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Shell Oil Company

One Shell Plaza
P.O. Box 4320
Houston, Texas 77210

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November 23, 1994

Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
ATTN: 8(e) Coordinator

89950000051

Dear Sir:

SUBJECT: SUPPLEMENTAL INFORMATION FOR TSCA 8(e) SUBMISSION ON VINYL 2-ETHYLHEXANOATE (CAS# 94-04-2)

A TSCA 8(e) submission on neurostructural changes in the brain and spinal cord of rats dosed orally with vinyl 2-ethylhexanoate in a 14-day toxicity study conducted by Bushy Run Research Center was filed by Shell Oil Company on June 22, 1994. A copy of the summary from the draft, unaudited report, which described the findings was provided. The study was jointly sponsored by Shell Chemical Company and Union Carbide Chemical and Plastics Company. The complete final report is now available along with an additional report of the results of the follow-up work to describe the electron microscopy of the neurostructural changes. Both final reports (attached) are provided as supplemental information to the original 8(e) filing (attached).

These supplemental reports are filed to provide information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Oil Company as the reporting corporation, its agents or employees. The reporting corporation, its agents and employees, reserve the right to object to this report's use or admissibility in any subsequent judicial or administrative proceeding against the corporation, its agents or employees.

These reports have been compiled based on information available as of the date of filing. The corporation, its agents and employees reserve the right to supplement the data contained in this report, and to revise and amend any conclusions drawn therefrom.

These reports contain no confidential business information.

1/2/95

SH9432701.W60

The following person should be contacted if you have questions or a need for discussion.

J. C. Willett
Manager, Product Safety and Compliance
Shell Oil Company
P.O. Box 4320
Houston, TX 77210
Telephone No. 713-241-6958
Fax. 713-241-3325

Very truly yours,

R. N. Shulman, General Manager
Health, Safety, and Environment
Shell Oil Company

THG/sjh

Attachments

SH9432701.W60

Shell Oil Company

One Shell Plaza
P.O. Box 4320
Houston, Texas 77210

June 22, 1994

VIA OVERNIGHT MAIL

Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
ATTN: 8(e) Coordinator

Dear Sir:

SUBJECT: NEUROSTRUCTURAL CHANGES IN THE BRAIN AND SPINAL CORD OF RATS DOSED ORALLY WITH VINYL 2-ETHYLHEXANOATE IN A 14-DAY TOXICITY STUDY

The following information is submitted under TSCA 8(e).

Neurostructural changes, which included vacuolation, myelinopathy and axonopathy of the brain and spinal cord, were observed in male and female rats that received two oral doses of 2000 mg/kg vinyl 2-ethylhexanoate (CAS Number 94-04-2) in a 14-day toxicity study conducted by Bushy Run Research Center. The study is jointly sponsored by Shell Chemical Company and Union Carbide Chemical and Plastics Company.

Attached is a copy of the summary from the draft, unaudited report, which describes the above findings. The complete final report will be sent to the Agency when available.

This report is filed to provide information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Oil Company as the reporting corporation, its agents or employees. The reporting corporation, its agents and employees, reserve the right to object to this report's use or admissibility in any subsequent judicial or administrative proceeding against the corporation, its agents or employees.

This report has been compiled based on information available as of the date of filing. The corporation, its agents and employees reserve the right to supplement the data contained in this report, and to revise and amend any conclusions drawn therefrom.

This report contains no confidential business information.

SH9417907.WPD

(k)

The following person should be contacted if you have questions or a need for discussion.

J. C. Willett
Manager, Product Safety and Compliance
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Telephone No. 713-241-6958
Fax. 713-241-3325

Very truly yours,

R. N. Shulman, General Manager
Health, Safety, and Environment
Shell Oil Company

THG/sjh

Attachments

SH9417907.WPD

UNION CARBIDE

BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
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STUDY TITLE

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats - Electron Microscopy of the Spinal Cord

TEST SUBSTANCE

Vinyl 2-Ethylhexanoate

DATA REQUIREMENT

Not Applicable

AUTHOR

P. E. Losco

STUDY COMPLETION DATE

October 20, 1994

PERFORMING LABORATORY

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

LABORATORY PROJECT ID

94U1428

SPONSORS

Union Carbide Corporation (UCC)
39 Old Ridgebury Road
Danbury, CT 06817-0001

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

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats - Electron Microscopy of the Spinal Cord

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 Fischer 344 Rats - Electron Microscopy of the Spinal Cord

NONCOMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

This study was performed at a non-GLP facility and does not meet the requirements of Toxic Substances Control Act (TSCA) Good Laboratory Practice Standards, 40 CFR Part 792.

Study Director: Patricia E. Losco 10-20-94

Patricia E. Losco, VMD
Diplomate, ACVP

Date

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Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats - Electron Microscopy of the Spinal Cord

SUMMARY

Electron microscopic evaluation of the cervical spinal cord was performed on Fischer 344 rats gavaged with 0 (corn oil control) or 2000 mg/kg/day of vinyl 2-ethylhexanoate (2-EH; CAS No. 94-04-2) for a 14-day range-finding study, in order to confirm and further characterize lesions of the spinal cord which were observed by light microscopy in treated animals. The 2000 mg/kg/day group rats used in this study only received 2 doses of chemical because of the high mortality which occurred in this treatment group. They were sacrificed on Day 14, along with the animals in the other dose groups. No lesions were found in the control group rat. Spinal cord lesions, characterized by disruption, vesicular degeneration, and fragmentation of the myelin sheaths of nerve fibers and shrinkage and disintegration of the axonal cylinders of demyelinated fibers, were observed in all 4 of the 2-EH-treated rats which were examined for this study.

BACKGROUND INFORMATION

In a 14-day peroral gavage study with vinyl 2-ethylhexanoate (BRRC Report 93U1318), light microscopic evaluation of nervous system tissues revealed that the spinal cord and brain stem were target organs of chemical exposure. The rats evaluated in this study received only 2 doses of 2-EH, as all the other animals in the 2000 mg/kg/day group died or were sacrificed moribund after 1-2 doses. Examined animals were sacrificed, as scheduled, on Day 14. Observed lesions, found only in the 2000 mg/kg/day group rats which survived to sacrifice (3 females and 1 male), included vacuolation of the ventral and, occasionally, lateral white matter tracts of the spinal cord (both sexes) and similar lesions in the pons and medulla of the brain stem (2 females only). The location of lesions was characteristic for affected animals. Special stains (Bielschowsky's technique) for axons also revealed that 2 females had degenerative changes of the axons of vacuolated fibers in the spinal cord. It was elected, in this study, to examine only the cervical spinal cord, as lesions occurred most consistently and characteristically at that site. Only the 4 rats which survived to sacrifice from the 2000 mg/kg/day group were examined, as they were the only study animals with light microscopic lesions of the spinal cord.

METHODS

Necropsy

Electron microscopic evaluations were performed on 1 control group female, gavaged with corn oil, and 3 females and 1 male, gavaged with 2000 mg/kg/day of 2-EH in corn oil vehicle for 2 consecutive days. The rats were sacrificed under anesthesia on Day 14 by means of an intraperitoneal injection with pentobarbital (Euthanasia-6 solution) and heparin and were then exsanguinated. They were immediately perfused with 10% neutral buffered formalin via intracardiac puncture at the time of bleeding. Tissues from the central and peripheral nervous systems were collected and fixed in formalin, embedded in paraffin, and sectioned and stained for light microscopy. (See BRRC Report 93U1318 for a detailed discussion of histology methods.) All 4 of the treated rats used in this study had lesions of their cervical spinal cords by light microscopy. Longitudinal and cross sectional samples of the cervical spinal cord, collected from sites immediately adjacent to the areas examined by light microscopy, were collected from each animal and submitted to Mellon Institute of Carnegie Mellon University (CMU) for electron microscopy.

Tissue Preparation

The formalin-fixed specimens were transferred into 2% glutaraldehyde buffered with phosphate buffered saline (PBS). After 30 minutes, they were washed in 3 changes of PBS and post fixed in 1% osmium tetroxide buffered with PBS for 1 hour. Specimens were then transferred to a solution of 0.5% osmium tetroxide for an additional hour. The specimens were washed in 3 changes of distilled water and stained with 0.5% uranyl acetate in distilled water overnight at 4°C. The following day, the specimens were washed in 3 changes of distilled water and dehydrated in an ethanol series (30%, 50%, 70%, 80%, 90%, and 3 times in 100%) for 5 minutes each. Two changes of propylene oxide, 5 minutes each, were used as a transitional solvent. The tissue was then infiltrated in a 1:1 mixture of EPON-Araldite and propylene oxide for 3 hours, and

transferred to 100% EPON-Araldite overnight. The following day, the 100% EPON-Araldite was changed, and the specimens were vacuum infiltrated for 3 hours. The specimens were placed in BEEM capsules and polymerized at 60°C for 48 hours. Thick (1 micron) sections of each specimen were cut and stained with toluidine blue, and were submitted to the study pathologist for review. The pathologist examined the slides and selected and marked areas for electron microscopic examination. The slides were returned to CMU where the designated areas were thin sectioned (at approximately 700 angstroms) on a Reichert-Jung Ultracut-E ultramicrotome. The sections were mounted on copper grids, stained for 7 minutes with 1% uranyl acetate and for 1 minute with Reynold's lead citrate. They were viewed by the study pathologist on a Philips 300 electron microscope at 60 kv. Representative photographs were taken of specimens from each animal and selected examples were printed and identified as follows:

Figure #	Animal #	Exposure Group (mg/kg/day)	Negative #	Magnification
1	9571	0	11546	33,000 X
2	9571	0	11543	53,900 X
3	9541	2000	11539	10,000 X
4	9541	2000	11536	21,300 X
5	9538	2000	11529	8,600 X
6	9538	2000	11528	21,300 X
7	9533	2000	11522	10,000 X
8	9533	2000	11523	26,000 X
9	9519	2000	11509	10,000 X
10	9519	2000	11511	17,750 X
11	9519	2000	11515	17,750 X

RETENTION OF RECORDS

All raw data material from this study, including microscopic thick sections, BEEM capsules, copper grids, and electron microscopic photographic negatives will be retained and will be submitted for archiving with the original study (BRRC Report 93U1318).

RESULTS

Only the white matter of the ventral funiculi of the cervical spinal cord was examined in this study. Most of the electron micrographs were taken of the cord in longitudinal or oblique section, as these views best revealed the structural appearance of the myelinated nerve fibers which were the presumed site of chemical toxicity.

The cervical spinal cord examined from the control group female displayed normal anatomic appearance and structural relationships. The anatomic features of the axonal cylinders included fine, longitudinally-oriented microfilaments and microtubules, with occasional scattered mitochondria, and infrequent foci of dilated endoplasmic reticulum (Figures 1 and 2). There were no Golgi complex or ribosomes seen within axons, as these structures are found in the main cell body adjacent to the nucleus. The myelin sheaths were symmetrical in density around each axon, and varied appropriately in density with the size of the nerve fiber, with larger fibers having thicker myelin sheaths than smaller fibers. There was a mild separation of myelin lamellae

present at scattered sites around many nerve fibers, which was interpreted as an artifact of the formalin fixative used on these tissues. Schwann cells, when present, exhibited normal appearance of their nucleus and cytoplasm with no swelling or disruption of organelles.

While all the 2-EH-treated rats had areas of normal appearance within their spinal cord sections, all of the animals examined for this study had foci of marked nerve fiber degeneration corresponding to the lesions of vacuolation observed by light microscopy. Lesions were characterized by disruption and degeneration of the myelin sheath lamellae and, in many cases, shrinkage and fragmentation of the axons. Degenerate myelin layers tended to separate and collapse into the axonal space (Figures 4, 6, and 9). Vesicular swelling between myelin layers was common, and fragmented myelin formed lamellar inclusions and condensed myelin droplets (Figures 3, 4, and 5). In most of the sections, axonal damage was profound. Many degenerating fibers had no visible axons (Figures 3 and 5). Others had condensed granular debris and occasional degenerating organelles intermixed with myelin fragments as the only axonal remnants which were recognizable (Figures 6, 8, 9, and 10). Degenerating fibers tended to occur in clusters, often with normal fibers intermixed. Larger fibers were more likely to be affected than small fibers (Figure 4). Although swelling of Schwann cell cytoplasm and organelles was occasionally observed adjacent to degenerate nerve fibers (Figure 7), Schwann cells, in general, were unaffected (Figure 11).

CONCLUSION

Peroral exposure of rats to 2000 mg/kg/day of vinyl 2-ethylhexanoate in this test system produced a moderate multifocal myelinopathy and axonopathy affecting the white matter of the spinal cord in the area of the ventral funiculus. The toxic effect involved primarily the larger nerve fibers and appeared consistently in each of the treated animals examined.

REVIEW AND APPROVAL

Study Director: Patricia E. Losco, VMD — Date: 10-20-94
Diplomate, ACVP

Manager: Edward H. Fowler, Ph.D., DVM — Date: 10-20-94
Diplomate, ACVP

Director: John P. Van Miller, Ph.D., DABT — Date: 10-20-94

KEY PERSONNEL

Study Director: P. E. Losco

Supervisor: M. A. McGee

Consultant: J. Suhan (CMU)

Additional personnel are listed in the raw data.

REFERENCE

BRRC Report 93U1318 (In Progress). Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats. Bushy Run Research Center, Export, PA. Prepared for Union Carbide Corporation and Shell Oil Company.

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 1

NEGATIVE 11546

MAGNIFICATION 33,000 X

CONTROL GROUP FEMALE RAT - ANIMAL 9571 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph shows the normal appearance of the myelinated fibers of the ventral white matter tracts of the spinal cord. Nerve fibers are shown in longitudinal section. The axons (A) are characterized by longitudinally running neurofilaments (small arrow) and microtubules which carry nourishment down the length of the fiber. A few mitochondria (M) are also present. The myelinated sheaths (S), which surround the axons, exhibit multifocal areas of lamellar separation, which are artifacts of formalin fixation (large arrow). The cytoplasm (C) of a Schwann cell is evident between nerve fibers.

0 1 1 5 4 6
A
C
1

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 2

NEGATIVE 11543

MAGNIFICATION 53,900 X

CONTROL GROUP FEMALE RAT - ANIMAL 9571 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This is a higher magnification of the white matter of the spinal cord of the same rat as shown in Figure 1. The longitudinally-aligned neurofilaments are clearly visible within the axons, as are mitochondria (M). The normal myelin sheath (S) appears electrodense, with finely visible period lines marking the fusion of 2 layers of the Schwann cell membrane (arrow). A few areas exhibit artifactual separation of lamellae (F) due to the formalin fixation.

0 1 1 5 4 3
F
2

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 3

NEGATIVE 11536

MAGNIFICATION 10,000 X

2000 MG/KG/DAY GROUP FEMALE RAT - ANIMAL 9541 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph of the white matter of the spinal cord of a treated rat shows several nerve fibers undergoing degeneration. The fibers are swollen with condensation and collapse of the myelin layers into the axonal space. The axon cylinder is lost, although some of the central debris may represent axonal fragments. There are a number of normal axons adjacent to the affected fibers (A). Formalin artifact of the myelin sheaths is also present (arrows).

0 1 1 5 3 6
A
3

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 4

NEGATIVE 11539

MAGNIFICATION 21,300 X

2000 MG/KG/DAY GROUP FEMALE RAT - ANIMAL 9541 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph shows a single large myelinated fiber undergoing degeneration. The entire fiber is greatly swollen and the lamellae of the myelin sheath have separated and collapsed into the axonal space. Condensed myelin droplets are present (M), and foci of granular debris, which may represent axonal remnants, are visible (arrow). Several smaller adjacent fibers (F) appear unaffected.

0 1 1 5 3 9

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 5

NEGATIVE 11529

MAGNIFICATION 8,600 X

2000 MG/KG/DAY GROUP FEMALE RAT - ANIMAL 9538 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This low magnification photomicrograph shows a cluster of fibers undergoing advanced vesicular degeneration of myelin. Most of the myelin sheaths are either condensed and collapsed (*) or swollen and fragmented. Axonal debris is present in one of the fiber cross sections (arrow).

0 1 1 5 2 9
5

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 6

NEGATIVE 11528

MAGNIFICATION 21,300 X

2000 MG/KG/DAY GROUP FEMALE RAT - ANIMAL 9538 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This is a higher magnification of an area adjacent to the lesion in Figure 5, which shows a single degenerate nerve fiber. The granular debris that represents condensed organelles of the disintegrated axon (arrows) is intermixed with lamellar inclusions of myelin. The edge of 2 Schwann cell nuclei are visible along the top and right of the photograph (N). The nucleus at the top is normal, but the one to the right is slightly swollen.

0 1 1 5 2 8
N
N
6

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 7

NEGATIVE 11522

MAGNIFICATION 10,000 X

2000 MG/KG/DAY GROUP FEMALE RAT - ANIMAL 9533 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph of the third affected female shows a longitudinal section of a single nerve fiber undergoing degeneration surrounded by several normal axons. The axon in the affected fiber (A) is shrunken and degenerate. There is both vesicular swelling and condensation of the myelin sheath. The mildly swollen cytoplasm of a Schwann cell (C) is present to the right.

0 1 1 5 2 2

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 8

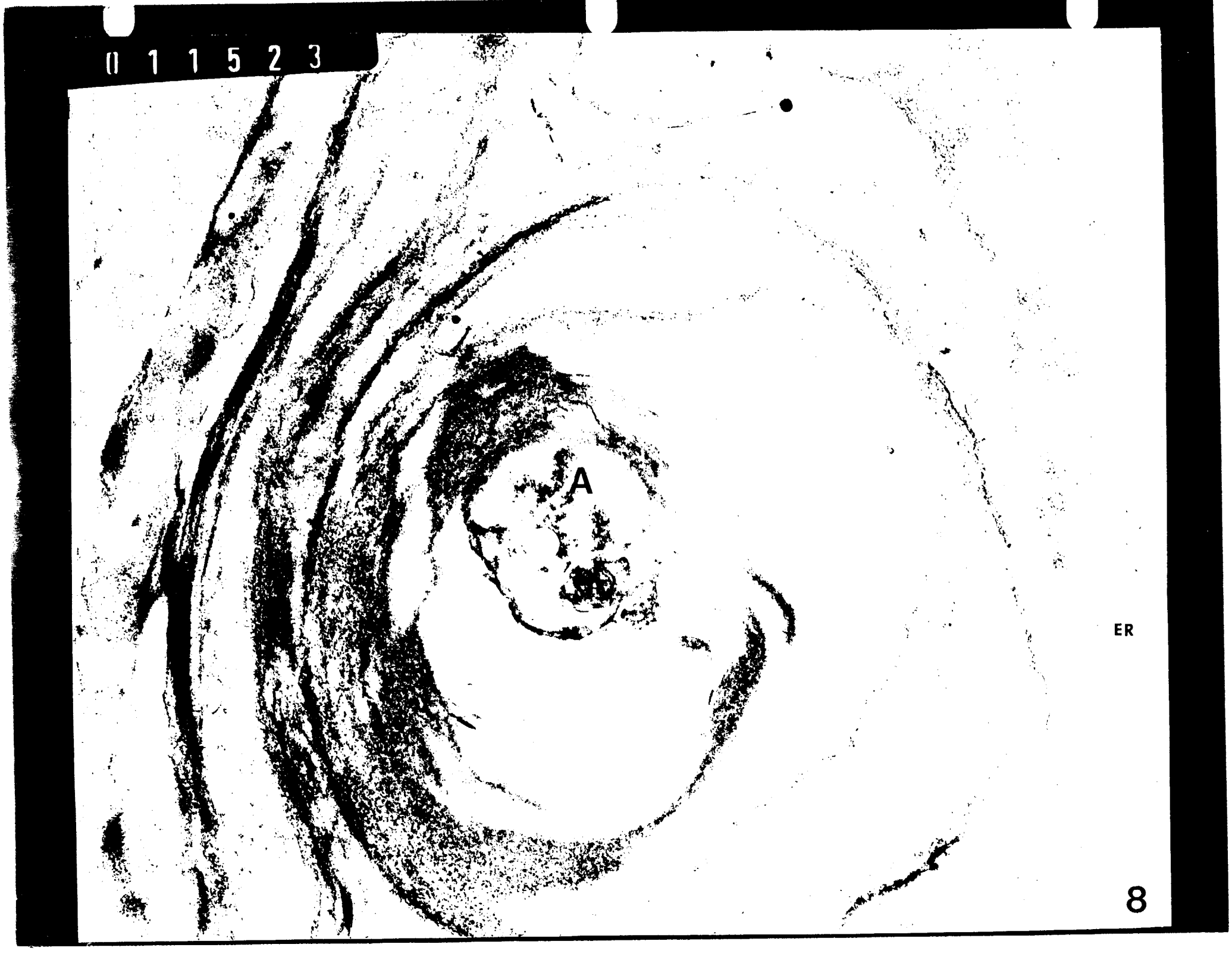
NEGATIVE 11523

MAGNIFICATION 26,000 X

2000 MG/KG/DAY GROUP FEMALE RAT - ANIMAL 9533 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph is a higher magnification of the previous lesion shown in Figure 7. The debris in the center is the remains of the disintegrating axon (A). The dilated structures on both sides of the fiber probably represent the endoplasmic reticulum (ER) of the Schwann cell.


0 1 1 5 2 3
A
ER
8

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 9

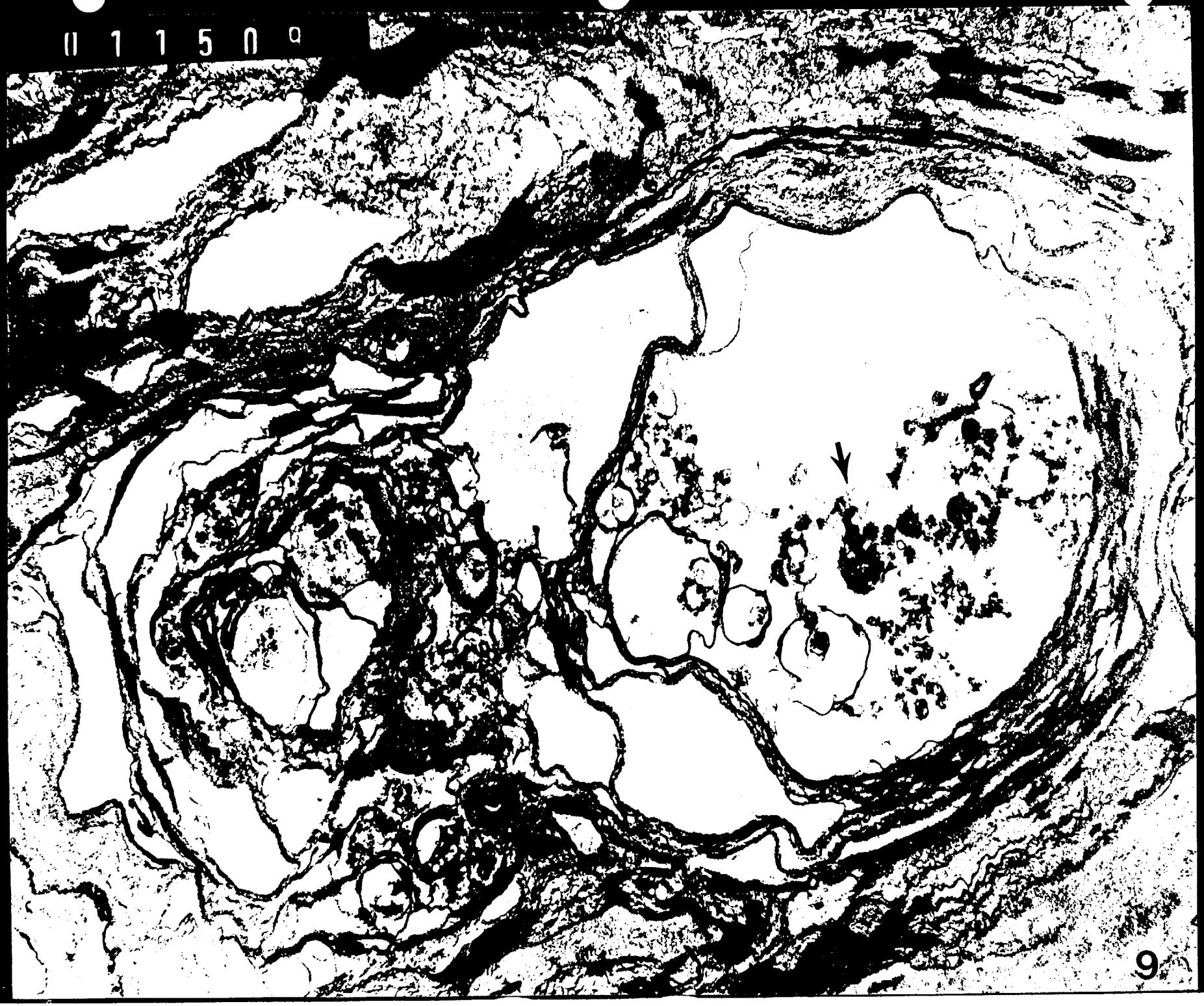
NEGATIVE 11509

MAGNIFICATION 10,000 X

2000 MG/KG/DAY GROUP MALE RAT - ANIMAL 9519 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph shows a lesion in a male rat which is similar to those found in females. There is swelling, separation, and fragmentation of the myelin sheath with occasional myelin droplet formation (M). Granular debris from the degenerating axon is present to the left (arrow).


11150a
9

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 10

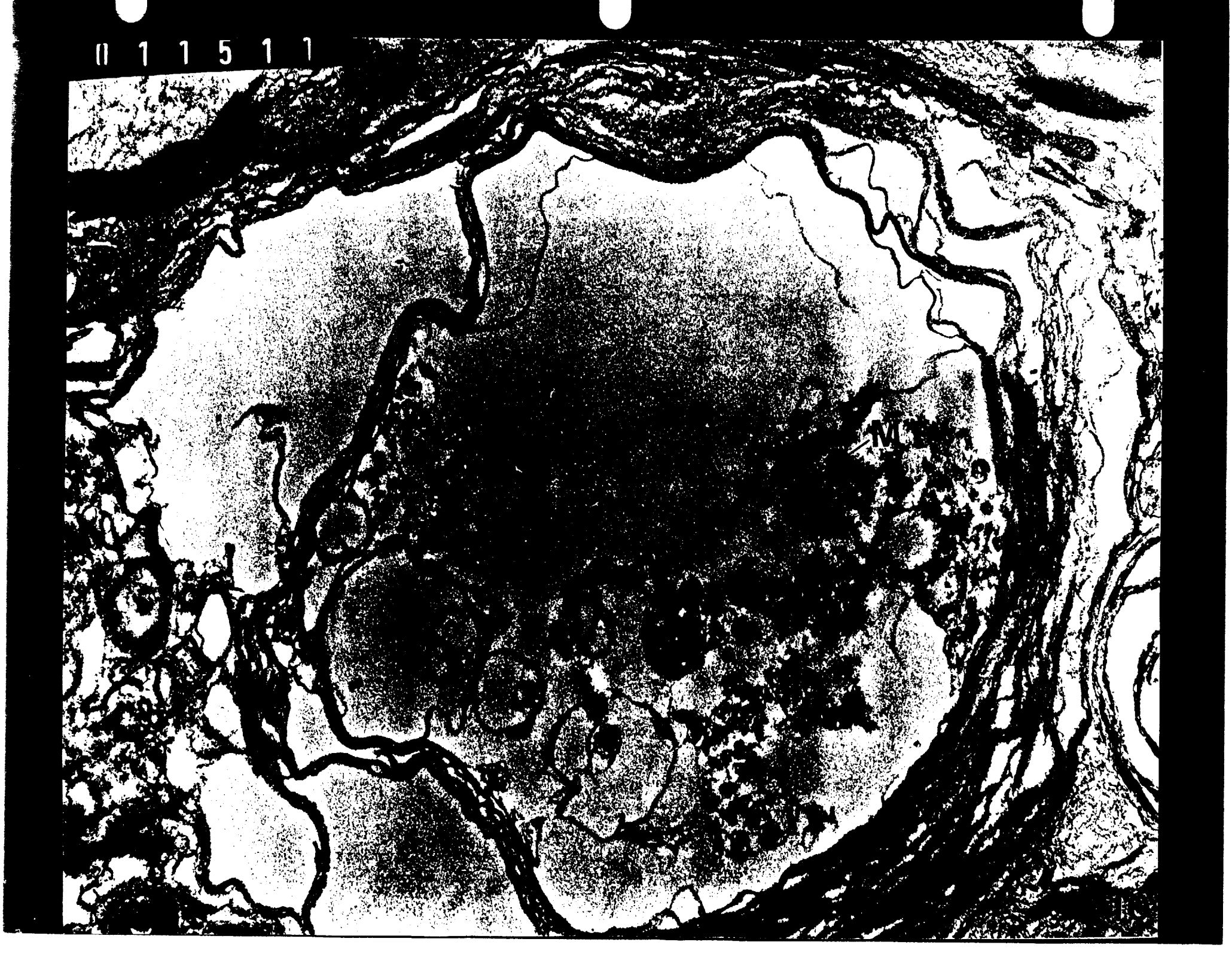
NEGATIVE 11511

MAGNIFICATION 17,750 X

2000 MG/KG/DAY GROUP MALE RAT - ANIMAL 9519 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This higher magnification of the lesion in Figure 9 shows the granular debris of condensed organelles from the disintegrating axon. A mitochondria (M) is still recognizable.


0 1 1 5 1 1
M

VINYL 2-ETHYLHEXANOATE

14-DAY PERORAL RANGE-FINDING STUDY IN RATS

FIGURE 11

NEGATIVE 11515

MAGNIFICATION 17,750 X

2000 MG/KG/DAY GROUP MALE RAT - ANIMAL 9519 - SACRIFICED ON DAY 14

CERVICAL SPINAL CORD - VENTRAL FUNICULUS

This electron micrograph shows a normal Schwann cell encircling a degenerate nerve fiber. (N) = nucleus. The nerve fiber exhibits complete disruption and separation of myelin lamellae. The axon is no longer present.

11

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats - Electron Microscopy of the Spinal Cord

Protocol

BUSHY RUN RESEARCH CENTER

UNION CARBIDE
6702 Mellon Road, Export, Pennsylvania 15632-8902
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PROTOCOL

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats - Electron Microscopy of the Spinal Cord.

BRRC PROJECT ID: 94U1428

SPONSOR:
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:

Patricia E. Losco, VMD — 6-10-94
Diplomate, ACVP — Date
Study Director

Edward H. Fowler — 6-10-94
Edward H. Fowler, DVM, Ph.D., Diplomate ACVP — Date
Associate Director

Linda J. Calisti, B.S. — 6/10/94
Manager, Good Laboratory Practices/Quality Assurance — Date

John P. Van Miller, Ph.D., DABT — 6/10/94
Director — Date

Union Carbide Corporation:

Tipton R. Tyler, Ph.D., DABT — 6/17/94
Associate Director of Applied Toxicology — Date

W. P. Miller, Ph.D. — 6/21/94
Manager of Product Safety — Date

Shell Oil Company:

Marcy L. Banton, DVM, Ph.D., DABVT — 6/30/94
Sponsor's Representative — Date

UNION CARBIDE CORPORATION

OBJECTIVE

The objective of this study is to further examine and characterize, by electron microscopy, possible morphologic changes in the spinal cord of rats which may have resulted from gavage treatment with Vinyl 2-Ethylhexanoate. This study is performed in support of the Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats (BRRC Report 93U1318).

Design and Basis for the Study

All of the tissues processed and examined in this study are portions of the same tissues which were collected for light microscopy in the original study, BRRC Report 93U1318, which was performed in compliance with Good Laboratory Practice standards at BRRC. The wet tissues will be shipped to Carnegie-Mellon Institute (CMU) where the processing, electron microscopic examination, and photography of the tissues will be performed. Carnegie-Mellon Institute is not a GLP laboratory and, therefore, this study is not being performed in full compliance with GLP standards.

PERSONNEL

Consultant: Joseph Suhan, Carnegie-Mellon Institute

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

PROJECT DATES

Proposed Date for Completion of Tissue Evaluation	May 15, 1994.
Proposed Date for Submission of Draft Final Report	June 15, 1994.
Proposed Date for Submission of Final Report	August 10, 1994.

METHODS

Tissues

Sections of formalin-fixed spinal cord will be collected from a small number of rats from both the control group and from rats gavaged with 2000 mg/kg/day of vinyl 2-ethylhexanoate 5 days/week for 2 consecutive weeks. The animals were sacrificed at Day 15. The tissues used in this evaluation will be from the same animals which had been previously examined by light microscopy. The methods of animal exposure, necropsy, and tissue collection are documented in BRRC Report 93U1318.

Tissue Preparation

The spinal cord sections will be submitted to the CMU Laboratory of Electron Microscopy, Mellon Institute, Pittsburgh, PA 15213, where they will be embedded, in entirety, in EPON-Araldite (BEEM capsules). Toluidine blue stained thick sections will be prepared and submitted to the study pathologist, who will identify areas of the sections which are to be further processed for electron microscopic examination. Thin sections of the selected areas will then be prepared and mounted on copper grids. A detailed description of the tissue preparation techniques will be included in the report.

The transportation of wet tissues, prepared slides of thick sections, and all electron microscopic materials including film negatives will be provided between BRRC and the CMU electron microscopy laboratory either by CMU courier, by hand of the study pathologist, or by a public mail or delivery service. All the tissues, slides, electron microscopy materials or specimens, including BEEM capsules, copper grids, and film negatives will be stored in the CMU electron microscopy laboratory for the duration of the study and will be returned to BRRC for archiving at the end of the study.

Electron Microscopy

The study pathologist will perform electron microscopic examination of the selected sections, and representative photomicrographs will be taken of both control and treated animal tissues. The study pathologist will evaluate the photomicrographs and prepare a report illustrated with representative prints.

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. BRRC 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. All protocol modifications will be signed by the Study Director and a representative of the Sponsor.

RETENTION OF RECORDS

All raw data material from this study, including microscopic thick sections, BEEM capsules, copper grids, and electron microscopic photographic negatives will be retained and will be submitted for archiving with the original study (BRRC Report 93U1318).

REPORTS

Draft Final Report

An unaudited draft of the final report will be submitted to the Sponsor approximately 1 month after the completion of the tissue evaluation. 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.

Final Report

The draft final report will be reviewed by the Sponsor, and comments on the report will be provided to BRRC within 6 weeks from the date of submission of the draft version. BRRC 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, BRRC will submit a final report within 8 weeks of the issuance of the draft report.

One copy of the final report will be submitted to each of the Sponsors.

REFERENCE

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Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

TEST SUBSTANCE

Vinyl 2-Ethylhexanoate

DATA REQUIREMENT

Not Applicable

AUTHORS

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STUDY COMPLETION DATE

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Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

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 Fischer 344 Rats

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: _____ 9/26/94

Steven J. Hermansky, Pharm.D., Ph.D., DABT — Date

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Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

SUMMARY

Fischer 344 rats (6/sex/group) were administered vinyl 2-ethylhexanoate in corn oil, CAS No. 94-04-2, by gavage at dosages of 50, 200, 1000, or 2000 mg/kg/day with a dose volume of 4.0 ml/kg/day. Animals were treated for 5 days/week for 2 weeks, excluding the 2000 mg/kg/day group which were dosed for only 2 days. 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, functional observations, hematologic evaluations, necropsy observations, and microscopic evaluations. Half of the surviving animals from the control, 50, 200 and 1000 mg/kg/day dose group (3/group/sex) were euthanized by perfusion fixation for a complete neuropathologic evaluation. In the 2000 mg/kg/day dose group, 2 male animals sacrificed in a moribund condition, and the 1 male and 3 female animals that survived to study termination were also euthanized by perfusion fixation.

Following dosing on Study Day 2, 3 female and 5 male animals from the 2000 mg/kg/day dose group were either found dead or sacrificed in a moribund condition. Animals from this dose group that survived the second daily dose of the test substance were not dosed throughout the remainder of the study and gradually recovered. Treatment-related clinical signs of toxicity were limited to animals from the 2000 mg/kg/day dose group after these animals received the second daily dose and included primarily urogenital wetness/urine stains, perinasal encrustation, labored respiration, loose feces, cold extremities, prostration and hypoactivity. Treatment-related clinical signs of toxicity, as well as decreased body weights and food consumption observed in animals from the 2000 mg/kg/day dose group resolved by the end of the study.

A neurological functional observational battery (FOB) was conducted on Study Days 12, 13, and 14. There were no changes in the FOB which were clearly attributed to treatment with the test substance. Slight increases in landing hind leg splay in female animals from the 1000 mg/kg/day dose group on Study Days 12 (the last day of dosing) and 13 were the only findings that may have been related to treatment.

In the 2000 mg/kg/day dose group, the 3 surviving female animals had decreased mean leukocyte count, hemoglobin, hematocrit, platelet count and lymphocyte count. In the 1000 mg/kg/day dose group, decreased mean erythrocyte, lymphocyte and platelet counts, hemoglobin and hematocrit values were observed in male and/or female rats. The biological or toxicological significance of these changes was not clear. Increases in mean neutrophil count in some male rats from the 1000 mg/kg/day dose group and female rats from the 2000 mg/kg/day dose group were of unknown etiology.

Slight decreases in the mean erythrocyte count, hemoglobin and hematocrit values observed in female rats from the 200 mg/kg/day dose group were considered to be of equivocal biological significance due to the small magnitude of the change and lack of effect in male animals of this dose group.

Increases were observed in the liver weights in the 1000 mg/kg/day dose group of both sexes. There were no treatment-related microscopic lesions observed in the liver and, therefore, the increased liver weights were likely an adaptive change in response to treatment with the test substance and not a direct toxic effect of the chemical.

In male rats from the 1000 mg/kg/day dose group, increases were observed in the kidney and spleen weights. There were no treatment-related microscopic lesions observed in the kidneys and the biological or toxicological significance of the increased weight of these organs was unknown. Slight increases in the weight of the livers and kidneys in male rats from the 200 mg/kg/day dose group were considered to be equivocal due to the slight (less than 10%) difference in the changes.

Dilation/distention of the urinary bladder was observed in 2 male rats from the 2000 mg/kg/day dose group which died or were sacrificed in a moribund condition during the study. While bladder distention can occur simply as a result of depression, it can be a sign of spinal cord damage with loss of nerve control to the bladder and may, therefore, have been related to treatment.

Treatment-related microscopic lesions were limited to minimal changes in the brain stem and spinal cord of some animals in the 2000 mg/kg/day dose group. Lesions were not observed for animals in the 1000 mg/kg/day group. Lesions observed included slight vacuolation/spongiosis of the white matter of the brain stem (medulla oblongata/pons area) and/or the spinal cord of the 3 females and the spinal cord of the 1 male from the 2000 mg/kg/day dose group which were sacrificed at Day 15. These animals were sacrificed by perfusion fixation 13 days after the last dose was administered. Degeneration of the nerve fibers of the cervical spinal cord was observed in 2 female animals in conjunction with vacuolation. Similar lesions were not observed in the 2000 mg/kg/day dose group rats which were found dead or sacrificed in a moribund condition during the dosing period.

Administration of vinyl 2-ethylhexanoate to rats resulted in mortality in some animals of both sexes following the second daily dose of 2000 mg/kg/day. Due to this mortality, surviving animals from this dose group were not treated for the remainder of the study. Clinical signs of toxicity in these surviving animals, as well as decreased food consumption and body weight, resolved following the termination of dosing. Microscopic lesions of the central nervous system were observed in the sacrificed animals but not in animals that died during the study. Repeated administration of 1000 mg/kg/day of vinyl 2-ethylhexanoate resulted in slight, reversible changes in the function of the nervous system (increased hind leg splay in female rats) that were not associated with microscopic lesions, hematology changes suggestive of mild anemia, and increased liver, kidney, and spleen weights. Equivocal hematology changes (females) and increased liver and kidney weights (males) were observed in the 200 mg/kg/day dose group. No effects were observed in any measurements or observations at 50 mg/kg/day. The no-observed-adverse-effect level of vinyl 2-ethylhexanoate under the conditions of this study was considered to be 200 mg/kg/day.

OBJECTIVES

The objectives of this study were to evaluate the toxicity of 4 dose levels of vinyl 2-ethylhexanoate in Fischer 344 (F344/NHSD) rats 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 LD_{50} 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 treatment 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 F344 male rat liver homogenates was measured. The auto-hydrolysis 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 any protocol amendments detailing the design and conduct of this study are included in Appendix 11. Protocol deviations are also included in Appendix 11.

Test Substance

Approximately 1 liter of vinyl 2-ethylhexanoate, Lot No. JGT-1092, was received on August 31, 1993, from the Union Carbide Corporation, South Charleston, WV, and assigned BRRC Sample Number 56-348. The test substance was a transparent colorless liquid and was stored in a 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 Number 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-five male and 45 female Fischer 344 rats arrived on October 12, 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 7, 1993) upon arrival. The females were nulliparous and nonpregnant.

Animals were housed in Room 174 from arrival to termination of the study. Within 2 days of receipt, the animals were examined by a Clinical Veterinarian and a pretest health screen for representative animals was initiated. The health screen included necropsy, and examinations for fecal parasites. Serology testing was conducted approximately 2 weeks after receipt using animals not selected for the study. 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 tail tattooing procedure.

Upon arrival at BRRC the animals, separated by sex, were housed 2/cage in stainless steel, wire mesh cages (22.5 x 15.5 x 18.0 cm). The purpose of the double housing was to help acclimate the animals to their new surroundings. Approximately 1 week 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. Animals were housed in clear polycarbonate cages (26.7 x 24.1 x 20.3 cm) during the days of FOB evaluations. A layer of ALPHA-dri® Bedding (Shepherd Specialty Papers, Inc.) was placed in each FOB observation cage. 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 PMI Feeds, 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 ± 20% of the population mean for each sex were included. The body weight range on the day of first treatment was 128.7 to 159.0 g for males and 103.1 to 122.3 g for females. The following table summarizes the organization of the study.

Group	Number of Animals Male	Female	Vinyl 2-Ethylhexanoate 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 October 25, 1993 (Study Day 1). Animals were treated for 5 days/week for 2 weeks, excluding the 2000 mg/kg/day group which was dosed for only 2 days. All surviving animals were sacrificed on November 8, 1993 (Study Day 15), 3 days following the last dose.

Administration of Test Substance

Dosing 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 a straight 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, 500 mg/ml) 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 (1.45 mg/ml for Study Week 1 and 1.52 mg/ml for Study Week 2) was prepared and standards ranging from 0.435 to 1.45 mg/ml and 0.456 to 1.52 mg/ml for Study Week 1 and 2, respectively, were prepared by diluting the stock solution (v/v) with toluene. For stability analyses (Days 7 and 14), 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. The details of these procedures are included in Appendix 1.

Observations and Measurements

Standard 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 Day 1 (first day of dosing) and shortly after dosing on all other dosing days with the exception of Study Day 4 when they were collected prior to dosing. 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), Study Days 4, 8, and 15 (prior to sacrifice).

Food consumption measurements were collected for intervals 1-4, 4-8, and 8-15.

Neurobehavioral Evaluations

The neurobehavioral function of all animals was evaluated using a screening battery of tests (FOB) designed to detect gross alterations in nervous system function. FOB evaluations were performed on Study Day 12 following the final treatment and again on Study Days 13 and 14. The animals were observed by trained technicians who were unaware of the animals' exposure group. The same observer was used to evaluate the animals of one sex at each testing period.

The endpoints included in the FOB are listed below. An overview of the FOB and the scoring criteria employed are included in Appendix 8.

cage posture	handling reactivity	involuntary muscular movements
vocalization	palpebral closure	unusual behavior
gait	body position	breathing pattern
arousal	defecation	urination
rears	approach response	startle response
tail pinch response	pupil size	muscle tone
piloerection	lacrimation	salivation
fur appearance	crusts	additional observations
visual placing	grip strength	core body temperature
body weight	air righting	hind leg splay
ataxia		

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 halothane 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:

<u>Hematology</u>

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

Details of the hematology procedures are included in Appendix 3.

Anatomic Pathology Evaluations

Necropsy - Non-Perfused Rats

All animals which were found dead during the dosing period, and 3 rats/group/sex from the animals sacrificed on Day 15 were subject to necropsy and tissues were fixed by standard immersion techniques.

Sacrificed rats not selected for perfusion were anesthetized with halothane and were euthanized by severing their brachial vessels to permit exsanguination. 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, adrenals, spleen, ovaries (females), testes (males), and brain were weighed for all nonperfused animals. The order of sacrifice was randomized in advance in order to reduce observation and handling biases. The following tissues were collected and preserved in 10% neutral buffered formalin:

gross lesions
lungs with mainstem bronchi
brain
  cerebral cortex
  cerebellar cortex
  medulla/pons
pituitary
thyroid/parathyroid
thymic region
trachea
heart
sternum (including marrow)
salivary gland
liver
spleen
kidneys
adrenals
pancreas
testes
epididymis
prostate
seminal vesicles
ovaries
vagina
uterus
  corpus and cervix
aorta
skin
esophagus
stomach
duodenum
jejunum
ileum
cecum
colon
rectum
urinary bladder
lymph nodes
  mesenteric
  non-mesenteric
mammary gland (females)
skeletal muscle
  (gastrocnemius)
peripheral nerve (sciatic)
tibial nerve
eyes
femur (including articular surface)
spinal cord

Tails were saved as animal identification.

Lungs were inflated with formalin by infusion through the trachea.

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

Rats, which died on study, were necropsied as they were found. Their tissues were collected and fixed by immersion. Organ weights were not obtained.

Histopathology - Non-Perfused Rats

Microscopic examinations were performed on the brains, sciatic nerves, tibial nerves, and gross lesions for all nonperfused rats. In addition, microscopic examinations were performed on the above underlined tissues for all nonperfused animals from the 0, 1000, and 2000 mg/kg/day groups.

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).

Necropsy - Perfused Rats

At termination, 3 rats/group/sex (control, 50, 200 and 1000 mg/kg/day dose groups), the 1 surviving male rat and the 3 surviving female rats from the 2000 mg/kg/day dose group were selected for perfusion. In addition, on Study Day 3, 2 male animals from the 2000 mg/kg/day dose group were sacrificed in a moribund condition and selected for perfusion. These animals were anesthetized with an i.p. injection of a mixture of Euthanasia-6 Solution (Veterinary Laboratories, Inc., Lenexa, KS), and heparin. When a deep plane of surgical anesthesia had been induced (as determined by the disappearance of all observable reflexes, including the toe pinch and corneal reflexes), the chest cavity was opened. A cannula was placed through the apex of the heart into the left ventricular chamber for perfusion fixation with 10 percent neutral (phosphate) buffered formalin (NBF).

After perfusion fixation, the animals received an abbreviated necropsy consisting of an examination of the tissues listed below. The calvaria and the dorsal arches of the vertebrae were removed and the sciatic nerve and its branches were exposed but left *in situ*. The following tissues were removed and immersion fixed in NBF:

- gross lesions
- brain
  - cerebral cortex
  - cerebellar cortex
  - medulla/pons
- spinal cord
- dorsal root ganglia
- dorsal and ventral nerve roots
- Gasserian ganglia
- sciatic nerve
- tibial nerve
- sural and peroneal nerves
- liver[1]
- kidneys[1]
- lungs[2]
- testes[1]
- ovaries[2]
- tail (animal identification)

1 These tissues were examined for animals from the control and high dose groups.

2 No microscopic examination was performed on these tissues.

Spinal cord sections included cervical, thoracic and lumbar regions. Two cross sections at the level of the cervical swelling, 1 cross section from the thoracic and lumbar sections, and 2 longitudinal sections from the cervical region (1 above and 1 below the level of the cervical swelling) were included.

Histopathology - Perfused Rats

Microscopic evaluations were performed on the above tissues for 3 rats/sex/group. The liver, kidneys, testes, and any gross lesions found in perfused rats were prepared and stained in the same manner as described above for the nonperfused animals. The findings for these tissues were reported in the same tables as the findings for the nonperfused rats in order to create an adequate sample for statistical evaluation.

The sections of brain, spinal cord, Gasserian ganglia, nerve roots, and dorsal root ganglia were embedded in paraffin. Five to 6 micron sections of each of these tissues were prepared and stained with hematoxylin and eosin, luxol fast blue, and the Bielschowsky's techniques. The peripheral nerves were embedded in glycol methacrylate, sectioned at 2 microns, and stained with hematoxylin and eosin, toluidine blue, and the Bielschowsky's technique.

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. Incidence data for select FOB endpoints with ordered severity scores were analyzed for group differences using Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somers' D measures of association. 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.

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, 8, 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.

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 (± standard deviation) 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. These results indicated that the solutions were uniformly prepared.

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 100.3 to 102.8% 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.

Three female and 5 male animals from the 2000 mg/kg/day dose group died or were sacrificed in a moribund condition following the second dose. Animals from this group that survived the third daily dose of the test substance were not dosed throughout the remainder of the study. No other animals from either sex died throughout the remainder of the study.

Treatment-related clinical signs of toxicity observed during the study were limited to animals from the 2000 mg/kg/day dose group. Following dosing on

Study Day 1, there were no clinical signs of toxicity observed in either sex. Following dosing on Study Day 2, all animals from the 2000 mg/kg/day dose group had urogenital wetness, labored respiration and cold extremities and were prostrate/hypoactive. Furthermore, all 6 male and 1 female animals from this dose group had loose feces, 1 male had urine stains and another male had perinasal encrustation.

On Study Day 3, one male and two female animals had recovered and had no overt signs of toxicity upon cageside observation. Many animals of both sexes from the 2000 mg/kg/day dose group had urogenital wetness, labored respiration and cold extremities and were prostrate/hypoactive and 4 male and 3 female animals from this dose group were found dead or sacrificed moribund. None of the surviving animals from the 2000 mg/kg/day dose group were dosed on Study Day 3.

Throughout the remainder of the study, the remaining male animal and 3 female animals recovered from treatment. By Study Day 8 (5 days after the last dose was administered to these animals), there were no clinical signs of toxicity considered to be related to treatment observed in any of these animals.

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.

Decreases in mean body weight and body weight gain in the surviving animals from the 2000 mg/kg/day dose group were considered to be related to treatment. Following the cessation of dosing in these animals, a complete recovery in mean body weight and body weight gain was observed. There were no changes in mean absolute body weights or body weight gains in any of the other dose groups of either sex that were considered to be related to treatment.

Food Consumption

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

Decreases in mean food consumption in the surviving animals from the 2000 mg/kg/day dose group were considered to be related to treatment. A complete recovery in food consumption was observed after treatment was stopped. These data must be interpreted cautiously due to the small number of animals in these groups (only 1 male and 3 female animals from this group survived the second daily dose of the test substance). There were no changes in mean food consumption in any of the other dose groups of either sex that were considered to be related to treatment.

Functional Observations

Summaries of the functional observations which were conducted on Study Days 12, 13 and 14 are presented in Tables 9 to 14. Individual animal data are included in Appendix 8.

Slight, non-statistically significant increases (approximately 20%) in landing hind leg splay were observed in female animals from the 1000 mg/kg/day dose

group on Study Days 12 (the last day of dosing) and 13. However, this questionable change was not associated with other alterations in neuromotor function or microscopic lesions and could not be clearly attributed to treatment with the test substance. A statistically significant increase in body temperature in the 1000 mg/kg/day dose group of female rats on Study Day 13 was not considered to be related to treatment due to the similarity of this value to the control value on Study Day 12. A statistically significant decrease in rears in the 200 mg/kg/day dose group on Study Day 14 was not considered to be related to treatment due to the lack of a dose response relationship. A significant correlation between exposure level and degree of palpebral closure in female rats also on Study Day 14 was not considered to be related to treatment due to the lack of similar findings in males or in females at previous evaluation periods. There were no other changes observed during the functional observational battery on Study Days 12, 13 or 14.

Clinical Pathology Evaluations

Summaries of the hematology measurements are presented in Tables 15 and 16. Individual clinical pathology data are included in Appendix 10. Detailed results and discussion of the clinical pathology measurements are included in Appendix 3.

In the 2000 mg/kg/day dose group, the 3 surviving female animals had decreased mean leukocyte count (20%), hemoglobin (4%), hematocrit (3%), platelet count (20%) and lymphocyte count (29%) and an increase in the mean neutrophil count (not statistically significant).

In the 1000 mg/kg/day dose group, rats of both sexes had a 6 to 7% decrease in mean erythrocyte count, hemoglobin and hematocrit values. Female rats from this dose group also had a 15% decrease in mean lymphocyte and platelet counts and several male rats had an increase in segmented neutrophils, but the mean value was not statistically significant.

In the 200 mg/kg/day dose group, female rats had a 2 to 3% decrease in the mean hemoglobin and hematocrit values with a slight, non-statistically significant decrease in the mean erythrocyte count. These changes were considered to be of equivocal biological significance due to the small magnitude of the change and lack of similar effects in male animals of this dose group.

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 17 to 22.

Summary results of necropsy observations are presented in Tables 23 to 26. Summary results of microscopic diagnoses are presented in Tables 27 to 35. Individual anatomic pathology data are included in Appendix 9. Detailed results and discussion of the anatomic pathology results are included in Appendix 2.

In male rats from the 1000 mg/kg/day dose group, increases were observed in the mean absolute and relative liver weights (approximately 35 to 50%), spleen weights (approximately 15 to 30%) and kidney weights (approximately 10 to

20%). The kidney weight changes and spleen weight relative to the final body weight were not statistically significant. In male rats from the 200 mg/kg/day dose group, there were slight increases (4 to 9%) in the mean absolute and relative weights of the liver and kidneys. The changes in the 200 mg/kg/day dose group were not statistically significant and the toxicological significance of the changes were considered to be equivocal due to the small magnitude of the changes.

In female rats from the 1000 mg/kg/day dose group, the mean absolute and relative weights of the liver were increased 13 to 20%. There were no other effects on organ weights in either male or female rats of either sex that were considered to be biologically significant.

The only gross lesion observed in this study which may be attributed to chemical treatment was the dilation/distention of the urinary bladder in 2 male rats from the 2000 mg/kg/day dose group which died or were sacrificed moribund during the study.

The only treatment-related microscopic lesions observed in the study were slight vacuolation/spongiosis of the white matter of the brain stem (medulla oblongata/pons area) and/or the spinal cord of the 3 females and the spinal cord of the 1 male from the 2000 mg/kg/day dose group which were sacrificed at Day 15. These animals were sacrificed by perfusion fixation 13 days after the last dose was administered to these animals. Brain lesions occurred mainly in the midline in the region of the medial longitudinal fasciculus. Spinal cord lesions occurred in the white matter of the ventral funiculi and affected 1 or more levels of the cord in each female but only the cervical spinal cord in the male animal. Degeneration of the nerve fibers of the cervical spinal cord was observed in 2 female animals in conjunction with vacuolation. Similar lesions were not observed in the 2000 mg/kg/day dose group rats which were found dead or sacrificed in a moribund condition during the dosing period.

There were no gross or microscopic lesions observed in any other dose group of either sex that were attributed to treatment with vinyl 2-ethylhexanoate.

CONCLUSIONS

Administration of vinyl 2-ethylhexanoate to rats resulted in mortality in 5 of 6 males and 3 of 6 females following the second daily dose of 2000 mg/kg/day. Due to this mortality, surviving animals from this dose group were not treated for the remainder of the study. Clinical signs of toxicity in these surviving animals, as well as decreased food consumption and body weight, resolved following the termination of dosing but microscopic lesions of the central nervous system were observed in these animals but not in animals that died during the study. Repeated administration of 1000 mg/kg/day of vinyl 2-ethylhexanoate resulted in slight, reversible changes in the function of the nervous system (increased hind leg splay in female rats) that were not associated with microscopic lesions of the central nervous system, hematology changes suggestive of mild anemia and increased liver, kidney and/or spleen weights. Equivocal hematology changes in females and increased liver and kidney weights of males were observed in the 200 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 200 mg/kg/day.

REVIEW AND APPROVAL

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Associate Director: Edward H. Fowler, DVM, Ph.D., Diplomate ACVP — Date: 9-26-94

Director: John P. Van Miller, Ph.D., DABT — Date: 9-27-94

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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 FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

MALES

CATEGORY FINDING (LOCATION)	GROUP:	GRADE	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)	5 (DAYS)
FATE							
FOUND DEAD		P	0	0	0	0	3(3- 4)
SACRIFICED MORIBUND		P	0	0	0	0	2 (3)
SCHEDULED SACRIFICE		P	3 (15)	3 (15)	3 (15)	3 (15)	0
SCHEDULED SACRIFICE-PERFUSED		P	3 (15)	3 (15)	3 (15)	3 (15)	1 (15)
BEHAVIOR/CNS							
HYPOACTIVE		P	0	0	0	0	6(2- 3)
PROSTRATION		P	0	0	0	0	6(2- 3)
BODY							
URINE STAINS		P	0	0	0	0	1 (2)
COLD EXTREMITIES (LEGS-ALL)		P	0	0	0	0	6(2- 3)
UROGENITAL AREA WETNESS		P	0	0	0	0	6(2- 3)
CARDIO-PULMONARY							
LABORED RESPIRATION		P	0	0	0	0	6(2- 3)

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 1 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

MALES

CATEGORY FINDING (LOCATION)	GROUP:	GRADE	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)	5 (DAYS)
CARDIO-PULMONARY							
EYES/EARS/NOSE							
EXOPHTHALMIA (EYE-LEFT)		P	0	0	1 (6)	0	0
LACRIMATION (EYE-BOTH)		P	0	0	0	0	1 (3)
PERINASAL ENCRUSTATION		P	0	0	0	0	1 (2)
EXCRETA							
LOOSE FECES		P	0	0	0	0	6 (2)

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.

TMOD_RPT:MRV2E2.CLS
091494

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

FEMALES

CATEGORY FINDING (LOCATION)	GROUP:	GRADE	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)	5 (DAYS)
FATE							
FOUND DEAD		P	0	0	0	0	3 (3)
SCHEDULED SACRIFICE		P	3 (15)	3 (15)	3 (15)	3 (15)	0
SCHEDULED SACRIFICE-PERFUSED		P	3 (15)	3 (15)	3 (15)	3 (15)	3 (15)
BEHAVIOR/CNS							
HYPOACTIVE		P	0	0	0	0	6(2- 3)
PROSTRATION		P	0	0	0	0	6(2- 3)
BODY							
UNKEMPT		P	0	0	0	0	1(4- 7)
URINE STAINS		P	0	0	0	0	1(6- 7)
COLD EXTREMITIES (LEGS-ALL)		P	0	0	0	0	6(2- 3)
UROGENITAL AREA WETNESS		P	0	0	0	0	6(2- 5)
CARDIO-PULMONARY							
LABORED RESPIRATION		P	0	0	0	0	6(2- 3)

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 2 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

FEMALES

CATEGORY FINDING (LOCATION)	GROUP:	GRADE	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)	5 (DAYS)
CARDIO-PULMONARY							
EYES/EARS/NOSE							
OPACITY (EYE-LEFT)		P	0	0	0	0	1(6- 15)
PERIOCULAR ENCRUSTATION (EYE-BOTH)		P	0	0	0	0	1(4- 5)
PERINASAL ENCRUSTATION		P	0	0	0	0	1(4- 5)
EXCRETA							
LOOSE FECES		P	0	0	0	0	1 (2)

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.

TMOD_RPT:FRV2E2.CLS
091494

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT (GRAMS)

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1					
MEAN	142.4	140.3	143.2	141.9	142.6
S.D.	9.44	7.77	6.93	6.83	7.91
N	6	6	6	6	6
DAY 4					
MEAN	150.0	147.4	152.7	149.1	140.7
S.D.	9.70	8.64	7.57	7.92	0.00
N	6	6	6	6	1
DAY 8					
MEAN	161.2	155.8	160.4	164.4	153.9
S.D.	10.07	9.09	8.04	10.83	0.00
N	6	6	6	6	1
DAY 15					
MEAN	180.9	173.5	181.9	190.4	178.5
S.D.	11.00	12.85	7.32	12.92	0.00
N	6	6	6	6	1

None significantly different from control group

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT GAIN (GRAMS)

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1 TO 4					
MEAN	7.7	7.1	9.6	7.2	-0.1
S.D.	1.30	3.38	3.41	3.13	0.00
N	6	6	6	6	1
DAY 1 TO 8					
MEAN	18.9	15.4	17.2	22.5	13.1
S.D.	2.75	6.09	3.98	5.02	0.00
N	6	6	6	6	1
DAY 1 TO 15					
MEAN	38.5	33.2	38.8	48.5*	37.6
S.D.	5.43	9.80	5.24	7.87	0.00
N	6	6	6	6	1

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

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT (GRAMS)

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1					
MEAN	112.1	114.4	113.0	112.9	113.9
S.D.	5.58	5.32	2.99	5.65	6.11
N	6	6	6	6	6
DAY 4					
MEAN	116.4	119.6	118.3	117.6	104.0**
S.D.	5.92	5.05	3.86	3.53	13.54
N	6	6	6	6	3
DAY 8					
MEAN	118.2	124.4	122.0	121.2	114.7
S.D.	8.39	5.03	3.48	5.62	3.03
N	6	6	6	6	3
DAY 15					
MEAN	132.2	136.8	133.6	134.3	132.2
S.D.	4.75	6.38	5.20	6.13	5.12
N	6	6	6	6	3

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

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT GAIN (GRAMS)

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1 TO 4					
MEAN	4.3	5.2	5.3	4.7	-8.5**
S.D.	1.04	1.51	2.01	3.49	5.87
N	6	6	6	6	3
DAY 1 TO 8					
MEAN	6.1	10.0*	9.0	8.3	2.2
S.D.	3.04	1.75	3.34	3.20	4.67
N	6	6	6	6	3
DAY 1 TO 15					
MEAN	20.1	22.4	20.6	21.4	19.7
S.D.	2.56	1.41	3.31	4.66	2.63
N	6	6	6	6	3

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

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1 TO 4					
MEAN	13.2	12.7	14.1	12.3	9.7**
S.D.	0.75	0.83	1.24	0.91	0.00
N	6	6	6	6	1
DAY 4 TO 8					
MEAN	14.7	14.5	14.5	15.3	16.4
S.D.	0.83	0.96	1.47	1.29	0.00
N	6	6	6	6	1
DAY 8 TO 15					
MEAN	13.4	12.8	13.8	14.6	15.9
S.D.	1.30	0.88	0.76	1.40	0.00
N	6	6	6	6	1

** Significantly different from control group ($p < .01$)
Data not included for animals removed from food consumption

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
DAY 1 TO 4					
MEAN	10.9	11.0	10.6	10.0	4.2*
S.D.	1.03	0.58	0.34	0.88	1.82
N	6	6	6	6	3
DAY 4 TO 8					
MEAN	11.2	12.3	12.1	11.7	13.3
S.D.	1.44	0.58	0.87	0.82	1.23
N	6	6	6	6	3
DAY 8 TO 15					
MEAN	10.6	10.4	10.4	10.6	13.2**
S.D.	0.15	2.08	0.55	0.40	0.72
N	6	6	6	6	3

* Significantly different from control group ($p < .05$)
** Significantly different from control group ($p < .01$)
Data not included for animals removed from food consumption

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 12

MALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Gait					
Normal	6	6	5	6	1
Other					
Present	0	0	1[a]	0	0
Defecation					
None	3	3	1	4	0
Normal	3	3	5	2	1
Urine					
None	2	1	3	2	0
Present	4	5	3	4	1
Rears (events)					
MEAN	13.33	15.67	17.50	15.67	12.00
S.D.	6.439	4.844	5.167	4.457	.000
N	6	6	6	6	1
Approach Response					
Noticeable	6	6	6	6	0
None	0	0	0	0	1
Pupil Size					
Normal	6	5	6	6	1
Decreased	0	1	0	0	0
Visual Placing					
Present	6	6	5	5	1
None	0	0	1	1	0
Grip Strength (fore) (kg)					
MEAN	.44	.47	.44	.45	.37
S.D.	.087	.136	.133	.183	.000
N	6	6	6	6	1
Grip Strength (hind) (kg)					
MEAN	.37	.33	.36	.36	.35
S.D.	.103	.125	.077	.090	.000
N	6	6	6	6	1
Body Temperature (degrees C)					
MEAN	38.03	38.40	38.55	38.32	38.70
S.D.	.596	.990	.274	.331	.000
N	6	6	6	6	1
Body Weight (grams)					
MEAN	169.11	163.07	169.76	174.23	164.78
S.D.	10.483	11.246	7.835	11.353	.000
N	6	6	6	6	1
Air Righting					
Feet/Coordinated	6	5	6	6	1
Back	0	1	0	0	0

None significantly different from control group
[a]Animal leaned to right side at all times

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 12

MALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Hind Leg Splay (cm)					
MEAN	4.97	4.55	4.34	5.22	4.75
S.D.	1.101	.720	.630	.512	.000
N	6	6	6	6	1

None significantly different from control group

In addition to the above observations, all animals were observed for the following endpoints. The incidence for these endpoints was zero or the same for all groups:
Cage Posture, Cage Palpebral Closure, Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions, Cage Tonic Convulsions, Handling Reactivity, Ataxia, Body Position, Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Arousal, Palpebral Closure, Piloerection, Startle Response, Tail Pinch Response, Muscle Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Additional Observations

Statistical analysis of grip strength and hind leg splay values was performed for all tests combined, not for individual tests. Details of the statistical analysis can be found in the raw data. No statistical analysis was performed for non-continuous parameters in which the same finding was entered for all animals in the control group and for all animals in the dose group being examined.

RPT_NT:MRV2E2F1.SFO

TABLE 10
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 13

MALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Cage Posture					
Normal/Awake	4	1	4	5	1
Normal/Asleep	2	5	2	1	0
Cage Palpebral Closure					
Wide Open	3	1	3	4	1
Slight Droop	1	0	1	0	0
Halfway Shut	0	0	0	1	0
Completely Shut	2	5	2	1	0
Unusual Behavior					
None	6	6	5	6	1
Other	0	0	1[a]	0	0
Arousal					
Active/Alert	5	5	6	6	1
Inactive/Alert	1	1	0	0	0
Palpebral Closure					
Wide Open	5	5	6	6	1
Slight Droop	0	1	0	0	0
Halfway Shut	1	0	0	0	0
Defecation					
None	3	5	4	4	0
Normal	3	1	2	2	1
Urine					
None	2	0	5	3	0
Present	4	6	1	3	1
Rears (events)					
MEAN	4.17	5.50	8.00	10.83	7.00
S.D.	3.189	3.146	4.243	4.070	.000
N	6	6	6	6	1
Visual Placing					
Present	6	6	5	6	1
None	0	0	1	0	0
Grip Strength (fore) (kg)					
MEAN	.53	.40	.43	.42	.56
S.D.	.134	.050	.125	.088	.000
N	6	6	6	6	1
Grip Strength (hind) (kg)					
MEAN	.33	.26	.28	.27	.38
S.D.	.105	.080	.069	.109	.000
N	6	6	6	6	1
Body Temperature (degrees C)					
MEAN	38.37	38.10	38.25	38.27	38.10
S.D.	.186	.063	.164	.137	.000
N	6	6	6	6	1
Body Weight (grams)					
MEAN	172.24	166.33	172.65	178.12	166.36
S.D.	9.725	12.305	7.207	11.614	.000
N	6	6	6	6	1

None significantly different from control group
[a]Animal leaned to right side at all times

TABLE 10
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 13

MALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Hind Leg Splay (cm)					
MEAN	3.92	3.92	4.76	4.58	4.50
S.D.	.444	.644	1.214	.577	.000
N	6	6	6	6	1

None significantly different from control group

In addition to the above observations, all animals were observed for the following endpoints. The incidence for these endpoints was zero or the same for all groups:
Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions, Cage Tonic Convulsions, Handling Reactivity, Ataxia, Gait, Body Position, Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic Convulsions, Tonic Convulsions, Piloerection, Approach Response, Startle Response, Tail Pinch Response, Pupil Size, Muscle Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Additional Observations, Air Righting

Statistical analysis of grip strength and hind leg splay values was performed for all tests combined, not for individual tests. Details of the statistical analysis can be found in the raw data. No statistical analysis was performed for non-continuous parameters in which the same finding was entered for all animals in the control group and for all animals in the dose group being examined.

RPT_NT:MRV2E2F2.SFO

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 14

MALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Cage Posture					
Normal/Awake	5	4	4	5	1
Normal/Asleep	1	2	2	1	0
Cage Palpebral Closure					
Wide Open	5	4	4	5	0
Halfway Shut	0	0	0	0	1
Completely Shut	1	2	2	1	0
Unusual Behavior					
None	6	6	5	6	1
Other	0	0	1[a]	0	0
Arousal					
Active/Alert	3	5	6	6	1
Inactive/Alert	3	1	0	0	0
Palpebral Closure					
Wide Open	5	6	6	6	1
Slight Droop	1	0	0	0	0
Defecation					
None	3	4	6	4	1
Normal	3	2	0	2	0
Urine					
None	4	4	5	3	0
Present	2	2	1	3	1
Rears (events)					
MEAN	2.67	5.83	5.67	6.17	10.00
S.D.	2.160	3.545	3.327	2.927	.000
N	6	6	6	6	1
Visual Placing					
Present	6	5	6	6	1
None	0	1	0	0	0
Grip Strength (fore) (kg)					
MEAN	.36	.40	.35	.41	.26
S.D.	.054	.114	.029	.125	.000
N	6	6	6	6	1
Grip Strength (hind) (kg)					
MEAN	.27	.26	.26	.31	.35
S.D.	.075	.103	.045	.080	.000
N	6	6	6	6	1
Body Temperature (degrees C)					
MEAN	38.48	38.33	38.25	38.38	38.60
S.D.	.445	.356	.243	.343	.000
N	6	6	6	6	1
Body Weight (grams)					
MEAN	174.64	167.76	176.59	182.64	171.48
S.D.	10.334	12.413	7.324	11.992	.000
N	6	6	6	6	1

None significantly different from control group
[a]Animal leaned to right side at all times

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 14

MALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Hind Leg Splay (cm)					
MEAN	4.73	4.40	4.90	4.81	5.15
S.D.	.807	.756	1.096	.589	.000
N	6	6	6	6	1

None significantly different from control group

In addition to the above observations, all animals were observed for the following endpoints. The incidence for these endpoints was zero or the same for all groups:
Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions, Cage Tonic Convulsions, Handling Reactivity, Ataxia, Gait, Body Position, Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic Convulsions, Tonic Convulsions, Piloerection, Approach Response, Startle Response, Tail Pinch Response, Pupil Size, Muscle Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Additional Observations, Air Righting

Statistical analysis of grip strength and hind leg splay values was performed for all tests combined, not for individual tests. Details of the statistical analysis can be found in the raw data. No statistical analysis was performed for non-continuous parameters in which the same finding was entered for all animals in the control group and for all animals in the dose group being examined.

RPT_NT:MRV2E2F3.SFO

TABLE 12
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Gait					
Normal	6	5	6	3	3
Uncoordinated Present	0	1	0	3	0
Defecation					
None	6	5	6	6	3
Normal	0	1	0	0	0
Urine					
None	4	3	5	4	3
Present	2	3	1	2	0
Rears (events)					
MEAN	19.17	18.33	19.17	21.00	14.00
S.D.	6.616	7.815	3.545	2.966	1.000
N	6	6	6	6	3
Startle Response					
Noticeable	6	5	5	6	3
Exaggerated	0	1	1	0	0
Tail Pinch Response					
Noticeable	6	5	6	6	3
Exaggerated	0	1	0	0	0
Pupil Size					
Normal	6	6	6	4	3
Decreased	0	0	0	2	0
Grip Strength (fore) (kg)					
MEAN	.62	.62	.64	.58	.52
S.D.	.043	.095	.060	.075	.058
N	6	6	6	6	3
Grip Strength (hind) (kg)					
MEAN	.32	.37	.31	.40	.39
S.D.	.058	.068	.055	.073	.042
N	6	6	6	6	3
Body Temperature (degrees C)					
MEAN	38.80	38.67	38.43	38.57	38.67
S.D.	.559	.653	.418	.589	.153
N	6	6	6	6	3
Body Weight (grams)					
MEAN	124.82	128.17	126.99	124.96	124.30
S.D.	6.742	5.603	4.107	4.555	3.923
N	6	6	6	6	3

None significantly different from control group

TABLE 12
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Hind Leg Splay (cm)					
MEAN	4.07	4.24	3.76	4.85	4.40
S.D.	.144	.860	.652	.488	.934
N	6	6	6	6	3

None significantly different from control group

In addition to the above observations, all animals were observed for the following endpoints. The incidence for these endpoints was zero or the same for all groups:
Cage Posture, Cage Palpebral Closure, Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions, Cage Tonic Convulsions, Handling Reactivity, Ataxia, Body Position, Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Arousal, Palpebral Closure, Piloerection, Approach Response, Muscle Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Additional Observations, Visual Placing, Air Righting

Statistical analysis of grip strength and hind leg splay values was performed for all tests combined, not for individual tests. Details of the statistical analysis can be found in the raw data. No statistical analysis was performed for non-continuous parameters in which the same finding was entered for all animals in the control group and for all animals in the dose group being examined.

RPT_NT:FRV2E2F1.SFO

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Cage Posture					
Normal/Awake	6	4	5	6	2
Normal/Asleep	0	2	1	0	1
Cage Palpebral Closure					
Wide Open	2	4	3	5	2
Slight Droop	1	0	1	0	0
Halfway Shut	3	0	1	1	0
Completely Shut	0	2	1	0	1
Arousal					
Active/Alert	6	4	5	6	3
Inactive/Alert	0	2	1	0	0
Urine					
None	4	3	4	6	2
Present	2	3	2	0	1
Rears (events)					
MEAN	9.67	12.33	8.50	13.67	11.33
S.D.	3.777	11.021	3.834	5.203	1.528
N	6	6	6	6	3
Pupil Size					
Normal	6	6	5	5	3
Decreased	0	0	1	1	0
Additional Observations					
None	6	6	6	6	2
Opacity - Left Eye	0	0	0	0	1
Grip Strength (fore) (kg)					
MEAN	.58	.55	.58	.54	.49
S.D.	.105	.075	.049	.063	.051
N	6	6	6	6	3
Grip Strength (hind) (kg)					
MEAN	.32	.34	.31	.34	.36
S.D.	.062	.043	.053	.069	.043
N	6	6	6	6	3
Body Temperature (degrees C)					
MEAN	38.23	38.37	37.97	38.85*	38.30
S.D.	.528	.197	.320	.677	.400
N	6	6	6	6	3
Body Weight (grams)					
MEAN	125.98	130.34	128.12	126.82	125.70
S.D.	5.109	4.480	3.591	4.736	4.210
N	6	6	6	6	3

* Significantly different from control group ($p < 0.05$)

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Hind Leg Splay (cm)					
MEAN	3.62	3.68	3.80	4.34	3.58
S.D.	.523	.473	.378	.838	.318
N	6	6	6	6	3

None significantly different from control group

In addition to the above observations, all animals were observed for the following endpoints. The incidence for these endpoints was zero or the same for all groups:
Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions, Cage Tonic Convulsions, Handling Reactivity, Ataxia, Gait, Body Position, Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Palpebral Closure, Defecation, Piloerection, Approach Response, Startle Response, Tail Pinch Response, Muscle Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Visual Placing, Air Righting

Statistical analysis of grip strength and hind leg splay values was performed for all tests combined, not for individual tests. Details of the statistical analysis can be found in the raw data. No statistical analysis was performed for non-continuous parameters in which the same finding was entered for all animals in the control group and for all animals in the dose group being examined.

RPT_NT:FRV2E2F2.SFO

TABLE 14
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Cage Palpebral Closure[a]					
Wide Open	6	6	5	3	2
Slight Droop	0	0	0	0	1
Halfway Shut	0	0	1	3	0
Arousal					
Active/Alert	6	6	2	6	3
Inactive/Alert	0	0	4	0	0
Urine					
None	4	3	6	6	3
Present	2	3	0	0	0
Rears (events)					
MEAN	9.50	7.17	3.50*	12.00	9.00
S.D.	5.822	2.041	2.950	5.254	1.000
N	6	6	6	6	3
Approach Response					
Noticeable	6	6	6	5	3
None	0	0	0	1	0
Startle Response					
Noticeable	6	6	6	6	2
Exaggerated	0	0	0	0	1
Additional Observations					
None	6	6	6	6	2
Opacity - Left Eye	0	0	0	0	1
Grip Strength (fore) (kg)					
MEAN	.50	.51	.61	.54	.50
S.D.	.101	.086	.102	.129	.039
N	6	6	6	6	3
Grip Strength (hind) (kg)					
MEAN	.28	.28	.31	.31	.28
S.D.	.042	.072	.036	.040	.060
N	6	6	6	6	3
Body Temperature (degrees C)					
MEAN	38.50	38.32	38.02	38.68	38.20
S.D.	.603	.527	.331	.534	.400
N	6	6	6	6	3
Body Weight (grams)					
MEAN	126.90	131.93	128.53	130.15	126.69
S.D.	5.915	5.537	5.735	5.732	1.653
N	6	6	6	6	3
Air Righting					
Feet/Coordinated	6	6	5	6	3
Feet/Uncoordinated	0	0	1	0	0

* Significantly different from control group ($p < 0.05$)
[a] A significant correlation was indicated between degree of palpebral closure and treatment level.

TABLE 14
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES

GROUP: (MG/KG/DAY)	0	50	200	1000	2000
Hind Leg Splay (cm)					
MEAN	3.98	4.35	4.01	4.19	3.73
S.D.	.566	.361	.560	.783	.725
N	6	6	6	6	3

None significantly different from control group

In addition to the above observations, all animals were observed for the following endpoints. The incidence for these endpoints was zero or the same for all groups:
Cage Posture, Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions, Cage Tonic Convulsions, Handling Reactivity, Ataxia, Gait, Body Position, Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Palpebral Closure, Defecation, Piloerection, Tail Pinch Response, Pupil Size, Muscle Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Visual Placing

Statistical analysis of grip strength and hind leg splay values was performed for all tests combined, not for individual tests. Details of the statistical analysis can be found in the raw data. No statistical analysis was performed for non-continuous parameters in which the same finding was entered for all animals in the control group and for all animals in the dose group being examined.

RPT_NT:FRV2E2F3.SFO

TABLE 15
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
LEUKOCYTES ($10^3/\mu l$)					
MEAN	6.7	6.7	6.7	6.5	6.0
S.D.	1.28	0.98	1.06	0.75	0.00
N	6	6	6	6	1
ERYTHROCYTES ($10^6/\mu l$)					
MEAN	7.99	8.16	7.96	7.53**	7.80
S.D.	0.192	0.329	0.313	0.204	0.000
N	6	6	6	6	1
HEMOGLOBIN (g/dl)					
MEAN	16.6	16.8	16.4	15.5**	16.2
S.D.	0.08	0.40	0.55	0.32	0.00
N	6	6	6	6	1
HEMATOCRIT (%)					
MEAN	44.6	45.3	44.3	41.8**	43.4
S.D.	0.97	1.43	1.74	1.14	0.00
N	6	6	6	6	1
MEAN CORPUSCULAR VOLUME (μm^3)					
MEAN	56.	56.	56.	56.	56.
S.D.	0.8	0.5	0.5	1.0	0.0
N	6	6	6	6	1
MEAN CORPUSCULAR HEMOGLOBIN (pg)					
MEAN	20.7	20.5	20.7	20.6	20.8
S.D.	0.42	0.36	0.42	0.27	0.00
N	6	6	6	6	1
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)					
MEAN	37.2	37.0	37.1	37.2	37.4
S.D.	0.66	0.43	0.67	0.91	0.00
N	6	6	6	6	1
PLATELETS ($10^3/\mu l$)					
MEAN	661.	620.	670.	658.	609.
S.D.	34.6	15.4	48.0	28.2	0.0
N	6	3	5	4	1
SEGMENTED NEUTROPHILS ($10^3/\mu l$)					
MEAN	0.48	0.57	0.55	0.96	0.47
S.D.	0.095	0.170	0.275	0.570	0.000
N	6	6	6	6	1
LYMPHOCYTES ($10^3/\mu l$)					
MEAN	6.00	5.94	5.90	5.29	5.31
S.D.	1.205	0.862	1.140	0.792	0.000
N	6	6	6	6	1
MONOCYTES ($10^3/\mu l$)					
MEAN	0.13	0.12	0.12	0.19	0.13
S.D.	0.051	0.073	0.027	0.098	0.000
N	6	6	6	6	1

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

TABLE 15 (continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
BASOPHILS ($10^3/\mu l$)					
MEAN	0.03	0.01	0.03	0.02	0.02
S.D.	0.020	0.013	0.015	0.020	0.000
N	6	6	6	6	1
EOSINOPHILS ($10^3/\mu l$)					
MEAN	0.05	0.04	0.05	0.05	0.03
S.D.	0.012	0.052	0.026	0.036	0.000
N	6	6	6	6	1
BANDED NEUTROPHILS (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
LARGE MONOCYTES (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
IMMATURE GRANULOCYTES (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
IMMATURE ERYTHROCYTES (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
NUCLEATED RBCs (cells/100 WBCs)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	

None significantly different from control group

TABLE 16
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
LEUKOCYTES ($10^3/\mu l$)					
MEAN	7.1	7.3	7.2	6.0	5.7*
S.D.	0.58	0.75	1.10	1.14	0.99
N	6	6	6	6	3
ERYTHROCYTES ($10^6/\mu l$)					
MEAN	7.95	7.95	7.75	7.49**	7.76
S.D.	0.097	0.235	0.152	0.192	0.272
N	6	6	6	6	3
HEMOGLOBIN (g/dl)					
MEAN	16.8	16.7	16.5*	15.8**	16.1**
S.D.	0.16	0.23	0.30	0.31	0.20
N	6	6	6	6	3
HEMATOCRIT (%)					
MEAN	44.6	44.6	43.4*	41.8**	43.1*
S.D.	0.69	1.37	0.90	0.93	0.83
N	6	6	6	6	3
MEAN CORPUSCULAR VOLUME (μm^3)					
MEAN	56.	56.	56.	56.	56.
S.D.	0.8	0.5	0.0	0.6	1.2
N	6	6	6	6	3
MEAN CORPUSCULAR HEMOGLOBIN (pg)					
MEAN	21.2	21.1	21.3	21.1	20.8
S.D.	0.33	0.46	0.31	0.23	0.52
N	6	6	6	6	3
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)					
MEAN	37.7	37.5	38.0	37.7	37.4
S.D.	0.50	0.75	0.57	0.23	0.34
N	6	6	6	6	3
PLATELETS ($10^3/\mu l$)					
MEAN	677.	697.	667.	575.**	544.**
S.D.	58.3	25.0	34.8	31.1	0.0
N	6	5	6	6	1
SEGMENTED NEUTROPHILS ($10^3/\mu l$)					
MEAN	0.50	0.66	0.51	0.45	0.95
S.D.	0.162	0.437	0.216	0.108	0.153
N	6	6	6	6	3
LYMPHOCYTES ($10^3/\mu l$)					
MEAN	6.37	6.45	6.52	5.40*	4.50**
S.D.	0.510	0.473	0.891	1.076	0.909
N	6	6	6	6	3
MONOCYTES ($10^3/\mu l$)					
MEAN	0.13	0.10*	0.12	0.09*	0.14
S.D.	0.025	0.028	0.038	0.022	0.040
N	6	6	6	6	3

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

TABLE 16 (continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
BASOPHILS ($10^3/\mu l$)					
MEAN	0.03	0.03	0.03	0.03	0.01**
S.D.	0.011	0.015	0.008	0.010	0.012
N	6	6	6	6	3
EOSINOPHILS ($10^3/\mu l$)					
MEAN	0.05	0.07	0.06	0.05	0.06
S.D.	0.020	0.018	0.005	0.011	0.066
N	6	6	6	6	3
BANDED NEUTROPHILS (cells/µl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
LARGE MONOCYTES (cells/µl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
IMMATURE GRANULOCYTES (cells/µl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
IMMATURE ERYTHROCYTES (cells/µl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
NUCLEATED RBCs (cells/100 WBCs)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2

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

TABLE 17
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF ORGAN WEIGHTS (GRAMS)
ANIMALS SACRIFICED AT DAY 15

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
FINAL BODY WEIGHT					
MEAN	180.9	173.5	181.9	190.4	178.5
S.D.	11.00	12.85	7.32	12.92	0.00
N	6	6	6	6	1
LIVER					
MEAN	7.777	7.410	8.070	11.366**	
S.D.	0.7642	1.1514	0.5563	0.6721	
N	3	3	3	3	
KIDNEYS					
MEAN	1.437	1.432	1.523	1.689	
S.D.	0.0996	0.1816	0.0879	0.0715	
N	3	3	3	3	
SPLEEN					
MEAN	0.422	0.406	0.415	0.529*	
S.D.	0.0355	0.0731	0.0093	0.0190	
N	3	3	3	3	
BRAIN					
MEAN	1.734	1.662	1.678	1.712	
S.D.	0.0218	0.0597	0.0689	0.0394	
N	3	3	3	3	
ADRENAL GL					
MEAN	0.031	0.030	0.035	0.037	
S.D.	0.0017	0.0032	0.0055	0.0021	
N	3	3	3	3	
TESTES					
MEAN	2.324	2.212	2.385	2.387	
S.D.	0.1773	0.2309	0.2028	0.1302	
N	3	3	3	3	

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

TABLE 18
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	4.246	4.304	4.495	5.723**	
S.D.	0.1666	0.2441	0.1617	0.1139	
N	3	3	3	3	
KIDNEYS					
MEAN	0.786	0.834	0.849	0.851	
S.D.	0.0086	0.0407	0.0292	0.0260	
N	3	3	3	3	
SPLEEN					
MEAN	0.231	0.236	0.232	0.267	
S.D.	0.0130	0.0207	0.0163	0.0106	
N	3	3	3	3	
BRAIN					
MEAN	0.951	0.973	0.936	0.863	
S.D.	0.0693	0.0660	0.0575	0.0269	
N	3	3	3	3	
ADRENAL GL					
MEAN	0.017	0.018	0.020	0.019	
S.D.	0.0007	0.0026	0.0032	0.0013	
N	3	3	3	3	
TESTES					
MEAN	1.271	1.290	1.328	1.202	
S.D.	0.0578	0.0277	0.0519	0.0225	
N	3	3	3	3	

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

TABLE 19
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	448.868	444.746	480.918	663.840**	
S.D.	49.1615	55.2473	26.1079	30.5248	
N	3	3	3	3	
KIDNEYS					
MEAN	82.943	86.046	90.769	98.695	
S.D.	6.6763	8.8879	3.7780	4.9389	
N	3	3	3	3	
SPLEEN					
MEAN	24.325	24.370	24.738	30.900**	
S.D.	2.1639	3.6056	1.0986	0.4423	
N	3	3	3	3	
ADRENAL GL					
MEAN	1.789	1.826	2.099	2.180	
S.D.	0.1214	0.1823	0.2477	0.0915	
N	3	3	3	3	
TESTES					
MEAN	134.144	132.923	142.334	139.471	
S.D.	11.8238	9.3911	13.5835	6.8857	
N	3	3	3	3	

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

TABLE 20
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF ORGAN WEIGHTS (GRAMS)
ANIMALS SACRIFICED AT DAY 15

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
FINAL BODY WEIGHT					
MEAN	132.2	136.8	133.6	134.3	132.2
S.D.	4.75	6.37	5.20	6.13	5.12
N	6	6	6	6	3
LIVER					
MEAN	5.447	5.426	5.608	6.200*	
S.D.	0.0996	0.3670	0.2718	0.2943	
N	3	3	3	3	
KIDNEYS					
MEAN	1.147	1.113	1.143	1.163	
S.D.	0.0188	0.0666	0.0512	0.0461	
N	3	3	3	3	
SPLEEN					
MEAN	0.370	0.343	0.369	0.369	
S.D.	0.0578	0.0140	0.0210	0.0423	
N	3	3	3	3	
BRAIN					
MEAN	1.591	1.654	1.635	1.515	
S.D.	0.0344	0.0579	0.0927	0.1164	
N	3	3	3	3	
ADRENAL GL					
MEAN	0.041	0.036	0.042	0.039	
S.D.	0.0021	0.0026	0.0096	0.0066	
N	3	3	3	3	
OVARIES					
MEAN	0.093	0.078	0.077	0.081	
S.D.	0.0061	0.0035	0.0173	0.0085	
N	3	3	3	3	

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

TABLE 21
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	4.174	4.061	4.267	4.734**	
S.D.	0.1347	0.0861	0.0663	0.1280	
N	3	3	3	3	
KIDNEYS					
MEAN	0.879	0.834	0.870	0.888	
S.D.	0.0307	0.0207	0.0167	0.0220	
N	3	3	3	3	
SPLEEN					
MEAN	0.283	0.257	0.282	0.282	
S.D.	0.0417	0.0039	0.0306	0.0361	
N	3	3	3	3	
BRAIN					
MEAN	1.219	1.240	1.245	1.157	
S.D.	0.0426	0.0395	0.0828	0.0873	
N	3	3	3	3	
ADRENAL GL					
MEAN	0.031	0.027	0.032	0.030	
S.D.	0.0029	0.0017	0.0062	0.0046	
N	3	3	3	3	
OVARIES					
MEAN	0.071	0.058	0.058	0.062	
S.D.	0.0015	0.0033	0.0110	0.0069	
N	3	3	3	3	

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

TABLE 22
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	342.470	327.872	343.868	410.577**	
S.D.	8.4314	15.4181	27.8022	30.8568	
N	3	3	3	3	
KIDNEYS					
MEAN	72.134	67.316	70.099	77.105	
S.D.	1.8164	3.7151	5.6737	7.5428	
N	3	3	3	3	
SPLEEN					
MEAN	23.194	20.712	22.630	24.570	
S.D.	3.1624	0.3524	1.9372	4.7692	
N	3	3	3	3	
ADRENAL GL					
MEAN	2.559	2.179	2.557	2.565	
S.D.	0.1872	0.1909	0.4633	0.2850	
N	3	3	3	3	
OVARIES					
MEAN	5.822	4.694	4.732	5.363	
S.D.	0.3021	0.1138	1.1939	0.2387	
N	3	3	3	3	

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

TABLE 23
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
STOMACH					
COLOR CHANGE, FOCAL/MULTIFOCAL	0	2	1	1	0
LYMPH ND, S-MAN					
COLOR CHANGE, FOCAL/MULTIFOCAL	1	0	0	0	0
SIZE INCREASE	0	0	0	1	0
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	3	2	3	0	0
COLOR CHANGE, DIFFUSE	0	1	0	2	0
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL	1	2	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 24
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	-	-	-	-	5
TOTAL BODY					
STAINED	-	-	-	-	5
STOMACH					
COLOR CHANGE, FOCAL/MULTIFOCAL	-	-	-	-	2
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE	-	-	-	-	5
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	-	-	-	-	2
BRAIN					
MENINGEAL HEMORRHAGE	-	-	-	-	3
LUNGS					
COLOR CHANGE, DIFFUSE	-	-	-	-	5
URINARY BLADDER					
DILATATION/DISTENTION	-	-	-	-	2
HEMORRHAGE	-	-	-	-	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 25
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
ADIPOSE TISSUE					
THICKER THAN NORMAL	0	1	0	0	0
STOMACH					
COLOR CHANGE, DIFFUSE	0	1	0	0	0
COLOR CHANGE, FOCAL/MULTIFOCAL	0	1	0	0	0
COLON					
HEMORRHAGE	0	1	0	0	0
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE	1	0	0	0	0
SIZE INCREASE	0	1	0	0	0
LYMPH ND, MED					
COLOR CHANGE, DIFFUSE	0	0	1	0	0
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	0	2	2	2	0
COLOR CHANGE, DIFFUSE	1	0	0	1	0
SPINAL CORD					
HEMORRHAGE	0	1	0	0	0
EYE					
OPACITY	0	0	0	0	1
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL	0	1	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

TABLE 26
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	-	-	-	-	3
TOTAL BODY					
STAINED	-	-	-	-	2
STOMACH					
COLOR CHANGE, DIFFUSE	-	-	-	-	1
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE	-	-	-	-	3
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	-	-	-	-	1
BRAIN					
MENINGEAL HEMORRHAGE	-	-	-	-	3
OVARIES					
COLOR CHANGE, DIFFUSE	-	-	-	-	1
LUNGS					
COLOR CHANGE, DIFFUSE	-	-	-	-	3

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 27
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
STOMACH					
TOTAL NUMBER EXAMINED	0	2	1	1	0
EXAMINED, UNREMARKABLE	-	0	0	1	-
GASTRITIS	-	**2**	**1**	**0**	-
MILD	-	2	1	0	-
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	1
EXAMINED, UNREMARKABLE	5	-	-	2	1
MONONUCLEAR CELL INFILTRATE(S)	**1**	-	-	**1**	**0**
MINIMAL	1	-	-	1	0
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	0	0	1	0
SINUS ERYTHROCYTOSIS	**1**	-	-	**0**	-
MILD	1	-	-	0	-
PLASMACYTOSIS	**0**	-	-	**1**	-
MODERATE	0	-	-	1	-
LYMPHOID HYPERPLASIA	**0**	-	-	**1**	-
MODERATE	0	-	-	1	-
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	2	0	1	1	0
SINUS ERYTHROCYTOSIS	**2**	-	**1**	**1**	-
MODERATE	2	-	1	0	-
MARKED	0	-	0	1	-
MASTOCYTOSIS	**1**	-	**0**	**0**	-
MODERATE	1	-	0	0	-
THYMIC REGION					
TOTAL NUMBER EXAMINED	3	3	3	2	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

None significantly different from control group

TABLE 27 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
THYMIC REGION (CONTINUED)					
HEMORRHAGE	**3**	**3**	**3**	**2**	-
MINIMAL	3	2	1	1	-
MILD	0	0	1	0	-
MODERATE	0	1	1	1	-
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	1	3	3	2	-
MENINGEAL HEMORRHAGE	**1**	**0**	**0**	**1**	-
MINIMAL	1	0	0	1	-
BRAIN HEMORRHAGE	**1**	**0**	**0**	**0**	-
MINIMAL	1	0	0	0	-
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
TESTES					
TOTAL NUMBER EXAMINED	6	0	0	3	1
EXAMINED, UNREMARKABLE	6	-	-	3	1
LUNGS					
TOTAL NUMBER EXAMINED	1	2	0	1	0
EXAMINED, UNREMARKABLE	0	2	-	0	-
ALVEOLAR HISTIOCYTOSIS	**1**	**0**	-	**0**	-
MILD	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

None significantly different from control group

TABLE 27 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
LUNGS (CONTINUED)					
HEMORRHAGE	**0**	**0**	**-**	**1**	**-**
MINIMAL	0	0	-	1	-
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	1
EXAMINED, UNREMARKABLE	5	-	-	3	1
TUBULAR REGENERATION/BASOPHILIA	**1**	**-**	**-**	**0**	**0**
MINIMAL	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

None significantly different from control group

TABLE 28
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
MENINGES					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	2	3	1
PERIVASCULAR INFILTRATES	**0**	**0**	**1**	**0**	**0**
MINIMAL	0	0	1	0	0
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
AMYGDALA					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	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 28 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
THALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
HYPOTHALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
MIDBRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SUBSTANTIA NIGRA					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CEREBELLAR W.M.					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
ANT COMMISSURE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
EXTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
INTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CORPUS CALLOSUM					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
FORNIX					
TOTAL NUMBER EXAMINED	3	2	3	3	1
EXAMINED, UNREMARKABLE	3	2	3	3	1
MISSING	0	1	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

TABLE 28 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
CEREBELLAR CTX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CEREBELLAR NUC					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
VESTIBULAR NUC					
TOTAL NUMBER EXAMINED	3	3	2	3	1
EXAMINED, UNREMARKABLE	3	3	2	3	1
MISSING	0	0	1	0	0
PONS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
MEDULLA OBL					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
OLFACTORY BULB					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
OPTIC N/CHIASM					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
TRIGEMINAL TRACT					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SPINAL CORD, CRV					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	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 28 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
SPINAL CORD, CRV(CONTINUED)					
VACUOLATION	**0**	**0**	**0**	**0**	**1**
MINIMAL	0	0	0	0	1
SPINAL CORD, THR					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	2	3	3	1
PERIVASCULAR INFILTRATES	**0**	**1**	**0**	**0**	**0**
MILD	0	1	0	0	0
GASSERIAN GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SCIATIC NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
TIBIAL NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED	3	2	3	3	1
EXAMINED, UNREMARKABLE	3	2	3	3	1
MISSING	0	1	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

TABLE 29
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	5
STOMACH					
TOTAL NUMBER EXAMINED	0	0	0	0	1
TOO AUTOLYZED TO EVALUATE	-	-	-	-	1
GASTRITIS	-	-	-	-	1
MINIMAL	-	-	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	0	0	0	0	5
EXAMINED, UNREMARKABLE	-	-	-	-	5
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	0	0	0	5
SINUS ERYTHROCYTOSIS	-	-	-	-	5
MILD	-	-	-	-	3
MODERATE	-	-	-	-	2
LYMPH ND, REN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
SINUS ERYTHROCYTOSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
THYMIC REGION					
TOTAL NUMBER EXAMINED	0	0	0	0	2
HEMORRHAGE	-	-	-	-	2
MILD	-	-	-	-	1
MODERATE	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	0	0	0	0	3
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 29 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	5
BRAIN (CONTINUED)					
MENINGEAL CONGESTION	-	-	-	-	2
MILD	-	-	-	-	1
MODERATE	-	-	-	-	1
MENINGEAL HEMORRHAGE	-	-	-	-	1
MINIMAL	-	-	-	-	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
TESTES					
TOTAL NUMBER EXAMINED	0	0	0	0	5
EXAMINED, UNREMARKABLE	-	-	-	-	5
LUNGS					
TOTAL NUMBER EXAMINED	0	0	0	0	5
CONGESTION	-	-	-	-	5
MODERATE	-	-	-	-	2
MARKED	-	-	-	-	3
INTRAALVEOLAR CELLULAR DEBRIS	-	-	-	-	1
MILD	-	-	-	-	1
HEMORRHAGE	-	-	-	-	1
MODERATE	-	-	-	-	1
PNEUMONITIS	-	-	-	-	1
MODERATE	-	-	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	0	0	0	0	5
EXAMINED, UNREMARKABLE	-	-	-	-	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

TABLE 29 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	5
URINARY BLADDER					
TOTAL NUMBER EXAMINED	0	0	0	0	3
ECTASIA	-	-	-	-	2
MODERATE	-	-	-	-	1
MARKED	-	-	-	-	1
HEMORRHAGE	-	-	-	-	2
MINIMAL	-	-	-	-	1
MODERATE	-	-	-	-	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 30
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
MENINGES					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
AMYGDALA					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 30 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
THALAMUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
HYPOTHALAMUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
MIDBRAIN					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SUBSTANTIA NIGRA					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CEREBELLAR W.M.					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
ANT COMMISSURE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
EXTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
INTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CORPUS CALLOSUM					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
FORNIX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CEREBELLAR CTX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 30 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
CEREBELLAR NUC					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
VESTIBULAR NUC					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PONS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
MEDULLA OBL					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
OLFACTORY BULB					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
OPTIC N/CHIASM					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
TRIGEMINAL TRACT					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL CORD, CRV					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL CORD, THR					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 30 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
GASSERIAN GANG					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SCIATIC NERVE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
TIBIAL NERVE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 31
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
STOMACH					
TOTAL NUMBER EXAMINED	0	2	1	1	1
EXAMINED, UNREMARKABLE	-	0	0	1	0
TOO AUTOLYZED TO EVALUATE	-	0	0	0	1
GASTRITIS	-	**2**	**1**	**0**	**1**
MINIMAL	-	0	0	0	1
MILD	-	2	1	0	0
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	5	-	-	2	6
MONONUCLEAR CELL INFILTRATE(S)	**1**	-	-	**1**	**0**
MINIMAL	1	-	-	1	0
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	0	0	1	5
SINUS ERYTHROCYTOSIS	**1**	-	-	**0**	**5**
MILD	1	-	-	0	3
MODERATE	0	-	-	0	2
PLASMACYTOSIS	**0**	-	-	**1**	**0**
MODERATE	0	-	-	1	0
LYMPHOID HYPERPLASIA	**0**	-	-	**1**	**0**
MODERATE	0	-	-	1	0
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	2	0	1	1	0
SINUS ERYTHROCYTOSIS	**2**	-	**1**	**1**	-
MODERATE	2	-	1	0	-
MARKED	0	-	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

None significantly different from control group

TABLE 31 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
LYMPH ND, MED (CONTINUED)					
MASTOCYTOSIS	1	-	0	0	-
MODERATE	1	-	0	0	-
LYMPH ND, REN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
SINUS ERYTHROCYTOSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
THYMIC REGION					
TOTAL NUMBER EXAMINED	3	3	3	2	2
HEMORRHAGE	3	3	3	2	2
MINIMAL	3	2	1	1	0
MILD	0	0	1	0	1
MODERATE	0	1	1	1	1
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	1	3	3	2	1
MENINGEAL CONGESTION	0	0	0	0	2
MILD	0	0	0	0	1
MODERATE	0	0	0	0	1
MENINGEAL HEMORRHAGE	1	0	0	1	1
MINIMAL	1	0	0	1	1
BRAIN HEMORRHAGE	1	0	0	0	0
MINIMAL	1	0	0	0	0
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 31 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
TESTES					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	6	-	-	3	6
LUNGS					
TOTAL NUMBER EXAMINED	1	2	0	1	5
EXAMINED, UNREMARKABLE	0	2	-	0	0
CONGESTION	**0**	**0**	**-**	**0**	**5**
MODERATE	0	0	-	0	2
MARKED	0	0	-	0	3
ALVEOLAR HISTIOCYTOSIS	**1**	**0**	**-**	**0**	**0**
MILD	1	0	-	0	0
INTRAALVEOLAR CELLULAR DEBRIS	**0**	**0**	**-**	**0**	**1**
MILD	0	0	-	0	1
HEMORRHAGE	**0**	**0**	**-**	**1**	**1**
MINIMAL	0	0	-	1	0
MODERATE	0	0	-	0	1
PNEUMONITIS	**0**	**0**	**-**	**0**	**1**
MODERATE	0	0	-	0	1
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	5	-	-	3	6
TUBULAR REGENERATION/BASOPHILIA	**1**	**-**	**-**	**0**	**0**
MINIMAL	1	-	-	0	0
URINARY BLADDER					
TOTAL NUMBER EXAMINED	0	0	0	0	3

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 31 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
URINARY BLADDER (CONTINUED)					
ECTASIA	-	-	-	-	**2**
MODERATE	-	-	-	-	1
MARKED	-	-	-	-	1
HEMORRHAGE	-	-	-	-	**2**
MINIMAL	-	-	-	-	1
MODERATE	-	-	-	-	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

None significantly different from control group

TABLE 32
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
ADIPOSE TISSUE					
TOTAL NUMBER EXAMINED	0	1	0	0	0
STEATITIS	-	1	-	-	-
MILD	-	1	-	-	-
STOMACH					
TOTAL NUMBER EXAMINED	0	2	0	0	0
LYMPHOCYTIC INFILTRATE(S)	-	1	-	-	-
MILD	-	1	-	-	-
GASTRITIS	-	2	-	-	-
MILD	-	2	-	-	-
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	3
EXAMINED, UNREMARKABLE	5	-	-	1	3
MONONUCLEAR CELL INFILTRATE(S)	1	-	-	2	0
MINIMAL	1	-	-	2	0
COLON					
TOTAL NUMBER EXAMINED	0	1	0	0	0
HEMORRHAGE	-	1	-	-	-
MARKED	-	1	-	-	-
COLITIS	-	1	-	-	-
MODERATE	-	1	-	-	-
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	1	0	0	0
EXAMINED, UNREMARKABLE	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

None significantly different from control group

TABLE 32 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
LYMPH ND, S-MAN (CONTINUED)					
SINUS ERYTHROCYTOSIS	1	0	-	-	-
MODERATE	1	0	-	-	-
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	0	1	1	2	0
SINUS ERYTHROCYTOSIS	-	1	1	2	-
MILD	-	1	0	1	-
MODERATE	-	0	0	1	-
MARKED	-	0	1	0	-
MASTOCYTOSIS	-	1	0	0	-
MILD	-	1	0	0	-
THYMIC REGION					
TOTAL NUMBER EXAMINED	1	2	3	3	0
EXAMINED, UNREMARKABLE	0	1	1	3	-
HEMORRHAGE	1	1	2	0	-
MINIMAL	0	0	1	0	-
MILD	1	1	1	0	-
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
EYE					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED	0	1	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

None significantly different from control group

TABLE 32 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
LUNGS (CONTINUED)					
PNEUMONITIS	-	1	-	-	-
MILD	-	1	-	-	-
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	3
EXAMINED, UNREMARKABLE	6	-	-	3	3

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 33
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
MENINGES					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
AMYGDALA					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 33 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
THALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
HYPOTHALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
MIDBRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SUBSTANTIA NIGRA					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
CEREBELLAR W.M.					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
ANT COMMISSURE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
EXTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
INTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
CORPUS CALLOSUM					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
FORNIX					
TOTAL NUMBER EXAMINED	2	3	1	2	1
EXAMINED, UNREMARKABLE	2	3	1	2	1
MISSING	1	0	2	1	2
CEREBELLAR CTX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 33 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
CEREBELLAR NUC					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
VESTIBULAR NUC					
TOTAL NUMBER EXAMINED	3	3	3	3	2
EXAMINED, UNREMARKABLE	2	3	3	3	2
MISSING	0	0	0	0	1
VACUOLATION/SPONGIOSIS	**1**	**0**	**0**	**0**	**0**
MINIMAL	1	0	0	0	0
PONS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION/SPONGIOSIS	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
MEDULLA OBL					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION/SPONGIOSIS	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
OLFACTORY BULB					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
OPTIC N/CHIASM					
TOTAL NUMBER EXAMINED	2	3	3	3	3
EXAMINED, UNREMARKABLE	2	3	3	3	3
MISSING	1	0	0	0	0
TRIGEMINAL TRACT					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SPINAL CORD, CRV					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	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 33 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
SPINAL CORD, CRV(CONTINUED)					
VACUOLATION	**0**	**0**	**0**	**0**	**3**
MINIMAL	0	0	0	0	2
MILD	0	0	0	0	1
NERVE FIBER DEGENERATION	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
SPINAL CORD, THR					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
GASSERIAN GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SCIATIC NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
TIBIAL NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	2	3

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 33 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
TIBIAL NERVE (CONTINUED)					
NERVE FIBER DEGENERATION	**0**	**0**	**0**	**1**	**0**
MINIMAL	0	0	0	1	0
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 34
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	3
STOMACH					
TOTAL NUMBER EXAMINED	0	0	0	0	1
CONGESTION	-	-	-	-	1
MODERATE	-	-	-	-	1
HYDROPIC DEGENERATION, SQUAMOUS MUCOSA	-	-	-	-	1
MODERATE	-	-	-	-	1
SQUAMOUS MUCOSAL HYPERPLASIA	-	-	-	-	1
MILD	-	-	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	1
HEPATOCELLULAR VACUOLATION	-	-	-	-	1
MINIMAL	-	-	-	-	1
HEPATOCELLULAR NECROSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	1
SINUS ERYTHROCYTOSIS	-	-	-	-	2
MILD	-	-	-	-	1
MARKED	-	-	-	-	1
MASTOCYTOSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
THYMIC REGION					
TOTAL NUMBER EXAMINED	0	0	0	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 34 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	3
THYMIC REGION (CONTINUED)					
HEMORRHAGE	-	-	-	-	**1**
MARKED	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	0	0	0	0	3
MENINGEAL CONGESTION	-	-	-	-	**3**
MILD	-	-	-	-	1
MODERATE	-	-	-	-	2
MENINGEAL HEMORRHAGE	-	-	-	-	**1**
MODERATE	-	-	-	-	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
OVARIES					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED	0	0	0	0	3
CONGESTION	-	-	-	-	**3**
MODERATE	-	-	-	-	1
MARKED	-	-	-	-	2
HEMORRHAGE	-	-	-	-	**1**
MODERATE	-	-	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3

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 35
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
ADIPOSE TISSUE					
TOTAL NUMBER EXAMINED	0	1	0	0	0
STEATITIS	-	1	-	-	-
MILD	-	1	-	-	-
STOMACH					
TOTAL NUMBER EXAMINED	0	2	0	0	1
CONGESTION	-	0	-	-	1
MODERATE	-	0	-	-	1
HYDROPIC DEGENERATION, SQUAMOUS MUCOSA	-	0	-	-	1
MODERATE	-	0	-	-	1
LYMPHOCYTIC INFILTRATE(S)	-	1	-	-	0
MILD	-	1	-	-	0
GASTRITIS	-	2	-	-	0
MILD	-	2	-	-	0
SQUAMOUS MUCOSAL HYPERPLASIA	-	0	-	-	1
MILD	-	0	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	5	-	-	1	4
HEPATOCELLULAR VACUOLATION	0	-	-	0	1
MINIMAL	0	-	-	0	1
MONONUCLEAR CELL INFILTRATE(S)	1	-	-	2	0
MINIMAL	1	-	-	2	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

None significantly different from control group

TABLE 35 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

: GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
LIVER (CONTINUED)					
HEPATOCELLULAR NECROSIS	**0**	**-**	**-**	**0**	**1**
MODERATE	0	-	-	0	1
COLON					
TOTAL NUMBER EXAMINED	0	1	0	0	0
HEMORRHAGE	**-**	**1**	**-**	**-**	**-**
MARKED	-	1	-	-	-
COLITIS	**-**	**1**	**-**	**-**	**-**
MODERATE	-	1	-	-	-
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	1	0	0	3
EXAMINED, UNREMARKABLE	0	1	-	-	1
SINUS ERYTHROCYTOSIS	**1**	**0**	**-**	**-**	**2**
MILD	0	0	-	-	1
MODERATE	1	0	-	-	0
MARKED	0	0	-	-	1
MASTOCYTOSIS	**0**	**0**	**-**	**-**	**1**
MODERATE	0	0	-	-	1
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	0	1	1	2	0
SINUS ERYTHROCYTOSIS	**-**	**1**	**1**	**2**	**-**
MILD	-	1	0	1	-
MODERATE	-	0	0	1	-
MARKED	-	0	1	0	-
MASTOCYTOSIS	**-**	**1**	**0**	**0**	**-**
MILD	-	1	0	0	-
THYMIC REGION					
TOTAL NUMBER EXAMINED	1	2	3	3	1
EXAMINED, UNREMARKABLE	0	1	1	3	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

None significantly different from control group

TABLE 35 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
THYMIC REGION (CONTINUED)					
HEMORRHAGE	**1**	**1**	**2**	**0**	**1**
MINIMAL	0	0	1	0	0
MILD	1	1	1	0	0
MARKED	0	0	0	0	1
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	0
MENINGEAL CONGESTION	**0**	**0**	**0**	**0**	**3**
MILD	0	0	0	0	1
MODERATE	0	0	0	0	2
MENINGEAL HEMORRHAGE	**0**	**0**	**0**	**0**	**1**
MODERATE	0	0	0	0	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
EYE					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
OVARIES					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED	0	1	0	0	3

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 35 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
LUNGS (CONTINUED)					
CONGESTION	-	**0**	-	-	**3**
MODERATE	-	0	-	-	1
MARKED	-	0	-	-	2
PNEUMONITIS	-	**1**	-	-	**0**
MILD	-	1	-	-	0
HEMORRHAGE	-	**0**	-	-	**1**
MODERATE	-	0	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	6	-	-	3	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

None significantly different from control group

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

QUALITY ASSURANCE UNIT INSPECTION SUMMARY

Inspection Date(s)	Inspection Type	Date QAU Report Issued To Study Director	Date QAU Report Issued To Management
09-08-93 to 09-09-93	PROTOCOL	09-09-93	09-15-93
10-12-93	EVENT-ANIMAL RECEIPT	10-12-93	10-12-93
11-08-93	EVENT-SACRIFICE PERFUSION	11-16-93	11-30-93
11-22-93	PROTOCOL AMENDMENT #1	11-22-93	12-13-93
02-23-94 to 02-24-94	CLINICAL PATHOLOGY DATA, REPORT	03-18-94	09-22-94
02-24-94 to 03-02-94	ANATOMIC PATHOLOGY DATA, REPORT	03-18-94	09-22-94
03-02-94 to 03-09-94	ANALYTICAL CHEMISTRY DATA, REPORT	03-18-94	09-22-94
03-09-94 to 03-18-94	RAW DATA, REPORT	03-18-94	09-22-94
05-28-94	PROTOCOL AMENDMENT #2	05-28-94	05-31-94
06-10-94	PROTOCOL AMENDMENT #2 REVISED	06-10-94	06-10-94
09-22-94	ARCHIVES	09-22-94	09-22-94

Craig A. Ferry 9.26.94

Craig A. Ferry — Date

Representative, Quality Assurance Unit

ARCH_DOC:93U1318:93U1318 QAU

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

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 Fischer 344 rats 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 100.3 to 102.8% 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 Number 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 Number 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 Number 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 were 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 the appropriate size 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 0.065 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 (1.45 mg/ml for Study Week 1 and 1.52 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 0.435 to 1.45 mg/ml and 0.456 to 1.52 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 were within ± 10% of nominal; the difference between duplicate analyses did not exceed ± 15%; and individual analyses were within ± 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 three separate regions (top, middle, and bottom) of the flask used for mixing each solution. The mean measured concentrations (± 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 100.3 to 102.8% of nominal. Vinyl 2-ethylhexanoate was not detected in the control dosing solutions.

Analytical Chemist: Marlene A. Vrbanic 9-26-94
Marlene A. Vrbanic, B.A. Date

TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

GAS CHROMATOGRAPHIC OPERATING PARAMETERS

Instrument:	Hewlett-Packard 5890A Gas Chromatograph (GC)
Column:	DB™-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 (Vinyl 2-ethylhexanoate):	Approximately 7.4 minutes
Limit of Quantification:	0.01 mg/ml[a]

[a]This 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 FISCHER 344 RATS

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

[a]These procedures were derived during the prestudy dosing solution stability study conducted by the analytical chemistry group, and assure accurate delivery of the dosing solutions to the animals.
[b]Priming 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 FISCHER 344 RATS

RESULTS OF DOSING SOLUTION HOMOGENEITY ANALYSES[a]

Nominal Concentration = 12.5 mg/ml

Area of Sampling	Measured Concentration (mg/ml)	% of Nominal
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

Area of Sampling	Measured Concentration (mg/ml)	% of Nominal
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

[a]Solutions were prepared on 9-15-93 and analyzed directly after preparation. Subsamples for analysis were removed from the flask used for mixing each solution.
[b]CV represents the percent coefficient of variation ((SD/Mean) x 100).

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

RESULTS OF DOSING SOLUTION STABILITY ANALYSES

Nominal Concentration = 12.5 mg/ml

Date of Analysis	Stability Day	Measured Concentration (mg/ml)[a]	% of Nominal[a]
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

Nominal Concentration = 500 mg/ml

Date of Analysis	Stability Day	Measured Concentration (mg/ml)[a]	% of Nominal[a]
09-15-93	0[b]	493.4 ± 6.6 (n=6)	98.7 ± 1.3
09-23-93	8[c,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

[a]The measured concentration and % of nominal represent a mean ± standard deviation.
[b]The 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.
[c]The 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.
[d]Due 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 FISCHER 344 RATS

RESULTS OF DOSING SOLUTION CONCENTRATION VERIFICATION ANALYSES

Date of Preparation	Date of Analysis	Nominal Concentration (mg/ml)	Measured Concentration (mg/ml)[a]	% of Nominal[a]
10-21-93[b]	10-21-93	0.0	ND[c]	NA[d]
10-21-93	10-21-93	12.5	12.84	102.7
10-21-93	10-21-93	50.0	51.38	102.8
10-21-93	10-21-93	250.0	252.2	100.9
10-21-93	10-21-93	500.0	502.9	100.6
10-28-93[e]	10-28-93	0.0	ND	NA
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

[a]The measured concentration and % of nominal represents a mean of duplicate analyses.
[b]Solutions prepared on 10-21-93 were designated for use in Study Week 1.
[c]ND - not detected.
[d]NA - not applicable.
[e]Solutions prepared on 10-28-93 were designated for use in Study Week 2.

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Test Substance Characterization Report

UNION CARBIDE

Union Carbide Corporation

STUDY TITLE

GLP Analysis-Final Report

TEST SUBTANCE

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 Divison
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

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

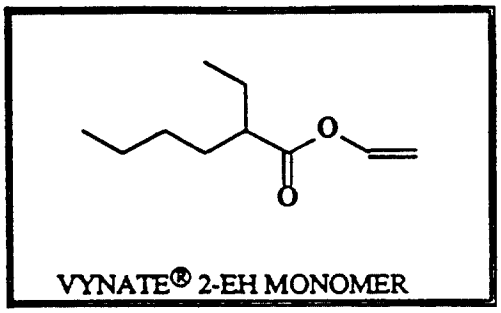
Vinyl 2-ethylhexanoate
Study # 37-AEG-110

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.



VYNATE® 2-EH MONOMER

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 ^{13}C flip angles were 30°; the $^{13}C\{^1H\}$ (proton decoupled ^{13}C) 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 deuterochloroform for analysis; tetramethylsilane (TMS) was added to provide an internal chemical shift reference. The TMS and deuterochloroform 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 $^{13}C\{^1H\}$ 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 CH_3 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 Hewlwtt-Packard (HP) 5890 gas chromatograph. The sample, 37-AEG-106, was analyzed by injecting 0.2 µL 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 µL) 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).

Component name	37-AEG-106	37-AEG-106R
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 — ^{1}H NMR Spectrum of 37-AEG-106 (vinyl 2-ethylhexanoate)

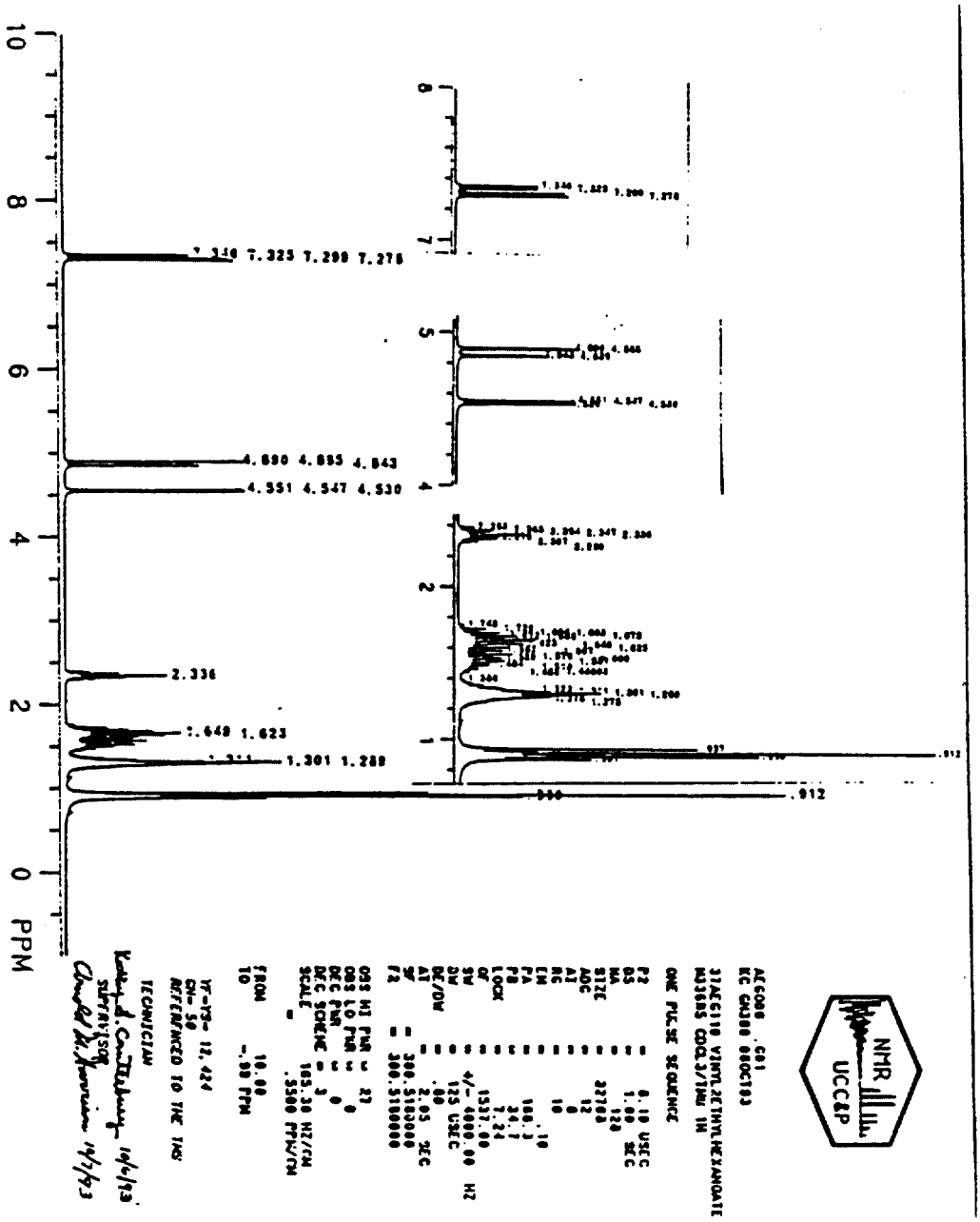


Figure 2 — ^{13}C NMR Spectrum of 37-AEG-106 (vinyl 2-ethylhexanoate)

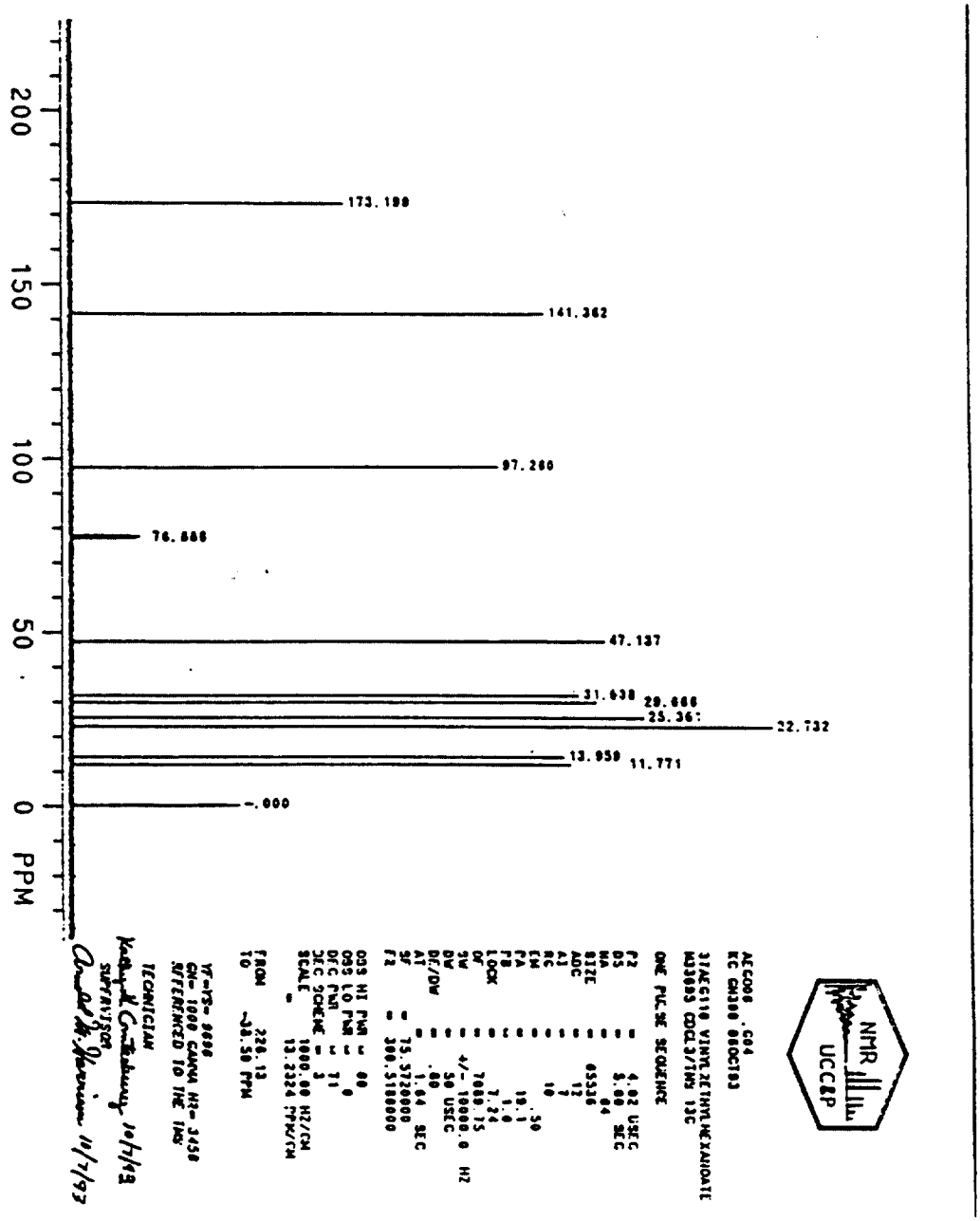


Figure 3 — Capillary GC/MS RIC of 37-AEG-106 (vinyl 2-ethylhexanoate)

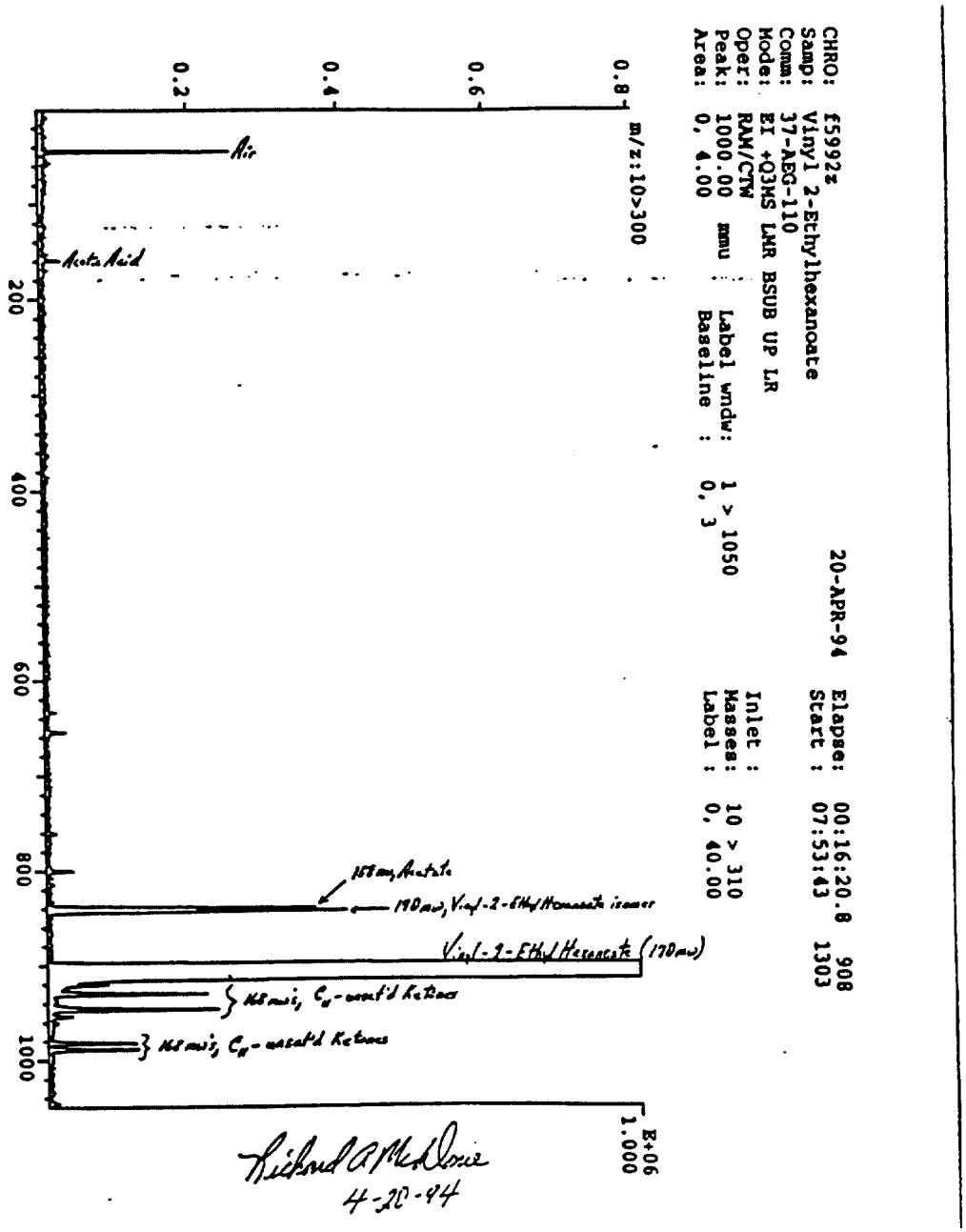


Figure 4 — Capillary Gas Chromatogram of 37-AEG-106 (vinyl 2-ethylhexanoate)

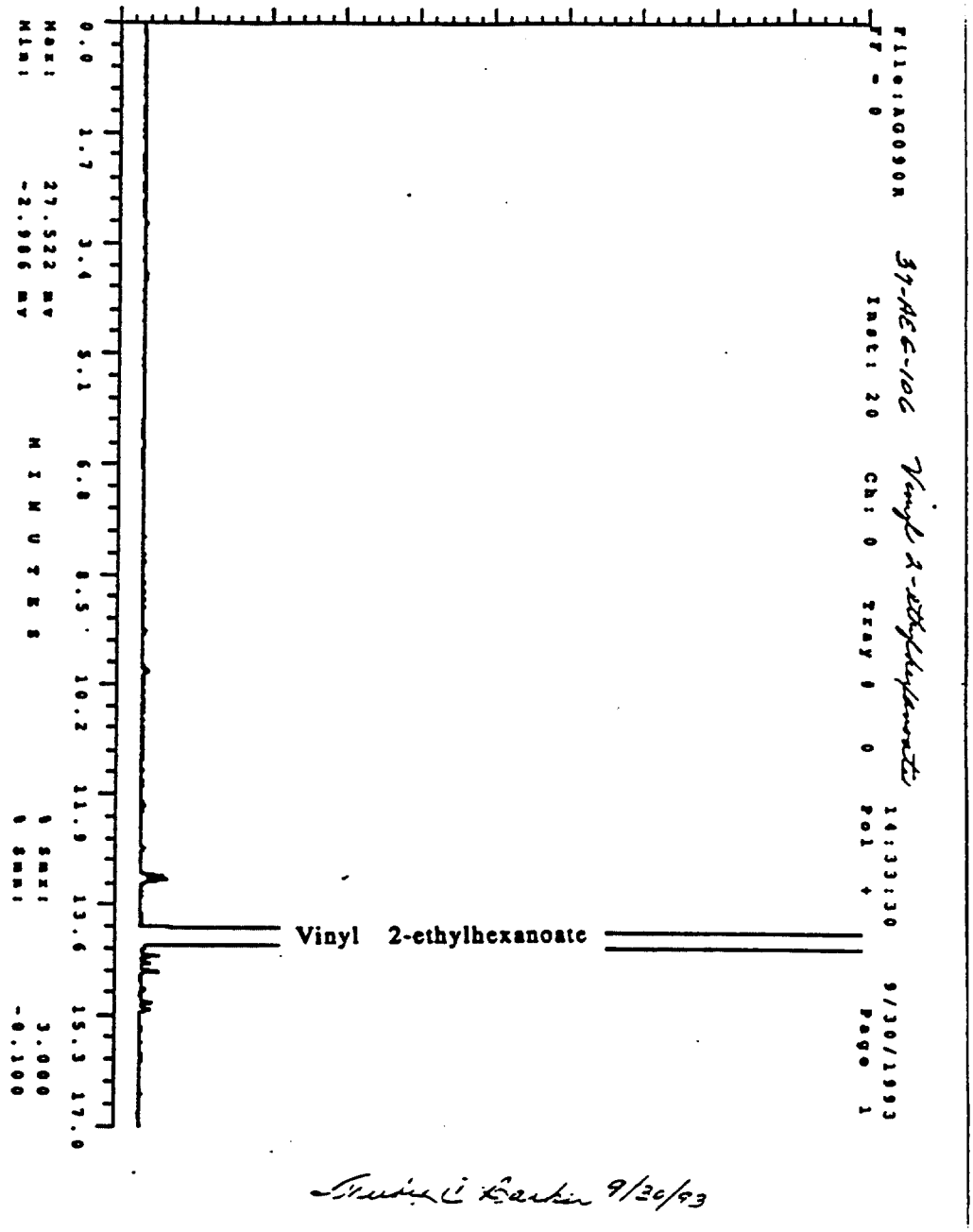
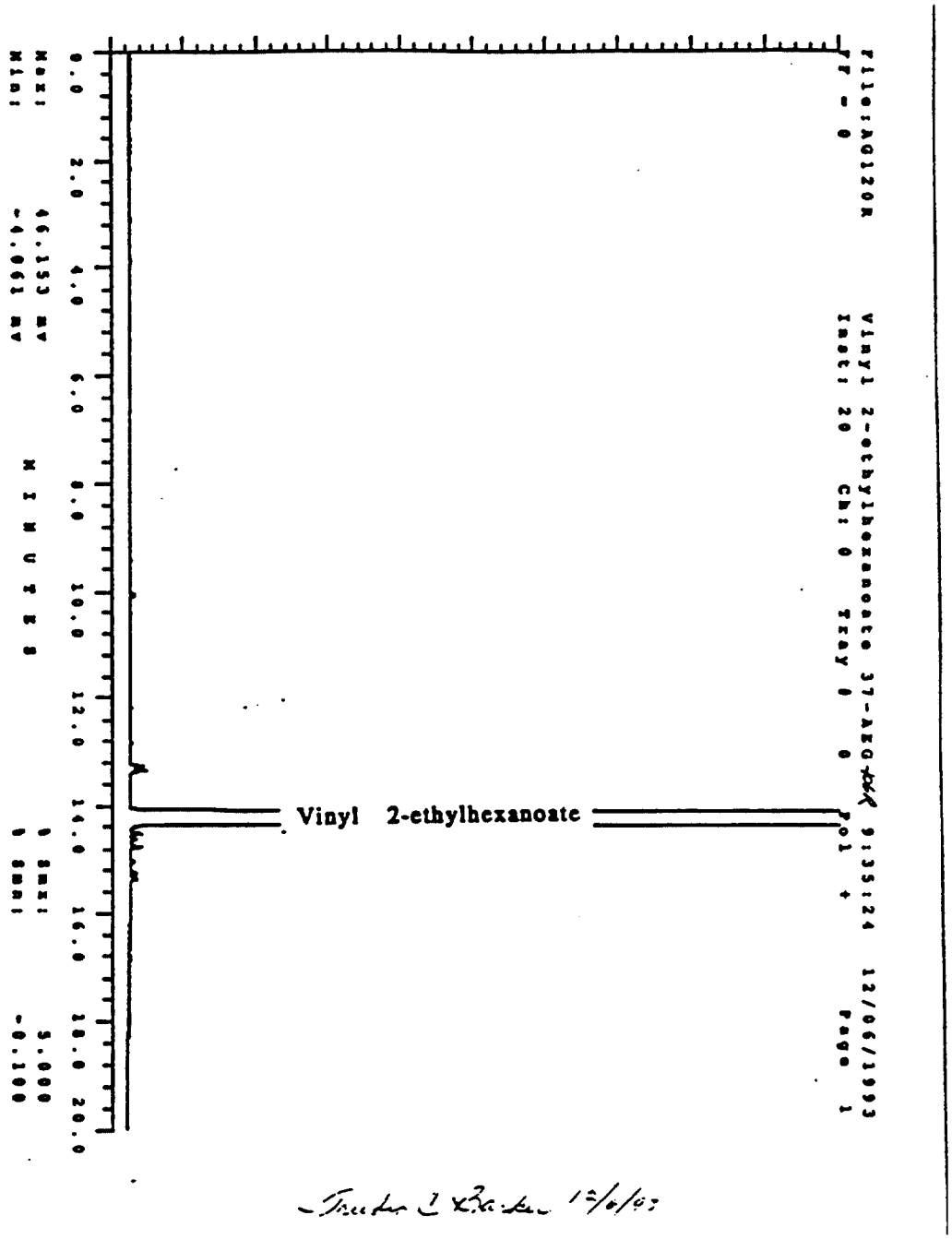


Figure 5 — Capillary Gas Chromatogram of 37-AEG-106R (vinyl 2-ethylhexanoate)



Study # 37-AEG-110

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:

9/27/93	9/29/93	10-8-93
Alexander E. Gabany, GLP Study Director	Denise L. Johnson, GLP Quality Assurance Unit (QAU) Representative	Richard C. Wise, Manager of Product Safety, SCMD, Sponsor
date	date	date

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 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.

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 5/10/94	Denise L. Johnson 5/11/94	Walter P. Miller 5/12/94
Nancy A. Broyles, Date	Denise L. Johnson, Date	Walter P. Miller, Ph. D., Date
GLP Study Director	GLP Quality Assurance Unit (QAU) Representative	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.

Inspection		Date QAU Report Issued	
Date	Type	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 5-19-94
Denise L. Johnson, QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Anatomic Pathology Report

(45 Pages)

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SUMMARY

Male and female Fischer 344 rats, purchased from Harlan Sprague Dawley Inc., Indianapolis, IN, were gavaged with 0, 50, 200, 1000, or 2000 mg/kg/day of vinyl 2-ethylhexanoate in corn oil vehicle for 10 doses over a 14 day period (except for the 2000 mg/kg/day group rats which only received 2 doses) to determine any possible toxic effects. Five males and 3 females in the 2000 mg/kg/day group died or were sacrificed moribund during the dosing period. The surviving high dose group rats and 6 rats/group/sex of the remaining dose groups were euthanized on Study Day 15. Because the nervous system tissues were considered to be potential target organs, 3 rats/group/sex from the sacrificed animal groups were perfused with fixative in preparation for a complete neurotoxicity examination. Two of the 2000 mg/kg/day group males which were sacrificed moribund were also perfused in an attempt to save their tissues for neuropathology evaluations. An abbreviated necropsy was performed on the perfused animals. A complete necropsy was performed on all of the nonperfused animals in the study, including those rats which died during the dosing period. Selected tissues were collected from all rats and preserved in fixative. Microscopic examinations were performed on selected tissues for all animals. A complete set of tissues from the nervous system was examined microscopically for the perfused rats.

The only gross lesions found in this study which may be attributed to chemical treatment were dilation/distention of the urinary bladder in 2 males from the 2000 mg/kg/day group which died or were sacrificed moribund during the study. The lesions may be indicative of loss of nerve function of the bladder.

Significant microscopic lesions, which were attributed to vinyl 2-ethylhexanoate treatment were found in the spinal cord and/or the brain stem (medulla oblongata/pons area) of the 3 females and the spinal cord only of 1 male from the 2000 mg/kg/day group which were sacrificed at Day 15 and were perfused. Both lesions were slight and were generally graded minimal. Brain lesions consisted of vacuolation/spongiosis of the white matter, mainly in the midline in the region of the medial longitudinal fasciculus. Spinal cord lesions consisted of vacuolation of the white matter of the ventral funiculi, affecting 1 or more levels of the cord in each female and the cervical cord only in the 1 male. Nerve fiber degeneration of the cervical spinal cord was evident in 2 high dose group females in conjunction with vacuolation. Similar lesions were not seen in the 2000 mg/kg/day group rats which were found dead or sacrificed moribund during the dosing period, nor in any rats receiving less than 2000 mg/kg/day.

INTRODUCTION

The objectives of this study were to evaluate the toxicity of 4 dose levels of vinyl 2-ethylhexanoate in Fischer 344 rats when administered by gavage and to establish dose levels for a potential 90-day gavage study. The nervous system was considered to be a potential target organ, based on the biochemical similarity of this chemical to other compounds previously tested.

MATERIALS AND METHODS

Necropsy - Nonperfused Rats

Three rats/sex/group, including all high dose group rats which died during the dosing period (3 females and 3 males), were immersion fixed in this study.

Surviving rats were anesthetized with halothane 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 with mainstem bronchi
- brain
  - cerebral cortex
  - cerebellar cortex
  - medulla/pons
- pituitary
- thyroid/parathyroid
- thymic region
- trachea
- heart
- sternum (including marrow)
- salivary gland
- liver
- spleen
- kidneys
- adrenals
- pancreas
- testes
- epididymis
- prostate
- seminal vesicles
- ovaries
- vagina
- uterus
  - corpus and cervix
- aorta
- skin
- esophagus
- stomach
- duodenum
- jejunum
- ileum
- cecum
- colon
- rectum
- urinary bladder
- lymph nodes
  - mesenteric
  - non-mesenteric
- mammary gland (females)
- skeletal muscle
  - (gastrocnemius)
- peripheral nerve (sciatic)
- tibial nerve
- eyes
- femur (including articular surface)
- spinal cord

Tails were saved as animal identification.

Lungs were inflated with formalin infusion through the trachea.

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

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

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

Rats which died on study or were sacrificed moribund were necropsied as they were found. Rats which died were necropsied and their tissues collected and fixed in the same manner as the nonperfused rats which were sacrificed, except that organ weights were not obtained.

Two male rats from the 2000 mg/kg/day group were sacrificed moribund during the dosing period. These rats were perfused when they were found and their tissues collected and processed as described below for perfused rats.

Histopathology - Nonperfused Rats

Microscopic examinations were performed on the brains, sciatic nerves, tibial nerves, and gross lesions for all nonperfused rats. In addition, microscopic examinations were performed on the livers and kidneys of all rats and the testes of males for all nonperfused animals from the 0, 1000, and 2000 mg/kg/day groups.

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. Statistical evaluations are considered to be valid only for tissues in which 6 animals were evaluated, as evaluations of fewer than 6 animals does not provide an adequate sample size.

Necropsy - Perfused Rats

Three rats/sex/group were anesthetized with an i.p. injection of a mixture of Euthanasia-6 Solution (Veterinary Laboratories, Inc., Lenexa, KS), and heparin. When a deep plane of surgical anesthesia had been induced (as determined by the disappearance of all observable reflexes, including the toe pinch and corneal reflexes), the chest cavity was opened and a cannula placed through the apex of the heart into the left ventricular chamber. Ten percent neutral (phosphate) buffered formalin (NBF) was then infused through this catheter into the left ventricle using a gravity feed perfusion apparatus. When the right ventricle began to bulge outward, the lateral wall of this ventricle was incised to allow the perfusion fluid to exit. Approximately 250 to 500 ml of fixative was perfused through each rat.

After perfusion fixation, the animals received an abbreviated necropsy consisting of an examination of the tissues listed below.
The calvaria and the dorsal arches of the vertebrae were removed and the sciatic nerve and its branches were exposed but left *in situ*. The following tissues were removed and immersion fixed in NBF:

- gross lesions
- brain
  - cerebral cortex
  - cerebellar cortex
  - medulla/pons
- spinal cord
- dorsal root ganglia
- dorsal and ventral nerve roots
- Gasserian ganglia
- sciatic nerve
- tibial nerve
- sural and peroneal nerves
- liver[1]
- kidneys[1]
- lungs[2]
- testes[1]
- ovaries[2]
- tail (animal identification)

[1]These tissues were examined for animals from the control and high dose groups only.

[2]No microscopic examination was performed on these tissues.

Spinal cord sections included cervical, thoracic and lumbar regions. Two cross sections at the level of the cervical swelling, 1 cross section from the thoracic and lumbar sections, and 2 longitudinal sections from the cervical region (1 above and 1 below the level of the cervical swelling) were included.

Histopathology - Perfused Rats

Microscopic examinations were performed on the above tissues for 3 rats/sex/group.

The liver, kidneys, testes, and any gross lesions found in perfused rats were prepared and stained in the same manner as is described above for the immersion fixed tissues. The findings for these tissues are reported in the same tables as the findings for the nonperfused rats in order to create an adequate sample for statistical evaluation.

The sections of brain, spinal cord, Gasserian ganglia, nerve roots, and dorsal root ganglia were embedded in paraffin. Five to 6 micron sections of each of these tissues were prepared and stained with hematoxylin and eosin, luxol fast blue, and the Bielschowsky's technique. The peripheral nerves were embedded in glycol methacrylate, sectioned at 2 microns, and stained with hematoxylin and eosin, toluidine blue, and the Bielschowsky's technique.

Microscopic findings for the nervous system tissues of perfused rats were recorded separately and are presented in separate tables which allow for input of findings for different neuroanatomic locations. Thirty-eight neuroanatomic locations were specifically designated, although many more (that is, all areas

of every section) were examined. If a designated neuroanatomic structure was not evaluated (because it was not present within the sections examined), it was designated as "missing." Microscopic findings were graded as to severity into five categories (minimal, mild, moderate, marked, and severe).

Statistics were not performed on the neuropathology findings for perfused rats because a sample size of 3 rats/group does not result in statistical significance with the Fischer's Exact Test regardless of the incidence of lesions.

RESULTS AND DISCUSSION

The gross lesions found in this study are presented in Tables 1-2 for male rats and 3-4 for females. Lesions for rats which were sacrificed and for those which died or were sacrificed moribund on study are presented separately in the tables. Gross lesions were infrequent in most tissues, and most lesions which were observed were related to changes in color, size, shape, or consistency of various organs or tissues. The only gross lesions which may represent a treatment related effect was dilation/distention of the urinary bladder, which was present in 2 males from the 2000 mg/kg/day group which died or were sacrificed moribund during the dosing period. While bladder distention can occur simply as a result of depression, it can be a sign of spinal cord damage with loss of nerve control to the bladder. An additional high dose group male which died had submucosal hemorrhage of the bladder wall. The cause was not determined.

Three rats/sex from the 2000 mg/kg/day group which died or were sacrificed moribund had meningeal hemorrhage of their brains. This lesion is commonly seen in rats which are found dead and which were not exsanguinated prior to death. It is attributed to a combination of meningeal congestion and autolytic degeneration of meningeal vessels. It is not considered to be due to treatment with vinyl 2-ethylhexanoate in this study. Spinal cord hemorrhage was reported in 1 sacrificed female from the 50 mg/kg/day group. The finding is believed to involve the meninges only, as there was no corroborating microscopic lesion of the spinal cord in this animal. Color change of various tissues was reported for many animals, particularly animals which died on study. In most cases, these findings were attributed to congestion in animals which were not exsanguinated prior to necropsy.

The microscopic lesions found in this study are presented in Tables 5 through 9 for males and 10 through 13 for females. As with the gross findings, the lesions for rats which were sacrificed and those which died on study are presented separately in the tables. Tables 9 (males) and 13 (females) present the combined findings for all animals on study, except for the findings of the nervous system tissues for the 3 rats/group which were perfused. Lesions of the nervous system for the perfused rats are presented separately in Tables 6 (rats sacrificed at day 15) and 8 (rats sacrificed moribund during the dosing period) for males and Table 11 for females.

Significant microscopic findings, which were attributed to treatment with vinyl 2-ethylhexanoate were found in the spinal cord and/or brain stem of the 3 perfused female rats from the 2000 mg/kg/day group, all of whom were

sacrificed at day 15, and in the spinal cord only of the 1 male from this group which survived to sacrifice and was perfused. Brain lesions consisted of minimal vacuolation/spongiosis of the pons and/or medulla of 2 of the 3 perfused females. Lesions were located along the midline of the brain stem in the region of the medial longitudinal fasciculus. Spinal cord lesions affected 2 or 3 levels of the cord of all 3 perfused females, with the cervical cord lesions being most prominent. Cord lesions were graded minimal or mild and consisted of vacuolation and/or fiber degeneration of the ventral funiculi. The cervical spinal cord was the only site of lesions in the 1 affected male. Neither brain nor spinal cord lesions were observed in the 2000 mg/kg/day group males which were sacrificed moribund during the dosing period and were then perfused. Brain lesions were also not observed in any of the 2000 mg/kg/day group rats which died on study.

One perfused female rat from the 1000 mg/kg/day group had a single focus of nerve fiber degeneration in the tibial nerve. Because the lesion did not occur in the high dose group females, it is considered to be an incidental finding in this study.

One perfused control group female had minimal vacuolation/spongiosis of the vestibular nuclei area of the brain of unknown cause.

One 2000 mg/kg/day group female, which was found dead, had hydropic degeneration and hyperplasia of the squamous mucosa of the stomach, which may be due to irritation from chemical treatment.

There were no microscopic lesions in tissues other than those discussed above which were attributed to treatment with vinyl 2-ethylhexanoate. A few lesions, although not related to chemical treatment, are worthy of mention, due to the frequency of their occurrence. These include congestion and/or hemorrhage in various tissues, particularly in rats which died on study from the high dose group. Tissues most commonly affected include the thymus, lungs, and the meningeal vessels of the brain. Congestion is an expected finding in rats which die on study, as these animals are not exsanguinated prior to necropsy. Hemorrhage, particularly in the thymus, may occur as an agonal finding. However, it can also result from chest compression during restraint of rats for blood collection prior to sacrifice. Thymic hemorrhage of varying severity occurred in similar frequency in all exposure groups, including controls, and was not considered to be related to chemical treatment. One 2000 mg/kg/day group female which was found dead had moderate multifocal liver necrosis which is attributed to an agonal impairment of the circulation. Two high dose group males, including 1 of the males with bladder distention reported grossly and a second male which was found dead, had submucosal hemorrhage of the bladder wall. The cause of the lesion was not determined. The tissues of the more severely affected male were too autolyzed to evaluate for contributing conditions such as cystitis.

CONCLUSION

Exposure of rats to vinyl 2-ethylhexanoate by gavage produced significant mortality to animals receiving 2000 mg/kg/day, with males being slightly more sensitive. Lesions suggestive of irritation of the nonglandular stomach were

present in only 1 high dose group female. Toxic lesions of the brain, consisting of characteristic vacuolation of the white matter tracts of the brain stem, affected the 3 females which survived to sacrifice from the 2000 mg/kg/day group. Similar brain lesions were not seen in the 1 male from this group which survived to sacrifice, nor in the lower dose group rats of either sex. Vacuolation and, in 2 females, nerve fiber degeneration, were present in the ventral white matter tracts of the spinal cord in the 3 females and 1 male of the 2000 mg/kg/day group which survived the dosing period. Spinal cord lesions were not evident in the lower dose group rats. There were no lesions of peripheral neuropathy which were attributed to chemical treatment. There were no lesions in tissues other than the stomach and nervous system which were attributed to vinyl 2-ethylhexanoate treatment in this test system.

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
STOMACH					
COLOR CHANGE, FOCAL/MULTIFOCAL	0	2	1	1	0
LYMPH ND, S-MAN					
COLOR CHANGE, FOCAL/MULTIFOCAL	1	0	0	0	0
SIZE INCREASE	0	0	0	1	0
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	3	2	3	0	0
COLOR CHANGE, DIFFUSE	0	1	0	2	0
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL	1	2	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 FISCHER 344 RATS
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	-	-	-	-	5
TOTAL BODY					
STAINED	-	-	-	-	5
STOMACH					
COLOR CHANGE, FOCAL/MULTIFOCAL	-	-	-	-	2
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE	-	-	-	-	5
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	-	-	-	-	2
BRAIN					
MENINGEAL HEMORRHAGE	-	-	-	-	3
LUNGS					
COLOR CHANGE, DIFFUSE	-	-	-	-	5
URINARY BLADDER					
DILATATION/DISTENTION	-	-	-	-	2
HEMORRHAGE	-	-	-	-	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 FISCHER 344 RATS
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	6	6	6	3
ADIPOSE TISSUE					
THICKER THAN NORMAL	0	1	0	0	0
STOMACH					
COLOR CHANGE, DIFFUSE	0	1	0	0	0
COLOR CHANGE, FOCAL/MULTIFOCAL	0	1	0	0	0
COLON					
HEMORRHAGE	0	1	0	0	0
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE	1	0	0	0	0
SIZE INCREASE	0	1	0	0	0
LYMPH ND, MED					
COLOR CHANGE, DIFFUSE	0	0	1	0	0
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	0	2	2	2	0
COLOR CHANGE, DIFFUSE	1	0	0	1	0
SPINAL CORD					
HEMORRHAGE	0	1	0	0	0
EYE					
OPACITY	0	0	0	0	1
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL	0	1	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

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	-	-	-	-	3
TOTAL BODY					
STAINED	-	-	-	-	2
STOMACH					
COLOR CHANGE, DIFFUSE	-	-	-	-	1
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE	-	-	-	-	3
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL	-	-	-	-	1
BRAIN					
MENINGEAL HEMORRHAGE	-	-	-	-	3
OVARIES					
COLOR CHANGE, DIFFUSE	-	-	-	-	1
LUNGS					
COLOR CHANGE, DIFFUSE	-	-	-	-	3

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 FISCHER 344 RATS
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	6	6	6	6	1
STOMACH					
TOTAL NUMBER EXAMINED	0	2	1	1	0
EXAMINED, UNREMARKABLE	-	0	0	1	-
GASTRITIS	-	**2**	**1**	**0**	-
MILD	-	2	1	0	-
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	1
EXAMINED, UNREMARKABLE	5	-	-	2	1
MONONUCLEAR CELL INFILTRATE(S)	**1**	-	-	**1**	**0**
MINIMAL	1	-	-	1	0
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	0	0	1	0
SINUS ERYTHROCYTOSIS	**1**	-	-	**0**	-
MILD	1	-	-	0	-
PLASMACYTOSIS	**0**	-	-	**1**	-
MODERATE	0	-	-	1	-
LYMPHOID HYPERPLASIA	**0**	-	-	**1**	-
MODERATE	0	-	-	1	-
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	2	0	1	1	0
SINUS ERYTHROCYTOSIS	**2**	-	**1**	1	-
MODERATE	2	-	1	0	-
MARKED	0	-	0	1	-
MASTOCYTOSIS	**1**	-	**0**	**0**	-
MODERATE	1	-	0	0	-
THYMIC REGION					
TOTAL NUMBER EXAMINED	3	3	3	2	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

None significantly different from control group

TABLE 5 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
THYMIC REGION (CONTINUED)					
HEMORRHAGE	**3**	**3**	**3**	**2**	-
MINIMAL	3	2	1	1	-
MILD	0	0	1	0	-
MODERATE	0	1	1	1	-
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	1	3	3	2	-
MENINGEAL HEMORRHAGE	**1**	**0**	**0**	**1**	-
MINIMAL	1	0	0	1	-
BRAIN HEMORRHAGE	**1**	**0**	**0**	**0**	-
MINIMAL	1	0	0	0	-
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
TESTES					
TOTAL NUMBER EXAMINED	6	0	0	3	1
EXAMINED, UNREMARKABLE	6	-	-	3	1
LUNGS					
TOTAL NUMBER EXAMINED	1	2	0	1	0
EXAMINED, UNREMARKABLE	0	2	-	0	-
ALVEOLAR HISTIOCYTOSIS	**1**	**0**	-	**0**	-
MILD	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

None significantly different from control group

TABLE 5 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	6	1
LUNGS (CONTINUED)					
HEMORRHAGE	**0**	**0**	**-**	**1**	**-**
MINIMAL	0	0	-	1	-
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	1
EXAMINED, UNREMARKABLE	5	-	-	3	1
TUBULAR REGENERATION/BASOPHILIA	**1**	**-**	**-**	**0**	**0**
MINIMAL	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

None significantly different from control group

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
MENINGES					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	2	3	1
PERIVASCULAR INFILTRATES	**0**	**0**	**1**	**0**	**0**
MINIMAL	0	0	1	0	0
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
AMYGDALA					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	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 6 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
THALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
HYPOTHALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
MIDBRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SUBSTANTIA NIGRA					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CEREBELLAR W.M.					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
ANT COMMISSURE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
EXTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
INTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CORPUS CALLOSUM					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
FORNIX					
TOTAL NUMBER EXAMINED	3	2	3	3	1
EXAMINED, UNREMARKABLE	3	2	3	3	1
MISSING	0	1	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

TABLE 6 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
CEREBELLAR CTX					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
CEREBELLAR NUC					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
VESTIBULAR NUC					
TOTAL NUMBER EXAMINED	3	3	2	3	1
EXAMINED, UNREMARKABLE	3	3	2	3	1
MISSING	0	0	1	0	0
PONS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
MEDULLA OBL					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
OLFACTORY BULB					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
OPTIC N/CHIASM					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
TRIGEMINAL TRACT					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SPINAL CORD, CRV					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	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 6 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	1
SPINAL CORD, CRV(CONTINUED)					
VACUOLATION	**0**	**0**	**0**	**0**	**1**
MINIMAL	0	0	0	0	1
SPINAL CORD, THR					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	2	3	3	1
PERIVASCULAR INFILTRATES	**0**	**1**	**0**	**0**	**0**
MILD	0	1	0	0	0
GASSERIAN GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
SCIATIC NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
TIBIAL NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	1
EXAMINED, UNREMARKABLE	3	3	3	3	1
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED	3	2	3	3	1
EXAMINED, UNREMARKABLE	3	2	3	3	1
MISSING	0	1	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

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	5
STOMACH					
TOTAL NUMBER EXAMINED	0	0	0	0	1
TOO AUTOLYZED TO EVALUATE	-	-	-	-	1
GASTRITIS	-	-	-	-	1
MINIMAL	-	-	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	0	0	0	0	5
EXAMINED, UNREMARKABLE	-	-	-	-	5
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	0	0	0	5
SINUS ERYTHROCYTOSIS	-	-	-	-	5
MILD	-	-	-	-	3
MODERATE	-	-	-	-	2
LYMPH ND, REN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
SINUS ERYTHROCYTOSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
THYMIC REGION					
TOTAL NUMBER EXAMINED	0	0	0	0	2
HEMORRHAGE	-	-	-	-	2
MILD	-	-	-	-	1
MODERATE	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	0	0	0	0	3
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 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	5
BRAIN (CONTINUED)					
MENINGEAL CONGESTION	-	-	-	-	**2**
MILD	-	-	-	-	1
MODERATE	-	-	-	-	1
MENINGEAL HEMORRHAGE	-	-	-	-	**1**
MINIMAL	-	-	-	-	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
TESTES					
TOTAL NUMBER EXAMINED	0	0	0	0	5
EXAMINED, UNREMARKABLE	-	-	-	-	5
LUNGS					
TOTAL NUMBER EXAMINED	0	0	0	0	5
CONGESTION	-	-	-	-	**5**
MODERATE	-	-	-	-	2
MARKED	-	-	-	-	3
INTRAALVEOLAR CELLULAR DEBRIS	-	-	-	-	**1**
MILD	-	-	-	-	1
HEMORRHAGE	-	-	-	-	**1**
MODERATE	-	-	-	-	1
PNEUMONITIS	-	-	-	-	**1**
MODERATE	-	-	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	0	0	0	0	5
EXAMINED, UNREMARKABLE	-	-	-	-	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

TABLE 7 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	5
URINARY BLADDER					
TOTAL NUMBER EXAMINED	0	0	0	0	3
ECTASIA	-	-	-	-	2
MODERATE	-	-	-	-	1
MARKED	-	-	-	-	1
HEMORRHAGE	-	-	-	-	2
MINIMAL	-	-	-	-	1
MODERATE	-	-	-	-	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 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
MENINGES					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
AMYGDALA					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 8 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
THALAMUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
HYPOTHALAMUS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
MIDBRAIN					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SUBSTANTIA NIGRA					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CEREBELLAR W.M.					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
ANT COMMISSURE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
EXTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
INTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CORPUS CALLOSUM					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
FORNIX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
CEREBELLAR CTX					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 8 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
CEREBELLAR NUC					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
VESTIBULAR NUC					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PONS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
MEDULLA OBL					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
OLFACTORY BULB					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
OPTIC N/CHIASM					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
TRIGEMINAL TRACT					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL CORD, CRV					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL CORD, THR					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 8 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ALL ANIMALS FOUND DEAD/SACRIFICED MORIBUND
PERFUSED MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS FOUND DEAD/SACRIFICED MORIBUND	-	-	-	-	2
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
GASSERIAN GANG					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
SCIATIC NERVE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
TIBIAL NERVE					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED	0	0	0	0	2
EXAMINED, UNREMARKABLE	-	-	-	-	2

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 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
STOMACH					
TOTAL NUMBER EXAMINED	0	2	1	1	1
EXAMINED, UNREMARKABLE	-	0	0	1	0
TOO AUTOLYZED TO EVALUATE	-	0	0	0	1
GASTRITIS	-	**2**	**1**	**0**	**1**
MINIMAL	-	0	0	0	1
MILD	-	2	1	0	0
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	5	-	-	2	6
MONONUCLEAR CELL INFILTRATE(S)	**1**	-	-	**1**	**0**
MINIMAL	1	-	-	1	0
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	0	0	1	5
SINUS ERYTHROCYTOSIS	**1**	-	-	**0**	**5**
MILD	1	-	-	0	3
MODERATE	0	-	-	0	2
PLASMACYTOSIS	**0**	-	-	**1**	**0**
MODERATE	0	-	-	1	0
LYMPHOID HYPERPLASIA	**0**	-	-	**1**	**0**
MODERATE	0	-	-	1	0
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	2	0	1	1	0
SINUS ERYTHROCYTOSIS	**2**	-	**1**	**1**	-
MODERATE	2	-	1	0	-
MARKED	0	-	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

None significantly different from control group

TABLE 9 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
LYMPH ND, MED (CONTINUED)					
MASTOCYTOSIS	**1**	**-**	**0**	**0**	**-**
MODERATE	1	-	0	0	-
LYMPH ND, REN					
TOTAL NUMBER EXAMINED	0	0	0	0	1
SINUS ERYTHROCYTOSIS	**-**	**-**	**-**	**-**	**1**
MODERATE	-	-	-	-	1
THYMIC REGION					
TOTAL NUMBER EXAMINED	3	3	3	2	2
HEMORRHAGE	**3**	**3**	**3**	**2**	**2**
MINIMAL	3	2	1	1	0
MILD	0	0	1	0	1
MODERATE	0	1	1	1	1
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	1	3	3	2	1
MENINGEAL CONGESTION	**0**	**0**	**0**	**0**	**2**
MILD	0	0	0	0	1
MODERATE	0	0	0	0	1
MENINGEAL HEMORRHAGE	**1**	**0**	**0**	**1**	**1**
MINIMAL	1	0	0	1	1
BRAIN HEMORRHAGE	**1**	**0**	**0**	**0**	**0**
MINIMAL	1	0	0	0	0
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 9 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
TESTES					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	6	-	-	3	6
LUNGS					
TOTAL NUMBER EXAMINED	1	2	0	1	5
EXAMINED, UNREMARKABLE	0	2	-	0	0
CONGESTION	**0**	**0**	**-**	**0**	**5**
MODERATE	0	0	-	0	2
MARKED	0	0	-	0	3
ALVEOLAR HISTIOCYTOSIS	**1**	**0**	**-**	**0**	**0**
MILD	1	0	-	0	0
INTRAALVEOLAR CELLULAR DEBRIS	**0**	**0**	**-**	**0**	**1**
MILD	0	0	-	0	1
HEMORRHAGE	**0**	**0**	**-**	**1**	**1**
MINIMAL	0	0	-	1	0
MODERATE	0	0	-	0	1
PNEUMONITIS	**0**	**0**	**-**	**0**	**1**
MODERATE	0	0	-	0	1
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	5	-	-	3	6
TUBULAR REGENERATION/BASOPHILIA	**1**	**-**	**-**	**0**	**0**
MINIMAL	1	-	-	0	0
URINARY BLADDER					
TOTAL NUMBER EXAMINED	0	0	0	0	3

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 9 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
MALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
URINARY BLADDER (CONTINUED)					
ECTASIA	-	-	-	-	**2**
MODERATE	-	-	-	-	1
MARKED	-	-	-	-	1
HEMORRHAGE	-	-	-	-	**2**
MINIMAL	-	-	-	-	1
MODERATE	-	-	-	-	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

None significantly different from control group

TABLE 10
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
ADIPOSE TISSUE					
TOTAL NUMBER EXAMINED	0	1	0	0	0
STEATITIS	-	1	-	-	-
MILD	-	1	-	-	-
STOMACH					
TOTAL NUMBER EXAMINED	0	2	0	0	0
LYMPHOCYTIC INFILTRATE(S)	-	1	-	-	-
MILD	-	1	-	-	-
GASTRITIS	-	2	-	-	-
MILD	-	2	-	-	-
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	3
EXAMINED, UNREMARKABLE	5	-	-	1	3
MONONUCLEAR CELL INFILTRATE(S)	1	-	-	2	0
MINIMAL	1	-	-	2	0
COLON					
TOTAL NUMBER EXAMINED	0	1	0	0	0
HEMORRHAGE	-	1	-	-	-
MARKED	-	1	-	-	-
COLITIS	-	1	-	-	-
MODERATE	-	1	-	-	-
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	1	0	0	0
EXAMINED, UNREMARKABLE	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

None significantly different from control group

TABLE 10 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
LYMPH ND, S-MAN (CONTINUED)					
SINUS ERYTHROCYTOSIS	**1**	**0**	-	-	-
MODERATE	1	0	-	-	-
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	0	1	1	2	0
SINUS ERYTHROCYTOSIS	-	**1**	**1**	**2**	-
MILD	-	1	0	1	-
MODERATE	-	0	0	1	-
MARKED	-	0	1	0	-
MASTOCYTOSIS	-	**1**	**0**	**0**	-
MILD	-	1	0	0	-
THYMIC REGION					
TOTAL NUMBER EXAMINED	1	2	3	3	0
EXAMINED, UNREMARKABLE	0	1	1	3	-
HEMORRHAGE	**1**	**1**	**2**	**0**	-
MINIMAL	0	0	1	0	-
MILD	1	1	1	0	-
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	0
EXAMINED, UNREMARKABLE	3	3	3	3	-
EYE					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED	0	1	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

None significantly different from control group

TABLE 10 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
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	6	6	6	3
LUNGS (CONTINUED)					
PNEUMONITIS	-	1	-	-	-
MILD	-	1	-	-	-
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	3
EXAMINED, UNREMARKABLE	6	-	-	3	3

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 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
MENINGES					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
AMYGDALA					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 11 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
THALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
HYPOTHALAMUS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
MIDBRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SUBSTANTIA NIGRA					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
CEREBELLAR W.M.					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
ANT COMMISSURE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
EXTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
INTERNAL CAPSULE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
CORPUS CALLOSUM					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
FORNIX					
TOTAL NUMBER EXAMINED	2	3	1	2	1
EXAMINED, UNREMARKABLE	2	3	1	2	1
MISSING	1	0	2	1	2
CEREBELLAR CTX					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 11 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
CEREBELLAR NUC					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
VESTIBULAR NUC					
TOTAL NUMBER EXAMINED	3	3	3	3	2
EXAMINED, UNREMARKABLE	2	3	3	3	2
MISSING	0	0	0	0	1
VACUOLATION/SPONGIOSIS	**1**	**0**	**0**	**0**	**0**
MINIMAL	1	0	0	0	0
PONS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION/SPONGIOSIS	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
MEDULLA OBL					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION/SPONGIOSIS	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
OLFACTORY BULB					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
OPTIC N/CHIASM					
TOTAL NUMBER EXAMINED	2	3	3	3	3
EXAMINED, UNREMARKABLE	2	3	3	3	3
MISSING	1	0	0	0	0
TRIGEMINAL TRACT					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SPINAL CORD, CRV					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	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 11 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
SPINAL CORD, CRV(CONTINUED)					
VACUOLATION	**0**	**0**	**0**	**0**	**3**
MINIMAL	0	0	0	0	2
MILD	0	0	0	0	1
NERVE FIBER DEGENERATION	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
SPINAL CORD, THR					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	1
VACUOLATION	**0**	**0**	**0**	**0**	**2**
MINIMAL	0	0	0	0	2
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
GASSERIAN GANG					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
SCIATIC NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
TIBIAL NERVE					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	2	3

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 11 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 15
PERFUSED FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	3	3	3	3	3
NUMBER OF ANIMALS SACRIFICED	3	3	3	3	3
TIBIAL NERVE (CONTINUED)					
NERVE FIBER DEGENERATION	**0**	**0**	**0**	**1**	**0**
MINIMAL	0	0	0	1	0
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3

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 12
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	3
STOMACH					
TOTAL NUMBER EXAMINED	0	0	0	0	1
CONGESTION	-	-	-	-	1
MODERATE	-	-	-	-	1
HYDROPIC DEGENERATION, SQUAMOUS MUCOSA	-	-	-	-	1
MODERATE	-	-	-	-	1
SQUAMOUS MUCOSAL HYPERPLASIA	-	-	-	-	1
MILD	-	-	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	1
HEPATOCELLULAR VACUOLATION	-	-	-	-	1
MINIMAL	-	-	-	-	1
HEPATOCELLULAR NECROSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	1
SINUS ERYTHROCYTOSIS	-	-	-	-	2
MILD	-	-	-	-	1
MARKED	-	-	-	-	1
MASTOCYTOSIS	-	-	-	-	1
MODERATE	-	-	-	-	1
THYMIC REGION					
TOTAL NUMBER EXAMINED	0	0	0	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 12 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

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	-	-	-	-	3
THYMIC REGION (CONTINUED)					
HEMORRHAGE	-	-	-	-	1
MARKED	-	-	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED	0	0	0	0	3
MENINGEAL CONGESTION	-	-	-	-	3
MILD	-	-	-	-	1
MODERATE	-	-	-	-	2
MENINGEAL HEMORRHAGE	-	-	-	-	1
MODERATE	-	-	-	-	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3
OVARIES					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED	0	0	0	0	3
CONGESTION	-	-	-	-	3
MODERATE	-	-	-	-	1
MARKED	-	-	-	-	2
HEMORRHAGE	-	-	-	-	1
MODERATE	-	-	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	0	0	0	0	3
EXAMINED, UNREMARKABLE	-	-	-	-	3

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 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
ADIPOSE TISSUE					
TOTAL NUMBER EXAMINED	0	1	0	0	0
STEATITIS	-	1	-	-	-
MILD	-	1	-	-	-
STOMACH					
TOTAL NUMBER EXAMINED	0	2	0	0	1
CONGESTION	-	0	-	-	1
MODERATE	-	0	-	-	1
HYDROPIC DEGENERATION, SQUAMOUS MUCOSA	-	0	-	-	1
MODERATE	-	0	-	-	1
LYMPHOCYTIC INFILTRATE(S)	-	1	-	-	0
MILD	-	1	-	-	0
GASTRITIS	-	2	-	-	0
MILD	-	2	-	-	0
SQUAMOUS MUCOSAL HYPERPLASIA	-	0	-	-	1
MILD	-	0	-	-	1
LIVER					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	5	-	-	1	4
HEPATOCELLULAR VACUOLATION	0	-	-	0	1
MINIMAL	0	-	-	0	1
MONONUCLEAR CELL INFILTRATE(S)	1	-	-	2	0
MINIMAL	1	-	-	2	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

None significantly different from control group

TABLE 13 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
LIVER (CONTINUED)					
HEPATOCELLULAR NECROSIS	**0**	-	-	**0**	**1**
MODERATE	0	-	-	0	1
COLON					
TOTAL NUMBER EXAMINED	0	1	0	0	0
HEMORRHAGE	-	**1**	-	-	-
MARKED	-	1	-	-	-
COLITIS	-	**1**	-	-	-
MODERATE	-	1	-	-	-
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED	1	1	0	0	3
EXAMINED, UNREMARKABLE	0	1	-	-	1
SINUS ERYTHROCYTOSIS	**1**	**0**	-	-	**2**
MILD	0	0	-	-	1
MODERATE	1	0	-	-	0
MARKED	0	0	-	-	1
MASTOCYTOSIS	**0**	**0**	-	-	**1**
MODERATE	0	0	-	-	1
LYMPH ND, MED					
TOTAL NUMBER EXAMINED	0	1	1	2	0
SINUS ERYTHROCYTOSIS	-	**1**	**1**	**2**	-
MILD	-	1	0	1	-
MODERATE	-	0	0	1	-
MARKED	-	0	1	0	-
MASTOCYTOSIS	-	**1**	**0**	**0**	-
MILD	-	1	0	0	-
THYMIC REGION					
TOTAL NUMBER EXAMINED	1	2	3	3	1
EXAMINED, UNREMARKABLE	0	1	1	3	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

None significantly different from control group

TABLE 13 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
THYMIC REGION (CONTINUED)					
HEMORRHAGE	**1**	**1**	**2**	**0**	**1**
MINIMAL	0	0	1	0	0
MILD	1	1	1	0	0
MARKED	0	0	0	0	1
BRAIN					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	0
MENINGEAL CONGESTION	**0**	**0**	**0**	**0**	**3**
MILD	0	0	0	0	1
MODERATE	0	0	0	0	2
MENINGEAL HEMORRHAGE	**0**	**0**	**0**	**0**	**1**
MODERATE	0	0	0	0	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
NERVE, TIBIAL					
TOTAL NUMBER EXAMINED	3	3	3	3	3
EXAMINED, UNREMARKABLE	3	3	3	3	3
EYE					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
OVARIES					
TOTAL NUMBER EXAMINED	0	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED	0	1	0	0	3

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 13 (Continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

DATA FOR ALL ANIMALS ON STUDY
FEMALES

GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	6	6	6	6	6
NUMBER OF ANIMALS	6	6	6	6	6
LUNGS (CONTINUED)					
CONGESTION	-	**0**	-	-	**3**
MODERATE	-	0	-	-	1
MARKED	-	0	-	-	2
PNEUMONITIS	-	**1**	-	-	**0**
MILD	-	1	-	-	0
HEMORRHAGE	-	**0**	-	-	**1**
MODERATE	-	0	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED	6	0	0	3	6
EXAMINED, UNREMARKABLE	6	-	-	3	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

None significantly different from control group

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Clinical Pathology Report

(9 Pages)

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SUMMARY

Male and female Fischer 344 rats (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. The 2000 mg/kg/day groups of rats were only dosed for 2 days then recovered for 13 days before blood was collected. Blood samples were collected for evaluation at Day 15.

Only 1 male and 3 female rats in the highest dose group lived to Day 15 for clinical pathology testing. Male rats in the 1000 mg/kg/day group had a decrease in erythrocyte count, hemoglobin, and hematocrit values with an increase in segmented neutrophils.

Female rats in the 200 and 1000 mg/kg/day groups had a decrease in total erythrocytes, hemoglobin and hematocrit values. Platelet counts and lymphocytes were decreased in the 1000 mg/kg/day group of female rats. The decreases in the 200 mg/kg/day group were considered to be equivocal due to the small magnitude of the change and the lack of a similar response in male rats. The surviving 2000 mg/kg/day group of female rats, which were not treated after the third dose, had a decrease in hemoglobin, hematocrit, platelet, total leukocytes, and lymphocyte values with an increase in neutrophils.

MATERIALS AND METHODS

In this study, male and female Fischer 344 rats were dosed with vinyl 2-ethylhexanoate by gavage dose 5 days/week for 2 weeks. The 2000 mg/kg/day groups of rats were only dosed for 2 days then recovered for 13 days before blood was collected. 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 rats prior to sacrifice. Rats were not fasted prior to bleeding. All analyses were performed in a predetermined alternating group order.

Hematology

Approximately 1.0 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 tests.

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 rats are presented in Tables 1 and 2. The individual results for these animals are included in Appendix 10.

Only 1 male and 3 female rats in the highest dose group lived to Day 15 for clinical pathology testing. These animals were not treated with the test substance after the second daily dose. The 2000 mg/kg/day group of female rats had 3 deaths in the group but the survivors had a decrease in hemoglobin, hematocrit, platelet, total leukocytes, lymphocyte and basophil values with an increase in neutrophils (not statistically significant). The change in basophil count was not considered to be biologically significant due to the small magnitude of the change and the rare occurrence of basophils in rats.

Male rats in the 1000 mg/kg/day group had a decrease in erythrocyte count, hemoglobin, and hematocrit values. Several rats in this group also had an increase in segmented neutrophils, although the mean value was not statistically significant.

Female rats showed the same indications of anemia. Female rats in the 200 and 1000 mg/kg/day groups had a decrease in hemoglobin and hematocrit values. Total erythrocyte counts were decreased in the 1000 mg/kg/day group of female rats with a trend toward lower values in the 200 mg/kg/day group. Platelet counts and lymphocytes were decreased in the 1000 mg/kg/day group of female rats. The decrease in monocytes in the 50 and 1000 mg/kg/day groups was not

considered to be biologically significant due to the small magnitude of the change and lack of a dose response.

CONCLUSION

Only 1 male and 3 female rats in the highest dose group lived to Day 15 for clinical pathology testing. The 2000 mg/kg/day group of female rats, which only received 2 doses, had 3 deaths in the group but the survivors had a decrease in hemoglobin, hematocrit, platelet, total leukocytes, and lymphocyte values with an increase in neutrophils. Both sexes displayed values consistent with a dose related anemia in the 1000 mg/kg/day male and female rats. Male rats in the 1000 mg/kg/day group had a decrease in erythrocyte count, hemoglobin, and hematocrit values with an increase in segmented neutrophils. Female rats in the 200 and 1000 mg/kg/day groups had a decrease in total erythrocytes, hemoglobin and hematocrit values. The decreases in the 200 mg/kg/day group were considered to be equivocal due to the small magnitude of the change and the lack of a similar response in male rats. Platelet counts and lymphocytes were decreased in the 1000 mg/kg/day group of female rats.

Clinical Pathologist: Douglas A. Neptun 9/22/94
Douglas A. Neptun, B.S., CC(NRCC), MT(ASCP) Date

REFERENCE

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

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SEPTEMBER 20, 1994

TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
LEUKOCYTES ($10^3/\mu l$)					
MEAN	6.7	6.7	6.7	6.5	6.0
S.D.	1.28	0.98	1.06	0.75	0.00
N	6	6	6	6	1
ERYTHROCYTES ($10^6/\mu l$)					
MEAN	7.99	8.16	7.96	7.53**	7.80
S.D.	0.192	0.329	0.313	0.204	0.000
N	6	6	6	6	1
HEMOGLOBIN (g/dl)					
MEAN	16.6	16.8	16.4	15.5**	16.2
S.D.	0.08	0.40	0.55	0.32	0.00
N	6	6	6	6	1
HEMATOCRIT (%)					
MEAN	44.6	45.3	44.3	41.8**	43.4
S.D.	0.97	1.43	1.74	1.14	0.00
N	6	6	6	6	1
MEAN CORPUSCULAR VOLUME (μm^3)					
MEAN	56.	56.	56.	56.	56.
S.D.	0.8	0.5	0.5	1.0	0.0
N	6	6	6	6	1
MEAN CORPUSCULAR HEMOGLOBIN (pg)					
MEAN	20.7	20.5	20.7	20.6	20.8
S.D.	0.42	0.36	0.42	0.27	0.00
N	6	6	6	6	1
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)					
MEAN	37.2	37.0	37.1	37.2	37.4
S.D.	0.66	0.43	0.67	0.91	0.00
N	6	6	6	6	1
PLATELETS ($10^3/\mu l$)					
MEAN	661.	620.	670.	658.	609.
S.D.	34.6	15.4	48.0	28.2	0.0
N	6	3	5	4	1
SEGMENTED NEUTROPHILS ($10^3/\mu l$)					
MEAN	0.48	0.57	0.55	0.96	0.47
S.D.	0.095	0.170	0.275	0.570	0.000
N	6	6	6	6	1
LYMPHOCYTES ($10^3/\mu l$)					
MEAN	6.00	5.94	5.90	5.29	5.31
S.D.	1.205	0.862	1.140	0.792	0.000
N	6	6	6	6	1
MONOCYTES ($10^3/\mu l$)					
MEAN	0.13	0.12	0.12	0.19	0.13
S.D.	0.051	0.073	0.027	0.098	0.000
N	6	6	6	6	1

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

TABLE 1 (continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

MALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
BASOPHILS ($10^3/\mu l$)					
MEAN	0.03	0.01	0.03	0.02	0.02
S.D.	0.020	0.013	0.015	0.020	0.000
N	6	6	6	6	1
EOSINOPHILS ($10^3/\mu l$)					
MEAN	0.05	0.04	0.05	0.05	0.03
S.D.	0.012	0.052	0.026	0.036	0.000
N	6	6	6	6	1
BANDED NEUTROPHILS (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
LARGE MONOCYTES (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
IMMATURE GRANULOCYTES (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
IMMATURE ERYTHROCYTES (cells/µl)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	
NUCLEATED RBCs (cells/100 WBCs)					
MEAN		0.	0.	0.	
S.D.		0.0	0.0	0.0	
N		3	1	2	

None significantly different from control group

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
LEUKOCYTES ($10^3/\mu l$)					
MEAN	7.1	7.3	7.2	6.0	5.7*
S.D.	0.58	0.75	1.10	1.14	0.99
N	6	6	6	6	3
ERYTHROCYTES ($10^6/\mu l$)					
MEAN	7.95	7.95	7.75	7.49**	7.76
S.D.	0.097	0.235	0.152	0.192	0.272
N	6	6	6	6	3
HEMOGLOBIN (g/dl)					
MEAN	16.8	16.7	16.5*	15.8**	16.1**
S.D.	0.16	0.23	0.30	0.31	0.20
N	6	6	6	6	3
HEMATOCRIT (%)					
MEAN	44.6	44.6	43.4*	41.8**	43.1*
S.D.	0.69	1.37	0.90	0.93	0.83
N	6	6	6	6	3
MEAN CORPUSCULAR VOLUME (μm^3)					
MEAN	56.	56.	56.	56.	56.
S.D.	0.8	0.5	0.0	0.6	1.2
N	6	6	6	6	3
MEAN CORPUSCULAR HEMOGLOBIN (pg)					
MEAN	21.2	21.1	21.3	21.1	20.8
S.D.	0.33	0.46	0.31	0.23	0.52
N	6	6	6	6	3
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)					
MEAN	37.7	37.5	38.0	37.7	37.4
S.D.	0.50	0.75	0.57	0.23	0.34
N	6	6	6	6	3
PLATELETS ($10^3/\mu l$)					
MEAN	677.	697.	667.	575.**	544.**
S.D.	58.3	25.0	34.8	31.1	0.0
N	6	5	6	6	1
SEGMENTED NEUTROPHILS ($10^3/\mu l$)					
MEAN	0.50	0.66	0.51	0.45	0.95
S.D.	0.162	0.437	0.216	0.108	0.153
N	6	6	6	6	3
LYMPHOCYTES ($10^3/\mu l$)					
MEAN	6.37	6.45	6.52	5.40*	4.50**
S.D.	0.510	0.473	0.891	1.076	0.909
N	6	6	6	6	3
MONOCYTES ($10^3/\mu l$)					
MEAN	0.13	0.10*	0.12	0.09*	0.14
S.D.	0.025	0.028	0.038	0.022	0.040
N	6	6	6	6	3

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

TABLE 2 (continued)
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 15

FEMALES

GROUP: MG/KG/DAY	0	50	200	1000	2000
BASOPHILS ($10^3/\mu l$)					
MEAN	0.03	0.03	0.03	0.03	0.01**
S.D.	0.011	0.015	0.008	0.010	0.012
N	6	6	6	6	3
EOSINOPHILS ($10^3/\mu l$)					
MEAN	0.05	0.07	0.06	0.05	0.06
S.D.	0.020	0.018	0.005	0.011	0.066
N	6	6	6	6	3
BANDED NEUTROPHILS (cells/μl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
LARGE MONOCYTES (cells/μl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
IMMATURE GRANULOCYTES (cells/μl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
IMMATURE ERYTHROCYTES (cells/μl)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2
NUCLEATED RBCs (cells/100 WBCs)					
MEAN		0.			0.
S.D.		0.0			0.0
N		1			2

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

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Individual Animal Fate Data

(4 pages)

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL ANIMAL FATE

MALES

GROUP	ANIMAL	TYPE OF DEATH	AGE IN WEEKS	DATE OF DEATH	DAYS ON STUDY
0 MG/KG/DAY	9499	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9518	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9507	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9509	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9495	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9517	SCHEDULED SACRIFICE	9	8-NOV-93	15
50 MG/KG/DAY	9487	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9500	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9496	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9485	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9513	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9510	SCHEDULED SACRIFICE	9	8-NOV-93	15
200 MG/KG/DAY	9504	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9489	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9523	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9482	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9512	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9497	SCHEDULED SACRIFICE	9	8-NOV-93	15
1000 MG/KG/DAY	9511	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9520	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9502	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9521	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9498	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9503	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
2000 MG/KG/DAY	9505	FOUND DEAD	7	27-OCT-93	3
	9514	SACRIFICED MORIBUND	7	27-OCT-93	3
	9519	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9506	SACRIFICED MORIBUND	7	27-OCT-93	3
	9484	FOUND DEAD	7	27-OCT-93	3
	9486	FOUND DEAD	8	28-OCT-93	4

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL ANIMAL FATE

FEMALES

GROUP	ANIMAL	TYPE OF DEATH	AGE IN WEEKS	DATE OF DEATH	DAYS ON STUDY
0 MG/KG/DAY	9537	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9532	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9571	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9540	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9552	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9531	SCHEDULED SACRIFICE	9	8-NOV-93	15
50 MG/KG/DAY	9557	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9566	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9559	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9570	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9556	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9563	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
200 MG/KG/DAY	9542	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9569	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9560	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9551	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9555	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9548	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
1000 MG/KG/DAY	9545	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9544	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9530	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9568	SCHEDULED SACRIFICE	9	8-NOV-93	15
	9543	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9553	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
2000 MG/KG/DAY	9549	FOUND DEAD	7	27-OCT-93	3
	9541	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9533	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9562	FOUND DEAD	7	27-OCT-93	3
	9538	SCHEDULED SACRIFICE-PERFUSED	9	8-NOV-93	15
	9561	FOUND DEAD	7	27-OCT-93	3

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Individual Clinical Observation Data

(9 Pages)

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TABLE 1

VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

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

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 MG/KG/DAY					
	9499	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9518	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9507	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9509	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9495	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9517	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
50 MG/KG/DAY					
	9487	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9500	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9496	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9485	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9513	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9510	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
200 MG/KG/DAY					
	9504	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9489	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9523	NORMAL	11	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
		BEHAVIOR/CNS	2	13- 14	ANIMAL ALWAYS LEANED TO RIGHT SIDE
		EYES/EARS/NOSE	1	6	EXOPHTHALMIA (EYL 1)
	9482	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9512	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9497	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
1000 MG/KG/DAY					
	9511	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 MG/KG/DAY					
	9520	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9502	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9521	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9498	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9503	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
2000 MG/KG/DAY					
	9505	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	FOUND DEAD
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	1	2	UROGENITAL AREA WETNESS
			1	2	COLD EXTREMITIES (LAL 1)
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
		EYES/EARS/NOSE	1	2	PERINASAL ENCRUSTATION
		EXCRETA	1	2	LOOSE FECES
	9514	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	SACRIFICED MORIBUND
		BEHAVIOR/CNS	2	2- 3	PROSTRATION
			2	2- 3	HYPOACTIVE
		BODY	2	2- 3	UROGENITAL AREA WETNESS
			2	2- 3	COLD EXTREMITIES (LAL 2)
		CARDIO-PULMONARY	2	2- 3	LABORED RESPIRATION
		EXCRETA	1	2	LOOSE FECES
	9519	NORMAL	13	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	1	2	UROGENITAL AREA WETNESS
			1	2	COLD EXTREMITIES (LAL 1)
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
		EXCRETA	1	2	LOOSE FECES
	9506	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	SACRIFICED MORIBUND
		BEHAVIOR/CNS	2	2- 3	PROSTRATION
			2	2- 3	HYPOACTIVE
		BODY	2	2- 3	UROGENITAL AREA WETNESS
			2	2- 3	COLD EXTREMITIES (LAL 2)
		CARDIO-PULMONARY	2	2- 3	LABORED RESPIRATION

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
2000 MG/KG/DAY					
	9506	EXCRETA	1	2	LOOSE FECES
	9484	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	FOUND DEAD
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	1	2	URINE STAINS
			1	2	COLD EXTREMITIES (LAL 1)
			1	2	UROGENITAL AREA WETNESS
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
		EXCRETA	1	2	LOOSE FECES
	9486	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	4	FOUND DEAD
		BEHAVIOR/CNS	2	2- 3	PROSTRATION
			2	2- 3	HYPOACTIVE
		BODY	2	2- 3	UROGENITAL AREA WETNESS
			2	2- 3	COLD EXTREMITIES (LAL 2)
		CARDIO-PULMONARY	2	2- 3	LABORED RESPIRATION
		EYES/EARS/NOSE	1	3	LACRIMATION (EYB 1)
		EXCRETA	1	2	LOOSE FECES

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 MG/KG/DAY					
	9537	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9532	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9571	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9540	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9552	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9531	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
50 MG/KG/DAY					
	9557	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9566	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9559	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9570	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9556	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9563	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
200 MG/KG/DAY					
	9542	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9569	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9560	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9551	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9555	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9548	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
1000 MG/KG/DAY					
	9545	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9544	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 MG/KG/DAY					
	9530	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9568	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE
	9543	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
	9553	NORMAL	14	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
2000 MG/KG/DAY					
	9549	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	FOUND DEAD
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	1	2	UROGENITAL AREA WETNESS
			1	2	COLD EXTREMITIES (LAL 1)
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
	9541	NORMAL	8	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
		BEHAVIOR/CNS	2	2- 3	PROSTRATION
			2	2- 3	HYPOACTIVE
		BODY	2	6- 7	URINE STAINS
			4	4- 7	UNKEMPT
			4	2- 5	UROGENITAL AREA WETNESS
			2	2- 3	COLD EXTREMITIES (LAL 2)
		CARDIO-PULMONARY	2	2- 3	LABORED RESPIRATION
		EYES/EARS/NOSE	2	4- 5	PERINASAL ENCRUSTATION
			2	4- 5	PERIOCULAR ENCRUSTATION (EYB 2)
	9533	NORMAL	4	1- 5	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	2	2- 3	UROGENITAL AREA WETNESS
			1	2	COLD EXTREMITIES (LAL 1)
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
		EYES/EARS/NOSE	10	6- 15	OPACITY (EYL 10)
	9562	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	FOUND DEAD
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	1	2	UROGENITAL AREA WETNESS
			1	2	COLD EXTREMITIES (LAL 1)
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
		EXCRETA	1	2	LOOSE FECES

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
2000 MG/KG/DAY					
	9538	NORMAL	11	1- 14	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	15	SCHEDULED SACRIFICE-PERFUSED
		BEHAVIOR/CNS	1	2	PROSTRATION
			1	2	HYPOACTIVE
		BODY	3	2- 4	UROGENITAL AREA WETNESS
			1	2	COLD EXTREMITIES (LAL 1)
		CARDIO-PULMONARY	1	2	LABORED RESPIRATION
	9561	NORMAL	1	1	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	3	FOUND DEAD
		BEHAVIOR/CNS	2	2- 3	PROSTRATION
			2	2- 3	HYPOACTIVE
		BODY	2	2- 3	UROGENITAL AREA WETNESS
			2	2- 3	COLD EXTREMITIES (LAL 2)
		CARDIO-PULMONARY	2	2- 3	LABORED RESPIRATION

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Individual Body Weight Data

(13 Pages)

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TABLE 1

VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

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 FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9499	130.4	136.5	146.9	165.7
9518	138.9	146.9	161.7	180.2
9507	139.1	146.8	154.8	172.6
9509	144.3	151.4	163.1	180.8
9495	142.5	152.5	163.8	190.8
9517	159.0	166.1	177.1	195.3
MEAN	142.4	150.0	161.2	180.9
S.D.	9.44	9.70	10.07	11.00
N	6	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9487	136.8	147.1	156.8	175.1
9500	128.7	134.5	142.0	153.9
9496	137.5	139.8	148.3	165.6
9485	143.6	152.6	165.9	186.1
9513	143.9	154.3	163.4	188.3
9510	151.4	156.0	158.2	172.3
MEAN	140.3	147.4	155.8	173.5
S.D.	7.77	8.64	9.09	12.85
N	6	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9504	133.5	141.8	150.5	170.8
9489	141.9	157.0	166.4	190.5
9523	140.4	152.1	153.4	177.6
9482	143.1	148.6	157.6	179.6
9512	145.4	152.7	163.0	185.0
9497	154.7	164.2	171.6	188.0
MEAN	143.2	152.7	160.4	181.9
S.D.	6.93	7.57	8.04	7.32
N	6	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9511	130.6	137.1	150.4	177.0
9520	142.1	154.6	165.9	189.7
9502	137.6	141.5	152.0	173.3
9521	145.6	150.9	168.8	200.9
9498	146.7	156.1	176.3	204.9
9503	149.0	154.6	173.0	196.8
MEAN	141.9	149.1	164.4	190.4
S.D.	6.83	7.92	10.83	12.92
N	6	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9505	134.1	dead		
9514	133.1	dead		
9519	140.9	140.7	153.9	178.5
9506	147.6	dead		
9484	147.6	dead		
9486	152.5	dead		
MEAN	142.6	140.7	153.9	178.5
S.D.	7.91	0.00	0.00	0.00
N	6	1	1	1

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9537	103.1	107.7	105.8	124.4
9532	111.3	114.8	114.5	131.1
9571	112.3	117.1	119.4	133.4
9540	111.4	114.1	117.7	130.4
9552	113.9	119.5	119.9	137.4
9531	120.5	125.4	131.6	136.4
MEAN	112.1	116.4	118.2	132.2
S.D.	5.58	5.92	8.39	4.75
N	6	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9557	109.9	113.1	118.8	130.9
9566	108.6	115.9	121.1	129.1
9559	111.4	117.0	121.1	135.2
9570	116.1	121.9	124.4	138.8
9556	118.2	123.8	129.9	140.6
9563	122.3	126.1	131.0	146.2
MEAN	114.4	119.6	124.4	136.8
S.D.	5.32	5.05	5.03	6.38
N	6	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9542	112.4	118.7	123.9	134.2
9569	108.2	112.2	119.5	124.1
9560	116.1	118.2	127.8	139.7
9551	113.3	119.3	122.3	136.1
9555	111.7	117.2	118.9	134.5
9548	116.2	124.2	119.4	133.3
MEAN	113.0	118.3	122.0	133.6
S.D.	2.99	3.86	3.48	5.20
N	6	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9545	105.6	112.9	118.7	134.0
9544	113.3	119.5	123.8	129.8
9530	112.7	117.1	116.9	129.4
9568	107.7	115.0	113.9	129.0
9543	118.2	123.0	124.8	143.1
9553	120.0	118.0	129.0	140.4
MEAN	112.9	117.6	121.2	134.3
S.D.	5.65	3.53	5.62	6.13
N	6	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	1	4	8	15
ANIMAL				
9549	114.0	dead		
9541	104.8	90.1	111.7	126.9
9533	112.4	104.7	114.7	132.7
9562	110.8	dead		
9538	120.2	117.1	117.7	137.1
9561	121.1	dead		
MEAN	113.9	104.0	114.7	132.2
S.D.	6.11	13.54	3.03	5.12
N	6	3	3	3

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Individual Food Consumption Data

(13 Pages)

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TABLE 1

VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

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 FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9499	12.1	13.4	12.6
9518	13.2	14.9	13.5
9507	12.5	14.1	11.4
9509	14.1	14.7	13.5
9495	13.3	15.8	15.0
9517	13.7	15.2	14.7
MEAN	13.2	14.7	13.4
S.D.	0.75	0.83	1.30
N	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9487	13.0	14.8	13.8
9500	12.1	12.9	11.7
9496	11.6	13.9	12.4
9485	13.6	15.8	13.8
9513	13.6	14.7	13.1
9510	12.3	14.6	12.2
MEAN	12.7	14.5	12.8
S.D.	0.83	0.96	0.88
N	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
MALES GROUP: 200 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9504	13.6	13.8	13.1
9489	15.3	16.1	13.5
9523	15.1	12.5	14.4
9482	12.7	14.4	13.8
9512	12.6	14.0	13.1
9497	15.1	16.4	15.0
MEAN	14.1	14.5	13.8
S.D.	1.24	1.47	0.76
N	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9511	11.1	13.5	13.4
9520	13.8	15.9	14.0
9502	11.6	13.9	12.8
9521	12.5	16.1	16.0
9498	12.7	16.6	16.1
9503	12.3	16.0	15.5
MEAN	12.3	15.3	14.6
S.D.	0.91	1.29	1.40
N	6	6	6

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9505	r/dead		
9514	r/dead		
9519	9.7	16.4	15.9
9506	r/dead		
9484	r/dead		
9486	r/dead		
MEAN	9.7	16.4	15.9
S.D.	0.00	0.00	0.00
N	1	1	1

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9537	9.5	9.4	10.6
9532	11.0	10.6	10.4
9571	11.8	11.7	10.8
9540	10.0	10.6	10.5
9552	10.7	11.2	10.5
9531	12.2	13.7	10.6
MEAN	10.9	11.2	10.6
S.D.	1.03	1.44	0.15
N	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9557	11.0	12.0	10.8
9566	10.2	11.9	6.5
9559	11.0	11.9	11.3
9570	10.7	11.8	11.0
9556	11.4	13.0	10.5
9563	11.9	13.0	12.6
MEAN	11.0	12.3	10.4
S.D.	0.58	0.58	2.08
N	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
FEMALES GROUP: 200 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9542	10.6	12.6	10.7
9569	10.1	13.0	9.5
9560	10.8	12.7	11.1
9551	11.1	12.1	10.2
9555	10.4	10.8	10.6
9548	10.9	11.4	10.5
MEAN	10.6	12.1	10.4
S.D.	0.34	0.87	0.55
N	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

DAY	4	8	15
ANIMAL			
9545	9.4	11.3	10.1
9544	11.1	12.9	10.6
9530	10.8	11.5	10.5
9568	10.2	10.4	10.2
9543	9.8	12.0	11.0
9553	8.8	12.0	11.1
MEAN	10.0	11.7	10.6
S.D.	0.88	0.82	0.40
N	6	6	6

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
FEMALES GROUP: 2000 MG/KG/DAY

DAY	4	8	15
ANIMAL			
9549	r/dead		
9541	2.1	14.2	13.8
9533	5.2	13.9	12.4
9562	r/dead		
9538	5.3	11.9	13.2
9561	r/dead		
MEAN	4.2	13.3	13.2
S.D.	1.82	1.23	0.72
N	3	3	3

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Functional Observational Battery Individual Data and Information

(56 Pages)

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Note: Units of measurements for the following are:

Grip Strength - Kilograms (kg)
Body Temperature - Degrees Celsius (°C)
Body Weight - Grams (g)
Hind Leg Splay - Centimeters (cm)

TABLE 1

VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

FUNCTIONAL OBSERVATIONAL BATTERY INDIVIDUAL DATA AND INFORMATION

ABBREVIATIONS

The following abbreviations and shortened names for the functional observations may appear in this appendix.

Parameter	Abbreviation	Corresponding Name
Cage Posture	NormAwake	Normal/awake
	NormAslee	Normal/asleep
	SideProst	On side/prostrate
	StomProst	On stomach/prostrate
Handling Reactivity	Resists	Slight/moderate resistance
	Limp	Animal limp
	HighResis	High resistance/aggressive
Gait	Uncoord	Uncoordinated
	Splayed	Limbs exaggerated/splayed
	OnToes	Walks on toes
Body Position	OnSide	On side
	OnStomach	On stomach
Breathing Pattern	Mthbreath	Mouthbreathing
	Rapid	Rapid respiration
Clonic Convulsions	RunFits	Running fits
(cageside and open field)	ExplJumps	Explosive jumps
Tremor or Jerk	WholeBody	Whole body
(cageside and open field)		
Unusual Behavior	Retropuls	Retropulsion
	HeadBob	Head bobbing/weaving
	Stereotyp	Stereotypy
Arousal	Active	Active/alert
	Hyperact	Hyperactive/hyperalert
	InacAlert	Inactive/alert
	NotAlert	Inactive/not alert
Palpebral Closure	WideOpen	Wide open
(cageside and open field)	SlDroop	Slightly drooping
	HalfShut	Halfway shut
	Shut	Completely shut
Approach, Startle, and	None	No reaction
Tail Pinch Responses	Noticable	Noticeable reaction
	Exagger	Exaggerated reaction
Fur Appearance	UrinStain	Urine stains/wetness
Additional Observations	Emaciated	Emaciation
	Dehydrat	Dehydration
	Exophthal	Exophthalmus
Air Righting	FeetCoord	Feet/coordinated
	FeetUncoor	Feet/uncoordinated

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9499	9518	9507	9509	9495	9517
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9487	9500	9496	9485	9513	9510
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9504	9489	9523	9482	9512	9497
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9511	9520	9502	9521	9498	9503
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9519
Cage Posture	NormAwake
Cage Palpebral Closure	WideOpen
Cage Twitch	None
Cage Tremor	None
Cage Spasm	None
Cage Jerk	None
Cage Clonic Convulsions	None
Cage Tonic Convulsions	None

RPT_NT:MRV2ECF1.IFO

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9499	9518	9507	9509	9495	9517
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	Normal	Normal	None	Normal	None
Urine	None	Present	Present	Present	Present	None
Piloerection	None	None	None	None	None	None
Rears	8	20	17	4	12	19
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.44	.71	.41	.49	.41	.56
Grip Strength #2 (fore)	.25	.48	.46	.36	.34	.33
Grip Strength #1 (hind)	.24	.35	.59	.51	.29	.39
Grip Strength #2 (hind)	.36	.11	.36	.44	.34	.46
Body Temperature	38.30	37.60	37.20	37.80	38.60	38.70
Body Weight	154.34	170.48	162.20	168.42	174.10	185.12
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.10	8.50	6.70	5.70	3.30	3.80
Hind Leg Splay #2	5.20	4.50	4.00	5.80	4.40	3.60

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9487	9500	9496	9485	9513	9510
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	Normal	Normal	None	None	Normal	None
Urine	Present	Present	Present	None	Present	Present
Piloerection	None	None	None	None	None	None
Rears	19	9	22	12	14	18
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Decreased
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.22	.47	.59	.43	.36	.77
Grip Strength #2 (fore)	.25	.68	.50	.37	.54	.42
Grip Strength #1 (hind)	.27	.24	.18	.33	.47	.38
Grip Strength #2 (hind)	.45	.45	.10	.15	.53	.41
Body Temperature	38.70	38.20	39.20	36.50	38.80	39.00
Body Weight	163.02	146.26	155.34	175.88	174.28	163.64
Air Righting	FeetCoord	FeetCoord	Back	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.20	4.60	4.70	4.00	3.40	5.80
Hind Leg Splay #2	4.80	6.00	3.40	5.00	3.40	4.30

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9504	9489	9523	9482	9512	9497
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Other[a]	Normal	Normal	Normal
			Present			
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	Normal	None	Normal	Normal	Normal	Normal
Urine	Present	None	Present	Present	None	None
Piloerection	None	None	None	None	None	None
Rears	19	19	8	20	23	16
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	None	Present	Present
Grip Strength #1 (fore)	.46	.42	.46	.29	.80	.38
Grip Strength #2 (fore)	.40	.51	.42	.25	.55	.38
Grip Strength #1 (hind)	.24	.34	.35	.34	.42	.36
Grip Strength #2 (hind)	.27	.59	.21	.43	.35	.39
Body Temperature	38.50	38.70	38.20	38.50	39.00	38.40
Body Weight	159.44	179.06	164.04	166.96	170.82	178.26
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.20	3.40	4.90	3.60	4.50	4.70
Hind Leg Splay #2	5.40	3.50	4.30	4.20	4.20	4.20

[a]Animal leaned to right side at all times

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9511	9520	9502	9521	9498	9503
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	Normal	Normal	None	None	None	None
Urine	Present	Present	None	Present	None	Present
Piloerection	None	None	None	None	None	None
Rears	15	19	22	14	15	9
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	None	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.27	.95	.50	.37	.34	.32
Grip Strength #2 (fore)	.39	.68	.43	.35	.38	.45
Grip Strength #1 (hind)	.35	.36	.18	.45	.40	.45
Grip Strength #2 (hind)	.21	.34	.38	.60	.32	.28
Body Temperature	37.80	38.50	38.50	38.50	38.60	38.00
Body Weight	161.22	176.50	159.24	180.40	186.86	181.14
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.10	6.00	6.00	4.70	5.30	4.00
Hind Leg Splay #2	4.90	5.40	4.80	5.90	5.90	4.60

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

MALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9519
Handling Reactivity	Resists
Ataxia	No
Gait	Normal
Body Position	Normal
Excessive Vocalization	None
Breathing Pattern	Normal
Twitch	None
Tremor	None
Spasm	None
Jerk	None
Clonic Convulsions	None
Tonic Convulsions	None
Unusual Behavior	None
Arousal	Active
Palpebral Closure	WideOpen
Defecation	Normal
Urine	Present
Piloerection	None
Rears	12
Approach Response	None
Startle Response	Noticable
Tail Pinch Response	Noticable
Pupil Size	Normal
Muscle Tone	Normal
Lacrimation	None
Salivation	None
Fur Appearance	Normal
Facial Crust	None
Additional Observations	None
Visual Placing	Present
Grip Strength #1 (fore)	.35
Grip Strength #2 (fore)	.39
Grip Strength #1 (hind)	.31
Grip Strength #2 (hind)	.39
Body Temperature	38.70
Body Weight	164.78
Air Righting	FeetCoord
Hind Leg Splay #1	4.70
Hind Leg Splay #2	4.80

RPT_NT:MRV2E2F1.IFO

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9499	9518	9507	9509	9495	9517
Cage Posture	NormAwake	NormAwake	NormAslee	NormAwake	NormAwake	NormAslee
Cage Palpebral Closure	WideOpen	WideOpen	Shut	WideOpen	SlDroop	Shut
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9487	9500	9496	9485	9513	9510
Cage Posture	NormAslee	NormAwake	NormAslee	NormAslee	NormAslee	NormAslee
Cage Palpebral Closure	Shut	WideOpen	Shut	Shut	Shut	Shut
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9504	9489	9523	9482	9512	9497
Cage Posture	NormAwake	NormAslee	NormAwake	NormAslee	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	Shut	WideOpen	Shut	SlDroop	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

TABLE 4
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9511	9520	9502	9521	9498	9503
Cage Posture	NormAwake	NormAwake	NormAslee	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	Shut	HalfShut	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9519
Cage Posture	NormAwake
Cage Palpebral Closure	WideOpen
Cage Twitch	None
Cage Tremor	None
Cage Spasm	None
Cage Jerk	None
Cage Clonic Convulsions	None
Cage Tonic Convulsions	None

RPT_NT:MRV2ECF2.IFO

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9499	9518	9507	9509	9495	9517
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	InacAlert
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	HalfShut
Defecation	None	Normal	Normal	None	Normal	None
Urine	None	Present	Present	Present	Present	None
Piloerection	None	None	None	None	None	None
Rears	7	1	8	5	4	0
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.68	.52	.58	.57	.61	.34
Grip Strength #2 (fore)	.51	.42	.37	.50	.87	.35
Grip Strength #1 (hind)	.39	.36	.49	.37	.39	.15
Grip Strength #2 (hind)	.33	.25	.37	.34	.38	.11
Body Temperature	38.50	38.60	38.40	38.20	38.10	38.40
Body Weight	158.96	173.26	166.20	170.06	177.76	187.20
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.00	3.40	4.50	4.40	3.70	2.80
Hind Leg Splay #2	3.90	4.10	4.60	3.60	4.50	3.60

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9487	9500	9496	9485	9513	9510
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	InacAlert	Active	Active	Active	Active
Palpebral Closure	WideOpen	SlDroop	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	Normal	None	None	None	None	None
Urine	Present	Present	Present	Present	Present	Present
Piloerection	None	None	None	None	None	None
Rears	7	2	11	5	4	4
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.38	.47	.32	.37	.39	.48
Grip Strength #2 (fore)	.27	.32	.54	.43	.38	.47
Grip Strength #1 (hind)	.39	.30	.28	.19	.25	.18
Grip Strength #2 (hind)	.19	.30	.30	.11	.46	.17
Body Temperature	38.20	38.00	38.10	38.10	38.10	38.10
Body Weight	165.48	147.32	158.84	177.48	180.88	168.00
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.40	3.90	2.80	3.80	3.80	4.30
Hind Leg Splay #2	4.20	4.20	3.20	3.70	4.00	5.70

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9504	9489	9523	9482	9512	9497
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	Other[a]	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	Normal	None	Normal
Urine	None	None	None	Present	None	None
Piloerection	None	None	None	None	None	None
Rears	8	14	2	11	8	5
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	None	Present	Present
Grip Strength #1 (fore)	.36	.73	.32	.53	.44	.49
Grip Strength #2 (fore)	.28	.58	.30	.40	.39	.37
Grip Strength #1 (hind)	.11	.33	.41	.41	.27	.33
Grip Strength #2 (hind)	.25	.21	.34	.26	.23	.17
Body Temperature	38.00	38.50	38.30	38.30	38.20	38.20
Body Weight	163.10	180.24	167.12	169.04	176.56	179.86
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.60	7.80	5.20	3.90	3.00	3.90
Hind Leg Splay #2	3.20	5.90	4.40	3.80	4.50	6.90

[a]Animal leaned to right side at all times

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9511	9520	9502	9521	9498	9503
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	Normal	None	None	Normal
Urine	None	None	None	Present	Present	Present
Piloerection	None	None	None	None	None	None
Rears	16	11	15	10	6	7
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.41	.37	.46	.56	.71	.37
Grip Strength #2 (fore)	.31	.32	.45	.37	.42	.32
Grip Strength #1 (hind)	.16	.42	.14	.30	.48	.45
Grip Strength #2 (hind)	.15	.23	.15	.15	.24	.35
Body Temperature	38.30	38.20	38.50	38.30	38.10	38.20
Body Weight	166.56	176.82	162.28	184.98	190.28	187.78
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	2.60	5.30	5.20	4.50	4.90	3.60
Hind Leg Splay #2	5.30	4.90	3.60	5.10	5.70	4.30

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

MALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9519
Handling Reactivity	Resists
Ataxia	No
Gait	Normal
Body Position	Normal
Excessive Vocalization	None
Breathing Pattern	Normal
Twitch	None
Tremor	None
Spasm	None
Jerk	None
Clonic Convulsions	None
Tonic Convulsions	None
Unusual Behavior	None
Arousal	Active
Palpebral Closure	WideOpen
Defecation	Normal
Urine	Present
Piloerection	None
Rears	7
Approach Response	Noticable
Startle Response	Noticable
Tail Pinch Response	Noticable
Pupil Size	Normal
Muscle Tone	Normal
Lacrimation	None
Salivation	None
Fur Appearance	Normal
Facial Crust	None
Additional Observations	None
Visual Placing	Present
Grip Strength #1 (fore)	.51
Grip Strength #2 (fore)	.60
Grip Strength #1 (hind)	.40
Grip Strength #2 (hind)	.36
Body Temperature	38.10
Body Weight	166.36
Air Righting	FeetCoord
Hind Leg Splay #1	4.90
Hind Leg Splay #2	4.10

RPT_NT:MRV2E2F2.IFO

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9499	9518	9507	9509	9495	9517
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAslee
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	Shut
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9487	9500	9496	9485	9513	9510
Cage Posture	NormAwake	NormAwake	NormAslee	NormAslee	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	Shut	Shut	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9504	9489	9523	9482	9512	9497
Cage Posture	NormAwake	NormAwake	NormAwake	NormAslee	NormAslee	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	Shut	Shut	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9511	9520	9502	9521	9498	9503
Cage Posture	NormAwake	NormAwake	NormAwake	NormAslee	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	Shut	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

MALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9519
Cage Posture	NormAwake
Cage Palpebral Closure	HalfShut
Cage Twitch	None
Cage Tremor	None
Cage Spasm	None
Cage Jerk	None
Cage Clonic Convulsions	None
Cage Tonic Convulsions	None

RPT_NT:MRV2ECF3.IFO

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9499	9518	9507	9509	9495	9517
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	InacAlert	Active	Active	InacAlert	Active	InacAlert
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	SlDroop
Defecation	None	Normal	Normal	Normal	None	None
Urine	None	Present	Present	None	None	None
Piloerection	None	None	None	None	None	None
Rears	2	3	6	0	4	1
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.41	.34	.42	.40	.51	.32
Grip Strength #2 (fore)	.41	.20	.26	.26	.30	.46
Grip Strength #1 (hind)	.20	.32	.35	.34	.52	.28
Grip Strength #2 (hind)	.15	.19	.29	.16	.26	.18
Body Temperature	38.30	39.00	38.20	39.10	38.10	38.20
Body Weight	161.96	174.36	166.72	171.92	182.90	189.96
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.60	4.50	4.10	5.60	3.90	4.90
Hind Leg Splay #2	5.60	4.00	3.20	5.90	4.60	5.90

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9487	9500	9496	9485	9513	9510
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	InacAlert
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	Normal	None	Normal
Urine	None	None	None	Present	Present	None
Piloerection	None	None	None	None	None	None
Rears	5	6	11	6	7	0
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	None	Present
Grip Strength #1 (fore)	.52	.50	.27	.26	.66	.39
Grip Strength #2 (fore)	.35	.43	.26	.25	.42	.45
Grip Strength #1 (hind)	.25	.21	.20	.23	.55	.20
Grip Strength #2 (hind)	.16	.22	.16	.19	.36	.39
Body Temperature	38.70	38.10	38.60	37.80	38.20	38.60
Body Weight	166.82	148.66	161.66	179.94	182.54	166.94
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.70	5.60	4.80	4.40	3.50	4.90
Hind Leg Splay #2	5.40	4.50	3.90	3.90	2.60	4.60

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9504	9489	9523	9482	9512	9497
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	Other[a]	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	Present	None	None	None	None
Piloerection	None	None	None	None	None	None
Rears	3	7	5	10	8	1
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.35	.44	.27	.35	.39	.50
Grip Strength #2 (fore)	.31	.25	.39	.33	.41	.26
Grip Strength #1 (hind)	.22	.21	.32	.39	.36	.25
Grip Strength #2 (hind)	.21	.22	.17	.25	.25	.30
Body Temperature	38.10	38.00	38.10	38.60	38.50	38.20
Body Weight	167.06	185.56	169.86	174.54	179.84	182.66
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.90	4.50	7.00	3.80	4.30	5.20
Hind Leg Splay #2	4.70	4.40	6.50	3.20	4.70	5.60

[a]Animal leaned to right side at all times

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9511	9520	9502	9521	9498	9503
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	Normal	Normal
Urine	None	None	Present	None	Present	Present
Piloerection	None	None	None	None	None	None
Rears	6	11	5	6	2	7
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.26	.33	.81	.38	.47	.46
Grip Strength #2 (fore)	.38	.32	.46	.26	.33	.48
Grip Strength #1 (hind)	.41	.26	.21	.18	.58	.34
Grip Strength #2 (hind)	.15	.28	.41	.29	.35	.29
Body Temperature	38.10	38.80	38.80	38.30	38.00	38.30
Body Weight	170.74	182.00	166.54	189.44	197.64	189.46
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.50	5.60	3.50	5.20	3.70	4.40
Hind Leg Splay #2	5.50	5.80	4.80	5.10	4.80	4.80

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

MALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9519
Handling Reactivity	Resists
Ataxia	No
Gait	Normal
Body Position	Normal
Excessive Vocalization	None
Breathing Pattern	Normal
Twitch	None
Tremor	None
Spasm	None
Jerk	None
Clonic Convulsions	None
Tonic Convulsions	None
Unusual Behavior	None
Arousal	Active
Palpebral Closure	WideOpen
Defecation	None
Urine	Present
Piloerection	None
Rears	10
Approach Response	Noticable
Startle Response	Noticable
Tail Pinch Response	Noticable
Pupil Size	Normal
Muscle Tone	Normal
Lacrimation	None
Salivation	None
Fur Appearance	Normal
Facial Crust	None
Additional Observations	None
Visual Placing	Present
Grip Strength #1 (fore)	.22
Grip Strength #2 (fore)	.31
Grip Strength #1 (hind)	.31
Grip Strength #2 (hind)	.39
Body Temperature	38.60
Body Weight	171.48
Air Righting	FeetCoord
Hind Leg Splay #1	4.80
Hind Leg Splay #2	5.50

RPT_NT:MRV2E2F3.IFO

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9537	9532	9571	9540	9552	9531
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9557	9566	9559	9570	9556	9563
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9542	9569	9560	9551	9555	9548
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9545	9544	9530	9568	9543	9553
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9541	9533	9538
Cage Posture	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None
Cage Tremor	None	None	None
Cage Spasm	None	None	None
Cage Jerk	None	None	None
Cage Clonic Convulsions	None	None	None
Cage Tonic Convulsions	None	None	None

RPT_NT:FRV2ECF1.IFO

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9537	9532	9571	9540	9552	9531
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	None	None	Present	Present	None
Piloerection	None	None	None	None	None	None
Rears	23	19	22	12	28	11
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.72	.60	.60	.60	.66	.59
Grip Strength #2 (fore)	.61	.59	.71	.71	.50	.55
Grip Strength #1 (hind)	.27	.36	.44	.29	.34	.35
Grip Strength #2 (hind)	.19	.29	.38	.32	.33	.30
Body Temperature	39.30	38.70	39.40	38.10	39.10	38.20
Body Weight	116.76	122.14	126.42	119.90	127.98	135.70
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.20	3.80	4.30	3.90	3.70	3.70
Hind Leg Splay #2	3.50	4.60	4.20	4.10	4.40	4.40

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9557	9566	9559	9570	9556	9563
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Uncoord Present	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	Normal	None	None	None	None
Urine	None	Present	Present	None	None	Present
Piloerection	None	None	None	None	None	None
Rears	24	24	11	16	8	27
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Exagger	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Exagger	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.72	.89	.62	.55	.55	.70
Grip Strength #2 (fore)	.70	.63	.55	.54	.49	.50
Grip Strength #1 (hind)	.22	.29	.30	.48	.36	.44
Grip Strength #2 (hind)	.38	.32	.34	.44	.45	.40
Body Temperature	39.30	39.50	38.60	38.00	37.90	38.70
Body Weight	120.92	123.16	127.46	130.26	130.82	136.38
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.30	4.40	3.10	3.40	5.10	3.60
Hind Leg Splay #2	5.70	4.70	3.50	4.40	4.50	3.20

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9542	9569	9560	9551	9555	9548
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	Present	None	None	None	None
Piloerection	None	None	None	None	None	None
Rears	14	19	20	25	18	19
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Exagger
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.68	.58	.62	.71	.62	.59
Grip Strength #2 (fore)	.58	.55	.74	.75	.58	.62
Grip Strength #1 (hind)	.25	.25	.43	.30	.34	.31
Grip Strength #2 (hind)	.22	.25	.33	.34	.33	.35
Body Temperature	38.10	38.20	38.10	39.10	38.80	38.30
Body Weight	128.66	120.48	131.98	129.94	126.02	124.84
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.60	3.80	4.10	3.40	3.00	3.10
Hind Leg Splay #2	5.20	3.10	4.10	3.30	3.20	4.20

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9545	9544	9530	9568	9543	9553
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Uncoord	Normal	Uncoord	Normal	Uncoord	Normal
	Present		Present		Present	
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	Present	None	Present	None	None
Piloerection	None	None	None	None	None	None
Rears	23	22	24	16	19	22
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Decreased	Normal	Decreased	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.57	.76	.61	.80	.57	.55
Grip Strength #2 (fore)	.51	.54	.33	.54	.51	.62
Grip Strength #1 (hind)	.35	.26	.28	.44	.38	.47
Grip Strength #2 (hind)	.51	.40	.42	.42	.33	.58
Body Temperature	38.60	39.60	38.50	37.80	38.60	38.30
Body Weight	122.40	124.14	122.84	119.44	131.04	129.92
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.80	5.10	5.40	4.40	4.40	4.10
Hind Leg Splay #2	5.20	4.80	4.50	5.80	3.80	4.90

TABLE 9
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 12

FEMALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9541	9533	9538
Handling Reactivity	Resists	Resists	Resists
Ataxia	No	No	No
Gait	Normal	Normal	Normal
Body Position	Normal	Normal	Normal
Excessive Vocalization	None	None	None
Breathing Pattern	Normal	Normal	Normal
Twitch	None	None	None
Tremor	None	None	None
Spasm	None	None	None
Jerk	None	None	None
Clonic Convulsions	None	None	None
Tonic Convulsions	None	None	None
Unusual Behavior	None	None	None
Arousal	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen
Defecation	None	None	None
Urine	None	None	None
Piloerection	None	None	None
Rears	13	15	14
Approach Response	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal
Lacrimation	None	None	None
Salivation	None	None	None
Fur Appearance	Normal	Normal	Normal
Facial Crust	None	None	None
Additional Observations	None	None	None
Visual Placing	Present	Present	Present
Grip Strength #1 (fore)	.46	.58	.48
Grip Strength #2 (fore)	.52	.59	.48
Grip Strength #1 (hind)	.42	.29	.45
Grip Strength #2 (hind)	.41	.40	.39
Body Temperature	38.80	38.50	38.70
Body Weight	120.80	123.56	128.54
Air Righting	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.60	3.60	5.60
Hind Leg Splay #2	4.50	3.20	4.90

RPT_NT:FRV2E2F1.IFO

TABLE 10
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9537	9532	9571	9540	9552	9531
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	SlDroop	HalfShut	WideOpen	HalfShut	HalfShut
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9557	9566	9559	9570	9556	9563
Cage Posture	NormAwake	NormAslee	NormAwake	NormAwake	NormAslee	NormAwake
Cage Palpebral Closure	WideOpen	Shut	WideOpen	WideOpen	Shut	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9542	9569	9560	9551	9555	9548
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAslee
Cage Palpebral Closure	WideOpen	SlDroop	WideOpen	HalfShut	WideOpen	Shut
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

TABLE 10
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9545	9544	9530	9568	9543	9553
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	HalfShut	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9541	9533	9538
Cage Posture	NormAwake	NormAslee	NormAwake
Cage Palpebral Closure	WideOpen	Shut	WideOpen
Cage Twitch	None	None	None
Cage Tremor	None	None	None
Cage Spasm	None	None	None
Cage Jerk	None	None	None
Cage Clonic Convulsions	None	None	None
Cage Tonic Convulsions	None	None	None

RPT_NT:FRV2ECF2.IFO

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9537	9532	9571	9540	9552	9531
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	Present	None	None	None	Present	None
Piloerection	None	None	None	None	None	None
Rears	12	13	7	7	14	5
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.70	.52	.74	.54	.52	.68
Grip Strength #2 (fore)	.43	.44	.82	.49	.61	.51
Grip Strength #1 (hind)	.24	.29	.35	.32	.37	.35
Grip Strength #2 (hind)	.19	.33	.33	.23	.37	.41
Body Temperature	38.80	37.40	38.60	38.00	38.60	38.00
Body Weight	118.78	125.26	127.66	123.48	126.40	134.28
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.20	2.70	3.30	3.80	4.00	3.80
Hind Leg Splay #2	3.60	2.80	3.60	4.10	4.00	4.50

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9557	9566	9559	9570	9556	9563
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	InacAlert	InacAlert	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	Present	Present	None	None	None	Present
Piloerection	None	None	None	None	None	None
Rears	29	11	3	1	8	22
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.70	.77	.50	.43	.53	.40
Grip Strength #2 (fore)	.57	.51	.59	.47	.50	.62
Grip Strength #1 (hind)	.27	.42	.38	.38	.29	.37
Grip Strength #2 (hind)	.32	.38	.36	.28	.30	.35
Body Temperature	38.50	38.70	38.20	38.30	38.20	38.30
Body Weight	125.92	125.46	128.48	132.66	132.66	136.88
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.20	4.30	2.80	3.90	4.00	4.00
Hind Leg Splay #2	3.90	3.80	2.90	4.10	2.90	3.30

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9542	9569	9560	9551	9555	9548
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	InacAlert
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	Present	None	None	None	Present
Piloerection	None	None	None	None	None	None
Rears	9	11	6	12	11	2
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Decreased
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.64	.61	.65	.62	.56	.46
Grip Strength #2 (fore)	.62	.48	.44	.54	.73	.59
Grip Strength #1 (hind)	.28	.28	.33	.36	.29	.38
Grip Strength #2 (hind)	.27	.25	.36	.31	.24	.41
Body Temperature	38.30	38.20	37.70	38.20	37.90	37.50
Body Weight	128.48	122.36	132.04	131.76	126.70	127.38
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.20	4.00	4.20	3.30	4.40	4.40
Hind Leg Splay #2	4.50	3.40	3.80	3.30	2.60	3.50

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9545	9544	9530	9568	9543	9553
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None
Rears	17	7	10	16	21	11
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Decreased	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.62	.58	.43	.70	.57	.59
Grip Strength #2 (fore)	.46	.55	.41	.46	.58	.58
Grip Strength #1 (hind)	.40	.29	.30	.31	.32	.42
Grip Strength #2 (hind)	.44	.28	.34	.23	.35	.45
Body Temperature	38.70	38.80	38.80	39.10	39.90	37.80
Body Weight	123.52	127.76	124.00	121.12	132.88	131.64
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.30	5.20	4.50	4.90	3.30	4.80
Hind Leg Splay #2	3.90	4.80	6.20	4.60	3.10	3.50

TABLE 11
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 13

FEMALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9541	9533	9538
Handling Reactivity	Resists	Resists	Resists
Ataxia	No	No	No
Gait	Normal	Normal	Normal
Body Position	Normal	Normal	Normal
Excessive Vocalization	None	None	None
Breathing Pattern	Normal	Normal	Normal
Twitch	None	None	None
Tremor	None	None	None
Spasm	None	None	None
Jerk	None	None	None
Clonic Convulsions	None	None	None
Tonic Convulsions	None	None	None
Unusual Behavior	None	None	None
Arousal	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen
Defecation	None	None	None
Urine	None	Present	None
Piloerection	None	None	None
Rears	13	10	11
Approach Response	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal
Lacrimation	None	None	None
Salivation	None	None	None
Fur Appearance	Normal	Normal	Normal
Facial Crust	None	None	None
Additional Observations	None	Other[a]	None
Visual Placing	Present	Present	Present
Grip Strength #1 (fore)	.47	.50	.59
Grip Strength #2 (fore)	.42	.45	.50
Grip Strength #1 (hind)	.37	.28	.44
Grip Strength #2 (hind)	.35	.36	.37
Body Temperature	38.70	37.90	38.30
Body Weight	123.84	122.74	130.52
Air Righting	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.10	3.50	3.60
Hind Leg Splay #2	3.80	3.30	3.20

[a]Opacity (Left Eye)

RPT_NT:FRV2E2F2.IFO

TABLE 12
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9537	9532	9571	9540	9552	9531
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9557	9566	9559	9570	9556	9563
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9542	9569	9560	9551	9555	9548
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	HalfShut	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

TABLE 12
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9545	9544	9530	9568	9543	9553
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	HalfShut	WideOpen	HalfShut	HalfShut	WideOpen
Cage Twitch	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None

FEMALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9541	9533	9538
Cage Posture	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	SlDroop	WideOpen	WideOpen
Cage Twitch	None	None	None
Cage Tremor	None	None	None
Cage Spasm	None	None	None
Cage Jerk	None	None	None
Cage Clonic Convulsions	None	None	None
Cage Tonic Convulsions	None	None	None

RPT_NT:FRV2ECF3.IFO

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:0 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9537	9532	9571	9540	9552	9531
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	Present	None	None	Present	None	None
Piloerection	None	None	None	None	None	None
Rears	18	5	8	8	15	3
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.62	.62	.49	.44	.44	.40
Grip Strength #2 (fore)	.63	.61	.55	.34	.42	.46
Grip Strength #1 (hind)	.26	.23	.34	.26	.31	.33
Grip Strength #2 (hind)	.20	.23	.32	.27	.28	.29
Body Temperature	39.40	37.80	38.00	38.20	38.80	38.80
Body Weight	117.58	125.60	126.64	125.40	131.16	135.02
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.50	3.30	3.50	4.10	4.90	4.60
Hind Leg Splay #2	3.60	5.50	3.10	3.30	4.70	3.70

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:50 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9557	9566	9559	9570	9556	9563
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	Present	None	Present	None	Present
Piloerection	None	None	None	None	None	None
Rears	8	4	6	7	8	10
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.72	.65	.55	.48	.44	.43
Grip Strength #2 (fore)	.59	.41	.56	.36	.52	.45
Grip Strength #1 (hind)	.18	.30	.32	.36	.20	.27
Grip Strength #2 (hind)	.20	.31	.40	.34	.21	.26
Body Temperature	39.30	38.20	38.20	38.20	37.70	38.30
Body Weight	126.94	125.80	129.58	132.50	137.44	139.32
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.20	5.10	4.90	3.90	4.50	3.90
Hind Leg Splay #2	3.00	4.00	4.60	4.30	4.90	3.90

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:200 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9542	9569	9560	9551	9555	9548
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	InacAlert	Active	InacAlert	Active	InacAlert	InacAlert
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None
Rears	4	7	1	7	1	1
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.64	.64	.46	.70	.53	.51
Grip Strength #2 (fore)	.63	.60	.48	.85	.64	.59
Grip Strength #1 (hind)	.29	.33	.34	.36	.28	.38
Grip Strength #2 (hind)	.31	.20	.31	.29	.25	.33
Body Temperature	38.10	38.40	38.00	38.10	38.10	37.40
Body Weight	126.74	118.28	135.30	130.74	130.68	129.44
Air Righting	FeetCoord	FeetUncoor	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.40	3.60	3.80	4.90	4.00	5.30
Hind Leg Splay #2	3.80	3.40	3.50	4.80	3.80	3.80

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:1000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9545	9544	9530	9568	9543	9553
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None
Tremor	None	None	None	None	None	None
Spasm	None	None	None	None	None	None
Jerk	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None
Urine	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None
Rears	12	3	13	18	16	10
Approach Response	Noticable	None	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None
Salivation	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.40	.61	.40	.59	.73	.53
Grip Strength #2 (fore)	.58	.57	.33	.49	.78	.47
Grip Strength #1 (hind)	.35	.32	.24	.31	.29	.29
Grip Strength #2 (hind)	.39	.31	.25	.29	.36	.32
Body Temperature	38.20	38.20	39.10	39.30	39.10	38.20
Body Weight	130.28	129.12	126.92	121.72	137.62	135.24
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.40	4.60	3.00	5.10	3.30	4.10
Hind Leg Splay #2	4.60	5.40	3.20	4.80	3.60	4.20

TABLE 13
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 14

FEMALES GROUP:2000 MG/KG/DAY

OBSERVATION	ANIMAL NUMBERS 9541	9533	9538
Handling Reactivity	Resists	Resists	Resists
Ataxia	No	No	No
Gait	Normal	Normal	Normal
Body Position	Normal	Normal	Normal
Excessive Vocalization	None	None	None
Breathing Pattern	Normal	Normal	Normal
Twitch	None	None	None
Tremor	None	None	None
Spasm	None	None	None
Jerk	None	None	None
Clonic Convulsions	None	None	None
Tonic Convulsions	None	None	None
Unusual Behavior	None	None	None
Arousal	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen
Defecation	None	None	None
Urine	None	None	None
Piloerection	None	None	None
Rears	8	9	10
Approach Response	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Exagger
Tail Pinch Response	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal
Lacrimation	None	None	None
Salivation	None	None	None
Fur Appearance	Normal	Normal	Normal
Facial Crust	None	None	None
Additional Observations	None	Other[a]	None
Visual Placing	Present	Present	Present
Grip Strength #1 (fore)	.40	.50	.46
Grip Strength #2 (fore)	.58	.59	.48
Grip Strength #1 (hind)	.34	.22	.30
Grip Strength #2 (hind)	.33	.21	.25
Body Temperature	37.80	38.60	38.20
Body Weight	124.98	126.80	128.28
Air Righting	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.00	3.10	4.00
Hind Leg Splay #2	3.90	2.90	3.50

[a]Opacity (Left Eye)

RPT_NT:FRV2E2F3.IFO

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

OVERVIEW OF THE FUNCTIONAL OBSERVATIONAL BATTERY (FOB)

The FOB involved the evaluation and documentation of the absence or presence (or severity if appropriate) of a predetermined set of behavioral and clinical signs for individual animals. During examination, all animals were observed in their observation cages for signs of involuntary muscular movements (twitches, tremors, spasms, jerks, and convulsions) and evaluated for posture and palpebral closure. One animal was then removed from its observation cage and handling reactivity was evaluated. The animal was placed on an observation cart and observed for signs of ataxia, involuntary muscular movements, excessive vocalization, piloerection, and unusual behavior. Gait, body position, breathing pattern, arousal, palpebral closure, defecation, urination, and rears were also evaluated during this observation period. Approach, startle, and tail pinch responses were then evaluated while the animal was still on the observation cart. The animal was then held, and pupil size, muscle tone, lacrimation, salivation, fur appearance, crusts, and visual placing were evaluated. Any additional clinical observations were also recorded. Grip strength, body temperature, body weight, air righting reflexes, and hind leg splay were subsequently evaluated. The same evaluations were then performed for the remaining animals. The FOB required approximately 6 minutes to perform for each animal.

Two technicians evaluated and documented neurobehavioral function of the test animals while blind to the animals' treatment.

I. Cageside Observations

Abbreviations or shortened names which are used during data collection are listed in parentheses.

Posture — The condition and body position of the animal in its observation cage. Scored as:

1. **Normal/Awake (NormAwake)** - Animal was in any normal awake position; i.e., standing, sitting, or rearing.
2. **Normal/Asleep (NormAslee)** - Animal was asleep in any normal position; i.e., lying on side or curled
3. **On side/Prostrate (SideProst)** - Animal was on its side with its legs out to the side and appeared to be unaware of its surroundings.
4. **On Stomach/Prostrate (StomProst)** - Animal was on its stomach with its legs splayed to the front or sides and appeared to be unaware of its surroundings.
5. **Other** - The animal was in an abnormal or unusual position which is not included above.

Palpebral Closure

The degree of closure of the eyelids. Scored as:
1. **Wide open (WideOpen)** - The animal's eyelids were fully open.
2. **Slightly Drooping (SlDroop)** - The animal's eyelids were slightly closed but were more than halfway open.
3. **Halfway Shut (HalfShut)** - The animal's eyelids were halfway closed or more but were not completely closed.
4. **Completely Shut (Shut)** - The animal's eyelids were completely closed.

Twitch

Brief, involuntary muscle contractions which caused the animal to abruptly move its extremities and/or individual isolated muscles or muscle groups. Recorded by location as:
1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Other**

Further scored by severity:
   1. **Present** (slight; fine)
   2. **Excessive** (pronounced; coarse)

Tremor

Continual, rhythmic quivering of the skeletal muscle involving or associated with a specific area. Recorded by location as:
1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Whole body (WholeBody)**
6. **Other**

Further scored by severity:
   1. **Present** (slight; fine)
   2. **Excessive** (pronounced; coarse)

Spasm

A sustained, involuntary contraction of a muscle or group of muscles without being rhythmic. Recorded by location as:
1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Other**

Further scored by severity:
   1. **Present** (single occurrence of short duration)
   2. **Excessive** (multiple occurrences or single occurrence of extended duration)

Jerk

A sudden involuntary movement. Recorded by location as:
1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Whole body (WholeBody)**
6. **Other**

Further scored by severity:
1. **Present** (1 or 2 occurrences)
2. **Excessive** (multiple occurrences)

Clonic Convulsions

Involuntary, repetitive, severe contractions of the voluntary (skeletal) muscles which may have been marked by movements similar to natural purposeful movements. Recorded by the movements associated with the convulsion as:
1. **None**
2. **Running Fits (RunFits)** - The animal's limbs moved in a running movement during the convulsions.
3. **Explosive Jumps (ExplJump)** - The animal jumped into the air with all 4 feet leaving the surface of the cart.
4. **Writhing** - The animal twisted and turned.
5. **Paddling** - The animal's limbs moved forward and back in a swimming motion.
6. **Other**

Further scored by severity:
1. **Present** (single occurrence of short duration)
2. **Excessive** (multiple occurrences or single occurrence of extended duration)

Tonic Convulsions

Involuntary, severe sustained contractions of the voluntary (skeletal) muscles which produced animal rigidity. Recorded as:
1. **None**
2. **Present**

Further scored by severity:
1. **Present** (single occurrence of short duration)
2. **Excessive** (multiple occurrences or single occurrence of extended duration)

II. Open Field Observations

Handling Reactivity

The reaction of the animal to being removed from the observation cage and handled. Scored as:
1. **Slight/Moderate Resistance (Resists)** - The animal was easy to handle although it may have struggled or vocalized occasionally.
2. **Animal Limp (Limp)** - The animal was limp/flaccid when handled.
3. **High Resistance/Aggressive (HighResis)** - The animal was difficult to handle, and/or struggled continuously, and/or tried to bite.

Ataxia

The animal showed a clear loss of balance while sitting or rearing. Recorded as:

1. **No**
2. **Yes**

Further scored by severity:

1. **Present** - The animal repeatedly began to fall while sitting and then caught itself or the animal had some difficulty holding itself erect while rearing. The animal may have fallen occasionally.
2. **Excessive** - The animal fell frequently while sitting or rearing.

Gait

The animal's manner of walking. Recorded as:

1. **Normal** - No obvious gait impairment
2. **Uncoordinated (Uncoord)** - The animal's movements were uncoordinated. Further scored by severity:
   1. **Present** - The animal walked with a noticeable sway and/or rocking and/or jerky movements when walking. Animal may have fallen on side occasionally.
   2. **Excessive** - The animal frequently fell on its back and/or side while moving. The animal may not have been able to move beyond a restricted area.
3. **Limbs Exaggerated/Splayed (Splayed)** - The hindlimbs and/or forelimbs showed exaggerated placement or movements. Further scored by severity:
   1. **Present** - The animal displayed slightly abnormal placement/movement of the limbs.
   2. **Excessive** - The limbs were moved in an extremely exaggerated motion when walking. The limbs were splayed at least 45 degrees from body.
4. **Walks on Toes (OnToes)** - The animal did not place its feet in a normal heel to toe manner when walking. The hindlimbs were drawn into the body. Further scored by severity:
   1. **Present** - There was a noticeable alteration in body position. The back may have appeared to be arched/hunched. The animal walked on its toes and the distal pads of its feet.
   2. **Excessive** - The animal walked only on its toes with a severely arched/hunched body position.
5. **Hypotonic** - The animal was unable to support its weight but was able to move in a straight line without lurching. Further scored by severity:
   1. **Present** - The animal moved slowly and dragged its abdomen on the surface of the observation cart.
   2. **Excessive** - The animal's limbs were apparently weak and obviously splayed. The animal dragged its abdomen on the surface of the observation cart and had labored locomotion.
6. **Other** - Any other abnormality or combination of abnormalities. Further scored by severity.

Body Position	The animal's posture while in the observation cart. Recorded as: 1. **Normal** - The animal's body position was normal. 2. **Hunched** - The animal's back was arched when standing normally or walking 3. **On side (OnSide)** - The animal lay on its side. It may have make occasional attempts to stand/walk but was unable to do so effectively. 4. **On stomach (OnStomach)** - The animal lay on its stomach with its limbs unable to support its weight. The animal may have attempted to stand/walk but was unable to so effectively. 5. **Other** - The animal was in an abnormal or unusual position which is not included above.
Excessive Vocalization	The animal vocalized without being provoked or vocalized continuously while being handled. Recorded as: 1. **None** 2. **Present**
Breathing Pattern	A characterization of the animal's respiration. Recorded as: 1. **Normal** 2. **Mouthbreathing (MthBreath)** - The animal appeared to have a normal breathing pattern but breathed with its mouth open. 3. **Labored** - The animal had difficulty breathing and may have appeared to be gasping. 4. **Audible** - Abnormal respiratory sounds were heard while listening to the animal breathing. 5. **Rapid respiration (Rapid)** - The animal breathed with excessively quick, short breaths. 6. **Other**
Twitch	As described above.
Tremor	As described above.
Spasm	As described above.
Jerk	As described above.
Clonic Convulsions	As described above.
Tonic Convulsions	As described above.

Unusual Behavior

Behavior which occurred out of context and/or with abnormally high frequency or behaviors not associated with the normal repertoire of the species. Recorded as:

1. **None**
2. **Retropulsion (Retropuls)** - The animal walked backward.
3. **Head Bobbing/Weaving (HeadBob)** - The animal moved its head up and down or from side to side continuously.
4. **Stereotypy (Stereotyp)** - The animal performed a normal behavior for an unusually long time.
5. **Prostrate** - The animal was lying down and showed little or no spontaneous movement. The animal appeared to be unaware of its surroundings, but was apparently awake.
6. **Other**

Arousal

An assessment of the level of unprovoked activity and alertness in the observation cart. Recorded as:

1. **Active/alert (Active)** - The animal went through a normal repertoire of behaviors consisting of periods of sniffing, rearing, exploring, grooming, etc.
2. **Hyperactive/hyperalert (Hyperact)** - The animal appeared excited and may have darted or froze during the observation period or may have sat in one place and jumped at any sound or movement.
3. **Inactive/alert (InacAlert)** - The animal generally sat in one place during the majority of the observation period but appeared to be aware of its surroundings.
4. **Inactive/not alert (NotAlert)** - The animal sat in one place during the observation period and appeared to be unaware of its surroundings or was in a stupor.

Palpebral Closure

As described above.

Defecation

The type or absence of excrement during the observation. Recorded as:

1. **None**
2. **Normal**
3. **Soft**
4. **Diarrhea**

Urine

The amount of urination during the observation period.

1. **None**
2. **Present**
3. **Excessive**

Piloerection

The animal's hair stood vertical to the plane of the skin surface. Recorded as:

1. **None**
2. **Present**

Rears

The number of times the animal lifted both front legs off the surface of the cart during the observation period. Any time the animal placed one or both front paws on the surface of the cart and then removes it/them another rear was counted.

III. Manipulative Observations

Approach Response

The animal's reaction to being approached by an object. The animal was approached at nose level with the end of a blunt object. The object was stopped approximately 3-4 cm from the animal's nose and held there for several seconds without making contact with the animal. The animal's reaction was recorded as:

1. **Noticeable reaction (Noticable)** - The animal froze, slowly approached the object, sniffed the object, or turned away from the object.
2. **No reaction (None)** - The animal made no noticeable reaction and apparently did not care or recognize that the object was there.
3. **Exaggerated reaction (Exagger)** - The animal attacked or fled from the object

Startle Response

The animal's response to acoustic stimuli. A hand held metal clicker was positioned approximately 5 cm above the animal and held out of sight. The clicker was quickly clicked and the animal's reaction was recorded as:

1. **Noticeable reaction (Noticable)** - The animal made a noticeable reaction. This reaction may have ranged from a slight flick of the ears to an obvious flinch.
2. **No reaction (None)** - The animal made no noticeable reaction.
3. **Exaggerated reaction (Exagger)** - The animal jumped at the sound or fled from the sound. Generally, the animal's front feet left the surface of the cart for a jump to have been considered an exaggerated reaction.

Tail Pinch Response

A pair of tweezers was used to pinch the tail approximately 2-3 cm from the tip. The animal's reaction to having its tail pinched was recorded as:

1. **Noticeable reaction (Noticable)** - The animal made a noticeable reaction. The animal may have flinched, walked away, or turned toward its tail.
2. **No reaction (None)** - The animal made no noticeable reaction.
3. **Exaggerated reaction (Exagger)** - The animal jumped, fled, or turned and attacked the tweezers or the technician's hand.

Pupil Size

The pupil's relative size to the normal size for the test species. The animals eye was held open and the size of the pupil was recorded as:
1. **Normal** - The pupil was less than approximately 50% of the eyeball but was not pinpoint.
2. **Increased** - The pupil was at least 50% of the eyeball.
3. **Decreased** - The pupil was pinpoint.

Muscle Tone

The animal was held and the technician felt the abdominal musculature and moved the hind legs to determine the range of their movement and resiliency. The relative rigidity or flaccidity of the limb and abdominal musculature was recorded as:
1. **Normal** - The animal's muscles were resilient and firm and the hindlimbs went through their full range of movement.
2. **Increased** - The animal's muscles were rigid and the hindlimbs would not go through their full range of movements.
3. **Decreased** - The animal's muscles were flaccid and the hindlimbs had resistance to movement.

Lacrimation

Secretion or discharge of tears causing the fur to appear wet around the eyes. Recorded as:
1. **None**
2. **Present** - Lacrimation was noticeable.
3. **Excessive** - The animal had a large amount of tearing.

Salivation

The presence of saliva around the mouth.
1. **None**
2. **Present** - Salivation was noticeable around the edges of the mouth.
3. **Excessive** - The salivation extended to the fur around the jaw.

Fur Appearance

The appearance of the animal's fur.
1. **Normal**
2. **Unkempt** - The animal had an unusually rough or ungroomed appearance.
3. **Urine Stains/Wetness (UrinStain)** - The animal's fur had stains or was wet from the discharge of urine.
4. **Other** - Any other discoloration or abnormal condition of the animal's fur.

Facial Crust

The presence or absence of a crust around the mouth, nose, or eyes. Recorded by location as:
1. **None**
2. **Eyes**
3. **Nose**
4. **Mouth**
5. **Multiple areas (Multiple)** - More than one location had a crust present.

Additional Observations

Any additional clinical observations were recorded as:
1. **None**
2. **Emaciation (Emaciated)** - An excessively lean appearance.
3. **Dehydration (Dehydrat)** - An abnormal depletion of body fluid. When present, if the animal's skin was pinched it remains in a pinched position when released.
4. **Exophthalmus (Exophthal)** - An abnormal protrusion of the eyeball from the eye socket.
5. **Other** - Additional observations, not included above, were present or more than 1 of the above observations were present.

Visual Placing

The presence or absence of forelimb extension in anticipation of grasping a surface while being held by the observer. The observer's palm was on the back of the animal with the fingers wrapped around the animal's midsection. The animal was held level with forelimb grip strength strain gauge (described below) with its body parallel to the floor. The animal was then slowly moved toward the strain gauge and the presence or absence of forelimb extension was recorded as:
1. **Present**
2. **None**

Grip Strength

The force, in kg, necessary to break the animal's grip on a wire screen attached to a strain gauge. Two strain gauges with wire mesh screens were secured to a Plexiglas® stand. One gauge was positioned parallel to the floor (forelimb gauge) and other was angled slightly down toward the floor (hindlimb gauge). The limbs to be tested were placed on the screen and the animal was allowed to grasp the screen with its toes. The animal was then pulled smoothly until its grip was broken and the reading of the strain gauge was recorded. Two trials were performed for the forelimbs and the hindlimbs.

Body Temperature

Core body temperature was measured using an digital thermometer. A vinyl rectal probe was dipped into petroleum jelly and inserted through the animal's rectum (approximately 6-8 cm depending on the size of the rat). The temperature in °C was recorded when the gauge had stabilized. The probe was wiped clean between animals.

Body Weight

The animal's body weight, in grams, was recorded using an electronic balance.

Air Righting

The ability of the animal to right itself while airborne. The animal was held upside down parallel to the surface of a padded cart with the observer's hands under its back. The animal was held approximately 30 cm above the surface of the cart and released. The test was not performed if the animal was considered by the observer to be impaired to the point that it could be injured if dropped. The manner in which the animal landed was recorded as:

1. **Feet/Coordinated (FeetCoord)** - The animal landed on its feet and appeared to have no problem with balance
2. **Feet/Uncoordinated (FeetUncoor)** - The animal landed on its feet but stumbled or staggered after landing.
3. **Side** - The animal landed on its side.
4. **Back** - The animal landed on its back.

Hind Leg Splay

The outside digit pads of the animal's hind paws were painted using non-toxic paint. The animal was then held in a prone position (the fingers of one hand under the animal's forelimbs and the other hand holding the base of its tail) approximately 40 cm above a cart. The animal was dropped 2 times onto a piece of paper and the paint marks left by the animals digit pads were marked. The distance, in cm, between the 2 paint marks (measured from the center of each paint mark) for each landing was recorded

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

FOB STATISTICAL SUMMARY

I. BMDP P7D:

The data for parameters that generate continuous data were intercompared for the dose and control groups by use of Levene's test for homogeneity of variances, by analysis of variance, and by pooled variance t-tests. The t-tests were used, if the analysis of variance was significant, to delineate which groups differed from the control groups. If Levene's test indicated heterogeneous variances, the groups were compared by an analysis of variance for unequal variances followed, if necessary, by separate variance t-tests.

II. BMDP P4F:

The incidence data were analyzed for group effects using Fisher's Exact Test on 2x2 tables.

Incidence data were collapsed to a single category, if necessary, prior to 2x2 table analysis (absence versus presence of a finding or normal versus abnormal). More than one response for a selected parameter may be considered normal and some parameters can be evaluated as either normal versus abnormal or present versus absent. The way in which the parameters were evaluated was determined after reviewing the data tables.

Additional analyses were performed on selected incidence data with ordered severity scores which do not conform to collapse into a 2x2 table analysis. For these, Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somers' D measures of association were computed.

Summary of the category designation for certain frequency parameters and additional P4F analyses in this study:

Cage Posture - Evaluated with awake as normal and asleep or any other finding as abnormal.
Cage Palpebral Closure - Any response could be considered normal; therefore, a P4F analysis examining the correlation between amount of closure and dose level was performed.
Handling Reactivity - Slight/moderate resistance was considered normal; any other response was considered abnormal.
Arousal - Alternating behaviors was considered normal; any other response was considered abnormal.
Urine - Evaluated as absent versus present.
Approach, Startle, and Tail Pinch Responses - Noticeable reactions were considered normal; any other response was considered abnormal.

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Individual Anatomic Pathology Data

(43 Pages)

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

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	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	COAGULATING GL
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 necropsy data for the 3 animals/group that were perfused were back entered into this computer protocol for reporting purposes because the microscopic examination of the liver, kidneys, and testes are reported in this computer protocol. The neuropathologic examination was completed in a different computer protocol. Only the following tissues/areas were examined for these animals:

brain
spinal cord
sciatic nerve
sural nerve
tibial nerve
peroneal nerve
gasserian ganglion
liver
kidneys
lungs
testes

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY MALE

ANIMAL 9499 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	165.7	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS
MICRO: (1) TUBULAR REGENERATION/BASOPHILIA
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER TESTES

ANIMAL 9518 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	180.2	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER TESTES KIDNEYS

ANIMAL 9507 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	7.003	4.056
KIDNEYS	1.340	0.776
SPLEEN	0.415	0.240
BRAIN	1.759	1.019
ADRENAL GL	0.029	0.017
TESTES	2.120	1.228
TERMINAL BODY WT.	172.6	

LYMPH ND, S-MAN
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL TAN AND RED
MICRO↑((2)) SINUS ERYTHROCYTOSIS
LYMPH ND, MED
MICRO: (3) SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL DARK RED FOCAL AREAS
MICRO↑((1)) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL TESTES KIDNEYS

ANIMAL 9509 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	7.796	4.313
KIDNEYS	1.433	0.793
SPLEEN	0.390	0.216
BRAIN	1.724	0.954
ADRENAL GL	0.032	0.018
TESTES	2.416	1.337
TERMINAL BODY WT.	180.8	

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL PINK FOCAL AREAS
MICRO↑((1)) HEMORRHAGE
BRAIN
MICRO: ((1)) MENINGEAL HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER NERVE, SCIATIC NERVE, TIBIAL
TESTES KIDNEYS

ANIMAL 9495 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	190.8	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER TESTES KIDNEYS

ANIMAL 9517 8-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 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY MALE

ANIMAL 9517 (CONTINUED)

LIVER	8.531	4.368
KIDNEYS	1.539	0.788
SPLEEN	0.460	0.236
BRAIN	1.719	0.880
ADRENAL GL	0.032	0.016
TESTES	2.437	1.248
TERMINAL BODY WT.	195.3	

MICRO: (1) MONONUCLEAR CELL INFILTRATE(S)
LYMPH ND, MED
MICRO: 3 SINUS ERYTHROCYTOSIS
3 MASTOCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
SCATTERED PINK FOCAL AREAS
MICRO+((1)) HEMORRHAGE
BRAIN
MICRO: ((1)) BRAIN HEMORRHAGE
POSSIBLE HANDLING ARTIFACT
LUNGS
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
SCATTERED RED FOCI, ALL LOBES
MICRO: ((2)) ALVEOLAR HISTIOCYTOSIS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
NERVE, SCIATIC NERVE, TIBIAL TESTES
KIDNEYS

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY MALE

ANIMAL 9487 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	175.1	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9500 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	6.227	4.045
KIDNEYS	1.296	0.842
SPLEEN	0.326	0.212
BRAIN	1.593	1.035
ADRENAL GL	0.029	0.019
TESTES	1.956	1.271
TERMINAL BODY WT.	153.9	

STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MOTTLED PINK AND TAN, NONGLANDULAR PORTION
MICRO: ((2)) GASTRITIS GLANDULAR STOMACH AND SQUAMOUS JUNCTION
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MOTTLED RED AND TAN
MICRO+((1)) HEMORRHAGE
LUNGS
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL DARK RED FOCAL AREA, 2X2 MM, RIGHT DIAPHRAGMATIC LOBE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
BRAIN NERVE, SCIATIC NERVE, TIBIAL
LUNGS

ANIMAL 9496 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	165.6	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9485 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	186.1	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9513 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	8.527	4.530
KIDNEYS	1.638	0.870
SPLEEN	0.469	0.249
BRAIN	1.701	0.904
ADRENAL GL	0.028	0.015
TESTES	2.404	1.277
TERMINAL BODY WT.	188.3	

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL RED FOCAL AREAS
MICRO+((1)) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9510 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	7.475	4.338
KIDNEYS	1.361	0.790
SPLEEN	0.424	0.246

STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MOTTLED PALE PINK AND TAN, NONGLANDULAR PORTION

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY MALE

ANIMAL 9510 (CONTINUED)

BRAIN	1.691	0.981
ADRENAL GL	0.034	0.020
TESTES	2.277	1.322
TERMINAL BODY WT.	172.3	

MICRO: ((2)) GASTRITIS
GLANDULAR STOMACH AND MAINLY SQUAMOUS JUNCTION
NEUTROPHILS AND EOSINOPHILS

THYMIC REGION
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, RIGHT SIDE
MICRO↑((3)) HEMORRHAGE

LUNGS
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
PUNCTATE RED FOCI, ALL LOBES

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

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 200 MG/KG/DAY MALE

ANIMAL 9504 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	7.742	4.533
KIDNEYS	1.481	0.867
SPLEEN	0.425	0.249
BRAIN	1.709	1.001
ADRENAL GL	0.038	0.022
TESTES	2.166	1.268
TERMINAL BODY WT.	170.8	

STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
MOTTLED PINK AND TAN, NONGLANDULAR PORTION
MICRO: (2) GASTRITIS
PRIMARILY AT THE SQUAMOUS/GLANDULAR JUNCTION
LYMPH ND, MED
MICRO: 3 SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
MOTTLED RED AND TAN
MICRO+((2)) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9489 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	190.5	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9523 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	177.6	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9482 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	7.755	4.317
KIDNEYS	1.464	0.815
SPLEEN	0.412	0.229
BRAIN	1.599	0.890
ADRENAL GL	0.029	0.016
TESTES	2.424	1.350
TERMINAL BODY WT.	179.6	

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
RED FOCAL AREAS
MICRO+((3)) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9512 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	185.0	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9497 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	8.712	4.634
KIDNEYS	1.624	0.864
SPLEEN	0.407	0.216
BRAIN	1.726	0.918
ADRENAL GL	0.039	0.021
TESTES	2.566	1.365
TERMINAL BODY WT.	188.0	

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
DARK RED FOCAL AREAS, MULTIPLE
MICRO+((1)) HEMORRHAGE
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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY MALE

ANIMAL 9511 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	177.0	

THYMIC REGION
GROSS: COLOR CHANGE, DIFFUSE
DARK RED
MICRO: ((3)) HEMORRHAGE

ANIMAL 9520 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	10.636	5.608
KIDNEYS	1.617	0.853
SPLEEN	0.524	0.276
BRAIN	1.692	0.892
ADRENAL GL	0.038	0.020
TESTES	2.237	1.179
TERMINAL BODY WT.	189.7	

LUNGS
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
DARK RED FOCI, PUNCTATE, ALL LOBES
MICRO+((1)) HEMORRHAGE
2 SMALL FOCI
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL TESTES KIDNEYS

ANIMAL 9502 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	173.3	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9521 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	11.503	5.725
KIDNEYS	1.760	0.876
SPLEEN	0.513	0.255
BRAIN	1.686	0.839
ADRENAL GL	0.035	0.017
TESTES	2.460	1.224
TERMINAL BODY WT.	200.9	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
BRAIN
MICRO: ((1)) MENINGEAL HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER NERVE, SCIATIC NERVE, TIBIAL
TESTES KIDNEYS

ANIMAL 9498 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	11.959	5.835
KIDNEYS	1.689	0.824
SPLEEN	0.550	0.268
BRAIN	1.757	0.857
ADRENAL GL	0.039	0.019
TESTES	2.465	1.203
TERMINAL BODY WT.	204.9	

STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
DARK RED FOCAL AREAS, THROUGHOUT
NON-GLANDULAR PORTION
LIVER
MICRO: (1) MONONUCLEAR CELL INFILTRATE(S)
LYMPH ND, S-MAN
GROSS: SIZE INCREASE
SLIGHT, LEFT SIDE
MICRO+ 3 LYMPHOID HYPERPLASIA
MICRO: 3 PLASMACYTOSIS
LYMPH ND, MED
MICRO: 4 SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, DIFFUSE
PINK
MICRO+((1)) HEMORRHAGE
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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY MALE :

ANIMAL 9498 (CONTINUED)

STOMACH	BRAIN	NERVE, SCIATIC
NERVE, TIBIAL	TESTES	KIDNEYS

ANIMAL 9503 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.		
TERMINAL BODY WT.	196.8		GROSS:	EXAMINED - NO SIGNIFICANT LESIONS
			MICRO:	N O T E X A M I N E D

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY MALE

ANIMAL 9505 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: FOUND DEAD

TOTAL BODY
GROSS: STAINED
PERINASAL REGION, RED
UROGENITAL REGION, BROWN
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, ALL NODES
MICRO+ 3 SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
RED FOCI
MICRO+((3)) HEMORRHAGE
BRAIN
GROSS: MENINGEAL HEMORRHAGE
MARKED
MICRO+((1)) MENINGEAL HEMORRHAGE
MICRO: 2 MENINGEAL CONGESTION
LUNGS
GROSS: COLOR CHANGE, DIFFUSE
ALL LOBES, BRIGHT RED
MICRO+ 4 CONGESTION
MICRO: ((3)) PNEUMONITIS
1 LOBE; MIXED INFLAMMATORY
INFILTRATE IN ALVEOLI
URINARY BLADDER
GROSS: DILATATION/DISTENTION
SLIGHT
MICRO+ 4 ECTASIA
MICRO: (1) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER NERVE, SCIATIC NERVE, TIBIAL
TESTES KIDNEYS

ANIMAL 9514 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: SACRIFICED MORIBUND

TOTAL BODY
GROSS: STAINED
YELLOW, UROGENITAL REGION
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
RED, ALL NODES
MICRO+ 2 SINUS ERYTHROCYTOSIS
LYMPH ND, REN
MICRO: 3 SINUS ERYTHROCYTOSIS
LUNGS
GROSS: COLOR CHANGE, DIFFUSE
RED, ALL LOBES
MICRO+ 3 CONGESTION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER TESTES KIDNEYS

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY MALE

ANIMAL 9519 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	178.5	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER TESTES KIDNEYS

ANIMAL 9506 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: SACRIFICED MORIBUND

TOTAL BODY
GROSS: STAINED
UROGENITAL REGION, YELLOW
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
DARK RED
MICRO+((2)) SINUS ERYTHROCYTOSIS
LUNGS
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, ALL LOBES
MICRO+((4)) CONGESTION
URINARY BLADDER
GROSS: DILATATION/DISTENTION
MILD
MICRO+ 3 ECTASIA
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER TESTES KIDNEYS

ANIMAL 9484 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: FOUND DEAD

TOTAL BODY
GROSS: STAINED
YELLOW, UROGENITAL REGION
STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
RED FOCAL AREAS, NONGLANDULAR PORTION
MICRO: (1) GASTRITIS
SUBMUCOSAL INFILTRATE, NONGLANDULAR STOMACH
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
RED, ALL NODES
MICRO+((3)) SINUS ERYTHROCYTOSIS
BRAIN
GROSS: MENINGEAL HEMORRHAGE
MODERATE
LUNGS
GROSS: COLOR CHANGE, DIFFUSE
ALL LOBES, RED
MICRO+ 3 CONGESTION
MICRO: (3) HEMORRHAGE
1 LOBE
INCLUDES HEMAGLOBIN CRYSTALS, CHRONIC LESION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER BRAIN NERVE, SCIATIC

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY MALE

ANIMAL 9484 (CONTINUED)

NERVE, TIBIAL TESTES KIDNEYS

ANIMAL 9486 28-OCT-93 STUDY DAY 4

TYPE OF DEATH: FOUND DEAD

TOTAL BODY
GROSS: STAINED
YELLOW, UROGENITAL REGION

STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
NONGLANDULAR PORTION, MULTIPLE PALE
RED FOCAL AREAS

LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, ALL NODES
MICRO+ 2 SINUS ERYTHROCYTOSIS

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
DARK RED FOCI
MICRO+((2)) HEMORRHAGE

BRAIN
GROSS: MENINGEAL HEMORRHAGE
SEVERE
MICRO+ 3 MENINGEAL CONGESTION

LUNGS
GROSS: COLOR CHANGE, DIFFUSE
BRIGHT RED, ALL LOBES
MICRO+ 4 CONGESTION
MICRO: ((2)) INTRAALVEOLAR CELLULAR DEBRIS

URINARY BLADDER
GROSS: HEMORRHAGE
MODERATE AMOUNT
MICRO+((3)) HEMORRHAGE
SUBMUCOSAL HEMORRHAGE SEVERAL SITES
THE TISSUE IS ALSO AUTOLYZED

THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER NERVE, SCIATIC NERVE, TIBIAL
TESTES KIDNEYS

THE FOLLOWING TISSUES WERE **TOO AUTOLYZED FOR EVALUATION:**
STOMACH

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 FISCHER 344 RATS

NECROPSY PROTOCOL

PERFUSED MALES

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

BRAIN, NOS	SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N	LUNG	TAIL
GROSS LESIONS				

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 0 MG/KG/DAY MALE

ANIMAL 9495 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9499 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9518 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 50 MG/KG/DAY . MALE

ANIMAL 9485 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
DORSAL ROOT GANG
MICRO: (2) PERIVASCULAR INFILTRATES
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE

THE FOLLOWING TISSUES WERE **MISSING:**
PERONEAL/SURAL N

ANIMAL 9487 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9496 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 50 MG/KG/DAY MALE

ANIMAL 9496 (CONTINUED)

PERONEAL/SURAL N
THE FOLLOWING TISSUES WERE MISSING:
FORNIX

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 200 MG/KG/DAY MALE

ANIMAL 9489 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MENINGES
MICRO: (1) PERIVASCULAR INFILTRATES
MONONUCLEAR CELLS; MIDBRAIN SECTION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:

PIRIFORM CORTEX	FRONTAL CORTEX	PARIETAL CORTEX
TEMPORAL CORTEX	OCCIPITAL CORTEX	SEPTAL NUCLEI
CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	AMYGDALA
HIPPOCAMPUS	THALAMUS	HYPOTHALAMUS
MIDBRAIN	SUBSTANTIA NIGRA	CEREBELLAR W.M.
ANT COMMISSURE	EXTERNAL CAPSULE	INTERNAL CAPSULE
CORPUS CALLOSUM	FORNIX	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

ANIMAL 9512 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9523 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 200 MG/KG/DAY MALE

ANIMAL 9523 (CONTINUED)

PERONEAL/SURAL N
THE FOLLOWING TISSUES WERE MISSING:
VESTIBULAR NUC

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 1000 MG/KG/DAY MALE

ANIMAL 9502 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9503 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9511 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

THYMIC REGION
GROSS: COLOR CHANGE, DIFFUSE
DARK RED
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 1000 MG/KG/DAY MALE

ANIMAL 9511 (CONTINUED)

DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE
TIBIAL NERVE PERONEAL/SURAL N

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 2000 MG/KG/DAY MALE

ANIMAL 9519 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
SPINAL CORD, CRV
MICRO: ((1)) VACUOLATION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

ANIMAL 9506 27-OCT-93
TYPE OF DEATH: SACRIFICED MORIBUND

LUNG
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, ALL LOBES
LN, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
DARK RED
TOTAL BODY
GROSS: STAINED
UROGENITAL REGION, YELLOW
URINARY BLADDER
GROSS: DILATATION/DISTENTION
MILD
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9514 27-OCT-93
TYPE OF DEATH: SACRIFICED MORIBUND

LUNG
GROSS: COLOR CHANGE, DIFFUSE

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 FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 2000 MG/KG/DAY MALE

ANIMAL 9514 (CONTINUED)

RED, ALL LOBES
LN, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
RED, ALL NODES
TOTAL BODY
GROSS: STAINED
YELLOW, UROGENITAL REGION
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

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

TABLE 5
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

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	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 necropsy data for the 3 animals/group that were perfused were back entered into this computer protocol for reporting purposes because the microscopic examination of the liver and kidneys are reported in this computer protocol. The neuropathologic examination was completed in a different computer protocol. Only the following tissues/areas were examined for these animals:

brain
spinal cord
sciatic nerve
sural nerve
tibial nerve
peroneal nerve
gasserian ganglion
liver
kidneys
lungs
ovaries

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 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 MG/KG/DAY FEMALE

ANIMAL 9537 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.382	4.328
KIDNEYS	1.137	0.914
SPLEEN	0.322	0.259
BRAIN	1.554	1.250
ADRENAL GL	0.043	0.035
OVARIES	0.086	0.069
TERMINAL BODY WT.	124.4	

LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
ONE NODE, RED
MICRO+((3)) SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, DIFFUSE
RIGHT SIDE, RED
MICRO: (2) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER BRAIN NERVE, SCIATIC
NERVE, TIBIAL KIDNEYS

ANIMAL 9532 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.398	4.118
KIDNEYS	1.136	0.867
SPLEEN	0.434	0.331
BRAIN	1.622	1.237
ADRENAL GL	0.039	0.030
OVARIES	0.094	0.072
TERMINAL BODY WT.	131.1	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER
MICRO: ((1)) MONONUCLEAR CELL INFILTRATE(S)
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
BRAIN NERVE, SCIATIC NERVE, TIBIAL
KIDNEYS

ANIMAL 9571 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	133.4	

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

ANIMAL 9540 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	130.4	

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

ANIMAL 9552 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	137.4	

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

ANIMAL 9531 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.562	4.077
KIDNEYS	1.169	0.857
SPLEEN	0.353	0.259
BRAIN	1.597	1.170
ADRENAL GL	0.040	0.029
OVARIES	0.098	0.072
TERMINAL BODY WT.	136.4	

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

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

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY FEMALE :

ANIMAL 9557 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.283	4.035
KIDNEYS	1.060	0.810
SPLEEN	0.342	0.261
BRAIN	1.680	1.283
ADRENAL GL	0.033	0.025
OVARIES	0.081	0.062
TERMINAL BODY WT.	130.9	

STOMACH
GROSS: COLOR CHANGE, DIFFUSE
GLANDULAR PORTION, PALE PINK
MICRO: ((2)) GASTRITIS
GLANDULAR STOMACH AND SQUAMOUS JUNCTION
MAINLY NEUTROPHILS AND EOSINOPHILS
(2) LYMPHOCYTIC INFILTRATE(S)

LYMPH ND, S-MAN
GROSS: SIZE INCREASE
SLIGHT

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
SEVERAL DARK RED FOCAL AREAS
MICRO+((2)) HEMORRHAGE

THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LYMPH ND, S-MAN BRAIN NERVE, SCIATIC
NERVE, TIBIAL

ANIMAL 9566 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.152	3.991
KIDNEYS	1.092	0.846
SPLEEN	0.329	0.255
BRAIN	1.588	1.230
ADRENAL GL	0.037	0.029
OVARIES	0.074	0.057
TERMINAL BODY WT.	129.1	

ADIPOSE TISSUE
GROSS: THICKER THAN NORMAL
RIGHT UTERINE FAT, NEAR HEMORRHAGE OF COLON
MICRO+ (2) STEATITIS
PROBABLY ASSOCIATED WITH THE COLON LESION

STOMACH
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
STRIATED RED FOCAL AREAS, NONGLANDULAR PORTION
MICRO: ((2)) GASTRITIS
GLANDULAR STOMACH AND SQUAMOUS JUNCTION

COLON
GROSS: HEMORRHAGE
10X5 MM AREA, NEAR PELVIC BONE
MICRO+ (4) HEMORRHAGE
SEROSAL SURFACE
MICRO: (3) COLITIS
AFFECTS THE SUBMUCOSA AT THE SAME SITE AS THE HEMORRHAGE

LUNGS
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
TWO BROWN FOCI, RIGHT DIAPHRAGMATIC LOBE
MICRO+((2)) PNEUMONITIS
SEVERAL SMALL FOCI

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 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 50 MG/KG/DAY FEMALE

ANIMAL 9559 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	135.2	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9570 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	138.8	

SPINAL CORD
GROSS: HEMORRHAGE
CERVICAL, 6X3 MM AREA
MICRO: N O T E X A M I N E D

ANIMAL 9556 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.843	4.157
KIDNEYS	1.188	0.845
SPLEEN	0.357	0.254
BRAIN	1.695	1.206
ADRENAL GL	0.038	0.027
OVARIES	0.078	0.055
TERMINAL BODY WT.	140.6	

LYMPH ND, MED
MICRO: 2 SINUS ERYTHROCYTOSIS
2 MASTOCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
SCATTERED PINK FOCAL AREAS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
THYMIC REGION BRAIN NERVE, SCIATIC
NERVE, TIBIAL

ANIMAL 9563 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	146.2	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

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

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 200 MG/KG/DAY FEMALE

ANIMAL 9542 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.811	4.331
KIDNEYS	1.185	0.883
SPLEEN	0.360	0.268
BRAIN	1.546	1.152
ADRENAL GL	0.038	0.028
OVARIES	0.092	0.069
TERMINAL BODY WT.	134.2	

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
RED FOCAL AREAS
MICRO+((1)) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9569 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.299	4.270
KIDNEYS	1.086	0.875
SPLEEN	0.393	0.317
BRAIN	1.627	1.311
ADRENAL GL	0.035	0.028
OVARIES	0.058	0.047
TERMINAL BODY WT.	124.1	

THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
DARK RED FOCAL AREAS
MICRO+((2)) HEMORRHAGE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
BRAIN NERVE, SCIATIC NERVE, TIBIAL

ANIMAL 9560 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	139.7	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9551 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.713	4.199
KIDNEYS	1.158	0.851
SPLEEN	0.354	0.260
BRAIN	1.731	1.272
ADRENAL GL	0.053	0.039
OVARIES	0.081	0.060
TERMINAL BODY WT.	136.1	

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

ANIMAL 9555 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	134.5	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9548 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	133.3	

LYMPH ND, MED
GROSS: COLOR CHANGE, DIFFUSE
SEVERAL NODES, DARK RED
MICRO: 4 SINUS ERYTHROCYTOSIS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
THYMIC REGION

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

Limbs exaggerated/ splayed	The hindlimbs and/or forelimbs show exaggerated placement or movements. Scoring criteria: Present - The animal displays slightly abnormal placement/movement of the limbs. Excessive - The limbs are moved in an extremely exaggerated motion when walking. The limbs are splayed at least 45 degrees from body.
Walks on Toes	The animal does not place its feet in a normal heel to toe manner when walking. The hindlimbs are drawn into the body. Scoring criteria: Present - There is a noticeable alteration in body position. The back may appear to be arched/hunched. The animal walks on its toes and the distal pads of its feet. Excessive - The animal walks on its toes only with a severely arched/hunched body position.
Hypotonic	The animal is unable to support its weight but is able to move in a straight line without lurching. Scoring criteria: Present - The animal moves slowly and drags abdomen on surface. Excessive - The animal's limbs are apparently weak and splayed. The animal drags its abdomen on surface and has labored locomotion.
Other	Any other gait abnormalities are recorded as other and described in the raw data.

Body Position

The animal's posture while in the observation arena will be recorded as normal, hunched, on side, or on stomach.

Breathing Pattern	A normal respiratory pattern is characterized by rapid and shallow breaths during movement and slower, deeper breaths when the animal is stationary. The respiratory pattern will be evaluated and recorded as either normal, mouth breathing, labored, or audible.
Arousal	The level of unprovoked activity in the open field will be evaluated. Scoring criteria: Hyperactive/hyperalert - The animal appears excited and may dart or freeze during the observation period or may sit in one place and jump at any sound or movement. Alternating behaviors - The animal goes through a normal repertoire of behaviors consisting of periods of sniffing, rearing, exploring, grooming, etc. Inactive/alert - The animal generally sits in one place during the majority of the observation period but appears to be aware of its surroundings. Inactive/not alert - The animal sits in one place during the observation period and appears to be unaware of its surroundings or is in a stupor.
Palpebral closure	As described above.
Defecation	The type or absence of excrement during the observation period will be recorded as normal, none, soft, or diarrhea.
Urination	The amount of urination during the observation period will be recorded as none, present, or excessive.
Rears	The number of times the animal lifts both front legs off the surface of the cart during the observation period will be recorded.

<u>Manipulative Observations</u>

Approach response	The animal's reaction to being approached by an object will be recorded as no reaction, noticeable reaction, or exaggerated reaction.
Startle response	The animal's response to acoustic stimuli will be recorded as no reaction, noticeable reaction, or exaggerated reaction.

Tail pinch response	The animal's reaction to having its tail pinched with tweezers will be recorded as no reaction, noticeable reaction, or exaggerated reaction.
Pupil size	The pupil's relative size to the normal size for the test species will be graded as normal (less than 50% of the size of the eyeball but not pinpoint), increased (greater than 50% of the size of the eyeball), or decreased (pinpoint).
Muscle tone	The relative rigidity or flaccidity of the limb and abdominal musculature will be recorded as normal, increased, or decreased.
Lacrimation	Secretion or discharge of tears causing the fur to appear wet around the eyes will be graded as none, present, or excessive.
Salivation	The presence of saliva around the mouth will be recorded as none, present, or excessive.
Exophthalmus	The absence or presence of an abnormal protrusion of the eyeball.
Emaciation	Whether the animal has an excessively lean appearance.
Dehydration	Whether the pinched skin remains in a pinched position when released.
Fur appearance	The appearance of the animal's fur will be recorded as normal, unkempt, or urine stains/wetness.
Crusts	The presence or absence of a crust around the mouth, nose, or eyes.
Visual placing	The presence or absence of forelimb extension, while being held by the observer, in anticipation of grasping a surface.
Grip strength	The animal is allowed to grasp with its forelimbs a wire mesh screen attached to a push-pull strain gauge. The animal is held by the base of the tail and pulled caudally (rapidly) parallel to the plane of the screen until its grip on the screen is broken. The animal is then allowed to grasp with its hindlimbs the leading edge of another wire mesh screen attached to a push-pull strain gauge. The animal is held by the base of the tail and pulled caudally (rapidly) parallel to and across the surface of the screen until its grip on the screen is broken. Forelimb and hindlimb measurements are performed in duplicate.

Body temperature	The animal's body temperature will be measured using an electronic thermistor inserted approximately 6 to 8 cm into the animal's rectum.
Body weight	The animal's body weight will be recorded at the time of testing.
Air righting	The ability of the animal to right itself while airborne will be recorded. The animal is held upside down, with the observer's hands under its back, approximately 30 cm above the surface of the cart. The animal is then released and the manner in which it lands is recorded either as feet/coordinated, feet/uncoordinated, back, or side.
Hind leg splay	The distance between the hindlimb digit pads after falling approximately 40 cm will be recorded. The outside digit pads of both hind paws are painted using a nontoxic paint. The animal is then held in a prone position above the cart and dropped onto a clean piece of paper. The distance between the two paint marks left upon landing is measured and recorded. The trial is performed in duplicate.

UNION CARBIDE

BUSHY RUN RESEARCH CENTER

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PROTOCOL AMENDMENT 2

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

BRRC PROJECT ID: 93U1318

SPONSORS:

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. Hermansky, Pharm.D., Ph.D., DABT — 6/10/94 Date
Study Director

Edward H. Fowler, DVM, Ph.D., Diplomate ACVP — 6-10-94 Date
Associate Director

Linda J. Calisti, B.S. — 6/10/94 Date
Manager, Good Laboratory Practices/Quality Assurance

John P. Van Miller, Ph.D., DABT — 6/10/94 Date
Director

Union Carbide Corporation:

Tipton R. Tyler, Ph.D., DABT — 6/17/94 Date
Associate Director of Applied Toxicology

W. P. Miller, Ph.D. — 6/21/94 Date
Manager of Product Safety

Shell Oil Company:

Marcy I. Banton, DVM, Ph.D., DABVT — 6/30/94 Date
Sponsor's Representative

UNION CARBIDE CORPORATION

The protocol is amended as follows:

Item 1

Location of Protocol Change	Page 1, Sponsors and Reviewed and Approved by
Description of Protocol Change	The references to the Union Carbide Corporation Division were removed.
Rationale	Union Carbide Corporation has been restructured and no longer has Divisions.

Item 2

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. Steven J. Hermansky received certification from the American Board of Toxicology.

Item 3

Location of Protocol Change	Page 1, Reviewed and Approved by
Description of Protocol Change	Dr. Tipton R. Tyler's title was changed to Associate Director of Applied Toxicology. Mr. W. P. Miller was added as signatory for Union Carbide Corporation in place of Mr. Richard C. Wise.
Rationale	These changes were made at Union Carbide Corporation due to promotion/retirement.

Item 4

Location of Protocol Change	Page 1, Sponsor's Representative
Description of Protocol Change	Marcy I. Banton will replace Thomas H. Gardiner as the Sponsor's Representative.
Rationale	Dr. Banton has assumed the responsibility of Sponsor's Representative for Shell Oil Company.

Item 5

Location of Protocol Change	Page 12, Histopathology
Description of Protocol Change	Tissues were taken from 1 male from the control group and 3 males from the high dose group to perform electron microscopy.
Rationale	This was done to aid in the characterization of the lesions observed by light microscopy. The results, interpretation and conclusions of this electron microscopy work will be submitted to the Sponsor as a separate report.

PROTOCOL DEVIATIONS

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

BRRC PROJECT NUMBER: 93U1318

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

1. Additional statistical analyses were conducted on incidence data for select FOB endpoints with ordered severity scores. They analyzed for group differences using Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somers' D measures of association.

2. Modifications were made to the FOB parameters included as Attachment 1 of the protocol in order to establish labwide consistency in terminology between behavioral signs recorded during routine clinical observations and those collected during functional observations. The major changes were the inclusion of additional involuntary muscular movement findings and a change in the definition of ataxia. See Appendix 8 for a listing of the parameters included in the FOB for this study and their definitions.

3. Sections of nervous system tissues collected from animals on this study were taken from one control and three high dose group animals for evaluation by electron microscopy. The methods, results and interpretation of this work will be reported under separate cover to the Sponsor. This additional work will be performed based upon a request by the Sponsor.

4. The cages were not changed and sanitized for one 16-day period. The protocol stated this procedure should be done every 2 weeks.

5. An 18-gauge oral dosing needle was used to dose the animals instead of a 16-gauge.

6. Animals were anesthetized with halothane instead of methoxyflurane prior to bleeding and sacrifice.

7. Due to the early mortality (following 2 doses) and subsequent cessation of dosing in the 2000 mg/kg/day dose group, the tissues to be examined in the high dose and control groups were also examined in the 1000 mg/kg/day dose group.

8. Heparin was mixed with sodium pentobarbital and this mixture was used to anesthetize the animals for perfusion. This was done to induce a state of anticoagulation in these animals to facilitate perfusion.

9. Organ weights were not collected for perfused animals.

10. The protocol states that stainless steel cages would be used throughout all phases of the study. Animals were housed in clear polycarbonate cages (26.7 x 24.1 x 20.3 cm) during the days of FOB evaluations.

11. The protocol states that the animals sacrificed for the pretest health screen would be identified by cage tags and a tail mark until sacrifice then toe-clipped for further identification. Toe clipping was not done.

12. The protocol states that stability would be determined using triplicate samples from the low and high dose concentrations. Actually 6 samples were evaluated.

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

BRRC Report 93U1318

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VINYL ESTERS

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(c/o Charlotte)
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Miller, W. P. - NC
Mazzolini, W. A. - DB (3 FULL)
Yalcinkaya, A. P. - TC

UCC HS&E

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Kuryla, W. C. - DB (FULL)
Leung, H-W. - DB
Tyler, T. R. - DB

NOTE: Please confirm changes on distribution list:

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Van Miller, John P.

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TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 MG/KG/DAY FEMALE

ANIMAL 9545 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	6.540	4.882
KIDNEYS	1.204	0.899
SPLEEN	0.332	0.248
BRAIN	1.565	1.168
ADRENAL GL	0.045	0.034
OVARIES	0.081	0.060
TERMINAL BODY WT.	134.0	

LYMPH ND, MED
MICRO: 3 SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, DIFFUSE
RED AREAS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
LIVER THYMIC REGION BRAIN
NERVE, SCIATIC NERVE, TIBIAL KIDNEYS

ANIMAL 9544 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	6.041	4.655
KIDNEYS	1.171	0.902
SPLEEN	0.415	0.320
BRAIN	1.382	1.065
ADRENAL GL	0.032	0.025
OVARIES	0.073	0.056
TERMINAL BODY WT.	129.8	

LIVER
MICRO: ((1)) MONONUCLEAR CELL INFILTRATE(S)
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
MOTTLED RED AND TAN
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
THYMIC REGION BRAIN NERVE, SCIATIC
NERVE, TIBIAL KIDNEYS

ANIMAL 9530 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	129.4	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9568 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	6.020	4.666
KIDNEYS	1.113	0.863
SPLEEN	0.359	0.278
BRAIN	1.598	1.239
ADRENAL GL	0.040	0.031
OVARIES	0.090	0.070
TERMINAL BODY WT.	129.0	

LIVER
MICRO: (1) MONONUCLEAR CELL INFILTRATE(S)
LYMPH ND, MED
MICRO: 2 SINUS ERYTHROCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
RED FOCAL AREAS, 2X2 MM
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**
THYMIC REGION BRAIN NERVE, SCIATIC
NERVE, TIBIAL KIDNEYS

ANIMAL 9543 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	143.1	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 9553 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	140.4	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

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

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY FEMALE

ANIMAL 9549 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: FOUND DEAD

TOTAL BODY
GROSS: STAINED
PERINASAL REGION, DARK RED
PERINEAL REGION, YELLOW
LIVER
MICRO: ((1)) HEPATOCELLULAR VACUOLATION
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, ALL NODES
MICRO+ 2 SINUS ERYTHROCYTOSIS
COLOR CHANGE IS MAINLY DUE TO
CONGESTION
MICRO: 3 MASTOCYTOSIS
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
DARK RED FOCI
MICRO+((4)) HEMORRHAGE
BRAIN
GROSS: MENINGEAL HEMORRHAGE
MARKED
MICRO+ 2 MENINGEAL CONGESTION
LUNGS
GROSS: COLOR CHANGE, DIFFUSE
DARK RED, ALL LOBES
MICRO+ 4 CONGESTION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
NERVE, SCIATIC NERVE, TIBIAL KIDNEYS

ANIMAL 9541 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	126.9	

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

ANIMAL 9533 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	132.7	

EYE
GROSS: OPACITY
LEFT, LINEAR
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER EYE KIDNEYS

ANIMAL 9562 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: FOUND DEAD

LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
RED, ALL NODES
BRAIN
GROSS: MENINGEAL HEMORRHAGE

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

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY FEMALE

ANIMAL 9562 (CONTINUED)

MICRO+ 3 MARKED MENINGEAL CONGESTION

OVARIES
GROSS: COLOR CHANGE, DIFFUSE DARK RED, BILATERAL

LUNGS
GROSS: COLOR CHANGE, DIFFUSE DARK RED, ALL LOBES
MICRO+ 4 CONGESTION
MICRO: (3) HEMORRHAGE

THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER, LYMPH ND, S-MAN, NERVE, SCIATIC, NERVE, TIBIAL, OVARIES, KIDNEYS

ANIMAL 9538 8-NOV-93 STUDY DAY 15
TYPE OF DEATH: SCHEDULED SACRIFICE-PERFUSED

ORGAN WEIGHT	ABS.(G)	REL.
TERMINAL BODY WT.	137.1	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS

THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:
LIVER, KIDNEYS

ANIMAL 9561 27-OCT-93 STUDY DAY 3
TYPE OF DEATH: FOUND DEAD

TOTAL BODY
GROSS: STAINED BROWN, PERINEAL REGION

STOMACH
GROSS: COLOR CHANGE, DIFFUSE PALE RED, GLANDULAR PORTION
MICRO+ 3 CONGESTION
MICRO: (3) HYDROPIC DEGENERATION, SQUAMOUS MUCOSA 1 FOCUS IN THE NONGLANDULAR STOMACH. EPITHELIUM IS SLIGHTLY THICKENED WITH VACUOLES, NUCLEAR DEGENERATION AND LOSS, OCCASIONAL NECROTIC CELLS.
((2)) SQUAMOUS MUCOSAL HYPERPLASIA 2 FOCI: THE GLANDULAR JUNCTION AND THE AREA OF HYDROPIC DEGENERATION. THE LATTER MAY BE DUE TO EDEMA RATHER THAN PROLIFERATION OF THE EPITHELIUM

LIVER
MICRO: ((3)) HEPATOCELLULAR NECROSIS BOTH LOBES HAVE MANY INDIVIDUAL CELLS UNDERGOING NECROSIS OR DEGENERATION. MAY BE AN AGONAL LESION DUE TO VASCULAR FAILURE?

LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE DARK RED, ALL NODES
MICRO+ 4 SINUS ERYTHROCYTOSIS

BRAIN
GROSS: MENINGEAL HEMORRHAGE

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

TABLE 6
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 2000 MG/KG/DAY FEMALE

ANIMAL 9561 (CONTINUED)

		SEVERE
MICRO+	3	MENINGEAL HEMORRHAGE
MICRO:	3	MENINGEAL CONGESTION
LUNGS		
GROSS:		COLOR CHANGE, DIFFUSE BRIGHT RED, ALL LOBES
MICRO+	3	CONGESTION

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

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

TABLE 7
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

NECROPSY PROTOCOL

PERFUSED FEMALES

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

BRAIN, NOS	SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N	LUNG	TAIL
OVARIES	GROSS LESIONS			

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 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 0 MG/KG/DAY FEMALE

ANIMAL 9571 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9552 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
VESTIBULAR NUC
MICRO: ((1)) VACUOLATION/SPONGIOSIS
BILATERAL
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

ANIMAL 9540 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	TRIGEMINAL TRACT
SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM
SPINAL NERVE RTS	DORSAL ROOT GANG	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 0 MG/KG/DAY FEMALE

ANIMAL 9540 (CONTINUED)

THE FOLLOWING TISSUES WERE MISSING:
FORNIX OPTIC N/CHIASM

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 50 MG/KG/DAY FEMALE

ANIMAL 9559 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9563 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9570 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

SPINAL CORD, CRV
GROSS: HEMORRHAGE
CERVICAL, 6X3 MM AREA
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 50 MG/KG/DAY FEMALE

ANIMAL 9570 (CONTINUED)

DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE
TIBIAL NERVE PERONEAL/SURAL N

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 200 MG/KG/DAY FEMALE

ANIMAL 9555 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9548 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

LYMPH ND, MED
GROSS: COLOR CHANGE, DIFFUSE
SEVERAL NODES, DARK RED
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

THE FOLLOWING TISSUES WERE **MISSING:**
FORNIX

ANIMAL 9560 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 200 MG/KG/DAY FEMALE

ANIMAL 9560 (CONTINUED)

TRIGEMINAL TRACT SPINAL CORD, CRV SPINAL CORD, THR
SPINAL CORD, LUM SPINAL NERVE RTS DORSAL ROOT GANG
GASSERIAN GANG SCIATIC NERVE TIBIAL NERVE
PERONEAL/SURAL N
THE FOLLOWING TISSUES WERE MISSING:
FORNIX

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 1000 MG/KG/DAY FEMALE

ANIMAL 9543 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 9553 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
TIBIAL NERVE
MICRO: (1) NERVE FIBER DEGENERATION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
PERONEAL/SURAL N		

ANIMAL 9530 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

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

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 1000 MG/KG/DAY FEMALE

ANIMAL 9530 (CONTINUED)

THE FOLLOWING TISSUES WERE MISSING:
FORNIX

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 2000 MG/KG/DAY FEMALE

ANIMAL 9541 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
SPINAL CORD, CRV
MICRO: ((2)) VACUOLATION
VENTRAL WHITE MATTER TRACTS
SPINAL CORD, THR
MICRO: ((1)) VACUOLATION
SPINAL CORD, LUM
MICRO: ((1)) VACUOLATION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

THE FOLLOWING TISSUES WERE **MISSING:**
FORNIX

ANIMAL 9538 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
PONS
MICRO: ((1)) VACUOLATION/SPONGIOSIS
VERY SLIGHT
MEDULLA OBL
MICRO: ((1)) VACUOLATION/SPONGIOSIS
VERY SLIGHT
SPINAL CORD, CRV
MICRO: ((1)) VACUOLATION
((1)) NERVE FIBER DEGENERATION
BEST SEEN ON LONGITUDINAL SECTION
SPINAL CORD, LUM
MICRO: ((1)) VACUOLATION
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL:**

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, THR
SPINAL NERVE RTS	DORSAL ROOT GANG	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N

THE FOLLOWING TISSUES WERE **MISSING:**
FORNIX

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

TABLE 8
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

PERFUSED

GROUP: 2000 MG/KG/DAY FEMALE

ANIMAL 9533 8-NOV-93
TYPE OF DEATH: SCHEDULED SACRIFICE

PONS
MICRO: ((1)) VACUOLATION/SPONGIOSIS
VERY SLIGHT, UNILATERAL FOCUS
MEDULLA OBL
MICRO: (1) VACUOLATION/SPONGIOSIS
MIDLINE SLIGHT
SPINAL CORD, CRV
MICRO: ((1)) VACUOLATION
VENTRAL WHITE MATTER TRACTS
((1)) NERVE FIBER DEGENERATION
SPINAL CORD, THR
MICRO: ((1)) VACUOLATION
EYE
GROSS: OPACITY
LEFT, LINEAR, WHITE
THE FOLLOWING TISSUES WERE **MICROSCOPICALLY NORMAL**:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, LUM
SPINAL NERVE RTS	DORSAL ROOT GANG	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N

THE FOLLOWING TISSUES WERE **MISSING**:
VESTIBULAR NUC

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 Fischer 344 Rats

Individual Clinical Pathology Data

(13 Pages)

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TABLE 1
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS
ABBREVIATIONS

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

WBC = LEUKOCYTES ($10^3/\mu l$)

RBC = ERYTHROCYTES ($10^6/\mu l$)

HGB = 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 ($10^3/\mu l$)

SEGS = SEGMENTED NEUTROPHILS ($10^3/\mu l$)

LYMP = LYMPHOCYTES ($10^3/\mu l$)

MONO = MONOCYTES ($10^3/\mu l$)

BASO = BASOPHILS ($10^3/\mu l$)

EOS = EOSINOPHILS ($10^3/\mu l$)

BAND = BANDED NEUTROPHILS ($10^3/\mu l$)

LMON = LARGE MONOCYTES ($10^3/\mu l$)

IGRN = IMMATURE GRANULOCYTES ($10^3/\mu l$)

IERY = IMMATURE ERYTHROCYTES ($10^3/\mu l$)

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 FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9499	6.4	8.10	16.6	44.9	55.	20.5	37.0	628.	0.33	5.91
9518	6.6	8.01	16.6	44.9	56.	20.7	37.0	692.	0.42	5.99
9507	5.2	7.98	16.6	44.6	56.	20.8	37.2	614.	0.48	4.57
9509	5.7	7.94	16.6	44.9	57.	20.9	37.0	697.	0.52	4.97
9495	8.7	7.67	16.4	42.7	56.	21.4	38.4	681.	0.55	7.94
9517	7.5	8.25	16.6	45.6	55.	20.1	36.4	655.	0.59	6.62
MEAN	6.7	7.99	16.6	44.6	56.	20.7	37.2	661.	0.48	6.00
S.D.	1.28	0.192	0.08	0.97	0.8	0.42	0.66	34.6	0.095	1.205
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9499	0.12	0.01	0.06					
9518	0.14	0.03	0.04					
9507	0.03	0.03	0.06					
9509	0.13	0.02	0.07					
9495	0.15	0.03	0.04					
9517	0.18	0.07	0.06					
MEAN	0.13	0.03	0.05					
S.D.	0.051	0.020	0.012					
N	6	6	6					

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9487	7.7	8.06	16.6	45.3	56.	20.6	36.7	CLOT	0.70	6.80
9500	5.1	8.44	17.0	46.5	55.	20.1	36.5	610.	0.46	4.51
9496	7.4	7.94	16.5	44.3	56.	20.8	37.3	638.	0.48	6.70
9485	7.1	8.05	16.8	44.6	55.	20.9	37.7	CLOT	0.85	6.02
9513	6.0	7.81	16.2	43.7	56.	20.8	37.1	613.	0.40	5.40
9510	6.9	8.68	17.4	47.5	55.	20.0	36.6	CLOT	0.55	6.18
MEAN	6.7	8.16	16.8	45.3	56.	20.5	37.0	620.	0.57	5.94
S.D.	0.98	0.329	0.40	1.43	0.5	0.36	0.43	15.4	0.170	0.862
N	6	6	6	6	6	6	6	3	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9487	0.23	0.00	0.00	0.	0.	0.	0.	0.
9500	0.04	0.03	0.05					
9496	0.18	0.01	0.03					
9485	0.07	0.00	0.14	0.	0.	0.	0.	0.
9513	0.08	0.02	0.04					
9510	0.14	0.00	0.00	0.	0.	0.	0.	0.
MEAN	0.12	0.01	0.04	0.	0.	0.	0.	0.
S.D.	0.073	0.013	0.052	0.0	0.0	0.0	0.0	0.0
N	6	6	6	3	3	3	3	3

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9504	6.1	7.56	15.5	42.1	56.	20.6	36.9	CLOT	1.10	4.88
9489	6.7	7.74	16.3	42.7	55.	21.1	38.2	731.	0.39	6.09
9523	8.0	7.99	16.6	44.9	56.	20.8	37.0	691.	0.50	7.27
9482	5.3	8.21	16.4	45.3	55.	20.0	36.3	603.	0.54	4.54
9512	7.8	7.83	16.5	44.0	56.	21.1	37.5	677.	0.40	7.14
9497	6.1	8.41	17.2	46.8	56.	20.5	36.7	647.	0.39	5.50
MEAN	6.7	7.96	16.4	44.3	56.	20.7	37.1	670.	0.55	5.90
S.D.	1.06	0.313	0.55	1.74	0.5	0.42	0.67	48.0	0.275	1.140
N	6	6	6	6	6	6	6	5	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9504	0.12	0.00	0.00	0.	0.	0.	0.	0.
9489	0.10	0.04	0.05					
9523	0.16	0.04	0.07					
9482	0.09	0.03	0.07					
9512	0.14	0.03	0.05					
9497	0.10	0.04	0.05					
MEAN	0.12	0.03	0.05	0.	0.	0.	0.	0.
S.D.	0.027	0.015	0.026	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 FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9511	7.4	7.25	15.1	40.5	56.	20.8	37.1	CLOT	2.01	5.20
9520	6.9	7.42	15.6	40.2	54.	21.1	38.9	668.	1.01	5.64
9502	6.0	7.86	16.0	43.1	55.	20.4	37.2	618.	0.50	5.31
9521	6.7	7.47	15.4	42.4	57.	20.7	36.4	684.	0.76	5.66
9498	5.3	7.56	15.4	42.4	56.	20.4	36.4	CLOT	1.06	3.82
9503	6.8	7.59	15.5	42.1	55.	20.5	36.9	662.	0.45	6.13
MEAN	6.5	7.53	15.5	41.8	56.	20.6	37.2	658.	0.96	5.29
S.D.	0.75	0.204	0.32	1.14	1.0	0.27	0.91	28.2	0.570	0.792
N	6	6	6	6	6	6	6	4	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9511	0.22	0.00	0.00	0.	0.	0.	0.	0.
9520	0.12	0.04	0.11					
9502	0.12	0.01	0.06					
9521	0.19	0.04	0.04					
9498	0.37	0.00	0.05	0.	0.	0.	0.	0.
9503	0.12	0.04	0.04					
MEAN	0.19	0.02	0.05	0.	0.	0.	0.	0.
S.D.	0.098	0.020	0.036	0.0	0.0	0.0	0.0	0.0
N	6	6	6	2	2	2	2	2

TABLE 2
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9519	6.0	7.80	16.2	43.4	56.	20.8	37.4	609.	0.47	5.31
MEAN	6.0	7.80	16.2	43.4	56.	20.8	37.4	609.	0.47	5.31
S.D.	0.00	0.000	0.00	0.00	0.0	0.00	0.00	0.0	0.000	0.000
N	1	1	1	1	1	1	1	1	1	1

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9519	0.13	0.02	0.03					
MEAN	0.13	0.02	0.03					
S.D.	0.000	0.000	0.000					
N	1	1	1					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9537	6.6	8.12	16.8	45.6	56.	20.7	36.9	627.	0.40	5.96
9532	7.8	7.87	16.9	44.6	57.	21.5	37.9	743.	0.81	6.74
9571	6.7	7.88	16.8	44.0	56.	21.3	38.2	667.	0.46	5.98
9540	7.8	7.89	16.6	43.7	55.	21.1	38.0	638.	0.36	7.15
9552	6.6	8.00	16.8	44.9	56.	21.0	37.4	757.	0.51	5.90
9531	7.1	7.93	17.1	44.9	57.	21.6	38.0	631.	0.44	6.48
MEAN	7.1	7.95	16.8	44.6	56.	21.2	37.7	677.	0.50	6.37
S.D.	0.58	0.097	0.16	0.69	0.8	0.33	0.50	58.3	0.162	0.510
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9537	0.13	0.03	0.05					
9532	0.16	0.03	0.08					
9571	0.17	0.01	0.02					
9540	0.13	0.04	0.06					
9552	0.11	0.03	0.06					
9531	0.11	0.04	0.06					
MEAN	0.13	0.03	0.05					
S.D.	0.025	0.011	0.020					
N	6	6	6					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9557	6.3	7.74	16.7	44.0	57.	21.6	38.0	682.	0.49	5.70
9566	7.7	7.94	16.8	44.3	56.	21.2	37.9	683.	0.49	6.97
9559	6.7	7.85	16.4	43.7	56.	20.9	37.6	685.	0.41	6.12
9570	7.3	7.94	16.9	44.9	57.	21.3	37.6	694.	0.38	6.70
9556	7.4	8.40	17.0	47.1	56.	20.2	36.0	741.	0.69	6.42
9563	8.5	7.81	16.5	43.4	56.	21.1	38.1	CLOT	1.53	6.79
MEAN	7.3	7.95	16.7	44.6	56.	21.1	37.5	697.	0.66	6.45
S.D.	0.75	0.235	0.23	1.37	0.5	0.46	0.75	25.0	0.437	0.473
N	6	6	6	6	6	6	6	5	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9557	0.09	0.03	0.04					
9566	0.10	0.04	0.08					
9559	0.09	0.03	0.05					
9570	0.07	0.04	0.08					
9556	0.15	0.03	0.08					
9563	0.08	0.00	0.08	0.	0.	0.	0.	0.
MEAN	0.10	0.03	0.07	0.	0.	0.	0.	0.
S.D.	0.028	0.015	0.018	0.0	0.0	0.0	0.0	0.0
N	6	6	6	1	1	1	1	1

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9542	5.4	7.62	16.5	42.7	56.	21.7	38.6	677.	0.30	4.95
9569	8.8	7.72	16.1	43.4	56.	20.9	37.2	662.	0.90	7.56
9560	7.6	7.60	16.3	42.7	56.	21.5	38.2	714.	0.46	6.96
9551	6.9	7.68	16.5	42.7	56.	21.5	38.6	686.	0.40	6.24
9555	7.7	7.91	16.6	44.0	56.	21.0	37.7	652.	0.60	6.91
9548	7.1	7.96	17.0	44.9	56.	21.4	37.8	611.	0.39	6.50
MEAN	7.2	7.75	16.5	43.4	56.	21.3	38.0	667.	0.51	6.52
S.D.	1.10	0.152	0.30	0.90	0.0	0.31	0.57	34.8	0.216	0.891
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9542	0.09	0.03	0.07					
9569	0.17	0.04	0.07					
9560	0.06	0.03	0.06					
9551	0.13	0.04	0.06					
9555	0.12	0.03	0.06					
9548	0.13	0.02	0.07					
MEAN	0.12	0.03	0.06					
S.D.	0.038	0.008	0.005					
N	6	6	6					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9545	4.9	7.43	15.6	41.5	56.	21.0	37.7	614.	0.40	4.37
9544	7.9	7.48	15.9	42.4	57.	21.3	37.5	565.	0.48	7.21
9530	6.6	7.85	16.3	43.4	55.	20.8	37.6	544.	0.46	6.03
9568	4.9	7.41	15.6	41.2	56.	21.1	38.0	558.	0.32	4.41
9543	6.0	7.28	15.5	40.9	56.	21.3	38.0	615.	0.64	5.21
9553	5.8	7.47	15.5	41.5	56.	20.8	37.5	556.	0.41	5.19
MEAN	6.0	7.49	15.8	41.8	56.	21.1	37.7	575.	0.45	5.40
S.D.	1.14	0.192	0.31	0.93	0.6	0.23	0.23	31.1	0.108	1.076
N	6	6	6	6	6	6	6	6	6	6

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9545	0.11	0.01	0.05					
9544	0.12	0.03	0.07					
9530	0.08	0.03	0.04					
9568	0.06	0.02	0.05					
9543	0.09	0.04	0.04					
9553	0.08	0.03	0.05					
MEAN	0.09	0.03	0.05					
S.D.	0.022	0.010	0.011					
N	6	6	6					

TABLE 3
VINYL 2-ETHYLHEXANOATE: FOURTEEN-DAY PERORAL (GAVAGE) RANGE-FINDING
STUDY IN FISCHER 344 RATS

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

ANIMAL	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	SEGS	LYMP
9541	4.5	7.45	15.9	42.1	57.	21.4	37.8	544.	0.86	3.47
9533	6.2	7.96	16.3	43.7	55.	20.5	37.3	CLOT	0.87	5.19
9538	6.3	7.87	16.1	43.4	55.	20.5	37.2	CLOT	1.13	4.84
MEAN	5.7	7.76	16.1	43.1	56.	20.8	37.4	544.	0.95	4.50
S.D.	0.99	0.272	0.20	0.83	1.2	0.52	0.34	0.0	0.153	0.909
N	3	3	3	3	3	3	3	1	3	3

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
9541	0.12	0.02	0.05					
9533	0.12	0.00	0.00	0.	0.	0.	0.	0.
9538	0.19	0.00	0.13	0.	0.	0.	0.	0.
MEAN	0.14	0.01	0.06	0.	0.	0.	0.	0.
S.D.	0.040	0.012	0.066	0.0	0.0	0.0	0.0	0.0
N	3	3	3	2	2	2	2	2

Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

Protocol, Protocol Amendments, and Protocol Deviations

(29 Pages)

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PROTOCOL

TITLE: Vinyl 2-Ethylhexanoate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats

BRRC PROJECT ID: 93U1318

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Excellence Through Quality

EQ

OBJECTIVES

The objectives of this study are to evaluate the toxicity of 4 dose levels of vinyl 2-ethylhexanoate in Fischer 344 rats 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

Starting Date of Acclimation	October 12, 1993
Starting Date of Test Substance Administration	October 25, 1993
Date for Completion of In-Life Phase	November 8, 1993
Proposed Date for Submission of Draft Final Report	February 11, 1994

METHODS

Test Substance

Product Name	VYNATE® 2-EH 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
BRRC 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	Fischer 344 rats
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 rat.

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 6 (3/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 rat, or whose absolute body weight at the second weighing is outside ± 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 3 animals/sex selected directly from the shipping cartons with as many cartons as possible being represented and will consist of examinations for fecal parasites and

necropsy. Serology testing on 5 animals/sex for Sendai virus, rat coronavirus/sialodacryoadenitis virus, and Mycoplasma pulmonis will be performed approximately 2 weeks after receipt using animals not selected for the study. Serology results will be available prior to the start of the study.

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)
Rat coronavirus/Sialodacryoadenitis virus (RCV/SDA)
Kilham rat virus (KRV)
Toolan's H-1 (H-1)
Reovirus type 3 (REO3)
Mycoplasma pulmonis (MPUL)
Mouse polio virus (GD-7)
Lymphocytic choriomeningitis (LCMV)
Mouse adenovirus FL/K87 (MAD)
Minute virus of mice (MVM)
Polyoma virus (POLY)

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 rats 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 tail tattoos. Animals sacrificed for use in the pretest health screen will be identified by cage tags and a tail mark until sacrifice and then toe-clipped for further identification. 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® (Deotized 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.

T. Taylor 9/30/93
[illegible] 10-12-93
JHG 10/22/93

Administration of Test Substance

Route and Justification

The route of administration will be by gavage. This route will ~~is considered to be a meaningful way to evaluate the toxicity of chemicals with the use pattern of vinyl 2-ethylhexanoate.~~ be used in the 90-day subchronic study as specified in the TSCA PMN consent order for the vinyl Ester family.

Dose Selection

Four graduated dosage levels of the test substance were selected by the Sponsor for evaluation in 4 groups of rats. Dosage levels will be expressed in terms of mg test substance/kg body weight/day.

12/13/93

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

The test substance will be administered as a single, daily dose using a 16-gauge, 3-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.

The dosing solution volume in all dose groups, including the control group, will be 4 ml/kg/day. Administered volumes will be based on the individual's body weight.

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 each 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 ± 10% of nominal; the difference between duplicate analyses will not exceed 15%; and individual analyses will be within ± 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 Male	Female	Vinyl 2-ethylhexanoate Volume (ml/kg/day)	Dosage (mg/kg/day)
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 0-4, 4-7, and 7-14. 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 lesions[1]
lungs with mainstem bronchi[2]
brain (cerebral cortex, cerebellar cortex, medulla/pons)
pituitary
thyroid - parathyroid complex[3]
thymic region[4]
trachea
heart
sternum (including marrow)
salivary gland
liver
spleen
kidneys[5]
adrenals
pancreas
testes
epididymis
prostate
seminal vesicles

ovaries
vagina
uterus (corpus and cervix)[6]
aorta
skin
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)

Tails will be saved for identification purposes.

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

[2]Lungs will be inflated with formalin by the trachea.

[3]Parathyroids 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.

[4]At 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.

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

[6]The 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)
spleen
brain (including brain stem)

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. BRRC 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 BRRC 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 BRRC 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 BRRC 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 BRRC within 8 weeks from the date of submission of the draft version. BRRC 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, BRRC 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.

UNION CARBIDE

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 Fischer 344 Rats

BRRC PROJECT ID: 93U1318

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:

11/17/93
Steven J. Hermansky, Pharm.D., Ph.D. / Date
Study Director

11/17/93
Edward H. Fowler, DVM, Ph.D., Date
Diplomate ACVP
Associate Director

12/14/93
Linda J. Calisti, B.S. Date
Manager, Good Laboratory Practices/Quality Assurance

12/14/93
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Corporation:

12/15/93
Tipton R. Tyler, Ph.D., DABT Date
Assistant Director of Applied Toxicology

Division:

12-20-93
Richard C. Wise Date
Manager of Product Safety

Shell Oil Company:

12/15/93
Thomas H. Gardiner, Ph.D. Date
Sponsor's Representative

The protocol is amended as follows:

Item 1

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.

Item 2

Location of Protocol Change	Page 9, Mortality Checks and Clinical Signs
Description of Protocol Change	Detailed clinical observations are to be performed daily.
Rationale	Detailed clinical observations are to be performed daily due to the short in-life phase of the study.

Item 3

Location of Protocol Change	Page 9, Body Weight
Description of Protocol Change	Individual body weights will be measured on Days 1, 4, 8, and 15 (prior to sacrifice).
Rationale	Days 7 and 14 were changed to accommodate scheduling.

Item 4

Location of Protocol Change	Page 9, Food Consumption
Description of Protocol Change	Individual food consumption measurements will be collected for intervals 1-4, 4-8, and 8-15.
Rationale	The intervals were changed to accommodate scheduling.

Item 5

Location of Protocol Change	Page 9, Functional Observational Battery (FOB)
Description of Protocol Change	A battery of tests designed to detect gross alterations in nervous system function will be performed for all animals on Days 12 (after dosing), 13, and 14. All animals will be examined by trained technicians who are unaware of the animals' dosing assignment. Animals of the same sex will be evaluated by the same technician to avoid the effects of possible variation between technicians. A detailed description of the measures included in the FOB and the scoring criteria used for these measures are presented in Attachment 1.
Rationale	Sponsor request.

Item 6

Location of Protocol Change	Page 10, Anatomic Pathology Evaluations
Description of Protocol Change	The brain and peripheral nerves (sciatic and tibial) will be included in the list of tissues that will be processed histologically and examined by light microscopy for all animals in all dose groups. Except as noted below, animals will not be perfused and peripheral nerves will be embedded in paraffin. Three animals/group/sex will be anesthetized with sodium pentobarbital and perfused in situ by intracardiac perfusion with a phosphate buffered solution of 10% formaldehyde. After perfusion, the calvaria overlying the brain and vertebral arches covering the spinal cord (down to the level of the lumbar swelling) will be removed, and the peripheral nerves in the hind legs will be exposed. The brain inside the skull (with Gasserian ganglia), the spinal column down to the level of the sacrum, and the hind legs (with the peripheral nerves) will be stored, until trimmed, in the same fixative as used for the perfusions. After further immersion fixation, the central and peripheral nervous systems will be further dissected. At the time of trimming, the brain will be divided into multiple coronal sections (with the exception of the olfactory bulbs which will be embedded sagitally), and all of the

sections will be processed for evaluation. At least the following neuroanatomic areas will be evaluated:

forebrain[1]
center of the cerebrum[1]
center of the midbrain[1]
cerebellum and pons[1]
medulla oblongata[1]
spinal cord (cervical)[2]
spinal cord (thoracic and lumbar)[1]
dorsal root ganglia and dorsal and ventral nerve roots[3]
Gasserian ganglia[3]
proximal sciatic nerve (above the knee)[2]
tibial nerve (below the knee)[2]
sural and peroneal (fibular) nerve (below the knee)[3]

[1]Cross sections of these tissues will be evaluated.

[2]Cross and longitudinal sections of these tissues will be evaluated.

[3]Longitudinal sections of these tissues will be evaluated.

The saved tissues in the list above for the 3 animals/group/sex will be processed using standard histologic procedures and will be examined microscopically. Gross lesions, livers, kidneys, testes (males), brains and spinal cords, along with ganglia and spinal nerve roots, will be processed for paraffin embedding, sectioned at 5-6 microns, and stained with hematoxylin and eosin. In addition, the luxol fast blue and Bielschowsky's techniques will be performed on the brains and spinal cords, along with ganglia and spinal nerve roots. Additional stains may also be used at the discretion of the pathologist evaluating the tissues. From 1 hind leg, the proximal sciatic nerve from above the knee level, as well as the tibial, peroneal (fibular) and sural nerves from below the knee, will be embedded in glycol methacrylate, sectioned at 2 microns, and stained with hematoxylin and eosin, toluidine blue, and Bielschowsky's technique.

Rationale Sponsor request.

OVERVIEW OF THE FUNCTIONAL OBSERVATIONAL BATTERY (FOB)

The FOB involves the evaluation and documentation of the absence or presence (or severity if appropriate) of a predetermined set of behavioral signs for individual animals. During examination, an animal will be observed in its observation cage for signs of convulsions or tremors and evaluated for posture and palpebral closure. The animal will then be removed from the observation cage and handling reactivity will be evaluated. The animal will be placed on a clean laboratory cart covered with a thin, disposable paper board. The surface of the cart will be surrounded by clear Plexiglas® walls. The animal will be observed for signs of convulsions, tremors, excessive vocalization, piloerection, and unusual behavior. Gait, body position, breathing pattern, arousal, palpebral closure, defecation, urination, and rears will also be evaluated during this initial observation period. Approach, startle, and tail pinch responses will then be evaluated using simple equipment. The animal will then be held, and pupil size, muscle tone, lacrimation, salivation, exophthalmus, emaciation, dehydration, fur appearance, crusts, and visual placing will be evaluated. Grip strength, body temperature, body weight, air righting reflexes, and hind leg splay will be subsequently evaluated using simple equipment. The FOB requires approximately 6 minutes to perform for each animal.

Two technicians will evaluate and document neurobehavioral function of the test animals while blind to the treatment of the animals.

FOB SCORING CRITERIA

Cageside Observations

Posture	The condition and body position of the animal will be evaluated in the observation cage. Observations will be recorded as normal/awake, normal/asleep, on side/prostrate, or on stomach/prostrate.
Convulsions	The presence or absence of convulsions and the type (tonic, clinic, or both) of convulsions will be recorded. Convulsions will be graded as either single or multiple.
Tremors	The presence or absence of tremors will be recorded. The type (coarse or fine) and location of the tremors will be recorded.
Palpebral closure	The degree of closure of the eyelids will be recorded as wide open, slightly drooping, halfway shut, or completely shut.

Open Field Observations

Handling reactivity	The reaction of the animal to being removed from the observation cage and handled will be recorded as animal limp, slight/moderate resistance, or high resistance/aggressive.
Convulsions	As described above.
Tremors	As described above.
Excessive Vocalization	The presence or absence of excessive vocalization will be recorded.
Piloerection	The presence or absence of piloerection (the animal's hair stands vertical to the skin surface) will be recorded.
Unusual behavior	Behavior which occurs out of context and/or with abnormally high frequency or behaviors not associated with the normal repertoire of the species will be recorded. This could include but is not limited to retropulsion, head bobbing, continuous nonpurposeful behavior, or prostration.
Gait	The absence of gait impairment or presence of the following types of gait impairment will be recorded. Gait impairments will be graded as either present or excessive.
Ataxia	The animal displays muscular incoordination, especially when voluntary muscle movements are attempted. Scoring criteria: Present - The animal walks with a noticeable sway and/or rocking and/or jerky movements when walking. Animal may fall on side occasionally. Excessive - The animal frequently falls on its back and/or side while moving. The animal may not be able to move beyond a restricted area.