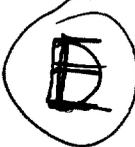




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Mr. Oscar Hernandez
Branch Chief, OPPT/CSRAD/RAB
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460



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Dear Mr. Hernandez,

In response to your February 2, 1995 letter (copy attached) attached is a complete copy (all 189 pages) of the report you requested.



8EHQ-94-12812
SP004 02/27/95

Regards,

William C. Kuryla, Ph.D.
Associate Director
Product Safety

- EPA letter
- BRRC 93U1319



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OFFICE OF
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February 2, 1995

William C. Kuryla, Ph.D.
Assistant Director, Product Safety
Union Carbide Chemicals and Plastics Company Inc.
Health, Safety and Environmental Affairs
39 Old Ridgebury Road
Danbury, Connecticut
06817-0001

Dear Dr. Kuryla:

RE: DOCUMENT NUMBER: 8EHQ-94-12812
CASNO: 94-04-2
CHEMNAME: VINYL 2-ETHYLHEXANOATE

In your submission of December 20, 1994 concerning the above referenced TSCA 8(e) submission, only the first 17 pages of the report "Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in B6CF₁ Mice", Bushy Run Researc, BRRC Report 93U1319, September 26, 1994 (189 pgs) were included. We would like to request the submission of the remainder of the study. If you have any questions please call Paul N. McMahon at 202-260-5047.

Thank you

Sincerely,

Oscar Hernandez, Branch Chief
OPPT/CSRAD/RAB

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BUSHY RUN RESEARCH CENTER

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STUDY TITLE

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in B6C3F₁ Mice

TEST SUBSTANCE

Vinyl 2-Ethylhexanoate

DATA REQUIREMENT

Not Applicable

AUTHORS

S. J. Hermansky and K. A. Loughran

STUDY COMPLETION DATE

September 26, 1994

PERFORMING LABORATORY

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93U1319

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Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice

CONFIDENTIALITY STATEMENT

This report is Union Carbide Corporation and Shell Oil Company Business Confidential and is not to be released outside of either Corporation/Company without the written consent of the Sponsors.

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in B6C3F₁ Mice

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

The portions of this study conducted by BRRC meet the requirements of the following Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA), 40 CFR Part 792, and Organisation for Economic Co-operation and Development (OECD), C(81)30(Final).

Study Director:

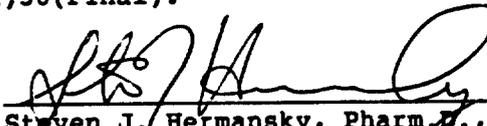

Steven J. Hermansky, Pharm.D., Ph.D., DABT
9/26/94 Date

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Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice

SUMMARY

B6C3F₁ Mice (6/sex/group) were administered vinyl 2-ethylhexanoate in corn oil, CAS No. 94-04-2, by gavage at dosages of 0 (control), 50, 200, 1000, or 2000 mg/kg/day at a dose volume of 4.0 ml/kg/day. Surviving animals were treated for 5 days/week for 2 weeks. Animals in the control group were administered Mazola® corn oil, CAS No. 8001-30-7, at a dose volume of 4.0 ml/kg/day. Monitors for toxic effects included detailed clinical observations, body and organ weights, food consumption, hematologic evaluations, necropsy observations, and microscopic evaluations.

Two female mice from the 2000 mg/kg/day dose group were prostrate approximately 5 hours after the first dose and 1 of these animals died the next day. There were no other chemical-related clinical signs of toxicity or animal deaths observed throughout the remainder of the study. In addition, hepatocellular hypertrophy was observed in all dose groups of both male and female mice. Based upon previous studies that indicated the hydrolysis of the test substance in liver homogenates was enzymatically mediated, the hepatocellular hypertrophy (and resulting increased liver weights in the 1000 mg/kg/day dose group of male mice and 2000 mg/kg/day dose group of both sexes) was likely an adaptive change in response to treatment with the test substance and not a direct toxic effect of the chemical on the liver. Decreased testes weights, but not testicular microscopic lesions, were observed in the 2000 mg/kg/day dose group. Therefore, the significance of the decreased weight of the testes was unknown. The no-observed-adverse-effect level of vinyl 2-ethylhexanoate under the conditions of this study was considered to be 1000 mg/kg/day since the increased liver weights observed in this dose group are considered to be an adaptive change and not a direct toxic effect of administration of the test substance.

OBJECTIVES

The objectives of this study were to evaluate the toxicity of 4 dose levels of vinyl 2-ethylhexanoate in B6C3F₁ mice when administered by gavage and to establish dose levels for a potential 90-day gavage study.

BACKGROUND INFORMATION

Several acute studies were conducted with vinyl 2-ethylhexanoate at BRRC (BRRC Report 53-130). Vinyl 2-ethylhexanoate was considered to be slightly toxic when administered perorally; the LD₅₀ for the male rat was 9.54 ml/kg and for the female rat was 5.47 ml/kg. When administered percutaneously, vinyl 2-ethylhexanoate had an extremely low order of toxicity; a 24-hour occluded dose of undiluted dose of 16.0 ml/kg killed 1 of 5 male rabbits and 2 of 5 female rabbits. When 5 male and 5 female rats were exposed to substantially saturated vapor (static) for 6 hours, there were no deaths. Minor to moderate erythema and edema occurred on all 6 rabbits that were occluded for 4 hours following the application of 0.5 ml of vinyl 2-ethylhexanoate to the clipped skin of the back. Minor irritation persisted 3 days after treatment, and the skin appeared normal 7 days after treatment. No corneal injury or iritis occurred in any of 6 rabbit eyes after instillation with 0.1 ml. Minor conjunctival irritation developed in all 6 eyes but resolved by 48 hours after treatment.

Vinyl 2-ethylhexanoate was also tested for potential mutagenic activity using the *Salmonella*/microsome (Ames) assay (BRRC Report 53-133). No indication of mutagenic activity was observed with any of 5 bacterial strains tested with or without metabolic activation. Vinyl 2-ethylhexanoate was not considered to be mutagenic under the conditions of this in vitro screening test.

A study to measure the rates of hydrolysis of various vinyl ester compounds in rat liver homogenates was conducted at BRRC (BRRC Report 92U1149). Analytical methodology for the hydrolysis work was developed and validated in an independent study (BRRC Report 92U1097). The following vinyl ester compounds were investigated in the study: vinyl acetate (CAS No. 108-05-04), vinyl propionate (CAS No. 105-38-4), vinyl pivalate (CAS No. 3377-92-2), vinyl 2-ethylhexanoate (CAS No. 94-04-2), divinyl adipate (CAS No. 4074-90-2), vinyl laurate (CAS No. 2146-71-6), vinyl neononanoate (CAS No. 54423-67-5), and vinyl neodecanoate (CAS No. 51000-52-3). The disappearance of each of the compounds in Fischer 344 male rat liver homogenates was measured. The autohydrolysis of selected compounds was also evaluated at pH 2, as well as evaluation of the effect of heat treatment on enzymatic hydrolysis. The nonenzymatic degradation rate of vinyl 2-ethylhexanoate at pH 2 was measured and was found to be 2 to 3 orders of magnitude slower than the metabolic degradation rates measured using rat liver homogenates. Furthermore, heat-inactivation (70°C/20 min) of liver homogenates inhibited hydrolysis. The nonenzymatic degradation rate would, therefore, not be expected to substantially influence the overall breakdown of vinyl 2-ethylhexanoate in vivo when compared to the enzymatic rates of degradation.

The Michaelis-Menten, first-order rate constants (K_m) and maximum velocities (V_{max}) of hydrolysis of vinyl 2-ethylhexanoate were measured in 3% (or less, w/w) rat liver homogenates with an incubation period of 1 minute or less. The

results from these studies indicated that vinyl 2-ethylhexanoate was metabolized by rat liver homogenate but not as readily as other vinyl esters that do not contain a neo group.

An additional investigation was conducted with male Fischer 344 rats to evaluate the potential for reactive intermediates to be produced during the metabolism of a number of vinyl esters (BRRC Report 92U1190). The depletion of rat liver reduced glutathione (GSH) was considered an indication of the production of reactive intermediates. The results from the investigation provided evidence of a low level of biochemically reactive intermediate production.

DOSE SELECTION

Based upon the above information, dose levels were selected to produce toxicity in the high dose group and no effect in at least one other dose group.

MATERIALS AND METHODS

The protocol and the protocol amendment detailing the design and conduct of this study are included in Appendix 10. Protocol deviations are also included in Appendix 10.

Test Substance

Approximately 1 liter of vinyl 2-ethylhexanoate, CAS No. 94-04-2, Lot No. JGT-1092, was received on August 31, 1993, from Union Carbide Corporation, South Charleston, WV, and assigned BRRC Sample No. 56-348. The test substance was a transparent, colorless liquid and was stored in an amber glass bottle at room temperature. Related correspondence from the supplier stated the purity of the test substance to be 99.9 (wt)%. The purity of the test substance was determined by the GLP Analytical Skill Center at the UCC South Charleston, WV, Technical Center to be 99.8 and the report is included as Attachment 1 of Appendix 1. No corrections for purity were made in any of the calculations. A reserve sample, approximately 8.7 g, was retained in the BRRC archives. This reserve sample will be discarded after issuance of the final report due to the potential for the test substance to form peroxides upon inhibitor depletion with long-term storage.

Vehicle and Control

Twenty-four 8-liter containers of Mazola® corn oil, CAS No. 8001-30-7, Research Lot No. 66580, were received from United States Cold Storage (supplied by Best Foods), Lyons, IL, on September 28, 1993, and assigned BRRC Sample Nos. 56-371-1 through 56-371-24. Sample 56-371-1 was used for the study. The corn oil was stored refrigerated.

Animals and Husbandry

Forty-four male and 46 female B6C3F₁ mice arrived on October 19, 1993, from Harlan Sprague Dawley, Inc. (Indianapolis, IN). They were designated by the supplier to be approximately 35 days old (the birth date was recorded as

September 14, 1993) upon arrival. The females were nulliparous and nonpregnant.

Animals were housed in Room 101 from arrival to termination of the study. Within 1 day of receipt, the animals were examined by a Clinical Veterinarian and a pretest health screen for representative animals was initiated. The health screen included a serology screen, necropsy, and examinations for fecal parasites. Based on the results of these data, the Clinical Veterinarian indicated that these animals were in good health and suitable for use.

All animals were assigned unique numbers and identified by cage tags. Animals considered available for the study were also identified by a toe-clipping procedure.

Upon arrival at BRRRC, the animals, separated by sex, were housed 2/cage (with the exception of 1 cage which housed 3 males) in stainless steel, wire mesh cages (22.5 x 10.0 x 12.5 cm). The purpose of the multiple housing was to help acclimate the animals to their new surroundings. Approximately 7 days later, the animals were individually housed until study termination. DACB® (Deotized Animal Cage Board; Shepherd Specialty Papers, Inc.) was placed under each cage and changed at least 3 times each week. An automatic timer was set to provide fluorescent lighting for a 12-hour photoperiod (approximately 0500 to 1700 hours for the light phase). Temperature and relative humidity were recorded (Cole-Parmer Hygrothermograph® Seven-Day Continuous Recorder, Model No. 8368-00, Cole-Parmer Instrument Co., Chicago, IL). Temperature was routinely maintained at 66-77°F; relative humidity was routinely maintained at 40-70%. Any minor exceptions to these specified ranges were noted in the raw data.

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) was available ad libitum and was delivered by an automatic watering system with demand control valves mounted on each rack. Water analyses were provided by the supplier, Halliburton NUS Environmental Laboratories, Chester Lab, and R. J. Lee Group, Inc. at regular intervals. EPA standards for maximum levels of contaminants were not exceeded. Ground Lab Diet™ The Richmond Standard™ Certified Rodent Diet #5002 (Purina Mills, Inc.; PMI, Inc.) was available ad libitum. Analyses for chemical composition and possible contaminants of each feed lot were performed by Purina Mills, Inc. (PMI, Inc.), and the results were included in the raw data.

Animal Acclimation

The acclimation period was approximately 2 weeks. During this period, the animals were weighed at least 2 times at scheduled intervals. Detailed clinical observations were conducted in conjunction with body weight measurements. Cage-side animal observations were conducted at least once daily, and mortality checks were conducted twice daily (morning and afternoon). The animals were examined just prior to the end of the acclimation period by a Clinical Veterinarian.

Study Organization

Following the second pretest body weight, the animals were assigned to 4 treatment groups and a control group using a stratified randomization procedure based on body weight. At the time of group assignment, only animals with body weight within $\pm 20\%$ of the population mean for each sex were included. The body weight range on the day of first treatment was 21.1 to 24.6 g for males and 17.6 to 21.1 g for females. The following table summarizes the organization of the study.

Group	Number of Animals		Vinyl 2-Ethylhexanoate	
	Male	Female	Volume (ml/kg/day)	Dosage (mg/kg/day)
Control	6	6	4.0	0
Low	6	6	4.0	50
Mid-1	6	6	4.0	200
Mid-2	6	6	4.0	1000
High	6	6	4.0	2000

The treatment began on November 1, 1993 (Study Day 1). Animals were treated for 5 days/week for 2 weeks. All surviving animals were sacrificed on November 15, 1993.

Administration of Test SubstanceDosing Solution Preparation

Dosing solutions were prepared by adding the appropriate amount of vinyl 2-ethylhexanoate (grams) to a volumetric flask and diluting to volume with corn oil. Each solution was mixed manually by repeated inversions. After mixing, the solutions were transferred to 30 ml Nalgene® dosing bottles specifically designed for use with a Hamilton® Microlab 900 automatic diluter/dispenser. The lids of the bottles had a small hole drilled through the top so Teflon® tubing, connected to the diluter dispenser and used for gavaging the animals, could be placed directly into the solution without removing the lid from the bottle. The hole was covered with electrical tape until needed for dosing. Each dosing bottle contained a sufficient quantity for a single day of dosing. These procedures minimized the potential for evaporation of the test substance from the solutions. Details of the dosing bottle design are included in Appendix 1.

Dosing

A fresh 30 ml bottle of dosing solution was utilized daily for each dose group. The dosing solutions were administered to the animals by gavage using an 18 gauge stainless steel animal feeding needle connected to the automatic diluter/dispenser via Teflon® tubing. The concentrations of the dosing solutions for each sex were graduated, 0, 12.5, 50, 250, and 500 mg/ml (which correspond to the dosages 0, 50, 200, 1000, and 2000 mg/kg, respectively), and

the dose volume (4.0 ml/kg/day) remained constant. Control animals were administered corn oil at a volume of 4.0 ml/kg/day. Individual dose volumes were calculated by a computer program based upon the most recent body weight of each animal.

Dosing Solution Analysis

The concentrations of vinyl 2-ethylhexanoate in corn oil were analyzed using a Gas Chromatograph (GC). A standard stock solution of vinyl 2-ethylhexanoate in toluene (1.52 mg/ml for Study Week 1 and 1.46 mg/ml for Study Week 2) was prepared and standards ranging from 0.456 to 1.52 mg/ml and 0.438 to 1.46 mg/ml for Study Week 1 and 2, respectively, were prepared by diluting the stock solution (v/v) with toluene. Dosing solutions were diluted for analysis using the automatic diluter/dispenser unit to ensure that concentration measurements were conducted under conditions identical to those utilized to dose the animals. Furthermore, procedures for priming and purging the dosing unit were recommended and validated utilizing this analytical methodology. For homogeneity and stability (Days 0 and 8) and concentration verification analyses (Study Weeks 1 and 2), dosing solutions were diluted for analysis using glass transfer pipettes.

For homogeneity and stability analyses, the measured concentration of each sample was determined by obtaining a value calculated by comparing the peak area or peak height of the sample to the peak area or peak height of the appropriate standard. For concentration verification analyses (Weeks 1 and 2), the measured concentration of each sample was determined by the equation for the standard curve developed by linear regression. Homogeneity and stability analyses were conducted for a study in rats (BRRC Report No. 93U1318) with this test substance. The data are presented in this report for completeness. The details of these procedures are included in Appendix 1.

Observations and Measurements

In-life Evaluations

Observations for mortality and overt signs were made twice daily (a.m. and p.m.). Detailed clinical observations were performed prior to dosing on Study Days 1 (first day of dosing), 4, and 8 and shortly after dosing on all other dosing days. In addition, following the first dose, all animals were observed for any overt clinical signs of toxicity at approximately hourly intervals for approximately 5 hours and the results recorded in the raw data.

Body weight data were collected for all animals on the morning prior to the initiation of dosing (denoted as Study Day 1 in the tables) and on Study Days 4, 8, and 15 (prior to sacrifice).

Food consumption measurements were collected for intervals 2-4, 4-8, and 9-15.

Clinical Pathology Evaluations

Prior to final sacrifice following the end of treatment, blood was obtained from all surviving animals for hematology determinations. Blood was obtained from the orbital sinuses of methoxyflurane anesthetized animals. The order of

bleeding and analysis was alternating (1 animal from each dose group then repeating) in order to reduce handling and time biases.

The following were measured or calculated:

Hematology

hematocrit	mean corpuscular hemoglobin
hemoglobin	concentration (MCHC)
erythrocyte count	total leukocyte count
mean corpuscular volume (MCV)	differential leukocyte count
mean corpuscular hemoglobin (MCH)	platelet count

Details of the hematology procedures are included in Appendix 3.

Anatomic Pathology Evaluations

At the end of treatment, all surviving animals were anesthetized with methoxyflurane and sacrificed by severing the brachial vessels. On the day of sacrifice, body weights were obtained to allow expression of relative organ weights. A complete necropsy was performed on all animals. The liver, kidneys, brain, adrenals, spleen, ovaries (females), and testes (males) were weighed for all sacrificed animals. The order of sacrifice and necropsy was randomized in advance in order to reduce observation and handling biases. The following tissues were collected and retained in 10% neutral buffered formalin:

<u>gross lesions</u>	vagina
lungs (with mainstem bronchi)	uterus (corpus and cervix)
<u>brain</u>	aorta
<u>cerebral cortex</u>	skin
<u>cerebellar cortex</u>	gall bladder
<u>medulla/pons</u>	esophagus
pituitary	stomach
thyroid/parathyroid	duodenum
thymic region	jejunum
trachea	ileum
heart	cecum
bone, sternum (including marrow)	colon
salivary gland	rectum
<u>liver</u>	urinary bladder
spleen	lymph node, mesenteric
<u>kidneys</u>	lymph node, other
adrenal gland	mammary gland
pancreas	skeletal muscle (gastrocnemius)
<u>testes</u>	<u>nerve, sciatic</u>
epididymis	<u>nerve, tibial</u>
prostate	eyes
seminal vesicles	femur
ovaries	spinal cord

Feet were saved for identification purposes.

The underlined tissues from the control and high dose groups were processed histologically and examined by light microscopy. In addition, gross lesions, liver, brain, sciatic and tibial nerves were examined microscopically from the low and mid dose groups.

Details of the anatomic pathology procedures are included in Appendix 2.

Data Analyses

The data for quantitative continuous variables were intercompared for the 4 treatment groups and the control group by use of Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. The t-tests were used when the F value from the ANOVA was significant. When Levene's test indicated similar variances, and the ANOVA was significant, a pooled t-test was used for pairwise comparisons. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances followed, when necessary, by a separate variance t-test for pairwise comparisons.

Nonparametric data were statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney U-test. Incidence data were compared using Fisher's Exact Test. For all statistical tests, the probability value of < 0.05 (two-tailed) was used as the critical level of significance.

Various models of calculators, computers, and computer programs may have been used to analyze data for this study. Since various models round or truncate numbers differently, values in some tables may differ slightly from those in other tables or from independently calculated data. The integrity of the study and interpretation of the data were unaffected by these differences.

RETENTION OF RECORDS

All raw data, documentation, the protocol and any amendments, specimens, and a copy of the final report generated as a result of this study will be retained in the BRRC Archives for at least 10 years. Due to the nature of the test substance, a reserve sample will not be retained following submission of the final report.

RESULTS AND DISCUSSION

All references of differences in group mean values in the following text refer to comparisons of statistically significant differences between the dose group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

Analytical Chemistry

Detailed results and discussion of the analytical chemistry measurements are included in Appendix 1.

Homogeneity of each solution (12.5 and 500 mg/ml) was evaluated to ensure that vinyl 2-ethylhexanoate was uniformly distributed throughout the solution. Duplicate samples were analyzed from 3 separate regions (top, middle, and bottom) of the mixing flask for each solution. The mean measured

concentrations (\pm standard deviation) of vinyl 2-ethylhexanoate in the 12.5 and 500 mg/ml solutions were 100.0 (\pm 1.1) and 98.7 (\pm 1.3) % of nominal, respectively. These results indicated that the solutions were uniformly prepared.

Stability analyses were conducted on 12.5 and 500 mg/ml solutions of vinyl 2-ethylhexanoate in corn oil. The solutions were analyzed for concentration of vinyl 2-ethylhexanoate directly after preparation (Day 0) and following 7 and 14 days of storage at room temperature in Nalgene® dosing bottles similar to those used for the dosing procedure. The mean measured concentrations for the 12.5 and 500 mg/ml solutions ranged from 100.0 to 100.2 and 93.6 to 98.9% of nominal, respectively. These results indicated that the solution remained stable at the specified concentrations and conditions for at least 14 days.

Dosing solutions were prepared weekly and analyzed for concentration prior to administration to the animals. The mean measured concentrations of the 12.5, 50, 250, and 500 mg/ml solutions ranged from 99.9 to 102.0% of nominal. Vinyl 2-ethylhexanoate was not detected in any of the control dosing solutions.

Clinical Observations

Summaries of the clinical observations are presented in Tables 1 and 2. Individual animal clinical observation data are included in Appendix 5. Individual animal fate data are included in Appendix 4.

On Study Day 1, there were no clinical signs of toxicity observed during the first 4 hours after treatment. However, 2 female animals from the 2000 mg/kg/day dose group were prostrate approximately 5 hours after dosing while all other animals appeared normal (see Table 4 of Appendix 5). One of these 2 animals was found dead the following day (Study Day 2). Upon examination of this animal at necropsy, there was no indication of a dosing error that may have contributed to the death of this animal. There were no overt clinical signs of toxicity observed in any animal prior to dosing on Study Day 2, including the surviving female animal that was prostrate 5 hours after dosing on Study Day 1.

There were no other clinical signs of toxicity observed in any animal throughout the study that were attributed to treatment with the test substance. One male animal from the control group and 1 female animal from the 50 mg/kg/day dose group died during the study. Necropsy observations of these animals indicated that the deaths were related to the dosing procedure and not due to chemical-induced toxicity. Clinical observations observed in these animals prior to death included limb paralysis, hypoactivity, prostration, cold extremities, labored respiration, urogenital area wetness, and/or lacrimation.

Body Weights

Summaries of absolute body weight and body weight gain are presented in Tables 3 to 6. Individual animal body weight data are included in Appendix 6.

There were no treatment-related effects on mean absolute body weight or body weight gain observed in any dose group of either sex throughout the study. Statistically significant increases in the mean body weight gains of male

animals from the 200, 1000 and 2000 mg/kg/day dose group during the Day 1 to 4 measurement interval were attributed to a slight decrease in the mean body weight gain of the control group. A statistically significant increase in the mean body weight gain in the 2000 mg/kg/day dose group of female mice was not considered to be related to treatment due to the transient nature of the change.

Food Consumption

Summaries of food consumption data are presented in Tables 7 and 8. Individual animal food consumption data are included in Appendix 7.

There were no treatment-related effects on mean food consumption observed in any dose group of either sex throughout the study.

Clinical Pathology Evaluations

Summaries of the hematology measurements are presented in Tables 9 and 10. Individual clinical pathology data are included in Appendix 9. Detailed results and discussion of the clinical pathology measurements are included in Appendix 3.

There were no effects on hematologic parameters observed in any dose group of either sex that were considered to be related to treatment.

Organ Weights, Necropsy Observations, and Microscopic Diagnoses

Summary results of organ weights, organ weights relative to final body weight, and organ weights relative to brain weight are presented in Tables 11 through 16. Summary results of necropsy observations are presented in Tables 17 through 20. Summary results of microscopic diagnoses are presented in Tables 21 through 24. Individual anatomic pathology data are included in Appendix 8. Detailed results and discussion of the anatomic pathology results are included in Appendix 2.

The mean absolute and relative weight of the liver were increased 5 to 8% and 12 to 13% in the 1000 (statistically significant only relative to the final body weight) and 2000 mg/kg/day dose groups of male animals, respectively. A 12 to 13% decrease in the mean absolute and weight of the testes was observed in the 2000 mg/kg/day dose group. There were no microscopic lesions observed in the testes and, therefore, the significance of the decreased weight of the testes was unknown. A statistically significant decrease in the mean weight of the testes relative to the brain weight in the 50 mg/kg/day dose group was not considered to be related to treatment due to the lack of a dose-response relationship.

The absolute and relative weight of the liver was slightly increased (5 to 12%) in the high dose group of female mice but only the weight of the liver relative to the brain weight was statistically significant. There were no other changes or trends in organ weights observed in female mice that were considered to be biologically significant.

There were no gross lesions observed in the study that were attributed to chemical-induced toxicity. Necropsy findings of the thoracic cavity in the

male animal from the control group and the female animal from the 50 mg/kg/day dose group that died on study indicated that effects secondary to errors in the dosing procedure caused the death of these animals.

Hepatocellular hypertrophy was observed in most animals of all dose groups of both sexes. The lesion was not observed in control animals. The severity of the lesion was slightly greater in the higher dose groups. There were no other microscopic lesions observed in any tissues of either sex that were considered to be related to treatment. The hepatocellular hypertrophy (and resulting increased liver weights in the 1000 and 2000 mg/kg/day dose groups of male and/or female mice) was likely an adaptive change in response to treatment with the test substance and not a direct toxic effect of the chemical on the liver.

CONCLUSIONS

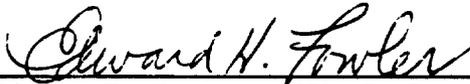
Repeated administration of vinyl 2-ethylhexanoate to mice resulted in prostration in 2 female mice approximately 5 hours after the first dose and death of 1 of these animals the next day. In addition, hepatocellular hypertrophy was observed in all dose groups of both male and female mice with an associated increase in liver weights in the 1000 mg/kg/day dose group of male mice and 2000 mg/kg/day dose group of both sexes. Decreased testes weights were also observed in the 2000 mg/kg/day dose group. The no-observed-adverse-effect level of vinyl 2-ethylhexanoate under the conditions of this study was considered to be 1000 mg/kg/day since the increased liver weights observed in this dose group are considered to be an adaptive change and not a direct toxic effect of administration of the test substance.

REVIEW AND APPROVAL

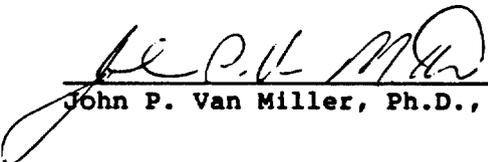
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Additional personnel are listed in the raw data.

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TABLE 1
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF CLINICAL OBSERVATIONS

MALES

CATEGORY FINDING (LOCATION)	GROUP:	GRADE (DAYS)	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)	5 (DAYS)
DEAD							
FOUND DEAD		P	1 (3)	0	0	0	0
SCHEDULED SACRIFICE		P	5 (15)	6 (15)	6 (15)	6 (15)	6 (15)
BEHAVIOR/CNS							
LIMB PARALYSIS (LEG-HIND-BOTH)		P	1 (3)	0	0	0	0
PROSTRATION		P	1(2- 3)	0	0	0	0
BODY							
COLD EXTREMITIES (LEGS-ALL)		P	1 (3)	0	0	0	0
CARDIO-PULMONARY							
LABORED RESPIRATION		P	1(2- 3)	0	0	0	0

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY

Grades: P = present, 1 = mild, 2 = moderate, 3 = severe.
 Numbers represent the number of animals exhibiting the finding at least once during the study.
 Parenthetical numbers "()" represent earliest to latest day a finding of the specified grade was observed.

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 9/20/94

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE
 SUMMARY OF CLINICAL OBSERVATIONS

FEMALES

CATEGORY FINDING (LOCATION)	GROUP:	GRADE (DAYS)	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)	5 (DAYS)
DEAD							
FOUND DEAD		P	0	1 (11)	0	0	1 (2)
SCHEDULED SACRIFICE		P	6 (15)	5 (15)	6 (15)	6 (15)	5 (15)
BEHAVIOR/CNS							
HYPOACTIVE		P	0	1 (11)	0	0	0
BODY							
COLD EXTREMITIES (LEGS-ALL)		P	0	1 (11)	0	0	0
UROGENITAL AREA WETNESS		P	0	1 (11)	0	0	0
CARDIO-PULMONARY							
LABORED RESPIRATION		P	0	1 (11)	0	0	0
EYES/EARS/NOSE							
LACRIMATION (EYE-BOTH)		P	0	1 (11)	0	0	0
SKIN							
ALOPECIA (CHEST)		P	1 (9-15)	0	0	1	0
(MULTIPLE AREAS-MOS)		P	0	0	0	1 (7-15)	0

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY

Grades: P = present, 1 = mild, 2 = moderate, 3 = severe.
 Numbers represent the number of animals exhibiting the finding at least once during the study.
 Parenthetical numbers "()" represent earliest to latest day a finding of the specified grade was observed.

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF BODY WEIGHT (GRAMS)

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
DAY 1						
MEAN	22.9	22.7	22.3	22.4	22.3	
S.D.	1.08	1.16	0.74	1.21	0.83	
N	6	6	6	6	6	
DAY 4						
MEAN	22.8	22.7	22.4	22.5	22.6	
S.D.	0.78	1.10	0.72	1.27	0.76	
N	5	6	6	6	6	
DAY 8						
MEAN	23.2	23.2	22.9	23.0	22.5	
S.D.	0.65	1.05	0.73	1.04	0.73	
N	5	6	6	6	6	
DAY 15						
MEAN	23.4	23.6	23.0	23.4	23.6	
S.D.	0.68	1.09	0.66	1.23	0.85	
N	5	6	6	6	6	

None significantly different from control group

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF BODY WEIGHT GAIN (GRAMS)

MALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1 TO 4					
MEAN	-0.3	0.0	0.2**	0.2**	0.3**
S.D.	0.30	0.33	0.36	0.15	0.17
N	5	6	6	6	6
DAY 1 TO 8					
MEAN	0.1	0.5	0.6	0.7	0.3
S.D.	0.59	0.48	0.50	0.27	0.23
N	5	6	6	6	6
DAY 1 TO 15					
MEAN	0.3	0.9	0.8	1.1	1.3
S.D.	0.91	0.66	0.55	0.51	0.43
N	5	6	6	6	6

** Significantly different from control group (p < .01)

TABLE 5
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF BODY WEIGHT (GRAMS)

		FEMALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
DAY 1						
MEAN	19.0	19.1	19.0	19.1	18.9	
S.D.	0.89	0.79	0.45	0.69	1.19	
N	6	6	6	6	6	
DAY 4						
MEAN	19.4	19.4	19.3	19.5	20.5	
S.D.	0.91	0.71	0.63	0.89	1.85	
N	6	6	6	6	5	
DAY 8						
MEAN	19.9	19.8	20.0	19.6	20.1	
S.D.	0.96	0.76	0.77	0.98	1.28	
N	6	6	6	6	5	
DAY 15						
MEAN	20.6	20.1	20.2	20.3	20.9	
S.D.	0.54	0.94	1.07	0.69	1.16	
N	6	5	6	6	5	
None significantly different from control group						

TABLE 6
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF BODY WEIGHT GAIN (GRAMS)

FEMALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1 TO 4					
MEAN	0.4	0.3	0.3	0.4	1.4**
S.D.	0.36	0.46	0.41	0.45	0.74
N	6	6	6	6	5
DAY 1 TO 8					
MEAN	0.9	0.7	1.0	0.5	1.0
S.D.	0.70	0.38	0.43	0.63	0.22
N	6	6	6	6	5
DAY 1 TO 15					
MEAN	1.6	1.1	1.2	1.2	1.9
S.D.	0.56	0.56	0.67	0.54	0.56
N	6	5	6	6	5

** Significantly different from control group (p < .01)

TABLE 7
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE
 SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
DAY 2 TO 4						
MEAN	7.2	7.3	7.8	8.0	6.5	
S.D.	1.81	1.01	2.23	2.72	2.10	
N	5	6	6	6	5	
DAY 4 TO 8						
MEAN	4.5	5.2	4.9	4.9	4.9	
S.D.	0.26	0.40	0.46	0.15	0.62	
N	5	6	6	5	6	
DAY 9 TO 15						
MEAN	5.4	5.9	6.3	5.4	5.0	
S.D.	0.65	0.95	0.85	1.42	0.25	
N	5	6	4	5	6	
None significantly different from control group						
Data not included for animals removed from food consumption						

TABLE 8
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

FEMALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 2 TO 4					
MEAN	7.3	9.6	8.4	10.0	6.9
S.D.	2.16	1.11	2.71	2.09	1.77
N	6	6	6	5	4
DAY 4 TO 8					
MEAN	4.9	4.9	5.4	5.5	5.1
S.D.	0.34	0.47	0.65	0.92	0.36
N	6	6	4	5	5
DAY 9 TO 15					
MEAN	6.1	6.1	5.9	5.9	6.0
S.D.	0.73	0.65	0.45	0.79	0.70
N	6	4	4	6	5
None significantly different from control group					
Data not included for animals removed from food consumption					

TABLE 9
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
ERYTHROCYTES (10⁶/μl)						
MEAN	8.62	8.49	8.50	8.58	8.64	
S.D.	0.250	0.136	0.122	0.244	0.242	
N	5	6	6	6	6	
HEMOGLOBIN (g/dl)						
MEAN	15.1	14.8	14.7	14.9	15.1	
S.D.	0.30	0.29	0.24	0.53	0.50	
N	5	6	6	6	6	
HEMATOCRIT (%)						
MEAN	43.2	42.5	42.5	43.0	43.3	
S.D.	1.15	0.65	0.55	1.34	1.23	
N	5	6	6	6	6	
MEAN CORPUSCULAR VOLUME (μm³)						
MEAN	50.	50.	50.	50.	50.	
S.D.	0.7	0.6	0.4	0.6	0.5	
N	5	6	6	6	6	
MEAN CORPUSCULAR HEMOGLOBIN (pg)						
MEAN	17.6	17.4	17.3	17.4	17.5	
S.D.	0.26	0.25	0.17	0.25	0.23	
N	5	6	6	6	6	
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)						
MEAN	35.0	34.8	34.6	34.7	34.9	
S.D.	0.34	0.53	0.26	0.40	0.29	
N	5	6	6	6	6	
PLATELETS (10³/μl)						
MEAN	673.	696.	659.	743.	706.	
S.D.	72.7	63.5	61.3	34.3	84.9	
N	5	6	6	6	6	
LEUKOCYTES (10³/μl)						
MEAN	4.0	4.6	4.4	5.2	4.0	
S.D.	0.91	1.22	1.91	1.50	0.69	
N	5	6	6	6	6	
SEGMENTED NEUTROPHILS (10³/μl)						
MEAN	0.67	0.79	0.60	0.83	0.70	
S.D.	0.137	0.198	0.112	0.271	0.074	
N	5	6	6	6	6	
LYMPHOCYTES (10³/μl)						
MEAN	3.30	3.79	3.78	4.28	3.26	
S.D.	0.777	1.005	1.814	1.230	0.626	
N	5	6	6	6	6	
MONOCYTES (10³/μl)						
MEAN	0.02	0.02	0.02	0.04	0.02	
S.D.	0.013	0.015	0.015	0.026	0.018	
N	5	6	6	6	6	

None significantly different from control group

TABLE 9 (continued)
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
BASOPHILS (10³/μl)						
MEAN	0.00	0.01	0.01	0.01	0.01	
S.D.	0.005	0.008	0.005	0.008	0.000	
N	5	6	6	6	6	
EOSINOPHILS (10³/μl)						
MEAN	0.02	0.01	0.02	0.03	0.02	
S.D.	0.012	0.008	0.009	0.037	0.010	
N	5	6	6	6	6	
BANDED NEUTROPHILS (10³/μl)						
MEAN	0.	0.	0.	0.		
S.D.	0.0	0.0	0.0	0.0		
N	1	1	1	1		
LARGE MONOCYTES (10³/μl)						
MEAN	0.	0.	0.	0.		
S.D.	0.0	0.0	0.0	0.0		
N	1	1	1	1		
IMMATURE GRANULOCYTES (10³/μl)						
MEAN	0.	0.	0.	0.		
S.D.	0.0	0.0	0.0	0.0		
N	1	1	1	1		
IMMATURE ERYTHROCYTES (10³/μl)						
MEAN	0.	0.	0.	0.		
S.D.	0.0	0.0	0.0	0.0		
N	1	1	1	1		
NUCLEATED RBCs (cells/100 WBCs)						
MEAN	0.	0.	0.	0.		
S.D.	0.0	0.0	0.0	0.0		
N	1	1	1	1		

None significantly different from control group

TABLE 10
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

FEMALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
ERYTHROCYTES (10⁶/μl)					
MEAN	8.13	8.18	8.12	7.99	8.07
S.D.	0.237	0.268	0.227	0.158	0.250
N	6	5	6	6	5
HEMOGLOBIN (g/dl)					
MEAN	14.2	14.4	14.3	14.1	14.2
S.D.	0.53	0.49	0.39	0.41	0.15
N	6	5	6	6	5
HEMATOCRIT (%)					
MEAN	40.6	41.0	40.6	40.7	40.9
S.D.	1.24	1.44	1.17	1.28	0.83
N	6	5	6	6	5
MEAN CORPUSCULAR VOLUME (μm³)					
MEAN	50.	50.	50.	51.	50.
S.D.	0.4	0.4	0.8	1.1	0.5
N	6	5	6	6	5
MEAN CORPUSCULAR HEMOGLOBIN (pg)					
MEAN	17.5	17.6	17.6	17.7	17.6
S.D.	0.17	0.31	0.23	0.22	0.43
N	6	5	6	6	5
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)					
MEAN	35.0	35.0	35.2	34.8	34.8
S.D.	0.37	0.70	0.36	0.82	0.47
N	6	5	6	6	5
PLATELETS (10³/μl)					
MEAN	668.	652.	646.	699.	717.
S.D.	39.2	25.3	50.6	55.3	96.9
N	6	4	5	6	5
LEUKOCYTES (10³/μl)					
MEAN	4.0	5.5	5.0	5.0	4.4
S.D.	1.28	1.14	0.92	1.62	1.32
N	6	5	6	6	5
SEGMENTED NEUTROPHILS (10³/μl)					
MEAN	0.67	0.96	0.74	0.86	0.63
S.D.	0.208	0.280	0.189	0.238	0.101
N	6	5	6	6	5
LYMPHOCYTES (10³/μl)					
MEAN	3.28	4.47	4.22	4.11	3.72
S.D.	1.028	0.910	0.912	1.467	1.300
N	6	5	6	6	5
MONOCYTES (10³/μl)					
MEAN	0.06	0.04	0.04	0.04	0.04
S.D.	0.090	0.013	0.020	0.026	0.022
N	6	5	6	6	5

None significantly different from control group

TABLE 10 (continued)
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

FEMALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
BASOPHILS (10³/μl)					
MEAN	0.01	0.01	0.01	0.01	0.01
S.D.	0.008	0.000	0.006	0.006	0.004
N	6	5	6	6	5
EOSINOPHILS (10³/μl)					
MEAN	0.02	0.01*	0.03	0.01*	0.02
S.D.	0.008	0.009	0.005	0.005	0.010
N	6	5	6	6	5

* Significantly different from control group (p < .05)

TABLE 11
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
FINAL BODY WEIGHT						
MEAN	23.4	23.6	23.0	23.4	23.6	
S.D.	0.68	1.09	0.66	1.23	0.85	
N	5	6	6	6	6	
LIVER						
MEAN	1.277	1.327	1.309	1.376	1.439**	
S.D.	0.1037	0.0941	0.0710	0.0840	0.0940	
N	5	6	6	6	6	
KIDNEYS						
MEAN	0.366	0.371	0.366	0.381	0.390	
S.D.	0.0265	0.0213	0.0256	0.0335	0.0226	
N	5	6	6	6	6	
SPLEEN						
MEAN	0.050	0.058	0.053	0.057	0.060	
S.D.	0.0059	0.0059	0.0054	0.0035	0.0135	
N	5	6	6	6	6	
BRAIN						
MEAN	0.438	0.458	0.452	0.450	0.438	
S.D.	0.0162	0.0139	0.0126	0.0122	0.0134	
N	5	6	6	6	6	
ADRENAL GL						
MEAN	0.005	0.005	0.005	0.004	0.005	
S.D.	0.0013	0.0015	0.0008	0.0013	0.0017	
N	5	6	6	6	6	
TESTES						
MEAN	0.201	0.189	0.202	0.204	0.176**	
S.D.	0.0164	0.0122	0.0089	0.0106	0.0094	
N	5	6	6	6	6	

** Significantly different from control group (p < .01)

TABLE 12
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
 ANIMALS SACRIFICED AT DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
LIVER						
MEAN	5.447	5.634	5.678	5.872*	6.102**	
S.D.	0.3947	0.2944	0.2405	0.2048	0.2328	
N	5	6	6	6	6	
KIDNEYS						
MEAN	1.560	1.576	1.587	1.624	1.655	
S.D.	0.1059	0.0703	0.0674	0.0669	0.1021	
N	5	6	6	6	6	
SPLEEN						
MEAN	0.212	0.248	0.230	0.242	0.255	
S.D.	0.0237	0.0291	0.0221	0.0137	0.0576	
N	5	6	6	6	6	
BRAIN						
MEAN	1.867	1.945	1.963	1.924	1.862	
S.D.	0.0801	0.0635	0.0424	0.0766	0.0856	
N	5	6	6	6	6	
ADRENAL GL						
MEAN	0.022	0.019	0.020	0.017	0.022	
S.D.	0.0056	0.0064	0.0034	0.0061	0.0081	
N	5	6	6	6	6	
TESTES						
MEAN	0.860	0.803	0.875	0.872	0.746**	
S.D.	0.0813	0.0635	0.0459	0.0345	0.0465	
N	5	6	6	6	6	

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)

TABLE 13
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF ORGAN WEIGHTS AS % OF BRAIN WEIGHT
 ANIMALS SACRIFICED AT DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
LIVER						
MEAN	291.546	289.978	289.319	305.570	328.339**	
S.D.	13.9402	18.6463	12.8262	13.8038	20.7781	
N	5	6	6	6	6	
KIDNEYS						
MEAN	83.624	81.075	80.870	84.582	88.989	
S.D.	5.7597	3.2867	4.3497	5.7098	6.1699	
N	5	6	6	6	6	
SPLEEN						
MEAN	11.372	12.714	11.705	12.581	13.746	
S.D.	1.1603	1.2976	0.9637	0.5383	3.1519	
N	5	6	6	6	6	
ADRENAL GL						
MEAN	1.185	0.988	0.996	0.889	1.184	
S.D.	0.2758	0.3443	0.1881	0.2864	0.4221	
N	5	6	6	6	6	
TESTES						
MEAN	46.086	41.293*	44.591	45.373	40.102**	
S.D.	4.3009	2.9380	2.5988	2.4922	2.6554	
N	5	6	6	6	6	

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)

TABLE 14
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT DAY 15

		FEMALES				
GROUP: MG/RG/DAY	0	50	200	1000	2000	
FINAL BODY WEIGHT						
MEAN	20.6	20.1	20.2	20.3	20.9	
S.D.	0.54	0.94	1.07	0.69	1.16	
N	6	5	6	6	5	
LIVER						
MEAN	1.165	1.149	1.140	1.170	1.247	
S.D.	0.0410	0.0663	0.1189	0.0650	0.1071	
N	6	5	6	6	5	
KIDNEYS						
MEAN	0.304	0.290	0.294	0.302	0.300	
S.D.	0.0142	0.0169	0.0233	0.0125	0.0268	
N	6	5	6	6	5	
SPLEEN						
MEAN	0.073	0.069	0.070	0.074	0.075	
S.D.	0.0023	0.0031	0.0074	0.0026	0.0087	
N	6	5	6	6	5	
BRAIN						
MEAN	0.471	0.450	0.454	0.453	0.448	
S.D.	0.0082	0.0164	0.0117	0.0178	0.0149	
N	6	5	6	6	5	
ADRENAL GL						
MEAN	0.007	0.008	0.007	0.008	0.007	
S.D.	0.0009	0.0011	0.0008	0.0015	0.0011	
N	6	5	6	6	5	
OVARIES						
MEAN	0.020	0.023	0.020	0.025	0.022	
S.D.	0.0015	0.0102	0.0020	0.0055	0.0048	
N	6	5	6	6	5	

None significantly different from control group

TABLE 15
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
 ANIMALS SACRIFICED AT DAY 15

		FEMALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
LIVER						
MEAN	5.662	5.700	5.627	5.766	5.955	
S.D.	0.2211	0.0951	0.3343	0.2140	0.2682	
N	6	5	6	6	5	
KIDNEYS						
MEAN	1.478	1.437	1.454	1.489	1.433	
S.D.	0.0581	0.0432	0.0767	0.0278	0.0705	
N	6	5	6	6	5	
SPLEEN						
MEAN	0.357	0.344	0.344	0.366	0.358	
S.D.	0.0114	0.0140	0.0271	0.0157	0.0286	
N	6	5	6	6	5	
BRAIN						
MEAN	2.289	2.236	2.246	2.235	2.144	
S.D.	0.0493	0.1013	0.0986	0.0834	0.0488	
N	6	5	6	6	5	
ADRENAL GL						
MEAN	0.034	0.038	0.034	0.040	0.032	
S.D.	0.0049	0.0065	0.0050	0.0078	0.0046	
N	6	5	6	6	5	
OVARIES						
MEAN	0.098	0.115	0.099	0.124	0.108	
S.D.	0.0091	0.0485	0.0132	0.0283	0.0274	
N	6	5	6	6	5	

None significantly different from control group

TABLE 16
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF ORGAN WEIGHTS AS % OF BRAIN WEIGHT
 ANIMALS SACRIFICED AT DAY 15

		FEMALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
LIVER						
MEAN	247.378	255.311	251.313	258.278	277.970**	
S.D.	8.8138	12.2956	23.3998	14.1004	15.5216	
N	6	5	6	6	5	
KIDNEYS						
MEAN	64.572	64.400	64.830	66.696	66.906	
S.D.	2.5872	4.0348	4.2398	2.7218	4.2562	
N	6	5	6	6	5	
SPLEEN						
MEAN	15.603	15.388	15.355	16.387	16.708	
S.D.	0.3027	0.7699	1.5159	0.9982	1.4976	
N	6	5	6	6	5	
ADRENAL GL						
MEAN	1.489	1.691	1.509	1.807	1.516	
S.D.	0.2146	0.2620	0.1898	0.3503	0.2267	
N	6	5	6	6	5	
OVARIES						
MEAN	4.287	5.159	4.413	5.571	5.023	
S.D.	0.3822	2.2581	0.4675	1.2864	1.2072	
N	6	5	6	6	5	

** Significantly different from control group (p < .01)

TABLE 17
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 15
 MALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED		5	6	6	6	6
SPLEEN						
COLOR CHANGE, FOCAL/MULTIFOVAL		0	0	0	0	1
EYE						
OPACITY		1	1	0	1	0
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY						

TABLE 18
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 MALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		1	-	-	-	-
THORACIC CAV HEMORRHAGE		1	-	-	-	-
PANCREAS COLOR CHANGE, DIFFUSE		1	-	-	-	-
EYE OPACITY		1	-	-	-	-
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY						

TABLE 19
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 15
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED		6	5	6	6	5
SKIN						
ALOPECIA		1	0	0	1	0
SUBCUTIS						
NODULE		0	0	0	1	0
SPLEEN						
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	0	0	1
LYMPH ND, S-MAN						
COLOR CHANGE, DIFFUSE		0	1	0	0	1
EYE						
OPACITY		0	3	3	1	2
LUNGS						
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	1	0	0
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY						

TABLE 20
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		-	1	-	-	1
THORACIC CAV CONTENTS ABNORMAL		-	1	-	-	0
STOMACH COLOR CHANGE, FOCAL/MULTIFOCAL		-	0	-	-	1
LYMPH ND, S-MAN COLOR CHANGE, DIFFUSE		-	0	-	-	1
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY-						

TABLE 21
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED	5	6	6	6	6
LIVER					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	0	2	0	0
HEPATOCELLULAR NECROSIS					
MILD	0	1	0	0	0
HEPATOCELLULAR HYPERTROPHY					
MINIMAL	0	2	0	0	0
MILD	0	2	1	2	3
MODERATE	0	2	3	4	3
SPLEEN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
HEMOSIDEROSIS					
MODERATE	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	6	6	6	6
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	6	6	6	6
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	6	6	6	6
EYE					
TOTAL NUMBER EXAMINED	1	1	0	1	0
EXAMINED, UNREMARKABLE	1	1	-	1	-
TESTES					
TOTAL NUMBER EXAMINED	5	0	0	0	6
EXAMINED, UNREMARKABLE	5	-	-	-	6
KIDNEYS					
TOTAL NUMBER EXAMINED	5	0	0	0	6
EXAMINED, UNREMARKABLE	5	-	-	-	6

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
5 is 2000 MG/KG/DAY

** Significantly different from control group (p < .01)

TABLE 22
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 MALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		1	-	-	-	-
LIVER						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
PANCREAS						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
BRAIN						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
NERVE, SCIATIC						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
NERVE, TIBIAL						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
EYE						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
TESTES						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
KIDNEYS						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

TABLE 23
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE
 ANIMALS SACRIFICED AT DAY 15
 FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED	6	5	6	6	5
LIVER					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	1	3	0	0
HEPATOCELLULAR NECROSIS					
MILD	0	0	1	0	0
HEPATOCELLULAR HYPERTROPHY					
MINIMAL	0	4*	2	6**	5**
MILD	0	2	1	1	1
MODERATE	0	2	1	4	1
SKIN					
TOTAL NUMBER EXAMINED	1	0	0	1	0
EXAMINED, UNREMARKABLE	1	-	-	1	-
SUBCUTIS					
TOTAL NUMBER EXAMINED	0	0	0	1	0
EPIDERMAL INCLUSION CYST					
PRESENT	-	-	-	1	-
SPLEEN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	1	0	0	1
SINUS ERYTHROCYTOSIS					
MILD	-	1	-	-	0
MODERATE	-	0	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	5	6	6	5
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	5	6	6	5
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY					
* Significantly different from control group (p < .05)					
** Significantly different from control group (p < .01)					

TABLE 23 (Continued)
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED		6	5	6	6	5
NERVE, TIBIAL						
TOTAL NUMBER EXAMINED		6	5	6	6	5
EXAMINED, UNREMARKABLE		6	5	6	6	5
EYE						
TOTAL NUMBER EXAMINED		0	3	3	1	2
EXAMINED, UNREMARKABLE		-	3	2	1	1
CORNEAL MINERALIZATION						
MODERATE		-	0	0	0	1
KERATITIS		-	0	0	0	1
MILD		-	0	0	0	1
SYMBECHIA		-	0	1	0	0
MODERATE		-	0	1	0	0
CATARACT		-	0	1	0	0
MODERATE		-	0	1	0	0
PTHRISIS BULBI		-	0	1	0	0
MARKED		-	0	1	0	0
LUNGS						
TOTAL NUMBER EXAMINED		0	0	1	0	0
EXAMINED, UNREMARKABLE		-	-	1	-	-
KIDNEYS						
TOTAL NUMBER EXAMINED		6	0	0	0	5
EXAMINED, UNREMARKABLE		6	-	-	-	5

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

None significantly different from control group

TABLE 24
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		-	1	-	-	1
STOMACH						
TOTAL NUMBER EXAMINED		0	0	0	0	1
EXAMINED, UNREMARKABLE		-	-	-	-	1
LIVER						
TOTAL NUMBER EXAMINED		0	1	0	0	1
CONGESTION		-	0	-	-	1
HEPATOCELLULAR HYPERTROPHY		-	1	-	-	0
LYMPH ND, S-MAN						
TOTAL NUMBER EXAMINED		0	0	0	0	1
EXAMINED, UNREMARKABLE		-	-	-	-	1
BRAIN						
TOTAL NUMBER EXAMINED		0	1	0	0	1
EXAMINED, UNREMARKABLE		-	1	-	-	1
NERVE, SCIATIC						
TOTAL NUMBER EXAMINED		0	1	0	0	1
EXAMINED, UNREMARKABLE		-	1	-	-	1
NERVE, TIBIAL						
TOTAL NUMBER EXAMINED		0	1	0	0	1
EXAMINED, UNREMARKABLE		-	1	-	-	1
KIDNEYS						
TOTAL NUMBER EXAMINED		0	0	0	0	1
CONGESTION		-	-	-	-	1

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F1 Mice

QUALITY ASSURANCE UNIT INSPECTION SUMMARY

<u>Inspection Date(s)</u>	<u>Inspection Type</u>	<u>Date QAU Report Issued To</u>	
		<u>Study Director</u>	<u>Management</u>
09-08-93	PROTOCOL	09-09-93	09-15-93
10-19-93	EVENT-ANIMAL RECEIPT	10-22-93	10-28-93
11-15-93	EVENT-SACRIFICE	11-15-93	11-30-93
01-11-94	PROTOCOL AMENDMENT #1	01-12-94	01-12-94
03-18-94 to 03-19-94	CLINICAL PATHOLOGY DATA, REPORT	03-28-94	09-26-94
03-19-94 to 03-24-94	ANATOMIC PATHOLOGY DATA, REPORT	03-28-94	09-26-94
03-21-94	ANALYTICAL CHEMISTRY DATA, REPORT	03-28-94	09-26-94
03-21-94 to 03-28-94	RAW DATA, REPORT	03-28-94	09-26-94
09-26-94	ARCHIVES	09-26-94	09-26-94



Craig A. Ferry
Representative, Quality Assurance Unit

9.26.94
Date

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Analytical Chemistry Report

(29 Pages)

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SUMMARY

A 14-day range-finding study with vinyl 2-ethylhexanoate, CAS No. 94-04-2, administered by gavage to B6C3F₁ mice, was conducted at the Bushy Run Research Center (BRRC). The solution concentrations of vinyl 2-ethylhexanoate designated for use in this study were 0, 12.5, 50, 250, and 500 mg/ml corresponding to dose levels of 0, 50, 200, 1000, and 2000 mg vinyl 2-ethylhexanoate/kg body weight, respectively. The concentration of vinyl 2-ethylhexanoate in corn oil was determined using gas chromatography. Chemical analyses for the dose range-finding study included stability, homogeneity, and concentration verification of the dosing solutions. The stability study showed that vinyl 2-ethylhexanoate remained stable in corn oil at concentrations of 12.5 and 500 mg/ml for at least 14 days when stored at room temperature in Nalgene® dosing bottles equipped with Nalgene® lids. The coefficients of variation of the percents of nominal from the homogeneity study conducted on a 12.5 and 500 mg/ml solution were 1.1 and 1.3%, respectively. These results indicated that the distribution of vinyl 2-ethylhexanoate in corn oil was uniform. Concentration verification analyses on solutions used for dosing showed analytical values ranging from 99.9 to 102.0% of nominal for the 2 periods of analysis.

MATERIALS AND METHODS

Test Substance

Approximately 1 liter of vinyl 2-ethylhexanoate, Lot No. JGT-1092, was received on August 31, 1993, from Union Carbide Corporation, South Charleston, WV, and assigned BRRC Sample No. 56-348. The test substance was a transparent, colorless liquid and was stored in an amber glass bottle at room temperature. Related correspondence from the supplier stated the purity of the test substance to be 99.9 (wt)%. Analyses of the test substance were performed by the GLP Analytical Skill Center at the UCC South Charleston, WV, Technical Center. The report issued by the Technical Center is included as Attachment 1 to this appendix. No corrections for purity were made in any of the calculations. A reserve sample, approximately 8.7 g, was retained in the BRRC archives and will be discarded after issuance of the final report.

Vehicle and Control

Eight 8-liter containers of Mazola® corn oil, CAS No. 8001-30-7, Research Lot No. 55295-030, were received from United States Cold Storage (supplied by Best Foods), Lyons, IL, on January 24, 1992, and assigned BRRC Sample No. 55-15 (A through H). Sample 55-15 B was used for prestudy testing.

Twenty-four 8-liter containers of Mazola® corn oil, CAS No. 8001-30-7, Research Lot No. 66580, were received from United States Cold Storage (supplied by Best Foods), Lyons, IL, on September 28, 1993, and assigned BRRC Sample Nos. 56-371-1 through 56-371-24. Sample 56-371-1 was used during this study for dosing solution preparation.

The corn oil samples were stored refrigerated at 4-5°C between each use. Information regarding the storage conditions, characteristics and composition of the corn oil was received from the supplier.

Procedures

The procedures for the determination of vinyl 2-ethylhexanoate in corn oil were developed at BRRC. These methods are described briefly below.

Analytical Instrumentation

A Hewlett-Packard 5890A Gas Chromatograph (GC) equipped with a flame ionization detector, Hewlett-Packard 7673A automatic sampler, and a Hewlett-Packard 3396A integrator was used for all dosing solution analyses. Samples were analyzed using a DB™-1 fused silica capillary column, 30 M x 0.53 mm ID, 5 µm film thickness (df), J & W Scientific, Folsom, CA. The GC operating parameters are listed in Table 1.

Dosing Solution Preparation and Storage Conditions

Dosing solutions were prepared by adding the appropriate amount of vinyl 2-ethylhexanoate (grams) to a 200 ml volumetric flask and diluting to volume with corn oil. Each solution was mixed manually by repeated inversions. After mixing and removal of subsamples for analysis, solutions were transferred to 30 ml Nalgene® dosing bottles equipped with Nalgene® lids. The lids had a 1/4 inch hole drilled through the top so the Teflon® tubing used for gavaging the animals could be placed directly in the solution without removing the lid from the bottle. These procedures minimized the potential for evaporation of the test substance from the solutions. The hole was covered with Scotch™ 3M electrical tape until needed for analysis or dosing. For the stability study, 3 Nalgene® bottles were filled with the 12.5 and 500 mg/ml solutions. For actual dosing, 5 Nalgene® bottles were filled for each concentration level. On each day of dosing, a fresh bottle of solution was used, then discarded.

Dilution of Dosing Solutions for Analysis

Dosing solutions were administered to the animals using the Hamilton Microlab® Diluter/Dispenser (gavaging unit). In order to verify that the gavaging unit would deliver the correct dose, prestudy tests were conducted to determine the appropriate procedures for operating the gavaging unit. The procedures developed are presented in Table 2.

The gavaging unit was used for stability Days 7 and 14. An aliquot (ranging from approximately 0.16 to 0.51 grams) of each dosing solution was transferred from the dosing Nalgene® bottle to an appropriately-sized (ml) volumetric flask, then the solution was diluted to volume with toluene (Burdick & Jackson, Muskegon, MI). Due to low recovery of the 500 mg/ml solution on stability Day 7, the solution was reanalyzed on Day 8. The low recovery on Day 7 was attributed to insufficient priming of the gavaging unit when changing dosing solution bottles. This was corrected by altering the priming procedures between dose groups. The improved procedures were verified on Day 14.

When the gavaging unit was not used for analysis, the solutions were diluted using glass transfer pipets. An aliquot (ranging from approximately 0.16 to 0.54 grams) of each dosing solution was transferred from the flask used for

mixing each solution to the appropriately-sized (ml) volumetric flask, then the solution was diluted to volume with toluene. One microliter of each diluted dosing solution was injected into the GC.

Calculation of Results

For homogeneity and stability analyses, the measured concentration of each sample was determined by obtaining a value calculated by comparing the peak area or peak height of the sample to the peak area or peak height of the appropriate standard. Standard solutions, approximately 0.7 and 1 mg/ml, were prepared by weighing the appropriate amount of vinyl 2-ethylhexanoate into a 100 ml flask and diluting to volume with toluene. For Days 0 and 7, corn oil was added to each standard solution so the amount of corn oil in the standard was similar to the amount of corn oil in the diluted dosing solution. Testing on Day 7 demonstrated that corn oil did not affect the signal response of the flame ionization detector. Therefore, for subsequent analyses, corn oil was not added to the standard solutions. The 0.7 and 1 mg/ml standards were used to quantitate the 12.5 and 500 mg/ml dosing solutions, respectively.

For concentration verification analyses (Study Weeks 1 and 2), the measured concentration of each sample was determined by the equation for the standard curve developed by linear regression. A standard stock solution of vinyl 2-ethylhexanoate in toluene (1.52 mg/ml for Study Week 1 and 1.46 mg/ml for Study Week 2) was prepared by weighing the appropriate amount of vinyl 2-ethylhexanoate into a 100 ml volumetric flask and diluting to volume with toluene. Additional standards were prepared by diluting the stock solution (v/v) with toluene. The standard curve generated for Study Weeks 1 and 2 ranged from 0.456 to 1.52 mg/ml and 0.438 to 1.46 mg/ml, respectively. One microliter of each standard solution was injected into the GC.

Standards for acceptable accuracy of mixing and analysis were: the mean of the analyzed samples was within $\pm 10\%$ of nominal; the difference between duplicate analyses did not exceed $\pm 15\%$; and individual analyses were within $\pm 15\%$ of nominal.

RESULTS AND DISCUSSION

Homogeneity Analyses

Homogeneity of each solution (12.5 and 500 mg/ml) was evaluated to ensure that vinyl 2-ethylhexanoate was uniformly distributed throughout the solution. Duplicate samples were analyzed from 3 separate regions (top, middle, and bottom) of the flask used for mixing each solution. The mean measured concentrations (\pm SD) of vinyl 2-ethylhexanoate in the 12.5 and 500 mg/ml solutions were 100.0 (± 1.1) and 98.7 (± 1.3)% of nominal, respectively. The coefficients of variation of the percents of nominal for the 12.5 and 500 mg/ml solutions were 1.1 and 1.3%, respectively. These results are presented in Table 3 and show that the solutions were uniformly prepared.

Stability Analyses

Table 4 contains a summary of results from the stability study conducted on 12.5 and 500 mg/ml solutions of vinyl 2-ethylhexanoate in corn oil. Dosing solutions were stored at room temperature during the stability study. The

solutions were analyzed for concentration of vinyl 2-ethylhexanoate directly after preparation (Day 0) and following 7 and 14 days of storage in the Nalgene® dosing bottles described above. Due to low recovery of the 500 mg/ml solution on stability Day 7, the solution was reanalyzed on Day 8. The gavaging unit was not used to dilute the solution on Day 8. The low recovery of the 500 mg/ml solution on Day 7 was attributed to the sampling procedures followed when using the gavaging unit. These procedures were improved and verified on Day 14. The mean measured concentrations of the 12.5 and 500 mg/ml solutions over the 14 day period ranged from 100.0 to 100.2 and 93.6 to 98.9% of nominal, respectively. These results indicated that vinyl 2-ethylhexanoate in corn oil remained stable at the specified concentrations for at least 14 days when stored at room temperature in Nalgene® dosing bottles.

Concentration Verification Analyses

Table 5 contains a summary of the results for the concentration verification analyses of vinyl 2-ethylhexanoate in corn oil. Dosing solutions were prepared weekly for dosing and analyzed for concentration of vinyl 2-ethylhexanoate prior to use. The mean measured concentrations of the 12.5, 50, 250, and 500 mg/ml solutions ranged from 99.9 to 102.0% of nominal. Vinyl 2-ethylhexanoate was not detected in the control dosing solutions.

Analytical Chemist:

Marlene A. Vrbanic
Marlene A. Vrbanic, B.A.

9-26-94

Date

TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

GAS CHROMATOGRAPHIC OPERATING PARAMETERS

Instrument:	Hewlett-Packard 5890A Gas Chromatograph (GC)
Column:	DB TM -1, 30 Meter x 0.53 mm ID fused silica capillary, 5 µm film thickness (df) ID# 2478646 J & W Scientific, Folsom, CA
Carrier Gas:	Ultra High Purity Helium
Column Flow Rate:	Approximately 10 ml/minute
Detector:	Flame-Ionization (FID)
Helium Auxiliary Flow Rate:	Approximately 30 ml/minute
Hydrogen Flow Rate:	Approximately 30 ml/minute
Air Flow Rate:	Approximately 400 ml/minute
Split Vent Flow Rate:	Approximately 60 ml/minute
Oven Temperature Program:	Initial Oven Temperature 90°C Initial Time 2 minutes Rate 10°C/minute Final Oven Temperature 250°C Final Time 10 minutes
Injection Temperature:	250°C
Detector Temperature:	300°C
Injection Volume:	1 µl
Retention Time (2-ethylhexanoate):	Approximately 7.4 minutes
Limit of Quantification:	0.01 µg/ml ^a

^aThis was the concentration of the lowest standard used for quantification during methods development. A limit of detection was not established for this study.

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

HAMILTON MICROLAB® DILUTER/DISPENSER RECOMMENDED PROCEDURES FOR DOSING^a

Procedure	# of Primes ^b	Priming Substance
Start-Up	10	1st Dosing Solution
Between Groups	6	Room Air
	14	Next Dosing Solution
After Dosing	6	Room Air
Clean-Up	15	Acetone
	6	Room Air

Pickup Speed = 8

Dispense Speed = 4

^aThese procedures were derived during the prestudy dosing solution stability study conducted by the analytical chemistry group, and ensure accurate delivery of the dosing solutions to the animals.

^bPriming the system is the process of filling and purging the gavaging unit Teflon® tubing with the appropriate substance. A prime is when the unit draws and dispenses approximately 1 ml of substance. Listed are the minimum number of primes.

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

RESULTS OF DOSING SOLUTION HOMOGENEITY ANALYSES^a

Nominal Concentration = 12.5 mg/ml

<u>Area of Sampling</u>	<u>Measured Concentration (mg/ml)</u>	<u>% of Nominal</u>
Top-1	12.54	100.3
Top-2	12.74	101.9
Middle-1	12.34	98.7
Middle-2	12.46	99.7
Bottom-1	12.38	99.0
Bottom-2	12.51	100.1
Mean	12.50	100.0
Standard Deviation	0.14	1.1
CV ^b		1.1

Nominal Concentration = 500 mg/ml

<u>Area of Sampling</u>	<u>Measured Concentration (mg/ml)</u>	<u>% of Nominal</u>
Top-1	497.8	99.6
Top-2	491.4	98.3
Middle-1	495.6	99.1
Middle-2	495.7	99.1
Bottom-1	481.0	96.2
Bottom-2	499.0	99.8
Mean	493.4	98.7
Standard Deviation	6.6	1.3
CV ^b		1.3

^aSolutions were prepared on 9-15-93 and analyzed directly after preparation. Subsamples for analysis were removed from the flask used for mixing each solution.

^bCV represents the percent coefficient of variation ((SD/Mean) x 100).

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

RESULTS OF DOSING SOLUTION STABILITY ANALYSES

<u>Nominal Concentration = 12.5 mg/ml</u>			
<u>Date of Analysis</u>	<u>Stability Day</u>	<u>Measured Concentration (mg/ml)^a</u>	<u>% of Nominal^a</u>
09-15-93	0 ^b	12.50 ± 0.14 (n=6)	100.0 ± 1.1
09-22-93	7 ^c	12.51 ± 0.08 (n=3)	100.1 ± 0.6
09-29-93	14 ^c	12.53 ± 0.11 (n=3)	100.2 ± 0.9
<u>Nominal Concentration = 500 mg/ml</u>			
<u>Date of Analysis</u>	<u>Stability Day</u>	<u>Measured Concentration (mg/ml)^a</u>	<u>% of Nominal^a</u>
09-15-93	0 ^b	493.4 ± 6.6 (n=6)	98.7 ± 1.3
09-23-93	8 ^d	494.5 ± 5.3 (n=3)	98.9 ± 1.0
09-29-93	14 ^c	468.2 ± 2.4 (n=3)	93.6 ± 0.5

^aThe measured concentration and % of nominal represent a mean ± standard deviation.

^bThe solution was prepared in a glass volumetric flask and analyzed directly after preparation for homogeneity. The results represent Day 0 reference data for subsequent stability analyses.

^cThe dosing solution was stored at room temperature in a 30 ml Nalgene® bottle equipped with a Nalgene® lid. The lid had a 1/4 inch hole drilled through the top so the Teflon® tubing used for gavaging the animals could be placed directly in the solution without removing the lid from the bottle. These procedures helped to minimize the potential evaporation of the test substance from the solutions. The hole was covered with Scotch™ 3M electrical tape until needed for analysis.

^dDue to insufficient priming of the gavaging unit, Day 7 results were out of the acceptable range of the protocol (approximately 84% of nominal). The 500 mg/ml solution was reanalyzed on Day 8.

TABLE 5
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

RESULTS OF DOSING SOLUTION CONCENTRATION VERIFICATION ANALYSES

<u>Date of Preparation</u>	<u>Date of Analysis</u>	<u>Nominal Concentration (mg/ml)</u>	<u>Measured Concentration (mg/ml)^a</u>	<u>% of Nominal^a</u>
10-28-93 ^b	10-28-93	0.0	ND ^c	NA ^d
10-28-93	10-28-93	12.5	12.59	100.7
10-28-93	10-28-93	50.0	51.00	102.0
10-28-93	10-28-93	250.0	253.8	101.5
10-28-93	10-28-93	500.0	501.6	100.3
11-04-93 ^e	11-04-93	0.0	ND	NA
11-04-93	11-04-93	12.5	12.65	101.2
11-04-93	11-04-93	50.0	50.18	100.4
11-04-93	11-04-93	250.0	252.0	100.8
11-04-93	11-04-93	500.0	499.4	99.9

^aThe measured concentration and % of nominal represent a mean of duplicate analyses.

^bSolutions prepared on 10-28-93 were designated for use in Study Week 1.

^cND - not detected.

^dNA - not applicable.

^eSolutions prepared on 11-04-93 were designated for use in Study Week 2.

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Test Substance Characterization Report



Union Carbide Corporation

STUDY TITLE

GLP Analysis-Final Report

TEST SUBSTANCE

VYNATE® 2-EH MONOMER
(Vinyl 2-ethylhexanoate)

DATA REQUIREMENT

U.S. FDA, 21 CFR Part 58
U.S. EPA TSCA, 40 CFR Part 792
U.S. EPA FIFRA, 40 CFR Part 160

STUDY DIRECTOR

Nancy A. Broyles

STUDY COMPLETED ON

May 17, 1994

PERFORMING LABORATORY

Union Carbide Corporation
PO Box 8361
South Charleston, West Virginia 25303

UCC R/D LABORATORY PROJECT ID

Study # 37-AEG-110

SPONSOR COMPANY

Union Carbide Corporation
Solvents and Coating Materials Division
Danbury, Conn. 06817-0001

STUDY COMPLIANCE STATEMENT

Study Compliance Statement for Union Carbide Corporation (UCC) Study # 37-AEG-110, vinyl 2-ethylhexanoate study for Bushy Run Research Center.

In accordance with UCC's intent that all tests conducted by our facility follow good laboratory practices, UCC's study director for the above test confirms that the study was conducted in compliance with the Good Laboratory Practice (GLP) standards: TSCA, 40 CFR Part 792; FIFRA, 40 CFR Part 160 and FDA, 21 CFR Part 58. All original raw data, records, protocols, samples, and final reports are being retained at UCC's South Charleston, WV, Technical Center.

Nancy A. Broyles 5/17/94
Nancy A. Broyles Date
Study Director

PROTOCOL DEVIATION STATEMENT

Protocol Deviation Statement for Union Carbide Corporation (UCC) Study # 37-AEG-110, vinyl 2-ethylhexanoate study for Bushy Run Research Center.

In accordance with UCC's intent that all tests conducted by our facility follow good laboratory practices, UCC's study director for the above test confirms that there were no protocol deviations taken during the study. The study was conducted in compliance with the protocol established and signed on 9/27/93 by Alexander E. Gabany, GLP Study Director. A protocol amendment was signed on May 10, 1994 to correct the test substance reference number and also to indicate a change in Study Director and Sponsor as of April 1, 1994.

Nancy A. Boyles 5/17/94
Nancy A. Boyles Date
Study Director

SIGNATURE PAGE

Submitted by: Union Carbide Corporation
P.O. Box 8361
South Charleston, West Virginia 25303

Prepared by:

Nancy A. Broyles 5/17/94
Nancy A. Broyles Date
Study Director

Quality Assurance Review by:

Denise L. Johnson 5/19/94
Denise L. Johnson Date
GLP Quality Assurance Unit
(QAU) Representative

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**VYNATE® 2-EH MONOMER
(Vinyl 2-ethylhexanoate)**

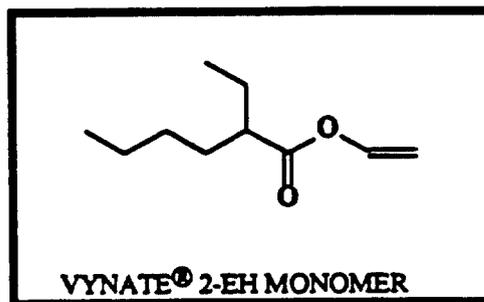
Vinyl 2-ethylhexanoate
Study # 37-AEG-110

ABSTRACT Vinyl 2-ethylhexanoate was analyzed to provide analytical data as part of the toxicity study at Bushy Run Research Center. The analyses were performed in compliance with Good Laboratory Practice (GLP) standards: TSCA, 40 CFR Part 792; FIFRA, 40 CFR Part 160 and FDA, 21 CFR Part 58. Gas chromatography-mass spectrometry (GC/MS) and nuclear magnetic resonance spectroscopy (NMR) techniques were independently used to confirm the sample's identity. Purity, measured by capillary GC, is ~99.8% for both the pre-study and the post-study sample. The samples were received from Bushy Run Research Center. All raw data, documentation, records, protocols, samples, and final reports are being retained.

INTRODUCTION Richard C. Wise, the study's original sponsor, requested that Bushy Run Research Center (BRRC) test vinyl 2-ethylhexanoate for toxicity. Such studies must follow GLP standards established by the EPA that require they be conducted with material whose identity and purity are verified analytically.

An ~8.65 gram sample of vinyl 2-ethylhexanoate (37-AEG-106) was received 9/3/93 in an amber glass bottle for analytical characterization. This sample is a subsample of a larger quantity of vinyl 2-ethylhexanoate (Lot # JGT-1092, BRRC# 56-348) tested at Bushy Run Research Center. A GLP protocol describing the analytical characterization of the sample was prepared (Appendix I). The protocol called for structural identification by NMR and GC/MS and for the capillary GC measurement of any impurities identified by GC/MS. The post-study sample (37-AEG-106R; BRRC# 56-348) was received on 11/17/93.

Shown at right is the structure of **VYNATE[®] 2-EH MONOMER** (vinyl 2-ethylhexanoate); its Chemical Abstracts Service Registry number (CAS #) is 94-04-2.



DISCUSSION The data from the analyses are summarized below.

NMR Analyses Proton and carbon NMR data were collected in the UCC NMR Skill Center using a General Electric GN-300NB spectrometer. The acquisition parameters are shown in the figures; for the ¹H NMR spectrum, the pulses used correspond to <3° flip angles; the ¹³C flip angles were 30°; the ¹³C(¹H) (proton decoupled ¹³C) spectrum used Waltz 16 modulation for ¹H decoupling. The spectra were not acquired under quantitative conditions; the acquisition conditions were established to identify the major component and to look for any substantial impurities. The sample was dissolved in deuteriochloroform for analysis; tetramethylsilane (TMS) was added to provide an internal chemical shift reference. The TMS and deuteriochloroform were used as received.

Figure 1 shows the ¹H NMR spectrum obtained from the sample of vinyl 2-ethylhexanoate. The observed chemical shifts, spin-spin coupling patterns, and relative intensities are appropriate for vinyl 2-ethylhexanoate. The two overlapping methyl triplets are at 0.8-1.0 ppm. The terminal vinyl protons are the two doublets of doublets at 4.5 and 4.8 ppm. The proton on the vinyl carbon next to the ether oxygen is another doublet of doublets at 7.3 ppm. The methine proton is the multiplet at 2.3 ppm. The methylene protons give the complex multiplets at 1.2 to 1.8 ppm.

Figure 2 shows the ¹³C(¹H) spectrum for the same sample. There are ten carbons in vinyl 2-ethylhexanoate and ten major lines are observed in the spectrum; no unusual or unexpected resonances are seen. The two CH₃ carbons are at 11.8 and 13.9 ppm; the four methylene carbons are at 22.7 - 31.6 ppm; the methine carbon is at 47.1 ppm; the terminal vinyl carbon is at 97.3 ppm; the vinyl ester carbon is at 141.4 ppm; and the carbonyl carbon is at 173.2 ppm. The triplet at 76.9 ppm is due to the solvent, and the 0 ppm singlet is due to TMS. The NMR spectra are appropriate for the sample being vinyl 2-ethylhexanoate with no substantial organic impurities.

GC/MS Analysis Electron ionization (EI) mass spectral data was collected in the UCC MS Skill Center using a Finnigan TSQ-70 mass spectrometer interfaced to a Hewlett-Packard (HP) 5890 gas chromatograph. The sample, 37-AEG-106, was analyzed by injecting 0.2 μ L aliquots onto a CP-Sil-5-CB capillary column held at 30°C for 4 minutes, and then programmed to 250°C at 8°/minute. Figure 3 shows the EI total ion current chromatogram for the sample (scanned from m/z 10 to m/z 310 EI mode). This chromatogram is annotated with identifications based on the components' EI spectrum.

Capillary GC A HP 5890 gas chromatograph equipped with a flame ionization detector was used to analyze the sample. Aliquots (1 μ L) were injected via autoinjector with a 100:1 split ratio onto a DB-1 capillary column started at 60°C and held for 4 minutes, then programmed to 250°C at 12°/minute and held for 5 minutes (see Figure 4). The averages of triplicate analysis are given below (normalized chromatogram area percent).

<u>Component name</u>	<u>37-AEG-106</u>	<u>37-AEG-106R</u>
vinyl 2-ethylhexanoate	99.76	99.76
170 molecular weight isomer	0.04	0.04
158 molecular weight acetate	0.03	0.03
168 mw's, C ₁₁ unsaturated ketones	0.10	0.10

CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC Skill Centers show that this sample is vinyl 2-ethylhexanoate. These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purity, measured by capillary GC, is = 99.8% for both the pre-study and the post-study sample.

ARCHIVES All raw data, records, protocols, samples, and final reports are being retained at UCC's South Charleston, WV, Technical Center as follows:

- raw data from GC, NMR, and GC/MS studies are in 770-361, 770-127, and 770-123, respectively;
- protocols, notebook, and other records are to be kept in the GLP archives;
- the remainder of each sample is being kept in a locked GLP sample box in 770-361.

ACKNOWLEDGEMENTS We would like to thank Trudy Barker and Susanne Chambers for sample handling, collecting the GC data, and preparing the bulk of the report, and Kathy Canterbury for collecting the NMR data.

NOTEBOOK REFERENCE: 37-AEG-110 and related pages

Confidentiality No claim of confidentiality is made for any information contained in this study as it pertains to use by any government agency to which it is submitted. This document, however, is proprietary to UCC and is confidential and trade secret information in all other countries and for all purposes other than those directly related to the purposes of the reviewing agency. Information contained in these studies should not be reviewed, abstracted or used by persons other than the agency without the expressed written consent of UCC except as required to carry out statutory requirements.

Figure 1 — ¹H NMR Spectrum of 37-AEG-106 (vinyl 2-ethylhexanoate)

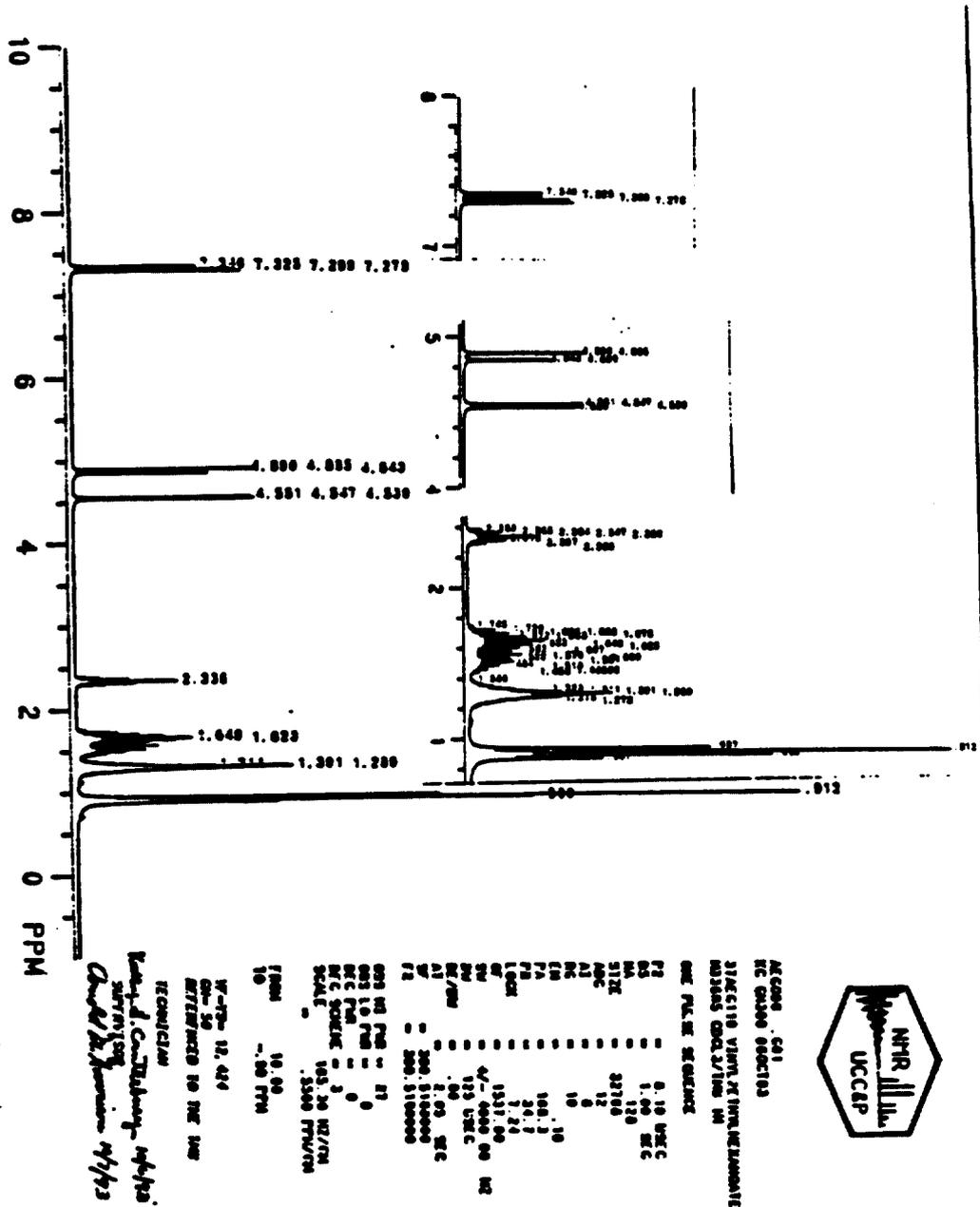


Figure 2 — ¹³C NMR Spectrum of 37-AEG-106 (vinyl 2-ethylhexanoate)

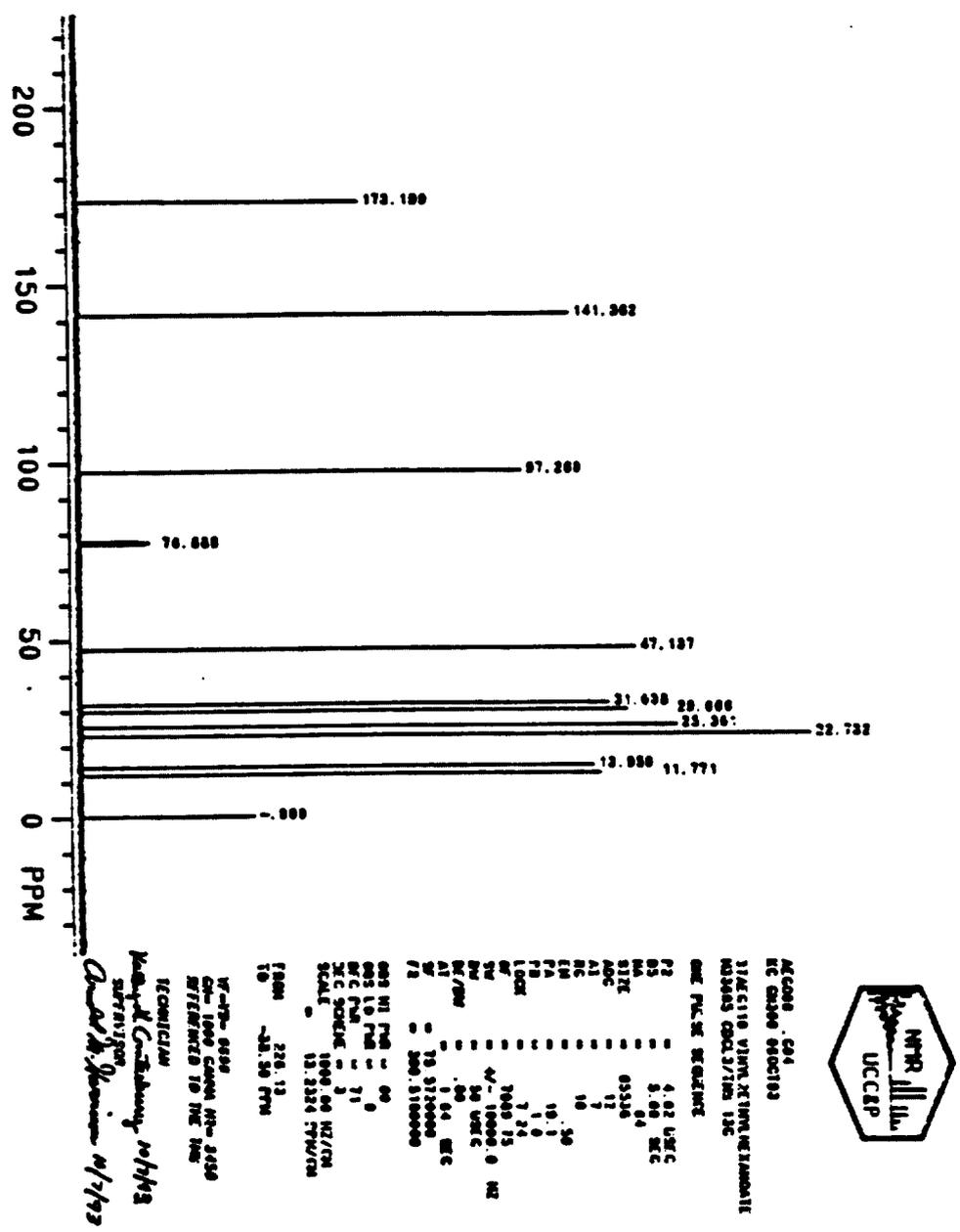
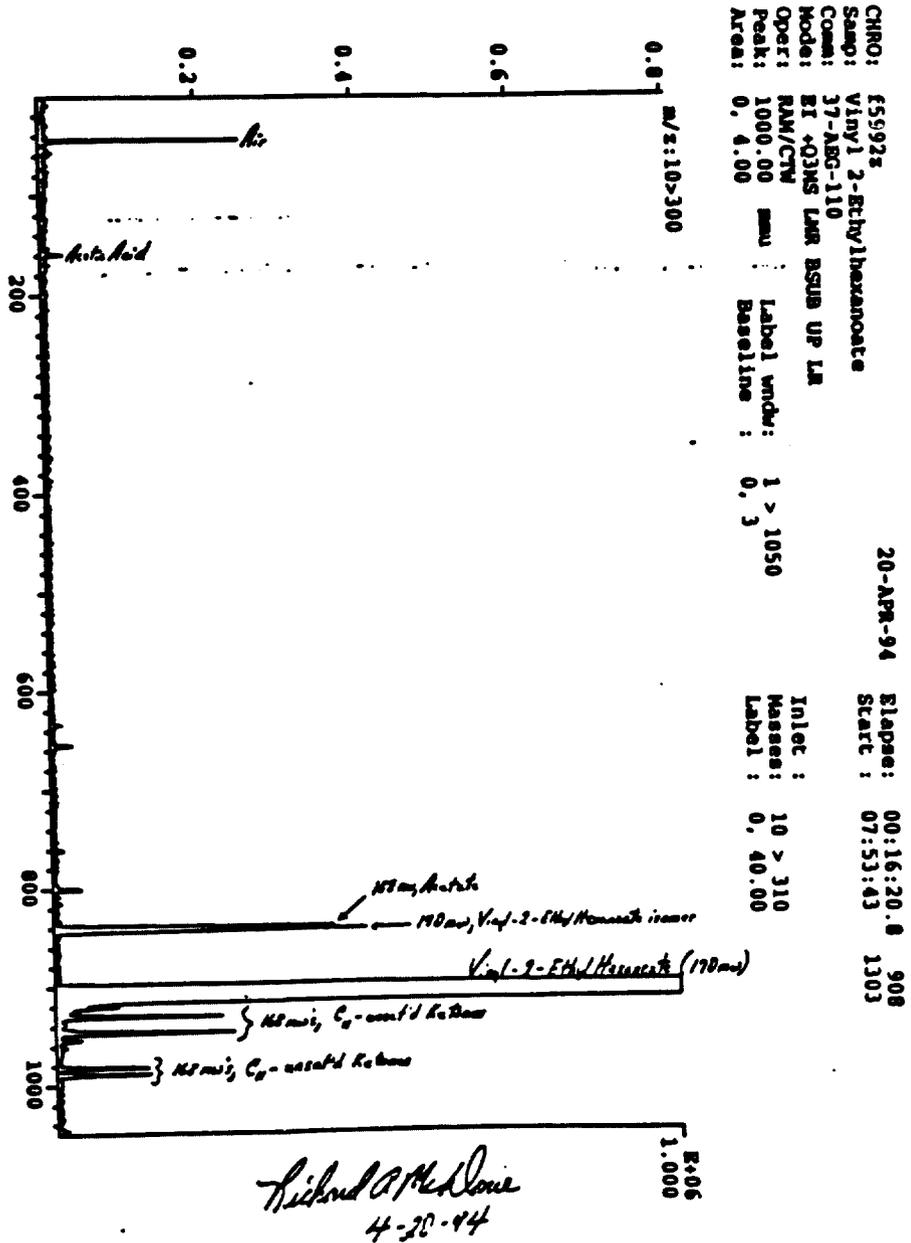


Figure 3 — Capillary GC/MS RIC of 37-AEG-106 (vinyl 2-ethylhexanoate)



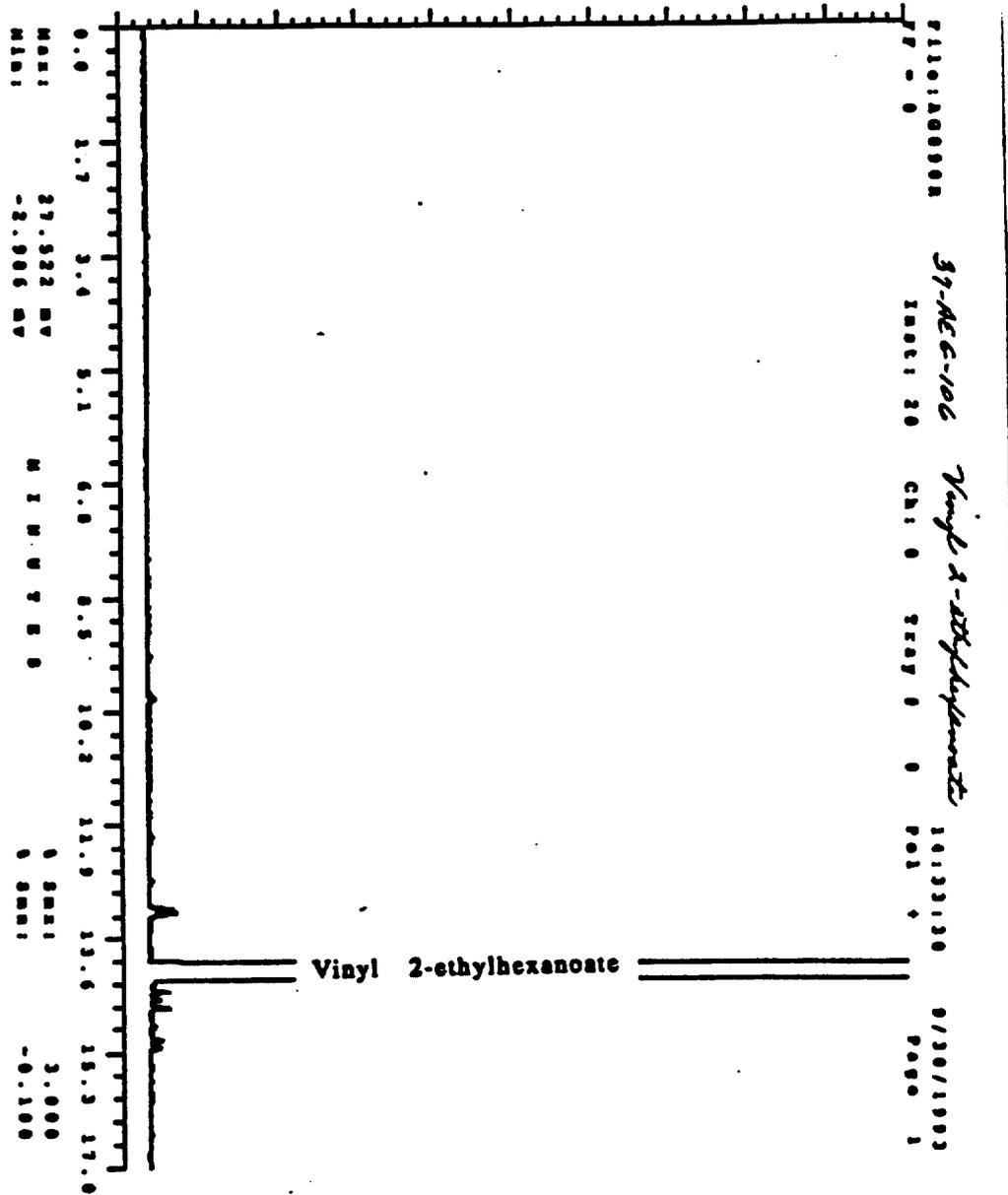
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 Samp: Vinyl 2-Ethylhexanoate
 Coma: 37-AEG-110
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 Oper: RAM/CTW
 Peak: 1000.00
 Area: 0.4.00

20-APR-94
 Elapse: 00:16:20.8
 Start: 07:53:43
 1303

Inlet: 10 > 310
 Masses: 0.40.00
 Label: 0.40.00

Label under: 1 > 1050
 Baseline: 0.3

Figure 4 — Capillary Gas Chromatogram of 37-AEG-106 (vinyl 2-ethylhexanoate)



APPENDIX I

Protocol

PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

title VYNATE™ 2-EH MONOMER

purpose Analytical Characterization of Sample(s) for Toxicology Studies at Bushy Run Research Center (BRRC)

study number 37-AEG-110

sponsor SOLVENTS AND COATING MATERIALS DIVISION (SCMD)
 Union Carbide Corporation (UCC)
 39 Old Ridgebury Road, Danbury, Conn. 06817-0001

testing facility UCC Technical Center,
 South Charleston, WV 25303 (Location 511)

Proposed Starting Date: Monday, September 27, 1993
Proposed Completion Date: February 1, 1994
Estimated Date of Final Report: March 1, 1994

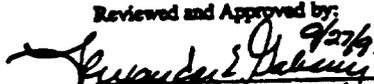
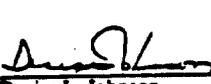
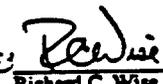
Test Substance(s) 37-AEG-18

Name	VYNATE™ 2-EH Monomer
Source	Lot # JGT-1092; UCC, South Charleston, WV
CAS Registry No.	94-04-2
Description	Transparent colorless liquid, sweet odor
Purity	>99% vinyl-2-ethyl hexanoate; 20 ppm monomethylether of hydroquinone inhibitor
Health/Safety	moderately toxic; stable. MSDS available upon request
Storage Conditions	room temperature

Study Design

- The test substance(s) will be characterized by:
- Verification of identity by proton- and carbon-NMR.
 - Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of ≥0.1 wt. %.
 - Quantitation of the identified impurities by capillary GC.

Reviewed and Approved by:

			10-8-93
Alexander E. Gabany GLP Study Director	date Denise L. Johnson GLP Quality Assurance Unit (QAU) Representative	date Richard C. Wise Manager of Product Safety, SCMD, Sponsor	

This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

APPENDIX II

Protocol Amendment

AMENDED 5/10/94

PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

Title VYNATE™ 2-EH MONOMER

Purpose Analytical Characterization of Sample(s) for Toxicology Studies at Bushy Run Research Center (BRRC)

Study Number 37-AEG-110

Sponsor SOLVENTS AND COATING MATERIALS DIVISION (SCMD)
Union Carbide Corporation (UCC)
39 Old Ridgebury Road, Danbury, Conn. 06817-0001

Testing Facility UCC Technical Center,
South Charleston, WV 25303 (Location 511)

Proposed Starting Date: Monday, September 27, 1993
Proposed Completion Date: February 1, 1994
Estimated Date of Final Report: March 1, 1994

Test Substance(s) 37-AEG-106

Name	VYNATE™ 2-EH Monomer
Source	Lot # JGT-1092; UCC, South Charleston, WV
CAS Registry No.	94-04-2
Description	Transparent colorless liquid, sweet odor
Purity	>99% vinyl-2-ethyl hexanoate; 20 ppm monomethyl ether of hydroquinone inhibitor
Health/Safety	moderately toxic; stable. MSDS available upon request
Storage Conditions	room temperature

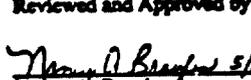
Study Design

The test substance(s) will be characterized by:

- Verification of identity by proton- and carbon-NMR.
- Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of ≥0.1 wt. %.
- Quantitation of the identified impurities by capillary GC.

This protocol amendment corrects the test substance reference number and also indicates a change in the Study Director and Sponsor as of April 1, 1994.

Reviewed and Approved by:

		
Nancy A. Broyles GLP Study Director	Denise L. Johnson GLP Quality Assurance Unit (QAU) Representative	Walter P. Miller, Ph. D. Health & Product Safety Manager Sponsor

This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

QAU STATEMENT

Quality Assurance Unit Study Inspection Summary

Test Substance: VYNATE® 2-EH MONOMER
(VINYL 2-ETHYLHEXANOATE)

Study No.: 37-AEG-110

Study Director: N.A. Broyles

The Quality Assurance Unit of the Union Carbide Technical Center conducted the inspections listed below and reported the results to the study director and management on the date indicated. It is the practice of this Quality Assurance Unit to report the results to both the study director and management.

Date	Inspection Type	Date OAU Report Issued	
		To Study Director	To Management
Feb. 10, 1992	Laboratory Compliance Review*	Feb. 10, 1992	May, 1992
Sept. 29, 1993	Protocol Compliance Review	Sept. 29, 1993	Sept. 29, 1993
May 11, 1994	Protocol Amendment #1 Compliance Review	May 11, 1994	May 11, 1994
May 19, 1994	Final Report Compliance Review	May 19, 1994	May 19, 1994

*The process of doing the GLP characterization studies is audited periodically to assure these studies comply with GLP requirements. The QA unit is exempted from performing in-life study inspections for studies designed to determine physical and chemical characteristics of a test substance as described in 40 CFR 792.135.


Denise L. Johnson, QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

Study # 37-AEG-110

page 17 of 17

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Anatomic Pathology Report

(14 Pages)

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SUMMARY

Male and female B6C3F₁ mice, purchased from Harlan Sprague Dawley Inc., Indianapolis, IN, were treated with 0, 50, 200, 1000, or 2000 mg/kg/day (6 mice/group/sex) of vinyl 2-ethylhexanoate (2-EH) by gavage 5 days/week for a 2 week period to determine any possible toxic effects. Surviving mice were euthanized at the end of the treatment period. All animals received a complete necropsy. Selected tissues were collected from all mice and preserved in fixative. Microscopic examinations were performed on selected tissues for all animals.

There were no gross lesions that could be attributed to 2-EH. The only microscopic change that could be attributed to the dosing with 2-EH was hepatocellular hypertrophy found in the centrilobular areas of the liver in all dosage groups. The frequency did not appear to be dose related, but the severity was slightly greater in the higher dosage groups. In no case was the severity greater than moderate. A no-observed-effect level (NOEL) was not found for 2-EH in this study.

MATERIALS AND METHODS

Necropsy

Mice were anesthetized with methoxyflurane and were euthanized by severing their brachial vessels to permit exsanguination. All animals received a complete necropsy and the following tissues were collected and preserved in 10% neutral buffered formalin:

gross lesions

lungs

brain

cerebral cortex

cerebellar cortex

medulla/pons

pituitary

thyroid/parathyroid

thymic region

trachea

heart

sternum (including marrow)

salivary gland

liver (2 lobes)

spleen

kidneys

adrenals

pancreas

testes

epididymis

prostate

seminal vesicles

ovaries (females)

vagina (females)

uterus (females)

corpus and cervix

aorta

skin

gallbladder

esophagus

stomach

duodenum

jejunum

ileum

cecum

colon

rectum

urinary bladder

lymph nodes

mesenteric

submandibular

mammary gland

(females)

skeletal muscle
(gastrocnemius)
eyes
femur (including
(articular surface)

spinal cord
sciatic nerve
tibial nerve
feet (animal identification)

Lung sections included 2 coronal cuts through all lobes and mainstem bronchi.

Spinal cord sections include cervical, thoracic and lumbar regions.

The right kidney was sectioned transversely and the left was cut longitudinally.

Organ weights were collected for the following tissues from all animals:

liver
kidneys
adrenals
testes (males)

ovaries (females)
brain
spleen

Histopathology

Microscopic examinations were performed on the above underlined tissues for all animals from the control and high dose groups from the Day 15 sacrifice. In addition, gross lesions, liver, brain, sciatic and tibial nerves were examined microscopically from the low and mid dose male and female mice.

All tissues to be examined were paraffin embedded, sectioned at approximately 5 microns and stained with hematoxylin and eosin. Lesions were graded, when possible, into 5 categories (minimal, mild, moderate, marked and severe).

Statistics

The frequency of histologic lesions was compared between each exposure and control group using the Fisher's Exact Test. The probability value of <0.05 (two-tailed) was used as the critical level of significance.

RESULTS AND DISCUSSION

Tables 1-4 list the gross lesions found at necropsy for the male and female mice, respectively, that were sacrificed at Day 15 or were found dead. The only gross lesions that could be attributed to gavage dosing with 2-EH were found in 2 mice (one 0 mg/kg/day male and one 50 mg/kg/day female) that had abnormal contents in their thoracic cavities due to being "lunged" during dosing. Eye opacities were observed in several male and female mice which were attributed to the loss of blood from the retinal vessels following bleeding.

Tables 5-8 list the microscopic lesions found in the male and female mice, respectively, that were sacrificed at Day 15 or were found dead. The only microscopic lesion that could be attributed to dosing with 2-EH was the hepatocellular hypertrophy found in the centrilobular areas of the livers of

mice dosed at all levels. There was no definite frequency distribution that was dose related, but the severity of the lesion seen in Tables 5 and 7 indicates that the hypertrophy was slightly more severe in the higher dosed mice. In no case was there a severity rating higher than moderate.

CONCLUSION

Mice dosed by gavage with 2-EH at doses of 50, 200, 1000, and 2000 mg/kg/day showed evidence of hepatocellular hypertrophy at all dosage levels, with the frequency of the lesion being similar over the dosage groups, but the severity being slightly greater in the higher dosage groups.

Pathologist:

Edward H. Fowler

Edward H. Fowler, DVM, Ph.D.
Diplomate, ACVP

9-26-94

Date

TABLE 1
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 15
 MALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED		5	6	6	6	6
SPLEEN						
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	0	0	1
EYE						
OPACITY		1	1	0	1	0
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY						

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 MALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		1	-	-	-	-
THORACIC CAV HEMORRHAGE		1	-	-	-	-
PANCREAS COLOR CHANGE, DIFFUSE		1	-	-	-	-
EYE OPACITY		1	-	-	-	-
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY						

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 15
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED		6	5	6	6	5
SKIN						
ALOPECIA		1	0	0	1	0
SUBCUTIS						
NODULE		0	0	0	1	0
SPLEEN						
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	0	0	1
LYMPH ND, S-MAN						
COLOR CHANGE, DIFFUSE		0	1	0	0	1
EYE						
OPACITY		0	3	3	1	2
LUNGS						
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	1	0	0
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, ^a 5 is 2000 MG/KG/DAY						

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF NECROPSY OBSERVATIONS

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		-	1	-	-	1
THORACIC CAV CONTENTS ABNORMAL		-	1	-	-	0
STOMACH COLOR CHANGE, FOCAL/MULTIFOCAL		-	0	-	-	1
LYMPH ND, S-MAN COLOR CHANGE, DIFFUSE		-	0	-	-	1
GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY, 5 is 2000 MG/KG/DAY						

TABLE 5
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE
 ANIMALS SACRIFICED AT DAY 15
 MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED	5	6	6	6	6
LIVER					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	0	2	0	0
HEPATOCELLULAR NECROSIS					
MILD	0	1	0	0	0
HEPATOCELLULAR HYPERTROPHY					
MINIMAL	0	6**	4	6**	6**
MILD	0	2	0	0	0
MODERATE	0	2	1	2	3
SPLEEN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
HEMOSIDEROSIS					
MODERATE	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	6	6	6	6
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	6	6	6	6
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	5	6	6	6	6
EXAMINED, UNREMARKABLE	5	6	6	6	6
EYE					
TOTAL NUMBER EXAMINED	1	1	0	1	0
EXAMINED, UNREMARKABLE	1	1	-	1	-
TESTES					
TOTAL NUMBER EXAMINED	5	0	0	0	6
EXAMINED, UNREMARKABLE	5	-	-	-	6
KIDNEYS					
TOTAL NUMBER EXAMINED	5	0	0	0	6
EXAMINED, UNREMARKABLE	5	-	-	-	6

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

** Significantly different from control group (p < .01)

TABLE 6
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 MALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND		1	-	-	-	-
LIVER						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
PANCREAS						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
BRAIN						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
NERVE, SCIATIC						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
NERVE, TIBIAL						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
EYE						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
TESTES						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-
KIDNEYS						
TOTAL NUMBER EXAMINED		1	0	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-	-

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

TABLE 7
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE
 ANIMALS SACRIFICED AT DAY 15
 FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED	6	5	6	6	5
LIVER					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	1	3	0	0
HEPATOCELLULAR NECROSIS					
MILD	0	0	1	0	0
HEPATOCELLULAR HYPERTROPHY					
MINIMAL	0	4*	2	6**	5**
MILD	0	2	1	1	1
MODERATE	0	2	1	4	1
SKIN					
TOTAL NUMBER EXAMINED	1	0	0	1	0
EXAMINED, UNREMARKABLE	1	-	-	1	-
SUBCUTIS					
TOTAL NUMBER EXAMINED	0	0	0	1	0
EPIDERMAL INCLUSION CYST					
PRESENT	-	-	-	1	-
SPLEEN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	1	0	0	1
SINUS ERYTHROCYTOSIS					
MILD	-	1	-	-	1
MODERATE	-	0	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	5	6	6	5
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	5	6	6	5

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)

TABLE 7 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE
ANIMALS SACRIFICED AT DAY 15
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS SACRIFICED	6	5	6	6	5
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	6	5	6	6	5
EXAMINED, UNREMARKABLE	6	5	6	6	5
EYE					
TOTAL NUMBER EXAMINED	0	3	3	1	2
EXAMINED, UNREMARKABLE	-	3	2	1	1
CORNEAL MINERALIZATION					
MODERATE	-	0	0	0	1
KERATITIS					
MILD	-	0	0	0	1
SYNECHIA					
MODERATE	-	0	1	0	0
CATARACT					
MODERATE	-	0	1	0	0
PHTHISIS BULBI					
MARKED	-	0	1	0	0
LUNGS					
TOTAL NUMBER EXAMINED	0	0	1	0	0
EXAMINED, UNREMARKABLE	-	-	1	-	-
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	0	5
EXAMINED, UNREMARKABLE	6	-	-	-	5

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
5 is 2000 MG/KG/DAY

None significantly different from control group

TABLE 8
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
 FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	1	-	-	1
STOMACH					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	0	1	0	0	1
CONGESTION	-	0	-	-	1
HEPATOCELLULAR HYPERTROPHY	-	1	-	-	0
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	0	1	0	0	1
EXAMINED, UNREMARKABLE	-	1	-	-	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	0	1	0	0	1
EXAMINED, UNREMARKABLE	-	1	-	-	1
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	0	1	0	0	1
EXAMINED, UNREMARKABLE	-	1	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	0	0	0	0	1
CONGESTION	-	-	-	-	1

GROUP LEGEND: 1 is 0 MG/KG/DAY, 2 is 50 MG/KG/DAY, 3 is 200 MG/KG/DAY, 4 is 1000 MG/KG/DAY,
 5 is 2000 MG/KG/DAY

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Clinical Pathology Report

(8 Pages)

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SUMMARY

Male and female B6C3F₁ mice (6/sex/group) were dosed with vinyl 2-ethylhexanoate (0, 50, 200, 1000, or 2000 mg/kg/day) by gavage dose 5 days/week for 2 weeks. Blood samples were collected for clinical pathology evaluation. One male mouse in the control group and 2 female mice (1 in the 50 and 1 in the 2000 mg/kg/day groups) died before blood samples were collected at Day 15.

No treatment-related differences in hematologic parameters were noted for male and female mice.

MATERIALS AND METHODS

In this study, male and female B6C3F₁ mice were dosed with vinyl 2-ethylhexanoate by gavage dose 5 days/week for 2 weeks. Doses were 0 (control), 50, 200, 1000, and 2000 mg/kg/day.

Blood samples for all clinical pathology analyses were collected by retroorbital bleeding from anesthetized mice prior to sacrifice. Mice were not fasted prior to bleeding. All analyses were performed in a predetermined, alternating group order.

Hematology

Approximately 0.5 ml of blood was collected into blood collection tubes containing EDTA as an anticoagulant for the hematologic determinations.

The following hematologic parameters were measured or calculated: erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, leukocyte count, segmented neutrophils, lymphocytes, monocytes, basophils, and eosinophils. These hematologic analyses were performed on a COBAS HELIOS™ 5DIFF on the day of the sample collection. Commercially available quality control samples were analyzed prior to the animal samples. Blood smears for differential leukocyte counts were prepared for all animals. The smears were not evaluated unless a value was not obtained for the instrument, to confirm the instrument results, or differentiate unusual patterns of cell populations. The source of the data is documented in the raw data.

Data Analyses

The results of the clinical pathology analyses for quantitative, continuous variables were intercompared for the dose and the control group by Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. If the ANOVA indicated statistical significance among experimental groups, the t-test was used to delineate which groups differ from the control group. If Levene's test indicated homogeneity of variances, the group was compared by an ANOVA for equal variances followed, when appropriate, by pooled variance t-tests. If Levene's test indicated heterogeneity of variances, the groups were

compared by an ANOVA for unequal variances followed, when appropriate, by a separate variance t-test.

All statistical analyses were performed using BMDP Statistical Software (Dixon, 1990). The probability value of less than 0.05 (two-tailed) was used as the critical level of significance for all test.

RESULTS AND DISCUSSION

All references to differences in group mean values in the following text refer to comparisons of statistically significant differences between the treatment group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

The summary results of hematology determinations for male and female mice are presented in Tables 1 and 2. The individual results for these animals are included in Appendix 9.

No treatment-related differences in hematologic parameters were noted for male and female mice. The slight decrease in eosinophil counts in the 50 and 1000, mg/kg/day groups of female mice was not considered to be biologically significant due to the small magnitude of the change and not exposure-related due to the lack of a dose response. One male mouse in the control group and 2 female mice (1 in the 50 and 1 in the 2000 mg/kg/day groups) died before blood samples were collected at Day 15.

CONCLUSION

No treatment-related differences in hematologic parameters were noted for male and female mice.

Clinical Pathologist: Douglas A. Neptun 9/26/94
Douglas A. Neptun, B.S., CC(NRCC), MT(ASCP) Date

REFERENCE

Dixon, W. J. (1990). BMDP Statistical Software. University of California Press, Berkeley, CA.

TABLE 1
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
ERYTHROCYTES (10⁶/μl)						
MEAN	8.62	8.49	8.50	8.58	8.64	
S.D.	0.250	0.136	0.122	0.244	0.242	
N	5	6	6	6	6	
HEMOGLOBIN (g/dl)						
MEAN	15.1	14.8	14.7	14.9	15.1	
S.D.	0.30	0.29	0.24	0.53	0.50	
N	5	6	6	6	6	
HEMATOCRIT (%)						
MEAN	43.2	42.5	42.5	43.0	43.3	
S.D.	1.15	0.65	0.55	1.34	1.23	
N	5	6	6	6	6	
MEAN CORPUSCULAR VOLUME (μm³)						
MEAN	50.	50.	50.	50.	50.	
S.D.	0.7	0.6	0.4	0.6	0.5	
N	5	6	6	6	6	
MEAN CORPUSCULAR HEMOGLOBIN (pg)						
MEAN	17.6	17.4	17.3	17.4	17.5	
S.D.	0.26	0.25	0.17	0.25	0.23	
N	5	6	6	6	6	
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)						
MEAN	35.0	34.8	34.6	34.7	34.9	
S.D.	0.34	0.53	0.26	0.40	0.29	
N	5	6	6	6	6	
PLATELETS (10³/μl)						
MEAN	673.	696.	659.	743.	706.	
S.D.	72.7	63.5	61.3	34.3	84.9	
N	5	6	6	6	6	
LEUKOCYTES (10³/μl)						
MEAN	4.0	4.6	4.4	5.2	4.0	
S.D.	0.91	1.22	1.91	1.50	0.69	
N	5	6	6	6	6	
SEGMENTED NEUTROPHILS (10³/μl)						
MEAN	0.67	0.79	0.60	0.83	0.70	
S.D.	0.137	0.198	0.112	0.271	0.074	
N	5	6	6	6	6	
LYMPHOCYTES (10³/μl)						
MEAN	3.30	3.79	3.78	4.28	3.26	
S.D.	0.777	1.005	1.814	1.230	0.626	
N	5	6	6	6	6	
MONOCYTES (10³/μl)						
MEAN	0.02	0.02	0.02	0.04	0.02	
S.D.	0.013	0.015	0.015	0.026	0.018	
N	5	6	6	6	6	

None significantly different from control group

TABLE 1 (continued)
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

		MALES				
GROUP: MG/KG/DAY	0	50	200	1000	2000	
BASOPHILS (10³/μl)						
MEAN	0.00	0.01	0.01	0.01	0.01	
S.D.	0.005	0.008	0.005	0.008	0.000	
N	5	6	6	6	6	
EOSINOPHILS (10³/μl)						
MEAN	0.02	0.01	0.02	0.03	0.02	
S.D.	0.012	0.008	0.009	0.037	0.010	
N	5	6	6	6	6	
BANDED NEUTROPHILS (10³/μl)						
MEAN	0.	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	0.0	
N	1	1	1	1	1	
LARGE MONOCYTES (10³/μl)						
MEAN	0.	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	0.0	
N	1	1	1	1	1	
IMMATURE GRANULOCYTES (10³/μl)						
MEAN	0.	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	0.0	
N	1	1	1	1	1	
IMMATURE ERYTHROCYTES (10³/μl)						
MEAN	0.	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	0.0	
N	1	1	1	1	1	
NUCLEATED RBCs (cells/100 WBCs)						
MEAN	0.	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	0.0	
N	1	1	1	1	1	

None significantly different from control group

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

FEMALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
ERYTHROCYTES (10 ⁶ /μl)					
MEAN	8.13	8.18	8.12	7.99	8.07
S.D.	0.237	0.268	0.227	0.158	0.250
N	6	5	6	6	5
HEMOGLOBIN (g/dl)					
MEAN	14.2	14.4	14.3	14.1	14.2
S.D.	0.53	0.49	0.39	0.41	0.15
N	6	5	6	6	5
HEMATOCRIT (%)					
MEAN	40.6	41.0	40.6	40.7	40.9
S.D.	1.24	1.44	1.17	1.28	0.83
N	6	5	6	6	5
MEAN CORPUSCULAR VOLUME (μm ³)					
MEAN	50.	50.	50.	51.	50.
S.D.	0.4	0.4	0.8	1.1	0.5
N	6	5	6	6	5
MEAN CORPUSCULAR HEMOGLOBIN (pg)					
MEAN	17.5	17.6	17.6	17.7	17.6
S.D.	0.17	0.31	0.23	0.22	0.43
N	6	5	6	6	5
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)					
MEAN	35.0	35.0	35.2	34.8	34.8
S.D.	0.37	0.70	0.36	0.82	0.47
N	6	5	6	6	5
PLATELETS (10 ³ /μl)					
MEAN	668.	652.	646.	699.	717.
S.D.	39.2	25.3	50.6	55.3	96.9
N	6	4	5	6	5
LEUKOCYTES (10 ³ /μl)					
MEAN	4.0	5.5	5.0	5.0	4.4
S.D.	1.28	1.14	0.92	1.62	1.32
N	6	5	6	6	5
SEGMENTED NEUTROPHILS (10 ³ /μl)					
MEAN	0.67	0.96	0.74	0.86	0.63
S.D.	0.208	0.280	0.189	0.238	0.101
N	6	5	6	6	5
LYMPHOCYTES (10 ³ /μl)					
MEAN	3.28	4.47	4.22	4.11	3.72
S.D.	1.028	0.910	0.912	1.467	1.300
N	6	5	6	6	5
MONOCYTES (10 ³ /μl)					
MEAN	0.06	0.04	0.04	0.04	0.04
S.D.	0.090	0.013	0.020	0.026	0.022
N	6	5	6	6	5

None significantly different from control group

TABLE 2 (continued)
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 SUMMARY OF HEMATOLOGY
 DAY 15

FEMALES					
GROUP: MG/KG/DAY	0	50	200	1000	2000
BASOPHILS (10³/μl)					
MEAN	0.01	0.01	0.01	0.01	0.01
S.D.	0.008	0.000	0.006	0.006	0.004
N	6	5	6	6	5
EOSINOPHILS (10³/μl)					
MEAN	0.02	0.01*	0.03	0.01*	0.02
S.D.	0.008	0.009	0.005	0.005	0.010
N	6	5	6	6	5

* Significantly different from control group (p < .05)

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Individual Animal Fate Data

(4 pages)

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TABLE 1
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL ANIMAL FATE

MALES

GROUP	ANIMAL	TYPE OF DEATH	AGE IN WEEKS	DATE OF DEATH	DAYS ON STUDY
0 MG/KG/DAY	9729	FOUND DEAD	7	3-NOV-93	3
	9728	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9734	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9709	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9708	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9711	SCHEDULED SACRIFICE	9	15-NOV-93	15
50 MG/KG/DAY	9705	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9721	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9717	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9715	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9697	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9724	SCHEDULED SACRIFICE	9	15-NOV-93	15
200 MG/KG/DAY	9731	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9733	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9719	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9710	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9707	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9696	SCHEDULED SACRIFICE	9	15-NOV-93	15
1000 MG/KG/DAY	9700	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9706	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9704	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9714	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9699	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9726	SCHEDULED SACRIFICE	9	15-NOV-93	15
2000 MG/KG/DAY	9732	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9730	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9712	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9716	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9698	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9701	SCHEDULED SACRIFICE	9	15-NOV-93	15

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL ANIMAL FATE

FEMALES

GROUP	ANIMAL	TYPE OF DEATH	AGE IN WEEKS	DATE OF DEATH	DAYS ON STUDY
0 MG/KG/DAY	9765	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9766	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9749	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9779	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9773	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9772	SCHEDULED SACRIFICE	9	15-NOV-93	15
50 MG/KG/DAY	9752	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9764	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9777	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9755	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9753	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9743	FOUND DEAD	9	11-NOV-93	11
200 MG/KG/DAY	9762	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9769	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9757	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9774	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9759	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9750	SCHEDULED SACRIFICE	9	15-NOV-93	15
1000 MG/KG/DAY	9767	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9754	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9768	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9760	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9744	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9780	SCHEDULED SACRIFICE	9	15-NOV-93	15
2000 MG/KG/DAY	9775	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9771	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9770	FOUND DEAD	7	2-NOV-93	2
	9745	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9748	SCHEDULED SACRIFICE	9	15-NOV-93	15
	9781	SCHEDULED SACRIFICE	9	15-NOV-93	15

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Individual Clinical Observation Data

(8 Pages)

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL CLINICAL OBSERVATION DATA

ABBREVIATIONS

The following is a list of three letter abbreviations for locations of clinical signs that may appear in the individual clinical observations tables.

ABD ABDOMEN	LHL LEG-HIND-LEFT
ANS ANUS	LHR LEG-HIND-RIGHT
AXB AXILLA-BOTH	LNS LOCATION NOT SPECIFIED
AXL AXILLA-LEFT	MTH MOUTH
AXR AXILLA-RIGHT	MUL MULTIPLE AREAS, NOS*
BCK BACK	NCK NECK
BDY ENTIRE BODY	NSE NOSE
CHS CHEST	PAL PAWS-ALL
EAB EAR-BOTH	PFB PAW-FORE-BOTH
EAL EAR-LEFT	PFL PAW-FORE-LEFT
EAR EAR-RIGHT	PFR PAW-FORE-RIGHT
ELB EYELID-BOTH	PFB PAW-HIND-BOTH
ELL EYELID-LEFT	PHL PAW-HIND-LEFT
ELR EYELID-RIGHT	PHR PAW-HIND-RIGHT
EYE EYE-BOTH	PNS PENIS
EYL EYE-LEFT	SCR SCROTUM
EYR EYE-RIGHT	SDB SIDE-BOTH
FAC FACE	SOL SIDE-LEFT
GEN GENITAL	SDR SIDE-RIGHT
HED HEAD	SHB SHOULDER-BOTH
HPB HIP-BOTH	SHL SHOULDER-LEFT
HPL HIP-LEFT	SHR SHOULDER-RIGHT
HPR HIP-RIGHT	TAL TAIL
INB INGUINAL-BOTH	TEE TEETH
INL INGUINAL-LEFT	TRA TREATMENT AREA
INR INGUINAL-RIGHT	TSE TESTIS-BOTH
LAL LEGS-ALL	TSL TESTIS-LEFT
LFB LEG-FORE-BOTH	TSR TESTIS-RIGHT
LFL LEG-FORE-LEFT	VAG VAGINA
LFR LEG-FORE-RIGHT	*NOS NOT OTHERWISE SPECIFIED
LHB LEG-HIND-BOTH	

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE

INDIVIDUAL CLINICAL OBSERVATIONS
 MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING	
0 MG/KG/DAY	9729	NORMAL FATE	3	-1- 1	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		BEHAVIOR/CNS	1	3	FOUND DEAD	
		BODY	1	3	PROSTRATION	
		CARDIO-PULMONARY	1	3	LIMB PARALYSIS (LHB 1) COLD EXTREMITIES (LAL 1)	
	9728	NORMAL FATE	2	2- 3	LABORED RESPIRATION	
		NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9734	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9709	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9708	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9711	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
50 MG/KG/DAY	9705	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9721	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9717	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9715	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9697	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	9724	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
	200 MG/KG/DAY	9731	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
			NORMAL FATE	1	15	SCHEDULED SACRIFICE
		9733	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
9719		NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
9710		NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
9707		NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
9696		NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
		NORMAL FATE	1	15	SCHEDULED SACRIFICE	
1000 MG/KG/DAY		9700	NORMAL FATE	16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
			NORMAL FATE	1	15	SCHEDULED SACRIFICE

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL CLINICAL OBSERVATIONS
 MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 MG/KG/DAY	9700	FATE	1	15	SCHEDULED SACRIFICE
	9706	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9704	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9714	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9699	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9726	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	FATE	1	15	SCHEDULED SACRIFICE	
2000 MG/KG/DAY	9732	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9730	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9712	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9716	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9698	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
9701	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	15	SCHEDULED SACRIFICE	

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 MG/KG/DAY	9765	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9766	NORMAL	10	-1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
		SKIN	7	9-15	ALOPECIA (CHS 7)
	9749	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9779	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9773	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9772	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	50 MG/KG/DAY	9752	NORMAL	16	-1-14
		FATE	1	15	SCHEDULED SACRIFICE
9764		NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
9777		NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
9755		NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
9753		NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
9743		NORMAL	12	-1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	FOUND DEAD
		BEHAVIOR/CNS	1	11	HYPOACTIVE
		BODY	1	11	UROGENITAL AREA WETNESS
		1	11	COLD EXTREMITIES (LAL 1)	
	CARDIO-PULMONARY	1	11	LABORED RESPIRATION	
	EYES/EARS/NOSE	1	11	LACRIMATION (EYB 1)	
200 MG/KG/DAY	9762	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9769	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9757	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9774	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9759	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
9750	NORMAL	16	-1-14	NO SIGNIFICANT CLINICAL OBSERVATIONS	

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE

INDIVIDUAL CLINICAL OBSERVATIONS
 FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
200 MG/KG/DAY	9750	FATE	1	15	SCHEDULED SACRIFICE
1000 MG/KG/DAY	9767	NORMAL FATE	8	-1- 6	NO SIGNIFICANT CLINICAL OBSERVATIONS
		SKIN	1	15	SCHEDULED SACRIFICE
	9754	NORMAL FATE	9	7- 15	ALOPECIA (MUL 9)
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	9768	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	9760	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	9744	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
2000 MG/KG/DAY	9780	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	9775	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	9771	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
	9770	NORMAL FATE	3	-1- 1	NO SIGNIFICANT CLINICAL OBSERVATIONS
			1	2	FOUND DEAD
	9745	NORMAL FATE	1	15	SCHEDULED SACRIFICE
			16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
9748	NORMAL FATE	1	15	SCHEDULED SACRIFICE	
		16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	
9781	NORMAL FATE	1	15	SCHEDULED SACRIFICE	
		16	-1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS	

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL CLINICAL OBSERVATION DATA FOR STUDY DAY 1 (NOVEMBER 1, 1993)
TRANSCRIBED FROM RAW DATA

FEMALES		
<u>Time (p.m)</u>	<u>Animal Number^a</u>	<u>FINDINGS</u>
3:45 (approx. 5 hours after dosing)	9775	Prostrate
	9770	Prostrate

^aBoth animals observed with findings were in the 2000 mg/kg/day dose group.

All animals, other than those specified above, appeared to be normal upon gross examination.

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Individual Body Weight Data

(13 Pages)

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Table 3 Females - Individual Body Weight (Grams).....	9

TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL BODY WEIGHT DATA

ABBREVIATIONS

The following is a list of abbreviations or words that may appear in the individual body weight tables.

dead = indicates that the animal died prior to the period in which this word appears.

sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

DAY	INDIVIDUAL BODY WEIGHT (GRAMS)			
	1	4	8	15
ANIMAL				
9729	21.6	dead		
9728	22.0	22.1	22.7	23.2
9734	22.5	22.4	23.1	23.9
9709	23.0	22.4	22.5	22.4
9708	23.5	23.1	23.6	23.5
9711	24.6	24.0	24.1	24.3
MEAN	22.9	22.8	23.2	23.4
S.D.	1.08	0.78	0.65	0.68
N	6	5	5	5

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL BODY WEIGHT (GRAMS)
 MALES GROUP: 50 MG/KG/DAY

DAY	1	4	8	15
ANIMAL				
9705	21.1	21.2	21.8	21.9
9721	21.9	21.9	22.5	23.7
9717	22.8	22.6	22.7	23.1
9715	22.6	22.3	23.3	23.3
9697	23.4	23.9	24.5	24.9
9724	24.4	24.0	24.3	24.5
MEAN	22.7	22.7	23.2	23.6
S.D.	1.16	1.10	1.05	1.09
N	6	6	6	6

TABLE 2
 VINYL 2-ETHYLHEXANOATE; FOURTEEN-DAY PERORAL (CAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL BODY WEIGHT (GRAMS)
 MALES GROUP: 200 MG/KG/DAY

DAY	1	4	8	15
ANIMAL				
9731	21.7	22.3	22.9	23.5
9733	21.5	21.5	22.2	22.5
9719	21.8	22.2	22.6	22.3
9710	22.3	21.9	22.1	22.6
9707	23.2	23.1	24.0	23.6
9696	23.1	23.4	23.4	23.8
MEAN	22.3	22.4	22.9	23.0
S.D.	0.74	0.72	0.73	0.66
N	6	6	6	6

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL BODY WEIGHT (GRAMS)
 MALES GROUP; 1000 MG/KG/DAY

DAY	1	4	8	15
ANIMAL				
9700	21.1	21.2	22.3	22.4
9706	21.9	22.1	22.5	23.8
9704	21.1	21.1	21.8	21.5
9714	22.9	23.1	23.2	23.9
9699	23.1	23.5	23.8	24.2
9726	24.1	24.2	24.6	24.8
MEAN	22.4	22.5	23.0	23.4
S.D.	1.21	1.27	1.04	1.23
N	6	6	6	6

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

DAY	INDIVIDUAL BODY WEIGHT (GRAMS)			
	1	4	8	15
ANIMAL				
9732	21.4	21.6	21.7	22.5
9730	21.5	22.1	21.9	22.5
9712	21.9	22.2	22.5	23.9
9716	22.4	22.8	22.6	23.8
9698	22.9	23.3	22.7	24.4
9701	23.5	23.6	23.8	24.3
MEAN	22.3	22.6	22.5	23.6
S.D.	0.83	0.76	0.73	0.85
N	6	6	6	6

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL BODY WEIGHT (GRAMS)
 FEMALES GROUP: 0 MG/KG/DAY

DAY	1	4	8	15
ANIMAL				
9765	17.6	18.0	18.6	19.8
9766	19.0	20.1	21.2	21.0
9749	18.3	18.7	18.9	20.3
9779	19.8	20.0	20.1	21.0
9773	19.4	19.4	19.8	20.2
9772	19.9	20.3	20.5	21.1
MEAN	19.0	19.4	19.9	20.6
S.D.	0.89	0.91	0.96	0.54
N	6	6	6	6

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)				
	1	4	6	15	
9752	18.3	18.2	18.9	19.5	
9764	18.3	19.1	18.8	18.9	
9777	20.1	19.8	20.2	21.0	
9755	19.7	19.9	20.4	20.7	
9753	18.6	19.1	19.7	20.7	
9743	19.5	20.1	20.6	dead	
MEAN	19.1	19.4	19.8	20.1	
S.D.	0.79	0.71	0.76	0.94	
N	6	6	6	5	

TABLE 3
 VINYL 2-ETHYLHEXANOATE; FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS) FEMALES GROUP; 200 MG/KG/DAY				
	1	4	8	15	
9762	18.8	18.9	19.3	19.0	
9769	18.9	18.5	19.3	19.6	
9757	18.5	19.0	19.5	19.7	
9774	19.2	20.1	20.6	20.7	
9759	19.8	20.0	21.1	22.0	
9750	19.1	19.5	20.3	20.4	
MEAN	19.0	19.3	20.0	20.2	
S.D.	0.45	0.63	0.77	1.07	
N	6	6	6	6	

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL BODY WEIGHT (GRAMS)
 FEMALES GROUP: 1000 MG/KG/DAY

ANIMAL	DAY 1	DAY 4	DAY 8	DAY 15
9767	18.6	18.4	18.4	19.5
9754	18.9	19.7	19.9	20.0
9768	19.1	19.2	19.1	19.6
9760	19.3	20.3	20.7	21.0
9744	18.5	18.7	18.9	20.4
9780	20.4	20.7	20.7	21.2
MEAN	19.1	19.5	19.6	20.3
S.D.	0.69	0.89	0.98	0.69
N	6	6	6	6

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (CAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 NICE

INDIVIDUAL BODY WEIGHT (GRAMS)
 FEMALES GROUP: 2000 MG/KG/DAY

ANIMAL	DAY 1	DAY 4	DAY 8	DAY 15
9775	21.1	23.1	22.3	22.6
9771	17.8	18.1	19.0	19.6
9770	18.0	dead		
9745	18.6	19.7	19.4	20.5
9748	18.6	20.1	19.7	21.4
9781	19.1	21.3	19.9	20.5
MEAN	18.9	20.5	20.1	20.9
S.D.	1.19	1.85	1.28	1.16
N	6	5	5	5

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Individual Food Consumption Data

(13 Pages)

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (CAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL FOOD CONSUMPTION DATA

ABBREVIATIONS

The following is a list of abbreviations or words that may appear in this appendix.

- r/s = indicates that the animal was removed from the consumption period due to spillage.
- r/e = indicates that the animal was removed from the consumption period due to excreta in the feeder.
- r/o = indicates that the animal was removed from the consumption period for reasons specified in the raw data.
- r/dead = indicates that the animal was removed from the consumption period because it died or was sacrificed during the period in which this abbreviation appears.
- dead = indicates that the animal died prior to the period in which this word appears.
- sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 MALES GROUP: 0 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9729	r/dead	4.5	4.7
9728	4.9	4.6	5.0
9734	6.6	4.9	6.4
9709	9.4	4.2	5.3
9708	8.5	4.3	5.7
9711	6.3	4.5	5.4
MEAN	7.2	4.5	5.4
S.D.	1.81	0.26	0.65
N	5	5	5

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 MALES GROUP: 50 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9705	6.9	5.4	4.5
9721	8.6	5.6	6.8
9717	7.9	5.5	6.4
9715	7.9	4.9	6.6
9697	6.9	5.3	4.9
9724	5.8	4.6	6.0
MEAN	7.3	5.2	5.9
S.D.	1.01	0.40	0.95
N	6	6	6

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 MALES GROUP: 200 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9731	7.7	4.4	5.0
9733	8.8	4.8	6.6
9719	7.4	5.4	r/s
9710	3.8	5.4	6.4
9707	9.7	5.2	r/s
9696	9.7	4.5	7.0
MEAN	7.8	4.9	6.3
S.D.	2.23	0.46	0.85
N	6	6	4

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 MALES GROUP; 1000 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9700	8.9	4.7	5.8
9706	11.1	5.0	4.7
9704	6.7	4.9	4.6
9714	6.4	5.1	7.7
9699	10.7	4.7	4.2
9726	4.1		
MEAN	8.0	4.9	5.4
S.D.	2.72	0.15	1.42
N	6	5	5

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 MALES GROUP; 2000 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9732	4.4	4.6	4.8
9730	5.2	4.4	4.7
9712	r/s	4.8	5.0
9716	8.6	6.1	5.2
9698	8.9	4.6	5.4
9701	5.4	5.0	4.9
MEAN	6.5	4.9	5.0
S.D.	2.10	0.62	0.25
N	5	6	6

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 FEMALES GROUP: 0 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9765	5.1	4.8	7.3
9766	6.9	4.5	5.4
9749	6.5	5.0	6.3
9779	6.9	5.5	5.7
9773	11.5	4.7	5.4
9772	7.0	4.9	6.3
MEAN	7.3	4.9	6.1
S.D.	2.16	0.34	0.73
N	6	6	6

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F1 MICE
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 FEMALES GROUP: 50 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9752	11.5	4.7	6.7
9764	9.8	5.6	r/s
9777	8.2	4.4	6.3
9755	9.8	4.4	5.1
9753	9.3	5.2	6.2
9743	9.0	4.9	r/dead
MEAN	9.6	4.9	6.1
S.D.	1.11	0.47	0.65
N	6	6	4

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 FEMALES GROUP; 200 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9762	8.6	6.3	5.5
9769	12.4	r/s	5.7
9757	5.4	r/s	r/s
9774	7.7	5.2	5.9
9759	5.8	5.2	6.5
9750	10.5	4.8	r/s
MEAN	8.4	5.4	5.9
S.D.	2.71	0.65	0.45
N	6	4	4

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 FEMALES GROUP: 1000 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9767	8.1	6.5	4.7
9754	r/s	r/s	6.2
9768	10.9	4.2	5.8
9760	9.0	4.9	5.6
9744	8.6	6.1	7.1
9780	13.2	5.0	6.3
MEAN	10.0	5.5	5.9
S.D.	2.09	0.92	0.79
N	5	5	6

TABLE 3
 VINYL 2-ETHYLHEXANOATE; FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 FEMALES GROUP; 2000 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9775	r/s	5.0	5.7
9771	5.2	4.0	5.9
9770	dead		
9745	6.9	5.0	5.9
9748	6.3	5.1	5.2
9781	9.4	5.1	7.1
MEAN	6.9	5.1	6.0
S.D.	1.77	0.36	0.70
N	4	5	5

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Individual Anatomic Pathology Data

(24 Pages)

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TABLE 1
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

NECROPSY PROTOCOL

MALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

TOTAL BODY	ADIPOSE TISSUE	MESENTERY/OM'TUM	PERITONEUM	PERITONEAL CAV
PLEURA	THORACIC CAV	HEART	PERICARDIAL CAV	AORTA
VASCULATURE	SALIVARY GL	ORAL/PHARYNGEAL	TONGUE	ESOPHAGUS
STOMACH	LIVER	GALLBLADDER	PANCREAS	DUODENUM
JEJUNUM	ILEUM	CECUM	COLON	RECTUM
ANUS	PITUITARY	THYROID GL	PARATHYROID GL	ADRENAL GL
SKIN	SUBCUTIS	HEAD	EARS	NARES/NOSE
MAMMARY GL	PAWS/FEET	TAIL	SPLEEN	LYMPH ND, S-MAN
LYMPH ND, MED	LYMPH ND, MES	THYMIC REGION	BONE/JOINT	BONE, STERNUM
BONE, FEMUR	BONE, VERTEBRA	SKELETAL MUSCLE	DIAPHRAGM	BRAIN
SPINAL CORD	NERVE, SCIATIC	NERVE, TIBIAL	EYE	HARDERIAN GL
LACRIMAL GL	TESTES	EPIDIDYMIDES	VASA DEFERENTIA	SEMINAL VESICLE
PROSTATE	PENIS	LARYNX	TRACHEA	LUNGS
KIDNEYS	URETER	URINARY BLADDER	URETHRA	GROSS LESIONS

The following organs were weighed at necropsy:

LIVER	ADRENAL GL	SPLEEN	BRAIN	TESTES
KIDNEYS				

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCAL, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY MALE

ANIMAL 9729 3-NOV-93 STUDY DAY 3
TYPE OF DEATH: FOUND DEAD

THORACIC CAV
GROSS: HEMORRHAGE
LARGE AMOUNT

PANCREAS
GROSS: COLOR CHANGE, DIFFUSE
WHITE

EYE
GROSS: OPACITY
LEFT, CORNEAL

MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
LIVER PANCREAS BRAIN
NERVE, SCIATIC NERVE, TIBIAL EYE
TESTES KIDNEYS

ANIMAL 9728 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL.
LIVER 1.291 5.560
KIDNEYS 0.342 1.473
SPLEEN 0.052 0.224
BRAIN 0.437 1.882
ADRENAL GL 0.004 0.017
TESTES 0.176 0.758
TERMINAL BODY WT. 23.2

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL TESTES KIDNEYS

ANIMAL 9734 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL.
LIVER 1.446 6.063
KIDNEYS 0.402 1.686
SPLEEN 0.058 0.243
BRAIN 0.463 1.941
ADRENAL GL 0.006 0.025
TESTES 0.199 0.834
TERMINAL BODY WT. 23.9

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL TESTES KIDNEYS

ANIMAL 9709 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL.
LIVER 1.175 5.236
KIDNEYS 0.369 1.644
SPLEEN 0.047 0.209
BRAIN 0.428 1.907
ADRENAL GL 0.005 0.022
TESTES 0.216 0.963
TERMINAL BODY WT. 22.4

EYE
GROSS: OPACITY
LEFT, CORNEAL

MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL EYE TESTES
KIDNEYS

ANIMAL 9708 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL.
LIVER 1.255 5.347
KIDNEYS 0.338 1.440

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY MALE

ANIMAL 9708 (CONTINUED)					
SPLEEN	0.042	0.179	LIVER	BRAIN	NERVE, SCIATIC
BRAIN	0.440	1.875	NERVE, TIBIAL	TESTES	KIDNEYS
ADRENAL GL	0.007	0.030			
TESTES	0.216	0.920			
TERMINAL BODY WT.	23.5				

ANIMAL 9711 15-NOV-93			STUDY DAY 15		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS		
LIVER	1.219	5.027	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
KIDNEYS	0.378	1.559	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
SPLEEN	0.050	0.206	LIVER	BRAIN	NERVE, SCIATIC
BRAIN	0.420	1.732	NERVE, TIBIAL	TESTES	KIDNEYS
ADRENAL GL	0.004	0.016			
TESTES	0.200	0.825			
TERMINAL BODY WT.	24.3				

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY MALE

ANIMAL	9705	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	1.244	5.691	LIVER	
KIDNEYS	0.353	1.615	MICRO: 2	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.062	0.284	EYE	
BRAIN	0.434	1.985	GROSS:	OPACITY
ADRENAL GL	0.005	0.023	LEFT, WHITE, CIRCULAR	
TESTES	0.186	0.851	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
TERMINAL BODY WT.	21.9		BRAIN	NERVE, SCIATIC NERVE, TIBIAL
			EYE	

ANIMAL	9721	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	1.346	5.689	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	0.384	1.623	LIVER	
SPLEEN	0.059	0.249	MICRO: 1	HEPATOCELLULAR HYPERTROPHY
BRAIN	0.471	1.991	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
ADRENAL GL	0.003	0.013	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
TESTES	0.186	0.786		
TERMINAL BODY WT.	23.7			

ANIMAL	9717	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	1.340	5.801	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	0.379	1.641	LIVER	
SPLEEN	0.061	0.264	MICRO: 1	HEPATOCELLULAR HYPERTROPHY
BRAIN	0.465	2.013	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
ADRENAL GL	0.005	0.022	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
TESTES	0.202	0.874		
TERMINAL BODY WT.	23.1			

ANIMAL	9715	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	1.208	5.187	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	0.338	1.451	LIVER	
SPLEEN	0.052	0.223	MICRO: 3	HEPATOCELLULAR HYPERTROPHY
BRAIN	0.452	1.941	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
ADRENAL GL	0.004	0.017	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
TESTES	0.179	0.769		
TERMINAL BODY WT.	23.3			

ANIMAL	9697	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	1.349	5.413	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	0.395	1.585	LIVER	
SPLEEN	0.065	0.261	MICRO: 3	HEPATOCELLULAR HYPERTROPHY
BRAIN	0.469	1.882	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
ADRENAL GL	0.003	0.012	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
TESTES	0.175	0.702		
TERMINAL BODY WT.	24.9			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY MALE

ANIMAL 9724 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.476	6.022
KIDNEYS	0.378	1.542
SPLEEN	0.050	0.204
BRAIN	0.455	1.856
ADRENAL GL	0.007	0.029
TESTES	0.205	0.836
TERMINAL BODY WT.	24.5	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

LIVER

MICRO: ((2)) HEPATOCELLULAR NECROSIS
 2 HEPATOCELLULAR HYPERTROPHY

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 200 MG/KG/DAY MALE

ANIMAL	9731	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.333	5.672	LIVER	
KIDNEYS	0.385	1.638	MICRO: 3 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.062	0.264	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.470	2.000	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.004	0.017		
TESTES	0.185	0.787		
TERMINAL BODY WT.	23.5			

ANIMAL	9733	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.367	6.067	MICRO: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	0.353	1.567	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
SPLEEN	0.055	0.244	LIVER BRAIN NERVE, SCIATIC	
BRAIN	0.452	2.006	NERVE, TIBIAL	
ADRENAL GL	0.005	0.022		
TESTES	0.203	0.901		
TERMINAL BODY WT.	22.5			

ANIMAL	9719	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.219	5.479	LIVER	
KIDNEYS	0.336	1.510	MICRO: 3 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.052	0.234	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.441	1.982	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.004	0.018		
TESTES	0.202	0.908		
TERMINAL BODY WT.	22.3			

ANIMAL	9710	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.228	5.434	LIVER	
KIDNEYS	0.342	1.513	MICRO: 2 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.046	0.204	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.437	1.934	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.004	0.018		
TESTES	0.202	0.894		
TERMINAL BODY WT.	22.6			

ANIMAL	9707	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.316	5.574	LIVER	
KIDNEYS	0.382	1.618	MICRO: 3 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.050	0.212	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.463	1.961	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.004	0.017		
TESTES	0.212	0.898		
TERMINAL BODY WT.	23.6			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 200 MG/KG/DAY MALE

ANIMAL	9696	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT		ABS.(G)	REL.	
LIVER		1.390	5.843	
KIDNEYS		0.398	1.673	
SPLEEN		0.053	0.223	
BRAIN		0.451	1.896	
ADRENAL GL		0.006	0.025	
TESTES		0.205	0.862	
TERMINAL BODY WT.		23.8		

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 LIVER BRAIN NERVE, SCIATIC
 NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY MALE

ANIMAL	9700	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.315	5.881	LIVER	
KIDNEYS	0.352	1.574	MICRO: 3 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.055	0.246	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.443	1.981	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.003	0.013		
TESTES	0.188	0.841		
TERMINAL BODY WT.	22.4			

ANIMAL	9706	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	LIVER	
LIVER	1.423	5.969	MICRO: 3 HEPATOCELLULAR HYPERTROPHY	
KIDNEYS	0.389	1.632	EYE	
SPLEEN	0.056	0.235	GROSS: OPACITY	
BRAIN	0.447	1.875	LEFT, CIRCULAR	
ADRENAL GL	0.003	0.013	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
TESTES	0.211	0.885	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
TERMINAL BODY WT.	23.8		EYE	

ANIMAL	9704	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.245	5.783	LIVER	
KIDNEYS	0.331	1.537	MICRO: 2 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.053	0.246	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.436	2.025	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.006	0.028		
TESTES	0.199	0.924		
TERMINAL BODY WT.	21.5			

ANIMAL	9714	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.464	6.118	LIVER	
KIDNEYS	0.388	1.621	MICRO: 3 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.061	0.255	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.453	1.893	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.003	0.013		
TESTES	0.209	0.873		
TERMINAL BODY WT.	23.9			

ANIMAL	9699	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.442	5.964	LIVER	
KIDNEYS	0.419	1.733	MICRO: 2 HEPATOCELLULAR HYPERTROPHY	
SPLEEN	0.061	0.252	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.472	1.952	BRAIN NERVE, SCIATIC NERVE, TIBIAL	
ADRENAL GL	0.005	0.021		
TESTES	0.200	0.827		
TERMINAL BODY WT.	24.2			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY MALE

ANIMAL	9726	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT		ABS. (G)	REL.	
LIVER		1.368	5.521	
KIDNEYS		0.408	1.646	
SPLEEN		0.054	0.218	
BRAIN		0.450	1.816	
ADRENAL GL		0.004	0.016	
TESTES		0.218	0.880	
TERMINAL BODY WT.		24.8		

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER
 MICRO: 3 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY MALE

ANIMAL	9732	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.305	5.800	LIVER	
KIDNEYS	0.392	1.742	MICRO: 3	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.064	0.284		CENTRILOBULAR DISTRIBUTION
BRAIN	0.416	1.849	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
ADRENAL GL	0.008	0.036	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
TESTES	0.178	0.791	TESTES	KIDNEYS
TERMINAL BODY WT.	22.5			

ANIMAL	9730	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.339	5.943	LIVER	
KIDNEYS	0.390	1.731	MICRO: 3	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.050	0.222	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.457	2.028	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
ADRENAL GL	0.006	0.027	TESTES	KIDNEYS
TESTES	0.173	0.768		
TERMINAL BODY WT.	22.5			

ANIMAL	9712	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.498	6.265	LIVER	
KIDNEYS	0.360	1.506	MICRO: 3	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.053	0.222	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.438	1.832	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
ADRENAL GL	0.005	0.021	TESTES	KIDNEYS
TESTES	0.161	0.673		
TERMINAL BODY WT.	23.9			

ANIMAL	9716	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.537	6.455	LIVER	
KIDNEYS	0.372	1.562	MICRO: 2	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.086	0.361	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.443	1.861	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
ADRENAL GL	0.004	0.017	TESTES	KIDNEYS
TESTES	0.185	0.777		
TERMINAL BODY WT.	23.8			

ANIMAL	9698	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.474	6.046	LIVER	
KIDNEYS	0.425	1.743	MICRO: 2	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.055	0.226	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
BRAIN	0.435	1.784	BRAIN	NERVE, SCIATIC NERVE, TIBIAL
ADRENAL GL	0.003	0.012	TESTES	KIDNEYS
TESTES	0.186	0.763		
TERMINAL BODY WT.	24.4			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY MALE

ANIMAL	9701	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	1.483	6.103	LIVER	
KIDNEYS	0.400	1.646	MICRO: 2	HEPATOCELLULAR HYPERTROPHY
SPLEEN	0.053	0.218	SPLEEN	
BRAIN	0.442	1.819	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL 2X2 MM DARK RED FOCUS
ADRENAL GL	0.005	0.021	MICRO: (3)	HEMOSIDEROSIS
TESTES	0.171	0.704	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
TERMINAL BODY WT.	24.3		BRAIN	NERVE, SCIATIC NERVE, TIBIAL
			TESTES	KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

NECROPSY PROTOCOL

FEMALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

TOTAL BODY	ADIPOSE TISSUE	MESENTERY/OM'TUM	PERITONEUM	PERITONEAL CAV
PLEURA	THORACIC CAV	HEART	PERICARDIAL CAV	AORTA
VASCULATURE	SALIVARY GL	ORAL/PHARYNGEAL	TONGUE	ESOPHAGUS
STOMACH	LIVER	GALLBLADDER	PANCREAS	DUODENUM
JEJUNUM	ILEUM	CECUM	COLON	RECTUM
ANUS	PITUITARY	THYROID GL	PARATHYROID GL	ADRENAL GL
SKIN	SUBCUTIS	HEAD	EARS	NARES/NOSE
MAMMARY GL	PAWS/FEET	TAIL	SPLEEN	LYMPH ND, S-MAN
LYMPH ND, MED	LYMPH ND, MES	THYMIC REGION	BONE/JOINT	BONE, STERNUM
BONE, FEMUR	BONE, VERTEBRA	SKELETAL MUSCLE	DIAPHRAGM	BRAIN
SPINAL CORD	NERVE, SCIATIC	NERVE, TIBIAL	EYE	HARDERIAN GL
LACRIMAL GL	OVARIES	OVIDUCT	UTERUS	CERVIX
VAGINA	VULVA	LARYNX	TRACHEA	LUNGS
KIDNEYS	URETER	URINARY BLADDER	URETHRA	GROSS LESIONS

The following organs were weighed at necropsy:

LIVER	ADRENAL GL	SPLEEN	BRAIN	OVARIES
KIDNEYS				

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:
 1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:
 ()=FOCAL, (())=MULTIFOCAL, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:
 ‡ = NEOPLASM, B = BENIGN, M = MALIGNANT, †PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY FEMALE

ANIMAL 9765 15-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER 1.179 5.943 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS 0.288 1.452 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPLEEN 0.071 0.358 LIVER BRAIN NERVE, SCIATIC
BRAIN 0.458 2.308 NERVE, TIBIAL KIDNEYS
ADRENAL GL 0.008 0.040
OVARIES 0.023 0.116
TERMINAL BODY WT. 19.8

ANIMAL 9766 15-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. SKIN GROSS: ALOPECIA
LIVER 1.206 5.751 20X35 MM AREA, CHEST
KIDNEYS 0.330 1.574 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
SPLEEN 0.076 0.362 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN 0.474 2.260 LIVER SKIN BRAIN
ADRENAL GL 0.007 0.033 NERVE, SCIATIC NERVE, TIBIAL KIDNEYS
OVARIES 0.019 0.091
TERMINAL BODY WT. 21.0

ANIMAL 9749 15-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER 1.086 5.342 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS 0.297 1.461 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPLEEN 0.071 0.349 LIVER BRAIN NERVE, SCIATIC
BRAIN 0.466 2.292 NERVE, TIBIAL KIDNEYS
ADRENAL GL 0.008 0.039
OVARIES 0.020 0.098
TERMINAL BODY WT. 20.3

ANIMAL 9779 15-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER 1.165 5.534 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS 0.300 1.425 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPLEEN 0.074 0.352 LIVER BRAIN NERVE, SCIATIC
BRAIN 0.480 2.280 NERVE, TIBIAL KIDNEYS
ADRENAL GL 0.006 0.029
OVARIES 0.020 0.095
TERMINAL BODY WT. 21.0

ANIMAL 9773 15-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER 1.177 5.835 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS 0.307 1.522 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPLEEN 0.076 0.377 LIVER BRAIN NERVE, SCIATIC
BRAIN 0.478 2.370 NERVE, TIBIAL KIDNEYS
ADRENAL GL 0.006 0.030
OVARIES 0.019 0.094
TERMINAL BODY WT. 20.2

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY FEMALE

ANIMAL	9772	15-NOV-93	STUDY DAY	15
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	1.177	5.568	MICRO: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	0.303	1.433	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
SPLEEN	0.073	0.345	LIVER	BRAIN
BRAIN	0.470	2.223	NERVE, TIBIAL	KIDNEYS
ADRENAL GL	0.007	0.033		NERVE, SCIATIC
OVARIES	0.020	0.095		
TERMINAL BODY WT.	21.1			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY FEMALE

 ANIMAL 9752 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.100	5.653
KIDNEYS	0.276	1.418
SPLEEN	0.068	0.349
BRAIN	0.451	2.318
ADRENAL GL	0.008	0.041
OVARIES	0.025	0.128
TERMINAL BODY WT.	19.5	

 GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER
 MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9764 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.057	5.604
KIDNEYS	0.274	1.453
SPLEEN	0.067	0.355
BRAIN	0.434	2.301
ADRENAL GL	0.008	0.042
OVARIES	0.015	0.080
TERMINAL BODY WT.	18.9	

 LIVER
 MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 EYE
 GROSS: OPACITY
 LEFT
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL
 EYE

ANIMAL 9777 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.186	5.640
KIDNEYS	0.313	1.488
SPLEEN	0.073	0.347
BRAIN	0.438	2.083
ADRENAL GL	0.006	0.029
OVARIES	0.020	0.095
TERMINAL BODY WT.	21.0	

 EYE
 GROSS: OPACITY
 LEFT
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 LIVER BRAIN NERVE, SCIATIC
 NERVE, TIBIAL EYE

ANIMAL 9755 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.206	5.820
KIDNEYS	0.301	1.453
SPLEEN	0.072	0.347
BRAIN	0.476	2.297
ADRENAL GL	0.007	0.034
OVARIES	0.016	0.077
TERMINAL BODY WT.	20.7	

 LIVER
 MICRO: 1 HEPATOCELLULAR HYPERTROPHY
 LYMPH ND, S-MAN
 GROSS: COLOR CHANGE, DIFFUSE
 DARK RED, ONE NODE
 MICRO: 2 SINUS ERYTHROCYTOSIS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9753 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.195	5.781
KIDNEYS	0.284	1.374
SPLEEN	0.066	0.319
BRAIN	0.451	2.182
ADRENAL GL	0.009	0.044
OVARIES	0.040	0.194

 LIVER
 MICRO: 1 HEPATOCELLULAR HYPERTROPHY
 EYE
 GROSS: OPACITY
 LEFT, WHITE, CIRCULAR
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY FEMALE

ANIMAL 9753 (CONTINUED)
TERMINAL BODY WT. 20.7

EYE

ANIMAL 9743 11-NOV-93 STUDY DAY 11
TYPE OF DEATH: FOUND DEAD

THORACIC CAV
GROSS:

CONTENTS ABNORMAL
CONTAINS SOFT CREAM MATERIAL

LIVER

MICRO: 2 HEPATOCELLULAR HYPERTROPHY
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN NERVE, SCIATIC NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 200 MG/KG/DAY FEMALE

ANIMAL 9762 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	0.989	5.205
KIDNEYS	0.284	1.495
SPLEEN	0.058	0.305
BRAIN	0.438	2.305
ADRENAL GL	0.008	0.042
OVARIES	0.023	0.121
TERMINAL BODY WT.	19.0	

EYE
 GROSS: OPACITY
 RIGHT, WHITE, CIRCULAR
 MICRO: 3 CATARACT
 PROBABLY DUE TO TRAUMA FROM BLEEDING
 MICRO: 3 SYNECHIA
 4 PHTHISIS BULBI
 PROBABLY DUE TO TRAUMA FROM
 RETROORBITAL BLEEDING
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 LIVER BRAIN NERVE, SCIATIC
 NERVE, TIBIAL

ANIMAL 9769 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.020	5.209
KIDNEYS	0.277	1.415
SPLEEN	0.072	0.368
BRAIN	0.455	2.324
ADRENAL GL	0.006	0.031
OVARIES	0.019	0.097
TERMINAL BODY WT.	19.6	

EYE
 GROSS: OPACITY
 LEFT
 LUNGS
 GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
 PUNCTATE RED FOCUS, RIGHT APICAL LOBE
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 LIVER BRAIN NERVE, SCIATIC
 NERVE, TIBIAL EYE LUNGS

ANIMAL 9757 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.119	5.689
KIDNEYS	0.262	1.332
SPLEEN	0.066	0.336
BRAIN	0.446	2.267
ADRENAL GL	0.007	0.036
OVARIES	0.019	0.097
TERMINAL BODY WT.	19.7	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER
 MICRO: (2) HEPATOCELLULAR NECROSIS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9774 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.226	5.923
KIDNEYS	0.306	1.478
SPLEEN	0.079	0.382
BRAIN	0.453	2.188
ADRENAL GL	0.007	0.034
OVARIES	0.018	0.087
TERMINAL BODY WT.	20.7	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER
 MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9759 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER		

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 200 MG/KG/DAY FEMALE

ANIMAL 9759 (CONTINUED)

LIVER	1.288	5.852
KIDNEYS	0.318	1.445
SPLEEN	0.075	0.341
BRAIN	0.456	2.072
ADRENAL GL	0.006	0.027
OVARIES	0.019	0.086
TERMINAL BODY WT.	22.0	

MICRO: 1 HEPATOCELLULAR HYPERTROPHY
EYE
GROSS: OPACITY
LEFT, CORNEAL
MICRO: MICROSCOPICALLY NORMAL
LENS FRACTURED DUE TO ARTIFACT IN
PROCESSING
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN NERVE, SCIATIC NERVE, TIBIAL
EYE

ANIMAL 9750 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.201	5.881
KIDNEYS	0.318	1.557
SPLEEN	0.068	0.333
BRAIN	0.473	2.316
ADRENAL GL	0.007	0.034
OVARIES	0.022	0.108
TERMINAL BODY WT.	20.4	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY FEMALE

 ANIMAL 9767 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.162	5.947
KIDNEYS	0.290	1.484
SPLEEN	0.074	0.379
BRAIN	0.457	2.339
ADRENAL GL	0.007	0.036
OVARIES	0.023	0.118
TERMINAL BODY WT.	19.5	

 LIVER MICRO: 3 HEPATOCELLULAR HYPERTROPHY
 SKIN GROSS: ALOPECIA
 VENTRAL SURFACE, 40X20 MM AREA
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 SKIN BRAIN NERVE, SCIATIC
 NERVE, TIBIAL

ANIMAL 9754 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.187	5.920
KIDNEYS	0.302	1.506
SPLEEN	0.078	0.389
BRAIN	0.425	2.120
ADRENAL GL	0.009	0.045
OVARIES	0.024	0.120
TERMINAL BODY WT.	20.0	

 LIVER MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 EYE GROSS: OPACITY
 LEFT, WHITE, CIRCULAR
 MICROSCOPICALLY NORMAL
 LENS FIBERS DISRUPTED DUE TO
 PROCESSING
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL
 EYE

ANIMAL 9768 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.070	5.456
KIDNEYS	0.290	1.479
SPLEEN	0.072	0.367
BRAIN	0.452	2.305
ADRENAL GL	0.010	0.051
OVARIES	0.029	0.148
TERMINAL BODY WT.	19.6	

 GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9760 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.237	5.902
KIDNEYS	0.322	1.536
SPLEEN	0.074	0.353
BRAIN	0.476	2.271
ADRENAL GL	0.009	0.043
OVARIES	0.025	0.119
TERMINAL BODY WT.	21.0	

 GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9744 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.128	5.535
KIDNEYS	0.298	1.462
SPLEEN	0.071	0.348

 LIVER MICRO: 2 HEPATOCELLULAR HYPERTROPHY
 SUBCUTIS GROSS: NODULE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY FEMALE

ANIMAL 9744 (CONTINUED)

BRAIN	0.444	2.179
ADRENAL GL	0.008	0.039
OVARIES	0.033	0.162
TERMINAL BODY WT.	20.4	

TOP OF HEAD, ADJACENT TO RIGHT EYE, 2
 MM, TAN
 MICRO+ P EPIDERMAL INCLUSION CYST
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9780 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE		
ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.237	5.835
KIDNEYS	0.311	1.467
SPLEEN	0.076	0.358
BRAIN	0.466	2.198
ADRENAL GL	0.006	0.028
OVARIES	0.017	0.080
TERMINAL BODY WT.	21.2	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER
 MICRO: 1 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY FEMALE

 ANIMAL 9775 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.401	6.188
KIDNEYS	0.340	1.502
SPLEEN	0.089	0.393
BRAIN	0.471	2.080
ADRENAL GL	0.008	0.035
OVARIES	0.018	0.080
TERMINAL BODY WT.	22.6	

LIVER
 MICRO: 1 HEPATOCELLULAR HYPERTROPHY
 SPLEEN
 GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
 DARK RED FOCAL AREA
 LYMPH ND, S-MAN
 GROSS: COLOR CHANGE, DIFFUSE
 DARK RED, ONE NODE
 MICRO+ 3 SINUS ERYTHROCYTOSIS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 SPLEEN BRAIN NERVE, SCIATIC
 NERVE, TIBIAL KIDNEYS

ANIMAL 9771 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.133	5.789
KIDNEYS	0.268	1.369
SPLEEN	0.068	0.347
BRAIN	0.432	2.207
ADRENAL GL	0.006	0.031
OVARIES	0.026	0.133
TERMINAL BODY WT.	19.6	

LIVER
 MICRO: 3 HEPATOCELLULAR HYPERTROPHY
 EYE
 GROSS: OPACITY
 LEFT, CORNEAL
 MICRO: (3) CORNEAL MINERALIZATION
 2 KERATITIS
 LENS FIBERS SEPARATED DUE TO
 PROCESSING ARTIFACT
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL
 KIDNEYS

ANIMAL 9770 2-NOV-93 STUDY DAY 2
 TYPE OF DEATH: FOUND DEAD
 STOMACH
 GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
 RED FOCI, NONGLANDULAR PORTION
 LIVER
 MICRO: 3 CONGESTION
 LYMPH ND, S-MAN
 GROSS: COLOR CHANGE, DIFFUSE
 ONE NODE, DARK RED
 KIDNEYS
 MICRO: 2 CONGESTION
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 STOMACH LYMPH ND, S-MAN BRAIN
 NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9745 15-NOV-93 STUDY DAY 15
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	1.289	6.285
KIDNEYS	0.291	1.419
SPLEEN	0.077	0.375
BRAIN	0.445	2.170
ADRENAL GL	0.006	0.029

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LIVER
 MICRO: 3 HEPATOCELLULAR HYPERTROPHY
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 BRAIN NERVE, SCIATIC NERVE, TIBIAL
 KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY FEMALE

ANIMAL 9745 (CONTINUED)

OVARIES 0.019 0.093
TERMINAL BODY WT. 20.5

ANIMAL 9748 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.253	5.852
KIDNEYS	0.292	1.364
SPLEEN	0.068	0.318
BRAIN	0.453	2.116
ADRENAL GL	0.006	0.028
OVARIES	0.020	0.093
TERMINAL BODY WT.	21.4	

LIVER

MICRO: 3 HEPATOCELLULAR HYPERTROPHY

EYE

GROSS: OPACITY
LEFT

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN NERVE, SCIATIC NERVE, TIBIAL
EYE KIDNEYS

ANIMAL 9781 15-NOV-93 STUDY DAY 15

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	1.161	5.661
KIDNEYS	0.310	1.511
SPLEEN	0.073	0.356
BRAIN	0.440	2.145
ADRENAL GL	0.008	0.039
OVARIES	0.029	0.141
TERMINAL BODY WT.	20.5	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

LIVER

MICRO: 2 HEPATOCELLULAR HYPERTROPHY

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN NERVE, SCIATIC NERVE, TIBIAL
KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Individual Clinical Pathology Data

(13 Pages)

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ Mice
ABBREVIATIONS

The following abbreviations appear in hematology reports when the parameter is reported.

WBC = LEUKOCYTES ($10^3/\mu\text{l}$)
RBC = ERYTHROCYTES ($10^6/\mu\text{l}$)
HB = HEMOGLOBIN (g/dl)
HCT = HEMATOCRIT (%)
MCV = MEAN CORPUSCULAR VOLUME (μm^3)
MCH = MEAN CORPUSCULAR HEMOGLOBIN (pg)
MCHC = MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)
PLT = PLATELETS ($10^3/\mu\text{l}$)
SEGS = SEGMENTED NEUTROPHILS (cells $10^3/\mu\text{l}$)
LYMPH = LYMPHOCYTES (cells $10^3/\mu\text{l}$)
MONO = MONOCYTES (cells $10^3/\mu\text{l}$)
BASO = BASOPHILS (cells $10^3/\mu\text{l}$)
EOS = EOSINOPHILS (cells $10^3/\mu\text{l}$)
BAND = BANDED NEUTROPHILS (cells $10^3/\mu\text{l}$)
LMON = LARGE MONOCYTES (cells $10^3/\mu\text{l}$)
IGRN = IMMATURE GRANULOCYTES (cells $10^3/\mu\text{l}$)
IERY = IMMATURE ERYTHROCYTES (cells $10^3/\mu\text{l}$)
NRBC = NUCLEATED RBCs (cells/100 WBCs)
RET = RETICULOCYTES (% of RBCs)
PT = PROTHROMBIN TIME (sec)
APTT = ACTIVATED PARTIAL THROMBOPLASTIN TIME (sec)
HBOD = HEINZ BODY (%)
MHGB = METHEMOGLOBIN (g/dl)
CLOT = CLOTTED
QNS = QUANTITY NOT SUFFICIENT
LA = LAB ACCIDENT
NOS = NO SAMPLE
DE = DATA ELIMINATED

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
MALES GROUP: 0 MG/KG/DAY
DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9728	8.43	14.8	42.1	50.	17.5	35.0	685.	4.4	0.75	3.63
9734	8.57	15.3	44.0	51.	17.8	34.7	756.	5.1	0.82	4.22
9709	8.70	15.4	43.7	50.	17.6	35.1	674.	3.0	0.46	2.53
9708	8.39	14.9	41.8	50.	17.7	35.5	556.	3.1	0.62	2.45
9711	9.01	15.4	44.3	49.	17.1	34.8	693.	4.4	0.68	3.68
MEAN	8.62	15.1	43.2	50.	17.6	35.0	673.	4.0	0.67	3.30
S.D.	0.250	0.30	1.15	0.7	0.26	0.34	72.7	0.91	0.137	0.777
N	5	5	5	5	5	5	5	5	5	5

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	MRBC
9728	0.03	0.01	0.00					
9734	0.03	0.01	0.03					
9709	0.02	0.00	0.02					
9708	0.00	0.00	0.03	0.	0.	0.	0.	0.
9711	0.03	0.00	0.02					
MEAN	0.02	0.00	0.02	0.	0.	0.	0.	0.
S.D.	0.013	0.005	0.012	0.0	0.0	0.0	0.0	0.0
N	5	5	5	1	1	1	1	1

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 50 MG/KG/DAY
 DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9705	8.38	14.5	42.1	50.	17.3	34.4	650.	4.7	0.71	3.89
9721	8.49	14.5	42.4	50.	17.0	34.1	695.	5.5	0.87	4.54
9717	8.32	14.8	42.4	51.	17.7	34.8	607.	2.8	0.51	2.32
9715	8.54	15.1	42.7	50.	17.6	35.2	690.	3.5	0.65	2.84
9697	8.49	14.9	41.8	49.	17.5	35.5	778.	5.9	1.04	4.85
9724	8.71	15.1	43.7	50.	17.4	34.7	754.	5.3	0.94	4.33
MEAN	8.49	14.8	42.5	50.	17.4	34.8	696.	4.6	0.79	3.79
S.D.	0.136	0.29	0.65	0.6	0.25	0.53	63.5	1.22	0.198	1.005
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9705	0.03	0.02	0.02					
9721	0.02	0.02	0.02					
9717	0.00	0.00	0.00	0.	0.	0.	0.	0.
9715	0.02	0.01	0.01					
9697	0.04	0.01	0.01					
9724	0.04	0.01	0.02					
MEAN	0.02	0.01	0.01	0.	0.	0.	0.	0.
S.D.	0.015	0.008	0.008	0.0	0.0	0.0	0.0	0.0
N	6	6	6	1	1	1	1	1

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 200 MG/KG/DAY
 DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9731	8.53	14.8	42.7	50.	17.3	34.5	673.	8.2	0.74	7.40
9733	8.39	14.4	42.1	50.	17.1	34.1	561.	4.3	0.61	3.67
9719	8.56	14.7	42.4	50.	17.1	34.6	679.	3.0	0.41	2.57
9710	8.69	15.1	43.4	50.	17.3	34.7	618.	3.5	0.63	2.78
9707	8.36	14.6	41.8	50.	17.4	34.8	738.	3.8	0.56	3.23
9696	8.45	14.9	42.7	51.	17.6	34.8	685.	3.7	0.67	3.02
MEAN	8.50	14.7	42.5	50.	17.3	34.6	659.	4.4	0.60	3.78
S.D.	0.122	0.24	0.55	0.4	0.17	0.26	61.3	1.91	0.112	1.814
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	PLRY	NRBC
9731	0.05	0.01	0.03					
9733	0.02	0.01	0.02					
9719	0.01	0.00	0.01					
9710	0.03	0.00	0.03	0.	0.	0.	0.	0.
9707	0.02	0.01	0.01					
9696	0.01	0.01	0.02					
MEAN	0.02	0.01	0.02	0.	0.	0.	0.	0.
S.D.	0.015	0.005	0.009	0.0	0.0	0.0	0.0	0.0
N	6	6	6	1	1	1	1	1

TABLE 2
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 1000 MG/KG/DAY
 DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9700	8.88	15.7	44.6	50.	17.7	35.3	760.	7.9	1.35	6.45
9706	8.30	14.7	41.8	50.	17.7	35.1	722.	4.7	0.76	3.85
9704	8.69	15.1	44.0	51.	17.3	34.2	722.	3.8	0.65	3.05
9714	8.34	14.4	41.8	50.	17.2	34.4	806.	4.0	0.59	3.33
9699	8.48	14.5	41.8	49.	17.1	34.6	727.	5.2	0.85	4.24
9726	8.80	15.4	44.0	50.	17.4	34.9	721.	5.7	0.80	4.78
MEAN	8.58	14.9	43.0	50.	17.4	34.7	743.	5.2	0.83	4.28
S.D.	0.244	0.53	1.34	0.6	0.25	0.40	34.3	1.50	0.271	1.230
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9700	0.06	0.02	0.01					
9706	0.06	0.00	0.02					
9704	0.00	0.00	0.11	0.	0.	0.	0.	0.
9714	0.01	0.01	0.02					
9699	0.04	0.00	0.03					
9726	0.05	0.01	0.02					
MEAN	0.04	0.01	0.03	0.	0.	0.	0.	0.
S.D.	0.026	0.008	0.037	0.0	0.0	0.0	0.0	0.0
N	6	6	6	1	1	1	1	1

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
MALES GROUP: 2000 MG/KG/DAY
DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9732	8.69	15.4	44.0	51.	17.7	34.9	780.	4.0	0.68	3.26
9730	8.68	15.0	43.4	50.	17.2	34.5	559.	5.3	0.82	4.37
9712	8.67	15.4	44.0	51.	17.8	35.1	782.	4.0	0.72	3.18
9716	8.82	15.5	44.0	50.	17.6	35.3	675.	3.2	0.70	2.43
9698	8.16	14.2	40.9	50.	17.4	34.7	751.	3.9	0.59	3.23
9701	8.80	15.3	43.7	50.	17.3	34.9	691.	3.8	0.69	3.08
MEAN	8.64	15.1	43.3	50.	17.5	34.9	706.	4.0	0.70	3.26
S.D.	0.242	0.50	1.23	0.5	0.23	0.29	84.9	0.69	0.074	0.626
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	ERY	NRBC
9732	0.02	0.01	0.02					
9730	0.03	0.01	0.04					
9712	0.05	0.01	0.03					
9716	0.01	0.01	0.01					
9698	0.00	0.01	0.03					
9701	0.03	0.01	0.02					
MEAN	0.02	0.01	0.02					
S.D.	0.018	0.000	0.010					
N	6	6	6					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
FEMALES GROUP: 0 MG/KG/DAY
DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9765	7.91	13.9	39.6	50.	17.6	35.1	707.	4.0	0.71	3.26
9766	7.87	13.6	39.6	50.	17.3	34.3	638.	2.7	0.33	2.27
9749	8.08	14.1	40.2	50.	17.4	35.0	705.	2.7	0.61	2.03
9779	8.46	15.1	42.7	51.	17.8	35.2	655.	6.0	0.96	4.73
9773	8.12	14.2	40.2	50.	17.5	35.3	611.	4.0	0.65	3.35
9772	8.36	14.7	41.5	50.	17.5	35.3	690.	4.9	0.78	4.05
MEAN	8.13	14.2	40.5	50.	17.5	35.0	668.	4.0	0.67	3.28
S.D.	0.237	0.53	1.24	0.4	0.17	0.37	39.2	1.28	0.208	1.028
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9765	0.03	0.01	0.02					
9766	0.02	0.02	0.04					
9749	0.01	0.01	0.02					
9779	0.24	0.02	0.03					
9773	0.01	0.01	0.02					
9772	0.03	0.00	0.02					
MEAN	0.06	0.01	0.02					
S.D.	0.090	0.008	0.008					
N	6	6	6					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
FEMALES GROUP: 50 MG/KG/DAY
DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9752	8.05	14.6	40.2	50.	18.1	36.2	630.	7.2	1.24	5.87
9764	7.77	13.5	39.0	50.	17.4	34.6	CLOT	4.1	0.53	3.46
9777	8.33	14.6	42.1	51.	17.5	34.6	688.	5.8	0.95	4.77
9755	8.29	14.6	41.5	50.	17.6	35.1	641.	5.3	1.18	4.05
9753	8.44	14.7	42.4	50.	17.4	34.6	647.	5.2	0.91	4.21
MEAN	8.18	14.4	41.0	50.	17.6	35.0	652.	5.5	0.96	4.47
S.D.	0.268	0.49	1.44	0.4	0.31	0.70	25.3	1.14	0.280	0.910
N	5	5	5	5	5	5	4	5	5	5

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9752	0.06	0.01	0.02					
9764	0.03	0.01	0.02					
9777	0.04	0.01	0.01					
9755	0.05	0.01	0.00					
9753	0.03	0.01	0.02					
MEAN	0.04	0.01	0.01					
S.D.	0.013	0.000	0.009					
N	5	5	5					

TABLE 3
VINYL 2-ETHYLBENZOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
FEMALES GROUP: 200 MG/KG/DAY
DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9762	8.52	15.1	42.7	50.	17.7	35.2	563.	5.5	0.64	4.76
9769	8.08	14.1	40.5	50.	17.4	34.7	CLOT	6.0	0.57	5.36
9757	8.17	14.1	40.2	49.	17.2	35.0	698.	3.9	0.64	3.17
9774	8.10	14.4	40.9	50.	17.8	35.2	662.	5.4	1.10	4.22
9759	8.02	14.2	39.6	49.	17.7	35.8	643.	5.6	0.76	4.70
9750	7.83	14.0	39.6	51.	17.9	35.3	666.	3.9	0.73	3.11
MEAN	8.12	14.3	40.6	50.	17.6	35.2	646.	5.0	0.74	4.22
S.D.	0.227	0.39	1.17	0.8	0.23	0.36	50.6	0.92	0.189	0.912
N	6	6	6	6	6	6	5	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9762	0.05	0.01	0.03					
9769	0.05	0.01	0.03					
9757	0.01	0.02	0.02					
9774	0.05	0.00	0.02					
9759	0.06	0.01	0.03					
9750	0.02	0.01	0.03					
MEAN	0.04	0.01	0.03					
S.D.	0.020	0.006	0.005					
N	6	6	6					

TABLE 3
 VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
 STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
 FEMALES GROUP: 1000 MG/KG/DAY
 DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9767	7.97	14.3	40.5	51.	17.9	35.2	772.	5.1	0.92	4.11
9754	7.84	13.8	39.3	50.	17.6	35.1	689.	4.0	0.71	3.21
9768	7.85	13.6	39.3	50.	17.3	34.6	613.	3.2	0.55	2.57
9760	7.96	14.1	42.4	53.	17.7	33.2	745.	4.5	1.15	3.29
9744	8.26	14.7	41.8	51.	17.8	35.1	680.	7.8	1.10	6.63
9780	8.08	14.5	40.9	51.	17.9	35.4	696.	5.7	0.72	4.86
MEAN	7.99	14.1	40.7	51.	17.7	34.8	699.	5.0	0.86	4.11
S.D.	0.158	0.41	1.28	1.1	0.22	0.82	55.3	1.62	0.238	1.467
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9767	0.03	0.01	0.01					
9754	0.04	0.01	0.02					
9768	0.02	0.01	0.01					
9760	0.03	0.01	0.01					
9744	0.09	0.00	0.01					
9780	0.06	0.02	0.02					
MEAN	0.04	0.01	0.01					
S.D.	0.026	0.006	0.005					
N	6	6	6					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN B6C3F₁ MICE

INDIVIDUAL HEMATOLOGY
FEMALES GROUP: 2000 MG/KG/DAY
DAY 15

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
9775	8.18	14.2	41.2	50.	17.3	34.4	609.	6.1	0.54	5.45
9771	8.03	14.1	40.5	50.	17.5	34.7	669.	5.2	0.61	4.47
9745	7.97	14.2	40.5	51.	17.8	35.0	868.	4.4	0.79	3.55
9748	7.76	14.2	39.9	51.	18.3	35.5	700.	3.8	0.64	3.10
9781	8.43	14.5	42.1	50.	17.2	34.4	739.	2.6	0.55	2.05
MEAN	8.07	14.2	40.9	50.	17.6	34.8	717.	4.4	0.63	3.72
S.D.	0.250	0.15	0.83	0.5	0.43	0.47	96.9	1.32	0.101	1.300
N	5	5	5	5	5	5	5	5	5	5

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IKRY	NRBC
9775	0.07	0.01	0.01					
9771	0.04	0.00	0.03					
9745	0.05	0.01	0.03					
9748	0.03	0.01	0.01					
9781	0.01	0.01	0.02					
MEAN	0.04	0.01	0.02					
S.D.	0.022	0.004	0.010					
N	5	5	5					

**Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding
Study in B6C3F₁ Mice**

Protocol, Protocol Amendment, and Protocol Deviations

(18 Pages)



BUSHY RUN RESEARCH CENTER

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PROTOCOL

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in B6C3F₁ Mice

BRRC PROJECT ID: 93U1319

SPONSORS: Solvents and Coatings Materials Division
Union Carbide Corporation
39 Old Ridgebury Road
Danbury, CT 06817-0001

Shell Oil Company
One Shell Plaza
P. O. Box 4320
Houston, TX 77210

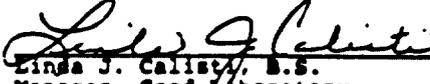
TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Corporation
6702 Mellon Road
Export, PA 15632-8902

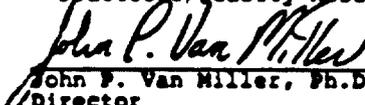
Reviewed and Approved by:

Bushy Run Research Center:

 9/13/93
Steven J. Hermansky, Pharm.D., Ph.D. Date
Study Director

 9/14/93
Edward H. Fowler, DVM, Ph.D., Date
Diplomate ACVP
Associate Director

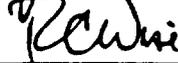
 9/15/93
Linda J. Calista, B.S. Date
Manager, Good Laboratory
Practices/Quality Assurance

 9/15/93
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Corporation:

 9/30/93
Tipton R. Tyler, Ph.D., DABT Date
Assistant Director of Applied Toxicology

Division:

 10-12-93
Richard C. Wise Date
Manager of Product Safety

Shell Oil Company:

 10/22/93
Thomas H. Gardiner, Ph.D. Date
Sponsor's Representative

Union Carbide Chemicals and Plastics Company Inc.
Excellence Through Quality

EQ

OBJECTIVES

The objectives of this study are to evaluate the toxicity of 4 dose levels of vinyl 2-ethylhexanoate in B6C3F₁ mice when administered by gavage and to establish dose levels for a potential 90-day gavage study.

Design and Basis for the Study

This study will consist of 4 treatment groups and a vehicle control group. Each group will consist of 6 animals/sex/group. Body weights, food consumption, and clinical signs will be assessed at specified intervals throughout the study. After at least 2 weeks of treatment, all surviving animals will be bled for hematology, all surviving animals will be killed, complete necropsies will be performed, and a microscopic evaluation will be made on a limited number of tissues.

The portions of this study conducted by BRRC will be in compliance with the following guidelines and standards:

U.S. Environmental Protection Agency (EPA), Toxic Substances Control Act (TSCA) Good Laboratory Practice (GLP) Standards, 40 CFR Part 792.

Organisation for Economic Co-operation and Development (OECD). OECD Principles of Good Laboratory Practice, C(81)30(Final).

PERSONNEL

All personnel who participate in the conduct of the study will be documented in the raw data.

PROJECT DATES

<u>Starting Date of Acclimation</u>	October 19, 1993
<u>Starting Date of Test Substance Administration</u>	November 1, 1993
<u>Date for Completion of In-Life Phase</u>	November 15, 1993
<u>Proposed Date for Submission of Draft Final Report</u>	February 18, 1994

METHODS

Test Substance

Product Name	VYNATE® 2-EE Monomer
Chemical Name	Vinyl 2-ethylhexanoate
CAS Registry Number	94-04-2
Source	Union Carbide Chemicals and Plastics Company Inc., South Charleston, WV

Sponsor Identification Number 11-ERE-52-1, Lot. No. JGT-1092

BRRRC Number 56-348

Description Transparent, colorless liquid.

Purity 99.9%

Stability The test substance is considered to be stable for the duration of the study.

Storage Conditions The test substance will be stored under well-ventilated conditions at ambient temperature in an appropriate storage area.

Quantity Approximately 1000 ml. After the assigned studies have been completed, all unused test substance will be returned to the Sponsor.

Reserve Sample A reserve sample of approximately 5 to 10 g will be retained in an amber bottle with a Teflon-lined cap from each container of test substance used during the study. The reserve sample will be stored at ambient temperature for 10 years. Prior to discarding the reserve sample, the Sponsor will be contacted.

Safety A Material Safety Data Sheet (MSDS) supplied by the Sponsor will be reviewed by all relevant personnel before their participation in the study. This review will be documented. Normal precautions for untested substances will be used. These procedures include the use of disposable Tyvek® or plastic coats or jumpsuits, hats, booties or shoe covers, and rubber gloves while in the animal rooms. Eye protection will include the use of safety glasses at all times. Disposable Tyvek® coats or smocks and appropriate gloves will be worn during administration of the test substance. In addition, monogoggles will be used when handling the test substance.

Test Animals

Species and Strain B6C3F₁ mice

Supplier Harlan Sprague Dawley Inc., Indianapolis, IN

Rationale This study is designed as a screen for aiding in selection of doses for a 90-day dose range-finding study in this strain of mouse.

Number and Sex A total of 45 males and 45 females will be ordered from which 30 animals/sex will be selected for the study.

Age and Weight The animals will be requested to be approximately 35 days of age on the scheduled animal receipt date.

Acclimation and Pretest Evaluations Shortly after their arrival at the laboratory, the animals will be transported to the room selected for the study. Once in the room, the animals will be removed from the shipping cartons and examined. All animals with evidence of disease or physical abnormalities will be discarded and the reason for rejection will be recorded. If an unusually large number of animals shows evidence of disease or physical abnormalities, the entire shipment of animals will be rejected for use in the study. A total of 10 (5/sex) will be randomly selected for a pretest health screen as discussed below.

All remaining animals will be housed 2 to a cage for at least one week during the acclimation period. After this period, animals will be housed individually.

During the acclimation period, animals will be fed the same diet that will be used during the study. Animals will be observed twice daily for any overt clinical signs of disease or abnormality. Individual detailed physical examinations will be conducted twice prior to study start. Animals showing abnormalities deemed by the Study Director or other appropriate personnel to render the animal unacceptable for placement on the study will be sacrificed and discarded on the day observed, and the reason for sacrifice will be recorded.

Approximately 10 days before the study is scheduled to begin, all animals will be weighed. The animals will be weighed again approximately 1 week later.

Any animal whose weight gain during the acclimation period is not considered normal for this age and strain of mouse, or whose absolute body weight at the second weighing is outside $\pm 20\%$ of the population mean for each sex, will not be considered for use in the study.

Pretest Health Screen A pretest health screen will be initiated within 2 days after the receipt of the animals. The pretest health screen will be performed on 5 animals/sex selected directly from the shipping cartons with as

many cartons as possible being represented and will consist of a serology screen, examinations for fecal parasites, and necropsy.

Animals not selected for the study may be held for possible random serology testing. The following organisms will be included in serologic testing conducted periodically throughout the facility:

Sendai virus (SEND)
Pneumonia virus of mice (PVM)
Mouse hepatitis virus (MHV)
Minute virus of mice (MVM)
Mouse polio virus (GD-7)
Reovirus type 3 (REO-3)
Mycoplasma pulmonis (MPUL)
Lymphocytic choriomeningitis (LCMV)
Mouse adenovirus FL/R87 (MAD)
Ectromelia virus (ECTRO)
Mouse pneumonitis virus (K)
Polyoma virus (POLY)
Epizootic diarrhea of infant mice virus (EDIM)
Mouse cytomegalovirus (MCMV)
Hantann virus (HANT)
Encephalitozoon cuniculi (ECUN)

Fecal examination for parasites will be conducted using a cellophane tape test as a prestudy screen and by zinc sulfate flotation from cecal contents obtained at necropsy.

The purpose of this screen is to determine the suitability of the population of animals proposed for this study. Therefore, the results of this screen will be available to the Study Director before the study begins.

All mice will be examined by a veterinarian shortly after their arrival and again prior to study start. The dates of the examinations will be documented in the raw data.

Identification

Each animal will be assigned a unique identification number prior to the initiation of the study. Animals considered for assignment to the study will be identified by cage tags and toe-clipped. Records will be kept documenting the fate of all animals received for the study.

Husbandry

Conditions

All animals will be housed in an appropriate animal room at BRRC from arrival until termination of the in-life phase of the study. Stainless steel cages with

wire mesh floors will be used throughout all phases of the study. Cages will be changed and sanitized at least once every 2 weeks. DACB® (Decontaminated Animal Cage Board; Shepherd Specialty Papers, Inc.) will be changed at least 3 times each week.

Temperature and humidity will be recorded continuously using an automatic recorder. Temperature will be maintained at 66-77°F and relative humidity will be maintained at 40-70%. The temperature and humidity will be checked by a technician at each room check and a record will be kept indicating that it was done. Appropriate corrective action will be taken whenever readings outside the specified limits are observed.

The accuracy of the temperature and humidity recording devices will be checked periodically and calibrated when necessary. The verification and calibration data will be recorded. In the event that continuous recording cannot be maintained, the temperature and humidity will be manually recorded at each room check.

An automatic timer will be set to provide fluorescent lighting for a 12-hour photoperiod (approximately 0500 to 1700 hours for the light phase). In the animal room, there will be at least 10 air changes each hour.

Diet

Ground Lab Diet™ The Richmond Standard™ Certified Rodent Diet #5002 (Purina Mills, Inc.; PMI, Inc.) will be available ad libitum. The analyses of chemical composition and possible contaminants of each batch of diet will be performed by Purina Mills, Inc. (PMI, Inc.), and the results of the analyses will be reviewed by the Study Director.

Water

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) will be available ad libitum by an automatic watering system with demand control valves mounted on each rack. Water pressure and function of the individual cage rack systems will be checked at each room check, and a record will be kept indicating it was done. Drinking water contaminant levels will be measured at approximately 9-month intervals according to the methods specified in the EPA Safe Drinking Water Act Regulations and will comply with human drinking water requirements. The results of the analyses will be reviewed by the Study Director.

Administration of Test Substance

Route and
Justification

The route of administration will be by gavage. This route will ~~be considered to be a meaningful way to evaluate the toxicity of chemicals with the use pattern of vinyl 3-ethylhexanoate~~ be used in the 90-day subchronic study as specified in the TSCA PMN consent order for the vinyl ester family.

T. Tybly 9/30/93
R.G. 10-12-93
J.H. 11/22/93

Dose Selection	Four graduated dosage levels of the test substance were selected by the Sponsor for evaluation in 4 groups of mice. Dosage levels will be expressed in terms of mg test substance/kg body weight/day.
Vehicle and Control Substance	Mazola® corn oil (Best Foods, CAS No. 8001-30-7) will be administered by gavage to the control group and serve as the vehicle for the test substance. Corn oil is an acceptable control substance for test substances of this type.
Dose Administration	<p>The test substance will be administered as a single, daily dose using an 18-gauge, 1 1/2-inch, commercial, ball-end stainless steel dosing needle attached to an automatic dispensing system. Attempts will be made to dose the animals at approximately the same time each day.</p> <p>The dosing solution volume in all dose groups, including the control groups, will be 4 ml/kg/day. Administered volumes will be based on the individual's body weight.</p>
Duration of Treatment	The dosing period will be 5 days/week for 2 consecutive weeks.
Preparation of Solutions	Dosing solutions will be prepared by direct addition of the test substance to corn oil. Solution concentrations will be prepared based on the test substance as received. Storage will be in a manner consistent with the stability of the test substance in the solutions as described below. Solutions will be prepared weekly. If the stability of vinyl 2-ethylhexanoate solutions proves to be less than 7 days, more frequent preparation will be necessary and will be at additional cost to the Sponsor.
Analysis of Dosing Solutions	Before initiating dosing, the test solutions will be prepared to assess the homogeneity and stability. Homogeneity (duplicate samples from the top, middle, and bottom of the mixing vessel) will be determined for the lowest and highest concentrations to be used for the study. Stability will be evaluated by determining the test substance concentration in triplicate samples from the low and high dose solution concentrations used for the study. Stability of the test substance in the solutions will be determined for at least 14 days under storage conditions identical to those used during dosing.

Dosing solutions will be prepared as necessary for the study. Each solution will be analyzed in duplicate for test substance concentration prior to administration to the animals.

Standards for acceptable accuracy of mixing will be: the mean of the analyzed samples must be within $\pm 10\%$ of nominal; the difference between duplicate analyses will not exceed 15% ; and individual analyses will be within $\pm 15\%$ of nominal. If one or more of these standards is not met, the solutions will not be administered to the animals. If additional analyses or solution preparations are necessary, these will be performed at no additional cost to the Sponsor. The Study Director and the Sponsor will be notified immediately when problems of this nature occur.

**Test Substance
Analysis**

Prior to initiation of the study, a sample of the test substance will be drawn, and a compositional analysis will be performed by the Sponsor.

Study Design

**Group
Assignment**

Based on the final pretest body weights, 30 males and 30 females will be selected for the study from the remaining population. These animals will be divided equally into 5 groups, each consisting of 6 males and 6 females, using a weight stratified randomization procedure.

Animals not assigned to the study will be used for other toxicity testing, training of BRRC staff, methods development, or possible random serology testing, or they will be humanely sacrificed and discarded. The fate of all animals not selected for use in this study will be documented in the raw data.

Following body weight measurement just prior to the first treatment, statistical evaluation of the body weights for all groups will be conducted, and statistical equivalence and homogeneity of variance will be examined. In the event that either criterion is not met, animals will be switched between groups to establish statistical equivalence and homogeneity of variance. Animals with any abnormal clinical signs will also be replaced prior to treatment and the statistical criteria will be repeated until statistically equivalent body weights for all groups are obtained.

Organization

Group	Number of Animals		Vinyl 2-ethylhexanoate Volume (ml/kg/day)	Dosage (mg/kg/day)
	Male	Female		
Control	6	6	4.0	0.0
Low	6	6	4.0	50.0
Mid-1	6	6	4.0	200.0
Mid-2	6	6	4.0	1000.0
High	6	6	4.0	2000.0

Experimental Evaluations

- Mortality Checks and Clinical Signs** All animals will be observed for mortality and signs of overt toxicity twice each day, 7 days a week. The first daily room check will generally be conducted before 8:30 a.m. and the second one will generally be conducted after 2:30 p.m. The times of daily room checks will be recorded. Should mortality and/or signs of overt toxicity be observed, it will be recorded on the day observed. Overt signs will also be recorded on subsequent days until the sign disappears or the animal dies. Detailed clinical observations will be performed weekly.
- Sacrifice of Distressed Animals** If any animal shows signs of extreme distress or is moribund, it will be sacrificed for humane reasons before the scheduled date and the Sponsor will be notified.
- Body Weight** Individual body weights will be measured on Days 1, 4, 7, 14, and prior to sacrifice.
- Food Consumption** Individual food consumption measurements will be collected for intervals 1-4, 5-7, and 8-14. The area under the cage will be examined for food spillage during each room check and significant food spillage will be noted. Significant food spillage will be defined as "piles" or "mounds" of feed but not a "dusting" or "sprinkling" of feed. Food consumption data for animals with recorded spills will not be used in summarization of results within a particular time interval.
- Clinical Pathology Evaluations** Clinical investigations (hematology) will be conducted on all surviving animals at termination. The order of bleeding and analysis will be alternating (1 animal from each dose group, then repeating) in order to reduce handling and time biases. All blood samples will be obtained from methoxyflurane anesthetized animals by puncture of the retroorbital sinus. Animals will not be fasted. The following procedures will be performed:

Hematology

hematocrit
hemoglobin
erythrocyte count
mean corpuscular volume (MCV)
mean corpuscular hemoglobin (MCH)
mean corpuscular hemoglobin
concentration (MCHC)
total leukocyte count
differential leukocyte count
platelet count

Anatomic
Pathology
Evaluations

At the end of treatment, all surviving animals will be anesthetized with methoxyflurane and killed by severing the brachial vessels. Any animal showing signs of severe debility, particularly if death appears imminent, will be sacrificed early to prevent loss of tissues through autolysis. All animals on the study will receive a complete necropsy and all retained tissues will be fixed in 10% neutral buffered formalin.

The order of sacrifice will be randomized in advance in order to reduce observation, tissue trimming, and organ weighing biases.

The following tissues will be collected for all animals:

gross lesions¹
lungs with mainstem bronchi²
brain (cerebral cortex, cerebellar cortex,
medulla/pons)
pituitary
thyroid - parathyroid complex³
thymic region⁴
trachea
heart
sternum (including marrow)
salivary gland
liver
spleen
kidneys⁵
adrenals
pancreas
testes
epididymis
prostate
seminal vesicles
ovaries
vagina

uterus (corpus and cervix)⁶
aorta
skin
gall bladder
esophagus
stomach
duodenum
jejunum
ileum
cecum
colon
rectum
urinary bladder
representative lymph nodes (mesenteric and
nonmesenteric)
mammary gland (females)
skeletal muscle (gastrocnemius)
peripheral nerve (sciatic)
eyes
femur (including articular surface)
spinal cord (cervical, midthoracic, and lumbar)

Feet will be saved for identification purposes.

¹Whenever possible, a border of normal appearing tissue will also be saved when gross lesions are taken.

²Lungs will be inflated with formalin by the trachea.

³Parathyroids cannot always be identified during slide preparation. They will be examined if they are in the plane of the section and in all cases where they are noted as grossly enlarged.

⁴At times, these tissues cannot be identified with the unaided eye because of anatomic variation in size. However, tissue from the region will be fixed for microscopic evaluation.

⁵The right kidney will be sectioned crosswise and the left kidney will be sectioned longitudinally for histologic processing.

⁶The cervix cannot always be identified during slide preparation. It will be examined when it is in the plane of the section and in all cases when gross lesions are present.

Organ Weights

The following organs from all surviving animals at the terminal sacrifice will be trimmed, blotted, and weighed:

liver
kidneys
adrenals
testes (males)
ovaries (females)
brain (including brain stem)
spleen

Histopathology

All tissues to be examined microscopically will be processed for paraffin embedding, sectioned at 5 microns, and stained with hematoxylin and eosin. Lesions will be graded as to severity, where possible, into 5 categories (minimal, mild, moderate, marked, or severe).

The underlined tissues in the list under Anatomic Pathology Evaluations will be processed histologically and examined by light microscopy for animals in the control and high dose groups. Animals that die or are killed during the study will be handled in a manner similar to those animals that survive to scheduled sacrifice, according to their respective dose groups.

If significant lesions are observed in the high dose group, those tissues will be examined for animals in the low and mid dose groups at an additional cost to the Sponsor.

Statistical Evaluations

The data for quantitative continuous variables will be intercompared for the dose and control groups by Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. The t-tests will be used following a significant ANOVA to delineate which groups differ from the control group. If Levene's test indicates homogeneous variances, the groups will be compared by an ANOVA for equal variances followed, when appropriate, by pooled variance t-tests. If Levene's test indicates heterogeneous variances, the groups will be compared by an ANOVA for unequal variances followed, when appropriate, by separate variance t-tests. For nonparametric data, the Kruskal-Wallis test followed, when appropriate, by Mann-Whitney U-tests, will be used. Incidence data will be compared using the appropriate statistical test, generally Fisher's Exact Test. Statistical analyses will be performed using either BMDP Statistical Software or other statistical programs, as deemed appropriate. The probability value of less than 0.05 (2-tailed) will be used as the critical level of significance for all tests.

ALTERATION OF PROTOCOL

Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. BRRRC reserves the right to revise the protocol or deviate therefrom solely at the discretion of the Study Director if prior approval of the Sponsor cannot be obtained and the integrity of the study is considered in jeopardy. In this event, the Sponsor will be notified of the alteration as soon as possible, and documentation of the change will be the responsibility of the Study Director.

RETENTION OF RECORDS

All raw data, documentation, the protocol and any amendments, specimens, and a copy of the final report generated as a result of this study will be retained in the BRRRC Archives for at least 10 years. A reserve sample of test substance from each container used during the study will also be stored in the BRRRC Archives.

Following the retention period specified above, the Sponsor will be contacted and given the option of taking receipt, destroying, or arranging for other storage of the data and materials. All data and materials mentioned above will remain the sole property of the Sponsor and can be removed from BRRRC at the Sponsor's discretion.

REPORTS

Draft Final Report

An unaudited draft of the final report will be submitted to the Sponsor approximately 3 months after the completion of the terminal sacrifice. This report will be a comprehensive report which will include all information necessary to provide a complete and accurate description and evaluation of the test procedures and results. It will include: a summary; appropriate text discussions of the experimental design, materials and methods, and results; and summary mean or incidence tables of in-life and pathology data. In addition, it will contain appendices with individual animal data and other pertinent information.

Final Report

The draft final report will be reviewed by the Sponsor, and comments on the report will be provided to BRRRC within 8 weeks from the date of submission of the draft version. BRRRC will consider these comments in preparing the final report. Assuming the Sponsor's comments are received at the specified time and no major revisions are required, BRRRC will submit a final report within 12 weeks of issuance of the draft report.

The final report will be audited by the Quality Assurance Unit and contain a signed quality assurance statement. It will conform to the formatting specifications of EPA PR notice 86-5.

ANIMAL USE POLICY

It is the goal of BRRC, through the establishment and activities of the Institutional Animal Care and Use Committee, to comply with the U.S. Animal Welfare Act and the subsequent rules promulgated by the U.S. Department of Agriculture and in effect on the date of this protocol. It has been determined that the work described herein minimizes the number of animals used, is necessary, and uses the most appropriate species and strain in order to provide meaningful results and the most useful information for comparative purposes relative to previous studies. Furthermore, this study will be conducted humanely, and to the best of our knowledge, neither unnecessarily duplicates any previous work, nor can it be accomplished using currently available, validated nonanimal models.

GOOD LABORATORY PRACTICE COMPLIANCE

BRRC, through the administration of a quality assurance program by the Good Laboratory Practice Committee and Quality Assurance Unit, assures compliance of all phases of studies conducted at BRRC with existing regulations and generally accepted good laboratory practices.

The study will be subjected to periodic inspections and the final report will be reviewed by the BRRC Quality Assurance Unit.



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL AMENDMENT 1

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in B6C3F₁ Mice

BRRC PROJECT ID: 93U1319

SPONSORS:

Solvents and Coatings Materials Division
Union Carbide Corporation
39 Old Ridgebury Road
Danbury, CT 06817-0001

Shell Oil Company
One Shell Plaza
P. O. Box 4320
Houston, TX 77210

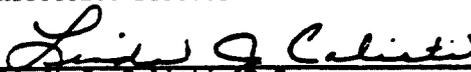
TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Corporation
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

Bushy Run Research Center:

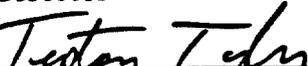

Steven J. Kernansky, Pharm.D.,
Ph.D., DABT
Study Director
1/10/94
Date


Edward H. Fowler, DVM, Ph.D.,
Diplomate ACVP
Associate Director
1/10/94
Date


Linda J. Calisti, M.S.
Manager, Good Laboratory
Practices/Quality Assurance
1/12/94
Date


John P. Van Miller, Ph.D., DABT
Director
1-12-94
Date

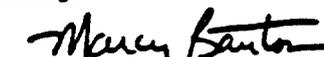
Union Carbide Corporation:


Tipton R. Tyler, Ph.D., DABT
Assistant Director of Applied Toxicology
2/3/94
Date

Division:


Richard C. Wise
Manager of Product Safety
2-3-94
Date

Shell Oil Company:


Marcy E. Banken, DVM, Ph.D.,
Diplomate ABVT
Sponsor's Representative
2/15/94
Date

UNION CARBIDE CORPORATION

The protocol is amended as follows:

Item 1

Location of
Protocol Change

Page 1, Reviewed and Approved by

Description of
Protocol Change

Diplomate, American Board of Toxicology (DABT) has been added to the degrees following Steven J. Hermansky's name.

Rationale

Dr. Hermansky has been certified as a Diplomate of the American Board of Toxicology.

Item 2

Location of
Protocol Change

Page 1, Sponsor's Representative

Description of
Protocol Change

Marcy I. Banton will replace Thomas E. Gardiner as the Sponsor's Representative.

Rationale

Dr. Banton has assumed the responsibility of Sponsor's Representative for Shell Oil Company.

Item 3

Location of
Protocol Change

Page 3, Reserve Sample and Page 13, Retention of Records

Description of
Protocol Change

A reserve sample will not be retained after the submission of the final report.

Rationale

The test substance may form peroxides upon inhibitor depletion with long-term storage.

CO_TORPROTOCOLVASEBGM1

PROTOCOL DEVIATIONS

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in B6C3F₁ Mice

BRRC PROJECT ID: 93U1319

The following deviations occurred from the written protocol for this study:

1. Detailed clinical observations were performed daily and body weights were measured on Days 1, 4, 8, and 15.
2. Food consumption measurements were collected for intervals 2-4, 4-8, and 9-15. Full feeder weights are collected on the day after the feeders are filled for mice.
3. The order of sacrifice was randomized in advance in order to reduce necropsy observation biases. The order of organ weighing did not necessarily follow this sacrifice order due to the varying performance of the different prosectors. Tissue trimming is not performed in random order.
4. The brain and peripheral nerves (sciatic and tibial) were included in the list of tissues that were processed histologically and examined by light microscopy for consistency between this study and the rat (93U1318).
5. Due to the number of male mice that arrived, the last 3 were housed together.
6. The liver was examined by light microscopy for all animals due to the lesion (hepatocellular hypertrophy) observed in the high dose group.
7. The protocol states that stability would be determined using triplicate samples from the low and high dose concentrations. Actually 6 samples were evaluated.