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BARTLESVILLE, OKLAHOMA 74004 918 661-6600

HEALTH, ENVIRONMENT AND SAFETY

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Environmental Protection Agency
401 M Street, SW
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Attn: Section 8(e) Coordinator
(CAP Agreement)

Gentlemen:

Phillips Petroleum Company is submitting the enclosed sixty (60) reports (two boxes, numbered 1 and 2) of toxicological studies pursuant to catagory II.B.2.b of the CAP Agreement 8ECAP-0075 Reports. Reports being submitted contain no confidential business information.

We are sending an additional five boxes (box numbers 3-7) of reports of studies that have, previously, been submitted to the FYI coordinator of the Office of Pollution Prevention and Toxics by the American Petroleum Institute (API). These are being provided solely for the Agency's convenience.

For questions concerning this correspondence, plese contact Fred Marashi at 918-661-8153.

Very truly yours,

Barbara J. Price

Barbara J. Price
Vice President
Health, Environment & Safety

Enclosure (Seven Boxes)

FFM/dh:29

3/7/95

Phillips Petroleum Company

CAP Identification Number: 8ECAP-0075
Pursuant to Category: II.B.2.b

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Title of Study: 26 Week Inhalation Toxicity Study of Toluene in the Rat

Name of Chemical: Toluene

CAS#: 108-88-3

Summary: After 7 days of inhalation, exposure to 1710 ppm, rats exhibited signs of central nervous system depression (ataxia, body tremors, prostration).

Fiche # 1684

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Medicine and Biological
Science Department

POOR QUALITY ORIGINAL

26 WEEK INHALATION TOXICITY STUDY OF TOLUENE IN THE RAT

STUDY PERFORMED BY:

Bio/dynamics Inc.

and

Institute of Neurotoxicity
Albert Einstein College of Medicine.

UNDER CONTRACT PS-29

April/May 1980

An equal opportunity employer

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Bio/dynamics Inc.

Drug Development and Safety Evaluation

PROJECT NO. 78-7234

A 26 WEEK INHALATION TOXICITY STUDY OF TOLUENE IN THE RAT

Submitted to: American Petroleum Institute
Washington, D.C.

Attention: Dr. Charles Holdsworth

Date: May 23, 1980

Bio dynamics Inc.

PROJECT NO. 78-7234

A 26 WEEK INHALATION TOXICITY STUDY

OF TOLUENE IN THE RAT

ABSTRACT

A twenty-six week inhalation toxicity study was performed with vapors of toluene. Groups of fifteen male and fifteen female Sprague-Dawley rats were exposed six hours per day, five days per week for twenty-six weeks with selected animals being removed following 8, 17, and 26 weeks of exposure, and a two-week post-exposure recovery period. The target concentrations had originally been set at 100 and 2,000 ppm of toluene, however following the observation of acute toxic responses during the second week of the study the high-level target concentration was lowered to 1,500 ppm for the remainder of the study. The cumulative mean exposure concentrations were 0, 100 and 1,481 ppm for Groups I, IV and V, respectively.

There were no treatment-related deaths during the study. During Week 2 the rats in the high-level chamber showed signs of central nervous system depression which was considered to be an acute response to the exposure. In addition to these signs, the only observations noted which may reflect treatment-related responses were increased incidences of dry rales and staining of the ano-genital fur in the high-level group relative to the control group.

Body weights for the high-level male rats were significantly higher than for the control rats during the latter part of the study. This was not considered to be a toxic response. No differences were found in the hematology parameters measured which were considered to be biologically significant. The urinalysis results were unremarkable.

Glucose levels in the female rats decreased in a dose-related pattern from the control group to the high-level group, however, all values fell within normal limits. A dose-related elevation in serum glutamic pyruvic transaminase levels was observed primarily in the female rats. The absolute values for all animals, except one high-level male and one high-level female rat, appeared to be within normal limits. The two animals mentioned above had SGPT levels approximately 4 and 5 times the average of their respective groups.

After termination of the exposure, all animals were submitted, live, to the sponsor for subsequent neurological examination at Albert Einstein College of Medicine.

P.O. Box 43 • Mettlers Road • East Millstone, New Jersey 08873 • (201) 873-2550 • Telex: 844597 • Cable: BIO/DYN

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I. INTRODUCTION

This study, conducted for the American Petroleum Institute, was designed to assess the inhalation toxicity of toluene administered to rats six hours per day, five days per week for 26 weeks at target concentrations of 100 and 1,500 parts per million (ppm). Three rats/sex/treated group, five rats/sex/group, and four rats/sex/group were randomly withdrawn from test on Weeks 9, 18, and 27, respectively, for neurohistopathological examination. All remaining animals were submitted for examination at Week 29. Hematology, clinical chemistry, and urinalysis parameters were evaluated in ten rats/sex/group after 13 weeks and in five/sex/group after 26 weeks of exposure.

II. MATERIALS

A. Test Material: Toluene

Grade:	Photrex
Supplier:	J.T. Baker Chemical Company Phillipsburg, New Jersey 08865
Dilutant:	None
Description:	Clear, colorless liquid
Date Received:	26 February, 1979
Label Information:	Toluene (for UV Spectrophotometry) 'Photrex' Reagent Lot 745849 J.T. Baker Chemical Company Phillipsburg, N.J. 08865
Amount Received:	48-1 gallon bottles

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II. MATERIALS (Cont.)

B. Test Animals: 90 rats (45/sex)

Strain: Sprague-Dawley

Supplier: Charles River Breeding Laboratories
Wilmington, Massachusetts 01887

Date Received: 29 March, 1979

Age Upon Receipt: 35 days

Dates of Exposure: 16 April, 1979 - 12 October, 1979

Age at Initial Exposure: 53 days

Baseline Weight (Last weight prior to exposure - grams):		Mean	Range
	Males:	286	258-321
	Female:	197	177-223

III. METHODS

A. In-Life:

Selection: More animals were purchased and equilibrated than were required for the study. Animals considered unsuitable for study on the basis of pre-test physical examinations were eliminated prior to initiation of exposure to the test substance. Animals were sorted into groups on a random basis from those animals considered suitable for study purposes using the procedure described in Appendix B (Methodology and References).

Identification: Individually ear-tagged after selection.

Equilibration: 17 days

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III. METHODS (Cont.)

A. In-Life (cont.)

Experimental Design:

Group	Target Concentration	Exposure Time[2]	Number of Animals[1] Exposed	Lab Test Week 13	Lab Test Week 26	Removed for Neurological Examination Week 9	Week 18	Week 27	Week 29
I[3]	None (Chamber Control)	6 hrs/day 5 days/week 26 weeks	30	20	10	0	10	8	A.S.[4]
IV	100 ppm	6 hrs/day 5 days/week 26 weeks	30	20	10	6	10	8	A.S.
V[5]	1500 ppm	6 hrs/day 5 days/week 26 weeks	30	20	10	6	10	8	A.S.
		TOTALS:	90	60	30	12	30	24	

[1]Number of animals equally divided male and female.
[2]Exposures were not run on the following holidays: Memorial Day, July Fourth, Labor Day.
[3]This group served as a common control for Bio/dynamics projects 78-7233 and 78-7234.
[4]A.S. = All survivors.
[5]The target concentration was lowered from 2000 ppm to 1500 ppm beginning at Test Day 11, at the request of the sponsor.

Husbandry:

Housing:	Individual in hung, stainless steel, wire mesh cages.
Food:	Standard laboratory pellet diet (Purina® Laboratory Chow - 5001) *ad libitum* (out of chamber)
Water:	Tap-city water (Elizabethtown Water Company) with automatic watering system *ad libitum* (out of chamber)
Lights:	12 hours on, 12 hours off Exposed during light period.
Temperature:	62°F - 79°F

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III. METHODS (Cont.)

A. In-Life (cont.)

Test Material Administration:

The test material was placed in a gas washing bottle (800-milliliter for the low-level exposure, 1,000-milliliter for the high-level exposure) which was suspended in a large Pyrex waterbath. The waterbath temperature was maintained at 34° by a Cole-Parmer Magnetic Stirrer/Hotplate with a temperature probe (Model 4812). Dry air was bubbled through the test material and the resulting vapors passed through glass tubing (with minimal Tygon tubing connections) into the entry portals of two one cubic meter stainless steel and glass exposure chambers. The vapor-laden airstreams were diluted with room air upon entering the chambers. Adjustments in the exposure concentrations were achieved by altering the air flow rate through the bubblers.

Chamber Operation:

The stainless steel and glass chambers in which the rats were exposed had a total volume of one cubic meter and an effective volume of 760 liters. They were operated dynamically at a flow rate of approximately 155-190 liters per minute with a mean value of 173 liters per minute. This flow rate provided for one air change every 5.8 minutes and a 99% equilibrium time (t_{99}) of 26.7 minutes.

Atmospheric Sampling:

Three samples were drawn from each exposure chamber each day using a Wilks Instrument Company, Miran Long Pathlength Infrared Analyzer Model IA. These samples were drawn at approximately the first, third, and fifth hour of exposure. The concentration of the test material was determined by comparing the adsorption of these samples to a calibration curve prepared using the same instrumental settings.

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III. METHODS (Cont.)

A. In-Life (cont.)

Animal Observations and Body Weights:

The test animals were observed twice daily for mortality and a full, recorded, physical assessment was recorded weekly. Individual body weights were recorded weekly.

Laboratory Studies:	(Methodology and References - Appendix B)
Number of Animals:	
Week 13: (9, 10 July, 1979)	10/sex/group
Week 26: (8 October, 1979)	5/sex/group
Blood Collection:	Retrobulbar venous plexus

Parameter Evaluated:

Hematology[6]

- hemoglobin
- hematocrit
- erythrocyte count
- leukocyte count (total and differential)
- clotting time

Clinical Chemistry[6]

- blood urea nitrogen
- serum glutamic pyruvic transaminase
- alkaline phosphatase
- glucose

---

[6]Rats were fasted overnight prior to orbital bleeding.

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III. METHODS (Cont.)

Urinalysis: (Methodology and References - Appendix B)

Number of Animals:

Week 13: (14, 15 July, 1979) 10/sex/group

Week 26: (13 October, 1979) 5/sex/group

Parameter Evaluated:

appearance
specific gravity
occult blood
pH
protein
bilirubin
ketones
glucose

B. Disposition of Animals

Animals were randomly withdrawn from test and submitted to Albert Einstein College of Medicine for neurological evaluation according to the following schedule:

Week 9:	3/sex/treatment group (Group IV and V)
Week 18:	5/sex/group (Groups I, IV, V)
Week 27:	4/sex/group (Groups I, IV, V)
Week 29:	All survivors

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III. METHODS (Cont.)

C. Post Mortem

Gross Necropsy: Performed on all animals dying spontaneously or killed *in extremis*

Tissues Fixed: The following tissues were taken from all animals dying spontaneously or killed *in extremis* for possible future histopathological examination.

- bone and bone marrow (costochondral junction)
- kidneys (2)
- liver
- lungs[7] with mainstembronchi
- lymph nodes (pulmonary and mesenteric)
- sciatic nerve
- spinal cord (cervical and thoracic)
- gross lesions

Fixative: 10% neutral-buffered formalin

D. Statistical Analysis (Methodology and References - Appendix B)

Hematology and clinical chemistry parameters and body weights were statistically analyzed. Mean values of all treatment groups were compared to the control group at each time interval. Statistically significant differences from the control are indicated in the mean tables.

E. Storage of Raw Data

All original records, raw data, and the protocol will be maintained at Bio/dynamics archives.

---

[7]Lungs were inflated with formalin via trachea with an amount of formalin approximately equal to 75% of the lung capacity.

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IV. RESULTS AND DISCUSSION

A. Chamber Concentration of the Test Material
(Cumulative Exposure Record - Table 1, page 15; Calibration Curves for the Miran IA Ambient Air Analyzer - Appendix A)

The target concentration for Group V was lowered from 2000 ppm to 1500 ppm after the seventh exposure (4/24/79 - test day 9) because the animals began showing acute effects of the test material on Days 6 and 7. The animals were not exposed the following day (4/25/79) so that the animals could recover from these acute effects and to allow for recalibration of the chamber at the new dose level. The Group V exposure was re-initiated on 4/26/79 and ran according to schedule for the remainder of the study.

The rats in Group IV (low-level) and in Group V (high-level) received exposure to cumulative mean concentrations of 100 parts per million (ppm) and 1481 ppm, respectively. These values are based on readings taken using the Miran IA Ambient Air Analyzer.

Closed loop injections were performed during the course of the study to recheck the calibration curves. All data used to generate the calibration curves is presented in Appendix A. These calibration checks were in agreement with the original curves.

Exposure Variations

On 5/17/79 at 9:15 AM, two liters of heptane was spilled in the chamber room after the animals had been loaded into the chambers. The heptane was cleaned up with the flammable liquid spill kit, however, the solvent odor did not clear for approximately 45 minutes. On 8/12/79 (a non-exposure day), the power in all rooms was off from 4:17 ppm to 5:00 ppm. The animals received 43 more minutes of light and 43 minutes less dark on that day. The light schedule was properly adjusted by the next morning.

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IV. RESULTS AND DISCUSSION (Cont.)

B. Physical Observations
(Summary of Physical Observations - Table 2, page 23)

The Group I rats (control) exhibited scattered observations of dry rales, dried material around the eyes, nasal area, and/or back, red and mucoid nasal discharge, excessive lacrimation, hair loss, open sores, scabbing, and a swollen ear lobe during the 28 weekly observations.

The Group IV (low-level) rats exhibited the same signs as did the control rats (except excessive lacrimation, hair loss, open sores, scabbing, and a swollen ear lobe) and in addition, yellow staining of the ano-genital fur, exophthalmia, and a damaged tail. These observations were generally scattered and do not represent a treatment effect when compared to the control.

The Group V (high-level) rats exhibited the same signs as did the control (except a swollen ear lobe) and in addition, yellow staining of the ano-genital fur and a single observation of soft stool. The incidence of dry rales and yellow staining of the ano-genital fur was higher than that observed in the control during the 28 weekly observations.

Additional observations were recorded on 4/23/79 through 4/26/79 for Group V (test days 8-11). On 4/23/79, 4/24/79, and 4/26/79, in-chamber observations were recorded. Also on 4/24/79, the rats were observed upon removal from the chamber after the six-hour exposure. On 4/25/79 (animals not exposed due to lowering of target chamber concentration), the animals were observed individually in the morning.

On Monday 4/23/79 (test day 8, exposure number 6), most rats exhibited excessive salivation, excessive lacrimation, rapid breathing, increased activity, and limb ataxia during the exposure. The mean chamber

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IV. RESULTS AND DISCUSSION (Cont.)

B. Physical Observations (cont.)

concentration for this day was 1760 ppm. On Tuesday 4/24/79 (test day 9, exposure number 7) most animals exhibited excessive lacrimation, excessive salivation, rapid shallow breathing, and body tremors; all animals exhibited increased activity and uncoordination in limb movements; and two rats were prostrate in the chamber. Upon removal from the chamber dry rales (12 of 30), excessive salivation (14 of 30), chromodacryorrhea (2 of 30), red nasal discharge (2 of 30), excessive lacrimation (3 of 30), mucoid nasal discharge (4 of 30), and yellow staining of the ano-genital fur, hair loss, dried material on the leg, and labored breathing (1 of 30, each) were noted. The mean chamber concentration on this day was 1710 ppm.

On these two days, the rats exhibited signs of central nervous system depression (ataxia, body tremors, prostration). The rats were not exposed on Wednesday 4/25/79 to allow for recovery from these acute effects. On the morning of 4/25/79, the rats exhibited dry rales (14 of 30), excessive salivation (1 of 30), hair loss (4 of 30), dried material on the leg (1 of 30), and matted fur (1 of 30). The sponsor requested the target concentration be lowered from 2000 ppm to 1500 ppm and exposure be re-initiated the following day.

On Thursday 4/26/79 (test day 11, exposure number 8) in-chamber observations included excessive lacrimation, excessive salivation and labored breathing in some rats and uncoordination in limb movements in all rats. The mean concentration for this day was 1370 ppm. The signs of central nervous system depression did not appear to be present in the rats during the exposure at the lower target concentration.

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IV. RESULTS AND DISCUSSION (cont'd)

C. Body Weights and Weight Gains

(Mean Values - Table 3, page 27; Individual Values - Appendix D)

The mean body weights in the females in Groups IV (low-level) and V (high-level) were comparable to the Group I (control) mean body weights throughout the duration of the study. The Group IV body weights were significantly decreased ($p \leq 0.05$) compared to the control during Week 2 in the males. During Weeks 18, 21, 22, 23, and 27, the mean male body weights in Group V were significantly increased ($p \leq 0.05$) compared to the control and during Week 28, the mean male body weight in this group was significantly increased ($p \leq 0.01$) compared to the control; these weight increases were linearly related to the dose levels. The weight decrease in the Group IV males during Week 2 and the weight increases in the Group V males during Weeks 18, 21, 22, 23, 27 and 28 did not appear to represent a significant treatment-related effect.

D. Hematology

(Mean Values - Table 4, page 30; Individual Values - Appendix E)

The mean hematology values for the Group IV (low-level) and Group V (high-level) males during Weeks 13 and 26 were comparable to the control (Group I). During Week 13 in the Group V females the mean hemoglobin and hematocrit values were significantly increased ($p \leq 0.05$) compared to the control and linearly related to the dose levels, but not to a degree considered to be biologically significant. During Week 26, the mean clotting time in the Group IV females was significantly decreased ($p \leq 0.05$) compared to the control. All other parameters were within normal biological limits and were unremarkable.

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IV. RESULTS AND DISCUSSION (Cont.)

F. Clinical Chemistry
(Mean Values - Table 5, page 32; Individual Values - Appendix F)

The mean serum glutamic pyruvic transaminase value in the Group IV (low-level) females during Week 26 was significantly ($p \leq 0.01$) increased compared to the control. The males during Week 26 did not show the same effect in serum glutamic pyruvic transaminase values as did the females. During Week 26, the mean glucose value in the Group V (high-level) females was significantly decreased ($p \leq 0.01$) compared to the control and was linearly related to the dose levels. The males showed the same pattern as the females of decreasing glucose values during Week 26 though no statisticantly significant differences occurred; this decreasing pattern was also present in the males and females at Week 13 (though no statiscally significant differences occurred). All other clinical chemistry parameters compared well with the control and were within normal biological limits.

In Group IV, male no. 401 and female no. 456 had serum glutamic pyruvic transaminase values at Week 26 that were approximately 4 times and 5 times, respectively, that of the average for the rest of the group. This parameter was reevaluated in both animals in the event of a possible error, but the original values were confirmed. Since these values are not representative of the rest of the group, they were not included in the calculation of the mean.

The glucose levels observed at Week 26 were all within normal limits and the differences do not appear to be biologically significant. The elevation in serum glutamic transaminase levels especially in the female rats may be a response to the exposure, with the exception of the two animals discussed above, however, these elevations are not considered to be significantly above normal levels.

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IV. RESULTS AND DISCUSSION (Cont.)

F. Urinalysis
(Individual Values - Appendix G)

Mild proteinuria was observed in all groups at Weeks 13 and 26. Proteinuria was most often seen in the Group V (high-level) males at Week 13 (through unremarkable in the Group V females at Week 13), and in the Group IV (low-level) females at Week 26 (though unremarkable in the Group IV males at Week 26). The specific gravity values in all groups were generally higher than those normally observed, but this is attributed to sample evaporation. Ketones were observed in one of the Group IV females during Week 26. None of these findings appear to be related to treatment.

George M. Rusch — 1/29/81

George M. Rusch, Ph.D.
Director, Inhalation Technology

Date

William E. Rinehart — 2/1/81

William E. Rinehart, Sc.D.
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TABLE 1

A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

POOR QUALITY ORIGINAL

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP IV (100 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
4/16/79	1	1	68	6.0	408	6.0	408	68
4/17/79	2	2	100	6.0	600	12.0	1008	84
4/18/79	3	3	102	6.0	612	18.0	1620	90
4/19/79	4	4	100	6.0	600	24.0	2220	93
4/20/79	5	5	95	6.0	570	30.0	2790	93
4/23/79	8	6	102	6.0	612	36.0	3402	95
4/24/79	9	7	93	6.0	558	42.0	3960	94
4/25/79	10	8	93	6.0	558	48.0	4518	94
4/26/79	11	9	88	6.0	528	54.0	5046	93
4/27/79	12	10	84	6.0	504	60.0	5550	93
4/30/79	15	11	90	6.0	540	66.0	6090	92
5/1/79	16	12	86	6.0	516	72.0	6606	92
5/2/79	17	13	102	6.0	612	78.0	7218	93
5/3/79	18	14	109	6.0	654	84.0	7872	94
5/4/79	19	15	144	6.0	864	90.0	8736	97
5/7/79	22	16	107	6.0	642	96.0	9378	98
5/8/79	23	17	100	6.0	600	102.0	9978	98
5/9/79	24	18	97	6.0	582	108.0	10560	98
5/10/79	25	19	113	6.0	678	114.0	11238	99
5/11/79	26	20	96	6.0	576	120.0	11814	98
5/14/79	29	21	102	6.0	612	126.0	12426	99
5/15/79	30	22	96	6.0	576	132.0	13002	99
5/16/79	31	23	96	6.0	576	138.0	13578	98
5/17/79	32	24	94	6.0	564	144.0	14142	98
5/18/79	33	25	80	6.0	480	150.0	14622	97
5/21/79	36	26	105	6.0	630	156.0	15252	98
5/22/79	37	27	111	6.0	666	162.0	15918	98
5/23/79	38	28	99	6.0	594	168.0	16512	98
5/24/79	39	29	98	6.0	588	174.0	17100	98
5/25/79	40	30	99	6.0	594	180.0	17694	98
5/29/79	44	31	90	6.0	540	186.0	18234	98
5/30/79	45	32	98	6.0	588	192.0	18822	98
5/31/79	46	33	101	6.0	606	198.0	19428	98
6/1/79	47	34	111	6.0	666	204.0	20094	99
6/4/79	50	35	91	6.0	546	210.0	20640	98

--CONTINUED--

[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)
A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

POOR QUALITY ORIGINAL

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP IV (100 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
6/5/79	51	36	103	6.0	618	216.0	21258	98
6/6/79	52	37	107	6.0	642	222.0	21900	99
6/7/79	53	38	109	6.0	654	228.0	22554	99
6/8/79	54	39	119	6.0	714	234.0	23268	99
6/11/79	57	40	101	6.0	606	240.0	23874	99
6/12/79	58	41	94	6.0	564	246.0	24438	99
6/13/79	59	42	105	6.0	630	252.0	25068	99
6/14/79	60	43	96	6.0	576	258.0	25644	99
6/15/79	61	44	117	6.0	702	264.0	26346	100
6/18/79	64	45	109	6.0	654	270.0	27000	100
6/19/79	65	46	98	6.0	588	276.0	27588	100
6/20/79	66	47	100	6.0	600	282.0	28188	100
6/21/79	67	48	97	6.0	582	288.0	28770	100
6/22/79	68	49	90	6.0	540	294.0	29310	100
6/25/79	71	50	84	6.0	504	300.0	29814	99
6/26/79	72	51	86	6.0	516	306.0	30330	99
6/27/79	73	52	98	6.0	588	312.0	30918	99
6/28/79	74	53	92	6.0	552	318.0	31470	99
6/29/79	75	54	107	6.0	642	324.0	32112	99
7/2/79	78	55	91	6.0	546	330.0	32658	99
7/3/79	79	56	104	6.0	624	336.0	33282	99
7/5/79	81	57	102	6.0	612	342.0	33894	99
7/6/79	82	58	95	6.0	570	348.0	34464	99
7/9/79	85	59	139	6.0	834	354.0	35298	100
7/10/79	86	60	103	6.0	618	360.0	35916	100
7/11/79	87	61	148	6.0	888	366.0	36804	101
7/12/79	88	62	134	6.0	804	372.0	37608	101
7/13/79	89	63	93	6.0	558	378.0	38166	101
7/16/79	92	64	100	6.0	600	384.0	38766	101
7/17/79	93	65	100	6.0	600	390.0	39366	101
7/18/79	94	66	100	6.0	600	396.0	39966	101
7/19/79	95	67	97	6.0	582	402.0	40548	101
7/20/79	96	68	100	6.0	600	408.0	41148	101
7/23/79	99	69	101	6.0	606	414.0	41754	101
7/24/79	100	70	97	6.0	582	420.0	42336	101

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[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)

A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

POOR QUALITY ORIGINAL

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP IV (100 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
7/25/79	101	71	102	6.0	612	426.0	42948	101
7/26/79	102	72	93	6.0	558	432.0	43506	101
7/27/79	103	73	98	6.0	588	438.0	44094	101
7/30/79	106	74	89	6.0	534	444.0	44628	101
7/31/79	107	75	102	6.0	612	450.0	45240	101
8/1/79	108	76	118	6.0	708	456.0	45948	101
8/2/79	109	77	112	6.0	672	462.0	46620	101
8/3/79	110	78	90	6.0	540	468.0	47160	101
8/6/79	113	79	105	6.0	630	474.0	47790	101
8/7/79	114	80	90	6.0	540	480.0	48330	101
8/8/79	115	81	81	6.0	486	486.0	48816	100
8/9/79	116	82	109	6.0	654	492.0	49470	101
8/10/79	117	83	115	6.0	690	498.0	50160	101
8/13/79	120	84	105	6.0	630	504.0	50790	101
8/14/79	121	85	68	6.0	408	510.0	51198	100
8/15/79	122	86	95	6.0	570	516.0	51768	100
8/16/79	123	87	102	6.0	612	522.0	52380	100
8/17/79	124	88	97	6.0	582	528.0	52962	100
8/20/79	127	89	95	6.0	570	534.0	53532	100
8/21/79	128	90	90	6.0	540	540.0	54072	100
8/22/79	129	91	95	6.0	570	546.0	54642	100
8/23/79	130	92	99	6.0	594	552.0	55236	100
8/24/79	131	93	107	6.0	642	558.0	55878	100
8/27/79	134	94	103	6.0	618	564.0	56496	100
8/28/79	135	95	98	6.0	588	570.0	57084	100
8/29/79	136	96	100	6.0	600	576.0	57684	100
8/30/79	137	97	109	6.0	654	582.0	58338	100
8/31/79	138	98	106	6.0	636	588.0	58974	100
9/4/79	142	99	132	6.0	792	594.0	59766	101
9/5/79	143	100	95	6.0	570	600.0	60336	101
9/6/79	144	101	88	6.0	528	606.0	60864	100
9/7/79	145	102	99	6.0	594	612.0	61458	100
9/10/79	148	103	97	6.0	582	618.0	62040	100
9/11/79	149	104	84	6.0	504	624.0	62544	100
9/12/79	150	105	93	6.0	558	630.0	63102	100

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[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)

A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

POOR QUALITY ORIGINAL

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP IV (100 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
9/13/79	151	106	95	6.0	570	636.0	63672	100
9/14/79	152	107	105	6.0	630	642.0	64302	100
9/17/79	155	108	104	6.0	624	648.0	64926	100
9/18/79	156	109	128	6.0	768	654.0	65694	100
9/19/79	157	110	99	6.0	594	660.0	66288	100
9/20/79	158	111	91	6.0	546	666.0	66834	100
9/21/79	159	112	102	6.0	612	672.0	67446	100
9/24/79	162	113	106	6.0	636	678.0	68082	100
9/25/79	163	114	104	6.0	624	684.0	68706	100
9/26/79	164	115	103	6.0	618	690.0	69324	100
9/27/79	165	116	100	6.0	600	696.0	69924	100
9/28/79	166	117	97	6.0	582	702.0	70506	100
10/1/79	169	118	81	6.0	486	708.0	70992	100
10/2/79	170	119	123	6.0	738	714.0	71730	100
10/3/79	171	120	100	6.0	600	720.0	72330	100
10/4/79	172	121	100	6.0	600	726.0	72930	100
10/5/79	173	122	95	6.0	570	732.0	73500	100
10/8/79	176	123	74	6.0	444	738.0	73944	100
10/9/79	177	124	107	6.0	642	744.0	74586	100
10/10/79	178	125	79	6.0	474	750.0	75060	100
10/11/79	179	126	81	6.0	486	756.0	75546	100
10/12/79	180	127	107	6.0	642	762.0	76188	100

[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)
A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

POOR QUALITY ORIGINAL

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP V (1500 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
4/16/79	1	1	1990	6.0	11940	6.0	11940	1990
4/17/79	2	2	2020	6.0	12120	12.0	24060	2005
4/18/79	3	3	1870	6.0	11220	18.0	35280	1960
4/19/79	4	4	1890	6.0	11340	24.0	46620	1943
4/20/79	5	5	1810	6.0	10860	30.0	57480	1916
4/23/79	8	6	1760	6.0	10560	36.0	68040	1890
4/24/79	9	7	1710	6.0	10260	42.0	78300	1864
4/26/79	11	8	1370	6.0	8220	48.0	86520	1803
4/27/79	12	9	1330	6.0	7980	54.0	94500	1750
4/30/79	15	10	1520	6.0	9120	60.0	103620	1727
5/1/79	16	11	1490	6.0	8940	66.0	112560	1705
5/2/79	17	12	1470	6.0	8820	72.0	121380	1686
5/3/79	18	13	1590	6.0	9540	78.0	130920	1678
5/4/79	19	14	1520	6.0	9120	84.0	140040	1667
5/7/79	22	15	1470	6.0	8820	90.0	148860	1654
5/8/79	23	16	1620	6.0	9720	96.0	158580	1652
5/9/79	24	17	1420	6.0	8520	102.0	167100	1638
5/10/79	25	18	1660	6.0	9960	108.0	177060	1639
5/11/79	26	19	1540	6.0	9240	114.0	186300	1634
5/14/79	29	20	1540	6.0	9240	120.0	195540	1630
5/15/79	30	21	1400	6.0	8400	126.0	203940	1619
5/16/79	31	22	1260	6.0	7560	132.0	211500	1602
5/17/79	32	23	1490	6.0	8940	138.0	220440	1597
5/18/79	33	24	1280	6.0	7680	144.0	228120	1584
5/21/79	36	25	970	6.0	5820	150.0	233940	1560
5/22/79	37	26	1560	6.0	9360	156.0	243360	1560
5/23/79	38	27	1420	6.0	8520	162.0	251940	1555
5/24/79	39	28	1310	6.0	7860	168.0	259800	1546
5/25/79	40	29	1430	6.0	8580	174.0	268380	1542
5/29/79	44	30	1300	6.0	7800	180.0	276180	1534
5/30/79	45	31	1570	6.0	9420	186.0	285600	1535
5/31/79	46	32	1420	6.0	8520	192.0	294120	1532
6/1/79	47	33	1440	6.0	8640	198.0	302760	1529
6/4/79	50	34	1440	6.0	8640	204.0	311400	1526
6/5/79	51	35	1450	6.0	8700	210.0	320100	1524

CONTINUED

[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)
A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP V (1500 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
6/6/79	52	36	1450	6.0	8700	216.0	328800	1522
6/7/79	53	37	1490	6.0	8940	222.0	337740	1521
6/8/79	54	38	1560	6.0	9360	228.0	347100	1522
6/11/79	57	39	1430	6.0	8580	234.0	355680	1520
6/12/79	58	40	1380	6.0	8280	240.0	363960	1517
6/13/79	59	41	1490	6.0	8940	246.0	372900	1516
6/14/79	60	42	1390	6.0	8340	252.0	381240	1513
6/15/79	61	43	1630	6.0	9780	258.0	391020	1516
6/18/79	64	44	1310	6.0	7860	264.0	398880	1511
6/19/79	65	45	1390	6.0	8340	270.0	407220	1508
6/20/79	66	46	1400	6.0	8400	276.0	415620	1506
6/21/79	67	47	1240	6.0	7440	282.0	423060	1500
6/22/79	68	48	1430	6.0	8580	288.0	431640	1499
6/25/79	71	49	1410	6.0	8460	294.0	440100	1497
6/26/79	72	50	1450	6.0	8700	300.0	448800	1496
6/27/79	73	51	1470	6.0	8820	306.0	457620	1495
6/28/79	74	52	1460	6.0	8760	312.0	466380	1495
6/29/79	75	53	1580	6.0	9480	318.0	475860	1496
7/2/79	78	54	1420	6.0	8520	324.0	484380	1495
7/3/79	79	55	1550	6.0	9300	330.0	493680	1496
7/5/79	81	56	1480	6.0	8880	336.0	502560	1496
7/6/79	82	57	1520	6.0	9120	342.0	511680	1496
7/9/79	85	58	1600	6.0	9600	348.0	521280	1498
7/10/79	86	59	1490	6.0	8940	354.0	530220	1498
7/11/79	87	60	1610	6.0	9660	360.0	539880	1500
7/12/79	88	61	1580	6.0	9480	366.0	549360	1501
7/13/79	89	62	1300	6.0	7800	372.0	557160	1498
7/16/79	92	63	1480	6.0	8880	378.0	566040	1497
7/17/79	93	64	1450	6.0	8700	384.0	574740	1497
7/18/79	94	65	1470	6.0	8820	390.0	583560	1496
7/19/79	95	66	1700	6.0	10200	396.0	593760	1499
7/20/79	96	67	1430	6.0	8580	402.0	602340	1498
7/23/79	99	68	1490	6.0	8940	408.0	611280	1498
7/24/79	100	69	1530	6.0	9180	414.0	620460	1499
7/25/79	101	70	1440	6.0	8640	420.0	629100	1498

--CONTINUED--

[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)
A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP V (1500 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
7/26/79	102	71	1530	6.0	9480	426.0	638580	1499
7/27/79	103	72	1520	6.0	9120	432.0	647700	1499
7/30/79	106	73	1300	6.0	8340	438.0	656040	1498
7/31/79	107	74	1560	6.0	9360	444.0	665400	1499
8/1/79	108	75	1520	6.0	9120	450.0	674520	1499
8/2/79	109	76	1400	6.0	8400	456.0	682920	1498
8/3/79	110	77	1320	6.0	7920	462.0	690840	1495
8/6/79	113	78	1610	6.0	9660	468.0	700500	1497
8/7/79	114	79	1530	6.0	9180	474.0	709680	1497
8/8/79	115	80	1210	6.0	7260	480.0	716940	1494
8/9/79	116	81	1440	6.0	8640	486.0	725580	1493
8/10/79	117	82	1490	6.0	8940	492.0	734520	1493
8/13/79	120	83	1450	6.0	8700	498.0	743220	1492
8/14/79	121	84	1510	6.0	9060	504.0	752280	1493
8/15/79	122	85	1530	6.0	9180	510.0	761460	1493
8/16/79	123	86	1490	6.0	8940	516.0	770400	1493
8/17/79	124	87	1520	6.0	9120	522.0	779520	1493
8/20/79	127	88	1390	6.0	8340	528.0	787860	1492
8/21/79	128	89	1170	6.0	7020	534.0	794880	1489
8/22/79	129	90	1580	6.0	9480	540.0	804360	1490
8/23/79	130	91	1380	6.0	8280	546.0	812640	1488
8/24/79	131	92	1450	6.0	8700	552.0	821340	1488
8/27/79	134	93	1560	6.0	9360	558.0	830700	1489
8/28/79	135	94	1500	6.0	9000	564.0	839700	1489
8/29/79	136	95	1480	6.0	8880	570.0	848580	1489
8/30/79	137	96	1530	6.0	9180	576.0	857760	1489
8/31/79	138	97	1500	6.0	9000	582.0	866760	1489
9/4/79	142	98	1570	6.0	9420	588.0	876180	1490
9/5/79	143	99	1550	6.0	9300	594.0	885480	1491
9/6/79	144	100	1330	6.0	7980	600.0	893460	1489
9/7/79	145	101	1420	6.0	8520	606.0	901980	1488
9/10/79	148	102	1320	6.0	7920	612.0	909900	1487
9/11/79	149	103	1400	6.0	8400	618.0	918300	1486
9/12/79	150	104	1440	6.0	8640	624.0	926940	1485
9/13/79	151	105	1480	6.0	8880	630.0	935820	1485

CONTINUED

[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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TABLE 1 (Cont.)
A 26 WEEK INHALATION TOXICITY STUDY
OF TOLUENE IN THE RAT

POOR QUALITY ORIGINAL

CUMULATIVE EXPOSURE CONCENTRATION[a]

GROUP V (1500 ppm)

DATE	TEST DAY	EXPO NUM	DAILY EXPO CONC	DAILY EXPO HRS	DAILY CONC HRS	TOTAL EXPO HRS	TOTAL CONC HRS	INT MEAN CONC
9/14/79	152	106	1460	6.0	8760	636.0	944520	1485
9/17/79	155	107	1540	6.0	9240	642.0	953820	1486
9/18/79	156	108	1540	6.0	9240	648.0	963060	1486
9/19/79	157	109	1440	6.0	8640	654.0	971700	1486
9/20/79	158	110	1550	6.0	9300	660.0	981000	1486
9/21/79	159	111	1570	6.0	9420	666.0	990420	1487
9/24/79	162	112	1540	6.0	9240	672.0	999660	1488
9/25/79	163	113	1450	6.0	8700	678.0	1008360	1487
9/26/79	164	114	1570	6.0	9420	684.0	1017780	1488
9/27/79	165	115	1480	6.0	8880	690.0	1026660	1488
9/28/79	166	116	1460	6.0	8760	696.0	1035420	1488
10/1/79	169	117	1340	6.0	8040	702.0	1043460	1486
10/2/79	170	118	1670	6.0	10020	708.0	1053480	1488
10/3/79	171	119	1530	6.0	9180	714.0	1062660	1488
10/4/79	172	120	1460	6.0	8760	720.0	1071420	1488
10/5/79	173	121	1460	6.0	8760	726.0	1080180	1488
10/8/79	176	122	1320	6.0	7920	732.0	1088100	1486
10/9/79	177	123	1520	6.0	9120	738.0	1097220	1487
10/10/79	178	124	1330	6.0	7980	744.0	1105200	1485
10/11/79	179	125	990	6.0	5940	750.0	1111140	1482
10/12/79	180	126	1430	6.0	8580	756.0	1119720	1481

[a]See Methodology and References (Appendix B) for the calculation of the Integrated Mean Concentration.

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Table 2
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Summary of Physical Observations
Group 1 - Control

	Week:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
RESPIRATORY	Dry Rales	2	4	3	2	2	2	1	2	3	2	3	2	4	2		5	5		3	2	2		1				6	1
SECRETORY	Dried Mat'l-Eyes, Nose, or Back		1											2	3			1			1	1			1		2		
	Red Nasal Discharge											1																	
	Mucoid Nasal Discharge			1																							1		
	Excessive Lacrimation																												
CUTANEOUS	Hair Loss	2	2	2	2	2	3	2	3	3	3	3	3	3	3	3	3	3	2	2	2	2	2	2	2	2	2	1	2
	Open Sore	2	2	2	1	1	1	2																					
	Scabbing								2	1																			
GENERAL	Swollen Ear Lobe															1	1												
	Yellow Ano-Genital Staining																												
	Exophthalmia																												
	Tail damaged																												
	Soft Stool																												
	No Observed Abnormalities	26	23	24	26	26	25	27	25	24	25	23	25	21	23	26	22	23	18	15	15	16	18	17	17	18	16	5	9
	Total Withdrawn From Test	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	18	18
	Cumulative Mortality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Total Remaining on Test	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	20	20	20	20	20	20	20	20	20	12	12

[a]The total number of observations may exceed 30 (number of animals) for any given week since an animal may have been observed with more than one abnormality during any given observation interval.

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Table 2 (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Summary of Physical Observations
Group IV - 100 ppm

	Week:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
RESPIRATORY	Dry rales	3	7	1		4	3	1	1	2	1			4	5	5	6	2	3	3	1	1		1	3	3		2	1
SECRETORY	Dried Mat'l-Eyes, Nose, or Back																			1	1	1	1	1		1	1		
	Red Nasal Discharge													1															
	Mucoid Nasal Discharge		1	1							2																		
	Excessive Lacrimation																												
CUTANEOUS	Hair Loss																												
	Open Sore																												
	Scabbing																												
GENERAL	Swollen Ear Lobe								1			1	1			2	1	2	1	1	1	1	2	1	1	2	1		
	Yellow Ano-Genital Staining																					1							
	Exophthalmia																1	1											
	Tail damaged																												
	Soft stool																												
	No Observed Abnormalities	27	22	28	30	26	27	29	28	22	21	23	23	19	19	18	16	19	10	10	11	11	11	12	10	8	12	5	1
	Total Withdrawn From Test	0	0	0	0	0	0	0	0	6	6	6	6	6	6	6	6	6	16	16	16	16	16	16	16	16	16	24	24
	Cumulative mortality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Total Remaining on Test	30	30	30	30	30	30	30	30	24	24	24	24	24	24	24	24	24	14	14	14	14	14	14	14	14	14	6	6

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Table 2 (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Summary of Physical Observations
Group V - 1500 ppm

	Week:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
RESPIRATORY	Dry Rales	11	11	5	7	7	5	4	6	7	9		1	3	13	6	4	6	2	2	1	1	2	3	2	3	1	1	1
SECRETORY	Dried Mat'l-Eyes, Nose, or Back										1							1											
	Red Nasal Discharge	2	1	1			1				5			1								1	2						1
	Mucoid Nasal Discharge		1	1			1	1		1	1		1	1			1	1	1	1				1	1	1	1		
	Excessive Lacrimation														3	1		3											
CUTANEOUS	Hair Loss		1	1	1	1	1	1	1																				
	Open Sore						1	1																					
	Scabbing		1	1	1	1	1		1										1										
GENERAL	Swollen Ear Lobe								1	3	2	2	3	2	1	3	2	2	2	1	1		2	1	1	2	2		
	Yellow Ano-Genital Staining			1																									
	Exophthalmia																							1					
	Tail damaged																												
	Soft stool																												
	No Observed Abnormalities	18	18	21	22	23	22	24	22	13	8	22	19	18	9	14	18	12	9	11	12	9	8	9	8	10	5	5	5
	Total Withdrawn From Test	0	0	0	0	0	0	0	0	6	6	6	6	6	6	6	6	6	16	16	16	16	16	16	16	16	16	24	24
	Cumulative mortality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Total Remaining on Test	30	30	30	30	30	30	30	30	24	24	24	24	24	24	24	24	24	14	14	14	14	14	14	14	14	14	6	6

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Preface to Tables 3, 4, and 5

A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Symbol			Statistical Statement
No Sig	$p \leq 0.05$	$p \leq 0.01$	
A^-			No statistical differences among the means (parametric ANOVA).
	A^+	A^{++}	The means differ significantly (parametric ANOVA).
	*	**	Significantly different from control (Dunnett's).
A^{+*}			The ANOVA indicates a difference among the means; Dunnett's test indicates the difference is not between the control and any of the treatment groups.
K^-			No statistical differences among the means (Kruskal-Wallis, nonparametric).
	K^+	K^{++}	The means differ significantly (Kruskal-Wallis, nonparametric).
	†	††	Significantly different from control (Dunn's Rank Sum).
	L	L^+	The response is linearly related to the dose levels.
	F	F^+	Lack of fit.
	J	J^+	There is an ordered response to dosage.

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Table 3
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Body Weight Values - grams[1]

Group ppm		Day 1	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
						Males					
I 0	Mean	A- 288	A- 326	A+ 361	A- 392	A- 422	A- 448	A- 472	A- 491	A- 513	A- 529
	S.E.	5	5	6	8	10	11	12	14	15	15
	N	15	14	15	15	14	15	15	14	15	15
IV 100	Mean	281	312	338*	371	402	422	444	469	485	499
	S.E.	5	7	7	9	11	10	11	11	12	13
	N	15	15	14	15	13	15	15	15	14	12
V 1500	Mean	288	320	347	385	419	450	481	506	525	551
	S.E.	3	4	4	6	8	8	10	12	13	17
	N	15	15	15	15	15	15	15	15	15	12
						Females					
I 0	Mean	A- 197	A- 214	A- 233	A- 245	A- 261	A- 270	A- 279	A- 291	A- 295	A- 302
	S.E.	3	4	5	5	6	6	7	7	8	8
	N	15	15	15	15	15	15	15	15	14	15
IV 100	Mean	197	215	229	241	258	268	275	285	294	304
	S.E.	2	4	5	6	5	7	7	9	8	9
	N	15	15	14	14	15	15	15	15	15	12
V 1500	Mean	198	213	228	239	252	263	274	278	290	297
	S.E.	3	3	4	5	5	5	5	6	6	6
	N	15	14	15	15	15	15	15	15	15	12

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more body weights were not used in computations (see Appendix D).

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Table 3 (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Body Weight Values - grams[1]

Group ppm		Week 10	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18	Week 19
						Males					
I 0	Mean	A- 547	A- 561	A- 577	A- 568	A- 581	A- 593	A- 603	A- 615	A+L 601	A+* 615
	S.E.	16	17	32	18	18	19	20	20	24	24
	N	15	15	5	15	15	15	15	15	10	10
IV 100	Mean	514	528	526	543	559	574	582	594	580	590
	S.E.	14	14	43	16	16	16	17	18	17	16
	N	12	12	2	12	12	12	12	12	7	7
V 1500	Mean	565	574	571	596	616	633	645	657	693*	704
	S.E.	18	19	46	20	21	22	23	24	37	38
	N	12	11	2	12	12	12	12	12	7	7
						Females					
I 0	Mean	A- 308	A- 315	A- 322	A- 316	A- 324	A- 332	A- 334	A- 339	A- 337	A- 345
	S.E.	9	9	10	9	11	11	10	10	15	15
	N	15	15	14	15	15	15	15	15	10	10
IV 100	Mean	307	316	319	316	322	331	338	338	345	350
	S.E.	10	10	10	10	9	10	10	12	16	16
	N	12	12	12	12	12	12	12	12	7	7
V 1500	Mean	301	306	312	310	316	321	328	332	339	343
	S.E.	5	6	6	7	8	7	7	8	15	16
	N	12	12	12	12	12	12	12	12	7	7

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more body weights were not used in computations (see Appendix D).

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Table 3 (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Body Weight Values - grams[1]

Group ppm		Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26	Week 27	Week 28
					Males					
I 0	Mean	A+*	A+L	A+L	A+L	A+*	A-	A+*	A+L	A++L
	S.E.	625	626	638	648	658	678	671	659	666
	N	27	25	26	27	29	5[illegible]	30	24	23
		10	10	10	10	10	5	10	6	6
IV 100	Mean	602	602	608	608	614	610	622	641	658
	S.E.	17	17	17	18	18	47	18	35	35
	N	7	7	7	7	7	2	7	3	3
V 1500	Mean	719	729*	738*	747*	755	818	755	803*	818**
	S.E.	38	40	41	41	44	71	42	31	30
	N	7	7	7	7	7	2	7	3	3
					Females					
I 0	Mean	A-	A-	A-	A-	A-	A-	A-	A-	A-
	S.E.	346	347	346	346	355	332	350	357	359
	N	14	15	16	18	19	30	21	28	30
		10	10	10	10	10	5	10	6	6
IV 100	Mean	354	356	359	361	369	364	365	338	345
	S.E.	16	16	17	17	19	14	19	24	28
	N	7	7	7	7	7	2	7	3	3
V 1500	Mean	351	355	354	358	367	426	367	399	404
	S.E.	17	18	19	18	19	50	21	58	62
	N	7	7	7	7	7	2	7	3	3

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more body weights were not used in computations (see Appendix D).

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Table 4
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Hematology Values[1]
Males

Group ppm		HGB g%	HCT %	RBC $10^6/mm^3$	CLOT X min	WBC $10^3/mm^3$
			Week 13			
I 0	Mean	A- 15.6	A- 51	A- 8.41	A- 2.9	A- 9.3
	S.E.	0.3	1	0.20	0.3	0.6
	N	8	10	8	10	8
IV 100	Mean	15.4	51	8.08	2.8	8.8
	S.E.	0.3	1	0.13	0.5	0.5
	N	9	10	9	10	9
V 1500	Mean	14.7	50	8.09	2.6	9.1
	S.E.	0.3	1	0.16	0.4	0.6
	N	10	10	10	10	10
			Week 26			
I 0	Mean	A+* 16.7	A- 48	A- 7.73	A- 3.5	A- 11.8
	S.E.	0.2	1	0.21	0.5	1.5
	N	5	5	5	5	5
IV 100	Mean	17.3	50	7.90	3.8	10.2
	S.E.	0.2	0	0.17	0.5	0.7
	N	5	5	5	5	5
V 1500	Mean	16.6	47	7.72	3.2	11.5
	S.E.	0.2	1	0.21	0.4	0.9
	N	5	5	5	5	5

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more samples were not available for analysis (see Appendix E).

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Table 4 (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Hematology Values[1]
Females

Group ppm		HGB g%	HCT %	RBC $10^6/mm^3$	CLOT X min	WBC $10^3/mm^3$
			Week 13			
		A+L	A+L	A-	A-	A-
I 0	Mean	15.4	45	7.26	2.6	9.1
	S.E.	0.2	1	0.11	0.4	0.3
	N	8	7	8	10	8
IV 100	Mean	15.6	47	7.36	2.3	9.1
	S.E.	0.2	1	0.07	0.4	0.4
	N	10	10	10	10	10
V 1500	Mean	16.2*	49*	7.60	2.8	9.2
	S.E.	0.1	0	0.16	0.5	0.6
	N	10	9	10	10	10
			Week 26			
		A-	A-	A-	A+	A-
I 0	Mean	14.9	44	7.25	3.3	8.3
	S.E.	0.1	1	0.11	0.6	0.6
	N	5	5	5	5	5
IV 100	Mean	15.1	46	6.99	1.3*	6.7
	S.E.	0.5	1	0.22	0.2	0.8
	N	3	4	3	5	3
V 1500	Mean	15.2	46	7.10	3.4	8.6
	S.E.	0.3	0	0.19	0.6	1.3
	N	5	4	5	5	5

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more samples were not available for analysis (see Appendix E).

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Table 5
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Clinical Chemistry Values[1]
Males

Group ppm		SGPT IU	ALK PHOS IU	BUN mg/dl	GLU mg/dl
			Week 13		
		K-	A-	A-	A-
I 0	Mean	19	98	15.6	113
	S.E.	2	4	0.5	3
	N	10	10	10	10
IV 100	Mean	22	110	16.5	130
	S.E.	3	9	0.6	9
	N	10	10	10	10
V 1500	Mean	17	96	15.6	114
	S.E.	1	5	0.3	7
	N	10	10	10	10
			Week 26		
		A-	A-	A+*	A-
I 0	Mean	23	92	16.7	142
	S.E.	3	3	0.7	7
	N	5	5	5	5
IV 100	Mean	22	90	18.3	127
	S.E.	3	6	0.5	7
	N	4	5	5	5
V 1500	Mean	19	84	14.9	126
	S.E.	3	10	0.7	8
	N	5	5	5	5

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more samples were not available for analysis (see Appendix F).

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Table 5 (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Mean Clinical Chemistry Values[1]
Females

Group ppm		SGPT IU	ALK PHOS IU	BUN mg/dl	GLU mg/dl
			Week 13		
		K-	A-	A-	A-
I	Mean	14	40	15.9	123
0	S.E.	2	5	0.8	3
	N	10	10	10	10
IV	Mean	13	33	16.5	121
100	S.E.	1	2	0.6	7
	N	10	10	10	10
V	Mean	12	44	18.3	114
1500	S.E.	1	4	0.8	4
	N	10	10	10	10
			Week 26		
		A++	K-	A-	A++L+
I	Mean	16	25	17.7	151
0	S.E.	1	1	1.9	4
	N	5	5	5	5
IV	Mean	26**	28	17.5	142
100	S.E.	2	1	0.8	1
	N	3	4	4	4
V	Mean	19	30	18.0	128**
1500	S.E.	2	7	0.3	5
	N	5	5	5	5

[1]When N (number of animals) was less than that specified in the Experimental Design (see page 3), one or more samples were not available for analysis (see Appendix F).

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Appendix A
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations

The Miran IA Ambient Air Analyzer was used to determine the concentration of the test material in the chamber by infrared analysis. The concentrations were determined by comparing the daily absorbance readings to a calibration curve prepared using the same instrumental settings.

Separate calibration curves were generated for Group IV (low-level) and Group V (high-level). The Miran settings, absorbance values, and typical calibration curves for each group are presented within this appendix. Also, one calibration curve is included which was generated to check the linearity of the calibrations from low-level to high-level and was found to be in agreement with the other curves.

During the low-level exposure, Miran #03 was used from 4/16/79 through 5/3/79 at which time it was sent out to be serviced. Miran #01 was used from 5/4/79 through 6/22/79. Injections were performed on 6/23/79 to confirm the validity of the first calibration curve presented on page A-5, generated using Miran #03 and it was then used for the remainder of the study.

During the high-level exposure, Miran #03 was used from 4/16/79 through 4/24/79 at which time the target concentration for Group V (high-dose) was lowered from 2000 ppm to 1500 ppm. Miran #02 was calibrated on 4/25/79 (no Group V exposure that day) and was used from 4/26/79 through 5/4/79 at which time it was sent out to be serviced. Miran #01 was used from 5/7/79 through 6/22/79. Additional calibration data was added to the original curve as a result of the target concentration being lowered and this curve is presented on page A-11.

The curve generated to check the linearly of the absorbance values using Miran #02 is presented on page A-12.

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Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Group IV - Low-Level Exposure

Project:	A-12 78-7234
Compound:	Toluene
Molecular Weight:	92.13 g/mole
Density:	.866 g/ml

MIRAN SETTINGS:

Wavelength:	3.4 μ
Pathlength:	14 (dial reading)
Range:	1 Å
Slit Width:	1 mm
Response Time:	4 sec.

Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #03
(4/16/79 - 5/3/79; 6/25/79 - 10/12/79)

Date	Injection Volume (µl)	Concentration (ppm)	Absorbance A_1	A_2	A_3	A_4
3/27/79	0.5	20.03	.03	.04	.03	.03
	1.0	40.07	.07	.08	.07	.06
	2.0	80.13	.14	.14	.13	.13
	2.49	99.77	.15	.17	.16	.16
	3.0	120.20	.19	.21	.19	.18
	5.0	200.34	.31	.32	.31	.31
	7.0	280.47	.42	.43	.42	.42
	9.0	360.60	.58	.54	.53	.52

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Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #01
(5/4/79 - 6/22/79)

Date	Injection Volume (µl)	Concentration (ppm)	Absorbance A_1	A_2	A_3	A_4
3/7/79	0.5	20.03	.03	.02	.04	.03
	1.0	40.07	.06	.05	.07	.06
	2.0	80.13	.13	.115	.135	.13
	2.49	99.77	.15	.15	.17	.16
	3.0	120.20	.19	.18	.21	.19
	5.0	200.34	.33	.31	.325	.32
	7.0	280.47	.44	.435	.45	.44
	9.0	360.60	.56	.55	.57	.56

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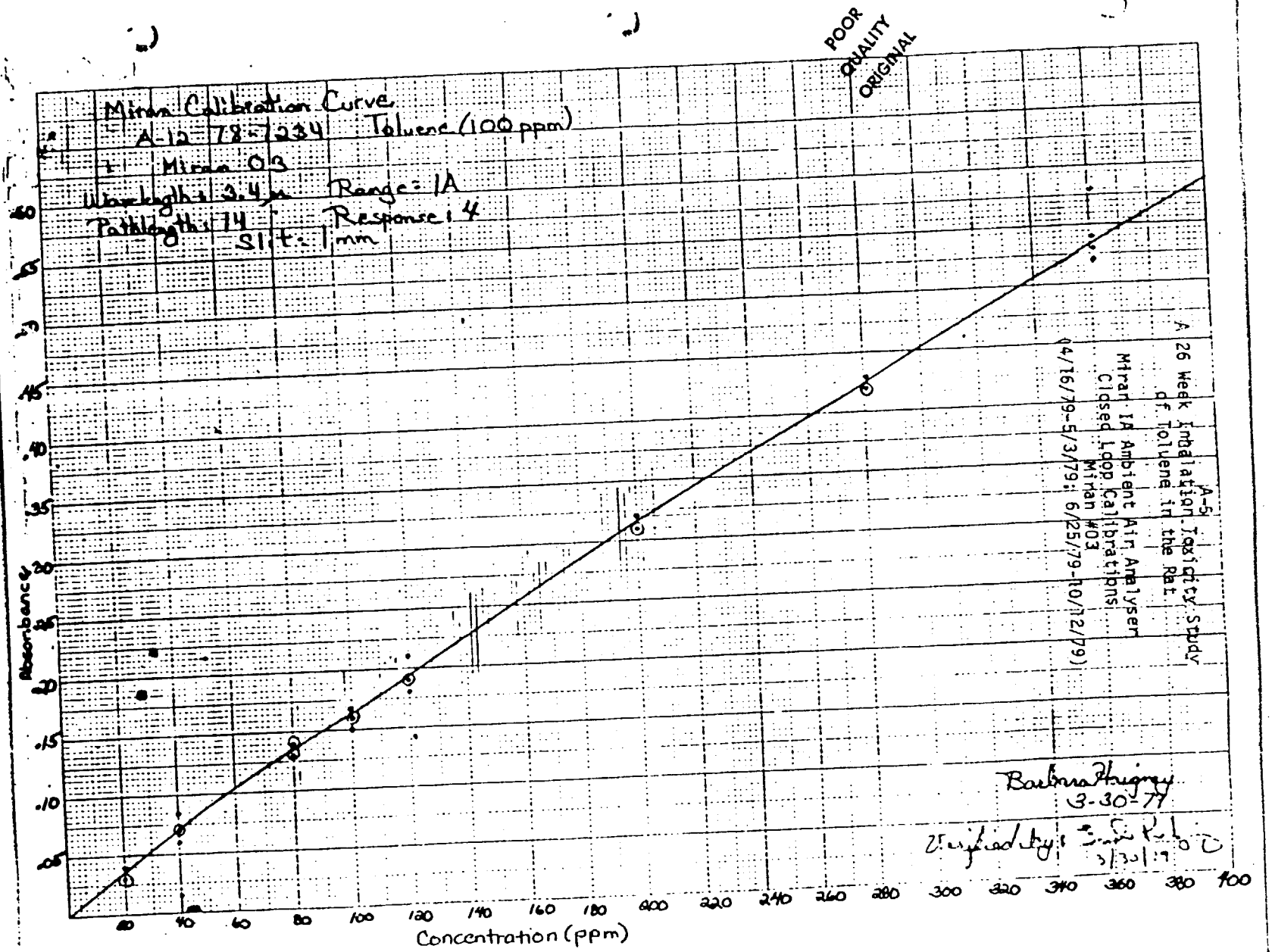

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Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Group V - High-Level Exposure

Project:	A-12 78-7234
Compound:	Toluene
Molecular Weight:	92.13 g/mole
Density:	.866 g/ml

MIRAN SETTINGS:

Wavelength:	3.4 μ
Pathlength:	3.5 (dial reading)
Range:	1 Å
Slit Width:	1 mm
Response Time:	4 sec.

Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #03
(4/16/79 - 4/24/79)

Date	Injection Volume (µl)	Concentration (ppm)	Absorbance A_1	A_2	A_3	A_4
3/28/79	40.0	1602.68	.62	.63	.61	.63
	42.0	1682.81	.65	.65	.64	.66
	45.0	1803.02	.69	.68	.68	.70
	47.0	1883.15	.71	.70	.71	.74
	49.0	1963.28	.74	.73	.73	.76
	49.89	1998.94	.75	.74	.74	.77
	51.0	2043.42	.76	.75	.75	.78
	53.0	2123.55	.77	.77	.77	.80
	56.0	2243.75	.81	.81	.80	.83
	58.0	2323.89	.84	.83	.82	.86
	60.0	2404.02	.86	.85	.84	.87

Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #02
(4/26/79 - 5/4/79)

Date	Injection Volume (ul)	Concentration (ppm)	Absorbance A_1	A_2	A_3	A_4
4/16/79	40.0	1602.68	.76	.76	.77	.77
	42.0	1682.81	.79	.80	.80	.80
	45.0	1803.02	.83	.84	.84	.84
	47.0	1883.15	.86	.87	.87	.88
	49.0	1963.28	.89	.90	.90	.91
	49.89	1998.94	.91	.92	.92	.92
	51.0	2043.42	.92	.93	.94	.94
	53.0	2123.55	.95	.96	.97	.97
	56.0	2243.75	1.00	1.00	1.02	1.01
	58.0	2323.89	-	-	-	-
	60.0	2404.02	-	-	-	-
4/19/79	0.5	20.03	.01	.01	-	-
4/25/79	1.0	40.07	.02	.02	-	-
	2.0	80.13	.03	.04	.05	.05
	2.5	100.17	.05	.05	.06	.06
	3.0	120.20	.06	.07	.07	.07
	5.0	200.34	.10	.11	.11	.11
	7.0	280.47	.14	.15	-	-
	9.0	360.60	.18	.19	-	-
	10.0	400.67	.20	.21	.23	.22
	15.0	601.01	.31	.31	.34	.32
	20.0	801.34	.40	.40	.44	.42
	25.0	1001.68	.51	.50	.53	.51
	30.0	1202.01	.59	.59	.62	.60
4/26/79	32.0	1282.14	.61	.62	.63	.63
	34.0	1362.28	.64	.65	.67	.66
	36.0	1442.41	.68	.69	.70	.70
	37.0	1482.48	.69	.71	.71	.71
	38.0	1522.55	.71	.72	.73	.73

Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #01
(5/7/79 - 6/22/79)

Date	Injection Volume (ul)	Concentration (ppm)	Absorbance A_1	A_2	A_3	A_4
3/8/79	40.0	1602.68	.65	.665	.64	.665
	42.0	1682.81	.68	.69	.67	.69
	45.0	1803.02	.72	.73	.72	.725
	47.0	1883.15	.745	.755	.735	.76
	49.0	1963.28	.77	.78	.76	.78
	49.89	1998.94	.78	.79	.77	.80
	51.0	2043.42	.79	.80	.785	.81
	53.0	2123.55	.815	.825	.81	.83
	56.0	2243.75	.85	.86	.84	.875
	58.0	2323.89	.88	.885	.87	.90
	60.0	2404.02	.90	.91	.89	.92

Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

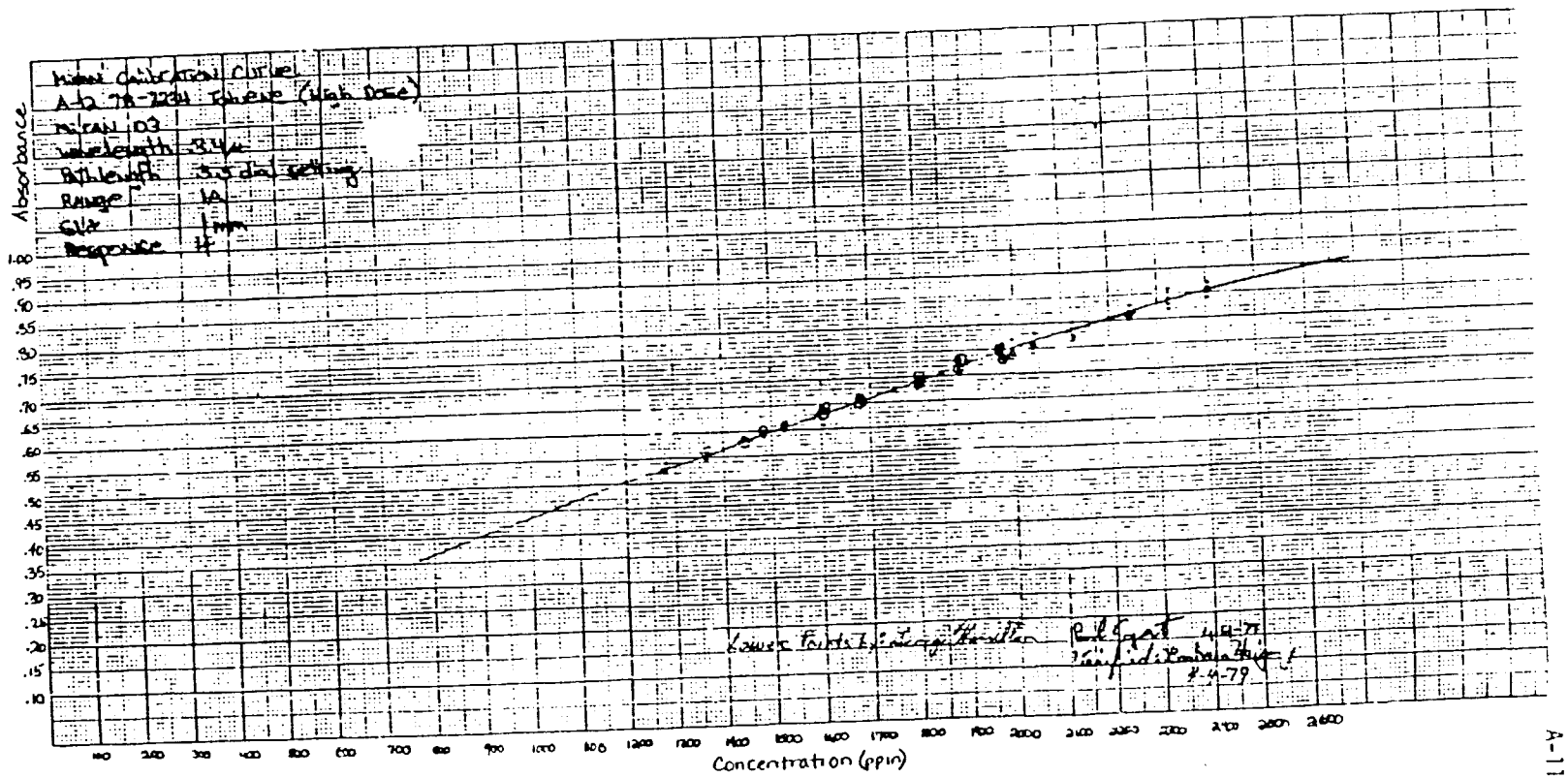
Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #03
(6/25/79 - 10/12/79)

Date	Injection Volume (µl)	Concentration (ppm)	Absorbance A_1	A_2	A_3	A_4
6/23/79	32.0	1282.14	.53	.54	.52	.53
6/25/79	34.0	1362.28	.56	.56	.55	.56
	36.0	1442.41	.58	.59	.58	.58
	37.0	1482.48	.60	.60	.59	.60
	38.0	1522.55	.61	.61	.60	.61
	40.0	1602.68	.63	.64	.63	.64
	42.0	1682.81	.66	.66	.65	.66
	45.0	1803.02	.70	.70	.69	.70
	47.0	1883.15	.72	.73	.71	.73
	49.0	1963.28	.75	.75	.74	.75

Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #03
(6/25/79-10/12/79)

POOR QUALITY ORIGINAL



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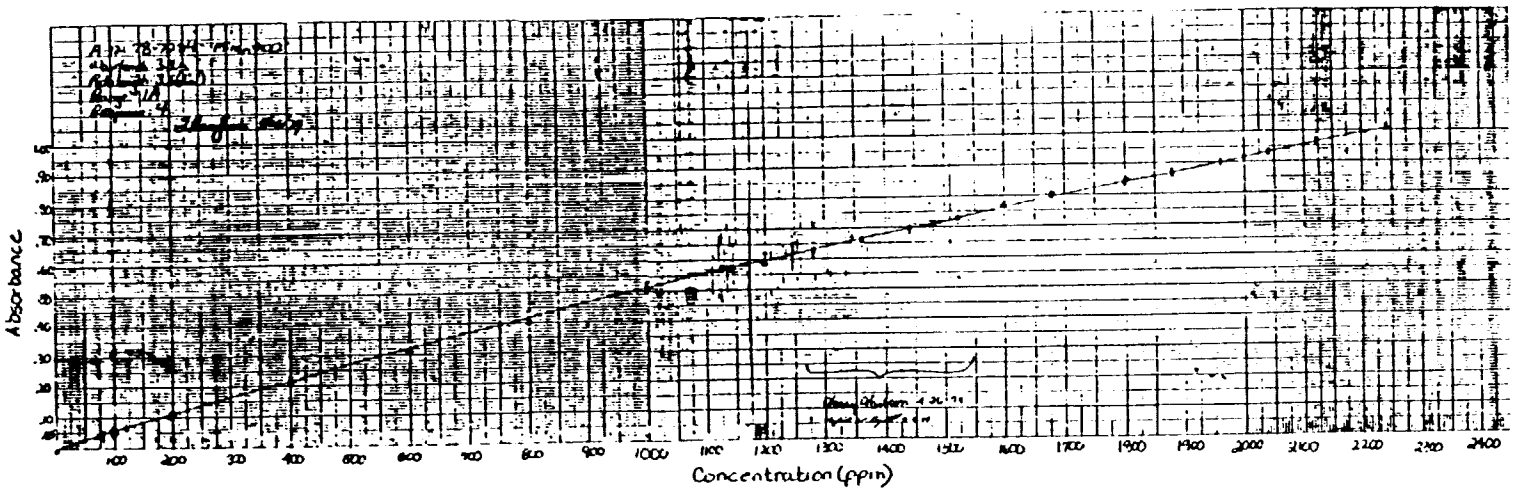
Appendix A (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Miran IA Ambient Air Analyzer
Closed Loop Calibrations
Miran #02
(4/26/79-5/4/79)

POOR QUALITY ORIGINAL



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Appendix B
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Methodology and References
General

Parameter	Reference or Description
Body Weight	INTEC Automatic Data Acquisition System.
Organ Weights	Mettler PL 200 Analytical Balance.
Selection	Similar groups of animals were selected by weight, using the Monroe 1860 Random Sorting Calculator Program, as follows: 1) After acclimatization, individually housed animals are given temporary numbers beginning with "1". 2) A mean body weight and its standard deviation are calculated for each sex. 3) At least three "ranges" of weight are designated arbitrarily in such a way that the number of animals in each weight range is as close to a multiple of the number of exposure groups as possible. 4) The animals in each range group are arbitrarily listed sequentially and distributed separately among the exposure groups, one animal per group at a time, as their sequence numbers are generated randomly. 5) Each animal receives a permanent number following randomization.
	Chamber Exposure Parameters
Integrated Mean Concentration	The integrated mean concentration was calculated by first multiplying the daily exposure concentration by the daily exposure hours to produce the daily concentration hours. This number was added to the previous value in the total concentration hours column to yield a new total concentration hours value. This value, divided by the total exposure hours for the exposure up to that time, gave the integrated mean concentration up to and including that day.

Appendix B (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Methodology and References
Statistical Analysis

Parameter	Reference or Description
Body Weight Hematology Clinical Chemistry	Statistical evaluation of equality of means was made by the appropriate one way analysis of variance technique, followed by a multiple comparison procedure if needed. First Bartlett's test was performed to determine if groups had equal variance. If the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. The parametric procedures were the standard one way ANOVA using the F distribution to assess significance. If significant differences among the means was indicated, Dunnett's test was used to determine which means were significantly different from the control. If a nonparametric procedure for testing equality of means was needed, the Kruskal-Wallis test was used, and if differences were indicated a summed rank test (Dunn) was used to determine which treatments differed from control. A statistical test for trend in the dose levels was also performed. In the parametric case (i.e. equal variance) standard regression techniques with a test for trend and lack of fit were used. In the nonparametric case Jonckheere's test for monotonic trend was used. The test for equal variance (Bartlett's) was conducted at the 1%, two-sided risk level. All other statistical tests were conducted at the 5% and 1%, two-sided risk levels. References for these techniques are Snedecor, G.W. and Cochran, W.G., Statistical Methods, 6th edition, Iowa State Univ. Press (1967), Hollander and Wolfe, Nonparametric Statistical Methods, John Wiley and Sons, New York (1973), Dunnett, C.W., J. Am. Sta. Assn., Vol. 50 (1955) and Biometrics, Vol. 20 (1964).

Bartlett's Test	pp. 296-298	S&C
ANOVA	pp. 277-279	S&C
Dunnett's Test	pp. 1096-1121, 482	D
Kruskal-Wallis	pp. 114-116	H&W
Summed Rank Test (Dunn)	pp. 131	H&W
Regression Analysis Trend	pp. 149-152	S&C
Lack of Fit	pp. 160-164	S&C
Jonckheere's Statistic	pp. 120-123	H&W

Appendix B (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Methodology and References
Laboratory Studies

Abbreviation	Parameter	Specimen	Reporting Units	Reference or Description
			Hematology	
HGB	Hemoglobin	Whole Blood	g%	Coulter Hemoglobinometer, Coulter Electronics, Inc.
HCT	Hematocrit	Whole Blood	%	Directions for Use-Adams Mechanical Hematocrit Tube Reader. Clay Adams, Inc., 1960.
RBC	Erythrocytes	Whole Blood	$10^6/mm^3$	Instruction Manual-Model Zf-Coulter Counter, Coulter Electronics, Inc.
WBC	Total Leukocytes	Whole Blood	$10^3/mm^3$	Instruction Manual-Model Zf-Coulter Counter, Coulter Electronics, Inc.
	Differential Leukocytes and Erythrocyte Morphology	Whole Blood	% WBC	Schermer, S. The Blood Morphology of Laboratory Animals; 3rd Edition. Philadelphia: F.A. Davis Co., 1967.
CLOT X	Clotting Time	Whole Blood	Minutes	Davidsohn, I. and B.B. Wells (Eds.). Todd-Sanford Clinical Diagnosis by Laboratory Methods (modified). 13th Edition. Philadelphia: W.B. Saunders Co., 1966, p. 416.

Appendix B (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Methodology and References
Laboratory Studies

Abbreviation	Parameter	Specimen	Reporting Units	Reference or Description
		Clinical Chemistry		
SGPT	Serum glutamic pyruvic transaminase	Serum	IU	CentrifiChem System 400® Modified Wroblewski Technique
ALK PHOS	Alkaline phosphatase	Serum	IU	CentrifiChem System 400® Modified Bessey-Lowry-Brock Technique
BUN	Blood urea nitrogen	Serum	mg/dl	CentrifiChem System 400® Modified Urease Technique
GLU	Fasting glucose	Serum	mg/dl	CentrifiChem System 400® Hexokinase Technique
		Urinalysis		
		Urine		Appropriate diagnostic labstick, Ames Company, Division of Miles Laboratory. Clinical Refractometer (National Instrument Company) for specific gravity.

Appendix C
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Animal Disposition History

Group ppm	Males An. No.	Males Days on Test	Males Date Sent	Males Week Sent	Females An. No.	Females Days on Test	Females Date Sent	Females Week Sent
I	100	197	10/29/79	29	150	183	10/15/79	27
0	101	120	8/13/79	18	151	120	8/13/79	18
	102	197	10/29/79	29	152	197	10/29/79	29
	103	183	10/15/79	27	153	197	10/29/79	29
	104	183	10/15/79	27	154	120	8/13/79	18
	105	197	10/29/79	29	155	183	10/15/79	27
	106	197	10/29/79	29	156	120	8/13/79	18
	107	183	10/15/79	27	157	120	8/13/79	18
	108	197	10/29/79	29	158	197	10/29/79	29
	109	120	8/13/79	18	159	197	10/29/79	29
	110	120	8/13/79	18	160	120	8/13/79	18
	111	183	10/15/79	27	161	183	10/15/79	27
	112	197	10/29/79	29	162	197	10/29/79	29
	113	120	8/13/79	18	163	183	10/15/79	27
	114	120	8/13/79	18	164	197	10/29/79	29

Appendix C (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Animal Disposition History

Group ppm	Males An. No.	Days on Test	Date Sent	Week Sent	Females An. No.	Days on Test	Date Sent	Week Sent
IV 100	400	183	10/15/79	27	450	120	8/13/79	18
	401	197	10/29/79	29	451	120	8/13/79	18
	402	120	8/13/79	18	452	183	10/15/79	27
	403	120	8/13/79	18	453	120	8/13/79	18
	404	120	8/13/79	18	454	57	6/11/79	9
	405	57	6/11/79	9	455	183	10/15/79	27
	406	120	8/13/79	18	456	197	10/29/79	29
	407	183	10/15/79	27	457	197	10/29/79	29
	408	183	10/15/79	27	458	57	6/11/79	9
	409	183	10/15/79	27	459	120	8/13/79	18
	410	57	6/11/79	9	460	183	10/15/79	27
	411	197	10/29/79	29	461	197	10/29/79	29
	412	57	6/11/79	9	462	183	10/15/79	27
	413	197	10/29/79	29	463	120	8/13/79	18
	414	120	8/13/79	18	464	57	6/11/79	9
V 1500	500	57	6/11/79	9	550	120	8/13/79	18
	501	197	10/29/79	29	551	183	10/15/79	27
	502	183	10/15/79	27	552	197	10/29/79	29
	503	120	8/13/79	18	553	57	6/11/79	9
	504	197	10/29/79	29	554	197	10/29/79	29
	505	183	10/15/79	27	555	57	6/11/79	9
	506	183	10/15/79	27	556	120	8/13/79	18
	507	120	8/13/79	18	557	197	10/29/79	29
	508	57	6/11/79	9	558	120	8/13/79	18
	509	120	8/13/79	18	559	120	8/13/79	18
	510	120	8/13/79	18	560	120	8/13/79	18
	511	57	6/11/79	9	561	183	10/15/79	27
	512	197	10/29/79	29	562	183	10/15/79	27
	513	120	8/13/79	18	563	183	10/15/79	27
	514	183	10/15/79	27	564	57	6/11/79	9

Appendix D
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Body Weight Values

Data Preface

[a]Body weight taken post-exposure, not used in the calculation of the mean.
[b]Animal sent to Albert Einstein College of Medicine for neurohistopathological examination. (Noted at time of removal from test, and once on each page thereafter).
[c]Animal fasted overnight prior to orbital bleeding, body weight not used in calculation of the mean.

78-7234 26WK INHAL-RAT-TOLUENE-BODY WT-M 4/16/79

RESPONSES 1-10; 3 GROUPS WITH SIZES 15 15 15

	DAY 1	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6	WEEK 7	WEEK 8	WEEK 9
100	264.	302.	341.	367.	390.	418.	426.	437.	445.	455.
101	321.	363.	411.	450.	484.	524.	555.	587.	609.	627.
102	272.	311.	349.	372.	403.	430.	460.	477.	495.	517.
103	296.	329.	354.	380.	-M-a	431.	445.	459.	474.	496.
104	266.	300.	329.	344.	368.	387.	393.	415.	434.	445.
105	260.	302.	343.	378.	414.	442.	475.	507.	531.	547.
106	269.	310.	337.	358.	370.	386.	407.	431.	453.	467.
107	296.	329.	360.	401.	444.	467.	491.	520.	553.	564.
108	300.	327.	352.	382.	405.	429.	448.	467.	474.	499.
109	306.	339.	366.	386.	416.	454.	478.	509.	530.	528.
110	283.	323.	357.	383.	416.	442.	468.	482.	488.	512.
111	300.	348.	391.	436.	472.	508.	537.	-M-a	589.	621.
112	294.	-M-a	358.	383.	406.	426.	448.	467.	480.	483.
113	293.	337.	378.	414.	444.	467.	500.	532.	550.	562.
114	305.	341.	386.	440.	479.	515.	544.	582.	592.	609.
GROUP AVERAGES	288.3	325.8	360.8	391.6	422.2	448.4	471.7	490.9	513.1	528.8
STANDARD ERRORS	4.7	5.1	5.8	8.0	10.0	10.8	12.4	13.9	14.5	15.1
400	280.	320.	348.	375.	-M-a	410.	430.	468.	474.	497.
401	258.	285.	313.	334.	-M-a	373.	399.	431.	444.	452.
402	287.	325.	368.	398.	429.	452.	474.	503.	514.	540.
403	265.	294.	312.	349.	383.	408.	425.	447.	459.	479.
404	321.	362.	-M-a	453.	489.	519.	555.	576.	594.	619.
405	304.	347.	373.	381.	416.	436.	441.	465.	465.	-M-b
406	260.	279.	298.	320.	339.	374.	400.	425.	443.	473.
407	288.	328.	356.	382.	409.	422.	440.	455.	461.	482.
408	266.	292.	330.	369.	403.	434.	458.	482.	501.	521.
409	263.	291.	316.	349.	371.	388.	405.	421.	446.	460.
410	308.	348.	388.	426.	458.	483.	507.	534.	562.	-M-b
411	278.	291.	326.	353.	381.	407.	431.	465.	485.	516.
412	285.	322.	341.	369.	391.	419.	451.	477.	492.	-M-b
413	272.	292.	325.	347.	373.	399.	426.	447.	-M-a	475.
414	277.	308.	339.	366.	383.	400.	411.	433.	448.	469.
GROUP AVERAGES	280.8	312.3	338.1	371.4	401.9	421.6	443.9	468.7	484.9	498.6
STANDARD ERRORS	4.8	6.7	7.0	8.9	11.0	10.2	10.9	11.0	12.2	13.3
500	292.	315.	338.	366.	399.	425.	450.	465.	487.	-M-b
501	292.	331.	375.	422.	463.	499.	542.	580.	608.	640.
502	267.	301.	329.	366.	395.	424.	454.	484.	504.	525.
503	281.	310.	326.	366.	396.	424.	452.	477.	496.	513.
504	279.	321.	357.	397.	433.	473.	507.	544.	570.	597.
505	286.	308.	327.	363.	401.	444.	476.	506.	534.	562.
506	285.	331.	357.	420.	473.	507.	558.	592.	629.	655.
507	282.	334.	362.	402.	434.	464.	497.	517.	545.	562.
508	307.	345.	363.	400.	433.	458.	485.	511.	505.	-M-b
509	271.	286.	320.	345.	379.	423.	459.	474.	489.	507.
510	292.	317.	339.	370.	397.	418.	449.	467.	488.	504.
511	299.	319.	359.	402.	437.	462.	491.	517.	538.	-M-b
512	296.	337.	357.	405.	443.	470.	496.	522.	536.	562.
513	290.	325.	357.	383.	424.	461.	480.	506.	512.	539.
514	293.	322.	344.	361.	378.	396.	412.	421.	439.	446.
GROUP AVERAGES	287.5	320.1	347.3	384.5	419.0	449.9	480.5	505.5	525.3	551.0
STANDARD ERRORS	2.7	3.9	4.3	6.1	7.6	8.1	9.7	11.5	12.7	17.1

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78-7239 26WK INHAL-RAT-TOLUENE-BODY WT-M 4/16/79
RESPONSES 11-26; 3 GROUPS WITH SIZES 15 15 15

	WEEK 10	WEEK 11	WEEK 12	WEEK 13	WEEK 14	WEEK 15	WEEK 16	WEEK 17	WEEK 18	WEEK 19
100	462.	475.	486.	496.	505.	507.	508.	523.	531.	529.
101	653.	674.	-M-c	691.	717.	728.	741.	762.	-M-b	-M-
102	528.	544.	-M-c	540.	561.	582.	593.	598.	609.	630.
103	512.	524.	-M-c	535.	539.	549.	557.	571.	574.	586.
104	456.	466.	-M-c	470.	478.	485.	493.	503.	505.	524.
105	570.	582.	-M-c	580.	582.	607.	625.	636.	648.	664.
106	493.	505.	-M-c	502.	520.	526.	542.	542.	558.	568.
107	584.	598.	617.	628.	633.	650.	646.	657.	672.	702.
108	518.	539.	-M-c	523.	544.	559.	566.	577.	592.	602.
109	559.	562.	578.	579.	580.	580.	589.	606.	-M-b	-M-
110	526.	533.	534.	534.	540.	550.	558.	573.	-M-b	-M-
111	633.	659.	671.	678.	698.	715.	734.	745.	759.	764.
112	490.	502.	-M-c	519.	529.	542.	546.	556.	561.	576.
113	576.	595.	-M-c	612.	631.	644.	653.	665.	-M-b	-M-
114	637.	658.	-M-c	637.	658.	676.	695.	706.	-M-b	-M-
GROUP AVERAGES	546.5	561.1	577.2	568.3	581.0	593.3	603.1	614.7	600.9	614.5
STANDARD ERRORS	16.1	17.0	32.1	17.5	18.4	19.2	19.9	20.3	23.7	24.2
400	512.	519.	-M-c	534.	548.	560.	569.	586.	606.	618.
401	469.	489.	-M-c	500.	511.	529.	531.	542.	559.	564.
402	559.	575.	-M-c	587.	608.	619.	626.	636.	-M-b	-M-
403	503.	514.	-M-c	538.	561.	565.	584.	597.	-M-b	-M-
404	639.	656.	-M-c	676.	694.	711.	729.	744.	-M-b	-M-
405	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
406	490.	510.	-M-c	534.	553.	572.	590.	597.	-M-b	-M-
407	490.	510.	-M-c	513.	529.	541.	549.	555.	559.	569.
408	539.	546.	-M-c	562.	580.	592.	598.	609.	611.	623.
409	460.	474.	483.	486.	502.	510.	514.	518.	535.	544.
410	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
411	537.	554.	568.	589.	600.	621.	629.	650.	654.	656.
412	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
413	493.	493.	-M-c	502.	513.	538.	541.	558.	536.	553.
414	478.	497.	-M-c	496.	510.	528.	522.	535.	-M-b	-M-
GROUP AVERAGES	514.1	528.1	525.5	543.1	559.1	573.8	581.8	593.9	580.0	589.6
STANDARD ERRORS	14.2	14.3	42.5	15.6	16.0	16.1	17.4	17.9	16.9	16.1
500	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
501	657.	-M-a	-M-c	690.	710.	729.	748.	761.	769.	780.
502	544.	556.	-M-c	567.	592.	610.	616.	633.	640.	656.
503	524.	551.	-M-c	557.	575.	599.	614.	620.	-M-b	-M-
504	611.	641.	-M-c	658.	678.	697.	711.	719.	735.	756.
505	584.	608.	616.	631.	652.	667.	674.	685.	701.	713.
506	659.	682.	-M-c	696.	736.	763.	780.	797.	812.	821.
507	590.	614.	-M-c	620.	638.	653.	672.	689.	-M-b	-M-
508	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
509	531.	542.	-M-c	538.	554.	562.	579.	592.	-M-b	-M-
510	511.	506.	525.	542.	552.	567.	571.	589.	-M-b	-M-
511	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
512	579.	596.	-M-c	606.	633.	650.	663.	672.	676.	682.
513	548.	565.	-M-c	577.	597.	614.	626.	630.	-M-b	-M-
514	445.	454.	-M-c	465.	472.	488.	480.	499.	516.	517.
GROUP AVERAGES	565.3	574.1	570.5	595.6	615.8	633.3	645.2	657.2	692.7	703.6
STANDARD ERRORS	17.7	19.2	45.5	19.6	21.4	22.1	23.3	23.5	36.6	37.8

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78-7254 20WK INHAL-RAT-TOLUENE-BODY WT-M 4/16/79
RESPONSES 21-29; 3 GROUPS WITH SIZES 15 15 15

	WEEK 20	WEEK 21	WEEK 22	WEEK 23	WEEK 24	WEEK 25	WEEK 26	WEEK 27	WEEK 28
100	535.	542.	551.	557.	568.	567.	568.	583.	587.
101	-M-	-M-	-M-	-M-	-M-	-M-c	-M-	-M-	-M-
102	640.	652.	662.	675.	680.	685.	697.	709.	714.
103	585.	594.	602.	608.	613.	-M-	626.	-M-b	-M-
104	531.	536.	545.	556.	556.	564.	578.	-M-b	-M-
105	676.	681.	685.	698.	711.	726.	730.	744.	741.
106	574.	579.	591.	599.	601.	-M-c	606.	625.	632.
107	732.	735.	751.	754.	767.	-M-c	777.	-M-b	-M-
108	606.	606.	616.	617.	632.	-M-c	640.	651.	659.
109	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
110	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
111	790.	757.	787.	813.	838.	847.	863.	-M-b	-M-
112	577.	577.	590.	601.	611.	-M-c	624.	642.	660.
113	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
114	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
GROUP AVERAGES	624.6	625.9	638.0	647.8	657.7	677.8	670.9	659.0	665.5
STANDARD ERRORS	26.9	24.5	25.9	27.0	28.7	53.0	30.0	23.8	22.7
400	638.	621.	633.	639.	649.	-M-c	658.	-M-b	-M-
401	566.	575.	564.	568.	578.	-M-c	581.	594.	608.
402	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
403	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
404	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
405	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
406	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
407	574.	575.	580.	571.	577.	-M-c	581.	-M-b	-M-
408	632.	637.	644.	629.	636.	657.	657.	-M-b	-M-
409	553.	554.	562.	562.	567.	563.	576.	-M-b	-M-
410	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
411	672.	679.	682.	689.	697.	-M-c	696.	708.	726.
412	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
413	576.	576.	590.	595.	594.	-M-c	603.	620.	639.
414	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
GROUP AVERAGES	601.6	602.4	607.[illegible]	607.6	614.0	610.0	621.7	640.7	657.7
STANDARD ERRORS	17.1	16.9	17.3	17.7	18.2	47.0	18.1	34.5	35.3
500	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
501	804.	809.	816.	820.	827.	-M-c	829.	847.	859.
502	670.	680.	694.	704.	709.	-M-c	720.	-M-b	-M-
503	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
504	773.	783.	794.	803.	819.	-M-c	779.	817.	837.
505	731.	741.	743.	756.	766.	-M-c	766.	-M-b	-M-
506	833.	855.	868.	882.	898.	889.	896.	-M-b	-M-
507	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
508	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
509	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
510	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
511	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
512	692.	701.	713.	725.	735.	747.	754.	744.	759.
513	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
514	532.	534.	536.	541.	532.	-M-c	542.	-M-b	-M-
GROUP AVERAGES	719.3	729.0	737.7	747.3	755.1	818.0	755.1	802.7	818.3
STANDARD ERRORS	38.2	39.8	40.7	41.3	44.2	71.0	41.6	30.6	30.3

POOR QUALITY ORIGINAL

BEST COPY AVAILABLE

RF-[illegible] DERK INHAL-RAT-TOLUENE-BODY WT-F

RE RANGE: 1-10; 3 GROUPS WITH SIZES: 15 15 15

	DAY 1	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6	WEEK 7	WEEK 8	WEEK 9
150	180.	201.	218.	223.	242.	251.	251.	268.	265.	274.
151	213.	234.	253.	274.	293.	300.	306.	322.	330.	337.
152	189.	206.	220.	224.	245.	258.	260.	283.	281.	287.
153	203.	215.	234.	247.	271.	268.	286.	291.	290.	299.
154	185.	193.	214.	222.	232.	242.	243.	253.	257.	265.
155	199.	216.	225.	244.	262.	266.	272.	290.	301.	305.
156	206.	223.	242.	254.	264.	279.	286.	291.	305.	304.
157	218.	231.	259.	272.	289.	290.	307.	318.	328.	324.
158	178.	194.	205.	208.	225.	233.	238.	241.	249.	253.
159	193.	206.	216.	243.	252.	254.	256.	273.	286.	288.
160	206.	228.	249.	255.	277.	292.	300.	302.	317.	324.
161	196.	213.	229.	252.	273.	283.	306.	318.	-M-a	346.
162	206.	235.	261.	268.	289.	311.	335.	350.	347.	358.
163	177.	191.	227.	231.	233.	250.	256.	267.	269.	275.
164	204.	223.	242.	259.	276.	277.	277.	291.	302.	304.
GROUP AVERAGES	196.9	213.9	232.9	245.1	261.1	270.3	279.3	290.5	294.8	302.1
STANDARD ERRORS	3.3	3.9	4.5	5.1	5.7	5.8	7.1	7.4	7.8	7.9
450	194.	207.	212.	234.	243.	250.	251.	260.	269.	268.
451	202.	218.	236.	-M-a	272.	278.	277.	296.	303.	303.
452	195.	214.	224.	229.	246.	256.	262.	283.	289.	286.
453	209.	244.	262.	285.	293.	318.	330.	342.	342.	354.
454	177.	188.	197.	208.	219.	223.	220	199.	233.	-M-b
455	214.	239.	255.	276.	292.	306.	315.	328.	343.	349.
456	192.	207.	-M-a	238.	253.	258.	269.	279.	286.	289.
457	190.	205.	210.	222.	240.	246.	251.	264.	278.	276.
458	202.	208.	231.	234.	256.	259.	267.	279.	278.	-M-b
459	195.	219.	237.	249.	264.	280.	290.	301.	309.	311.
460	186.	210.	221.	240.	256.	267.	278.	293.	299.	299.
461	193.	204.	206.	220.	231.	242.	242.	247.	255.	258.
462	200.	225.	243.	258.	278.	294.	307.	324.	337.	348.
463	198.	214.	236.	239.	261.	267.	280.	295.	291.	305.
464	206.	224.	236.	241.	264.	278.	287.	288.	302.	-M-b
GROUP AVERAGES	196.9	215.1	229.0	240.9	257.9	268.1	275.1	285.2	294.3	303.8
STANDARD ERRORS	2.4	3.6	5.0	5.6	5.4	6.5	7.4	.0	8.0	9.2
550	209.	-M-a	241.	256.	262.	272.	285.	293.	297.	317.
551	204.	216.	226.	234.	246.	259.	267.	277.	281.	291.
552	183.	204.	227.	235.	244.	260.	273.	276.	288.	302.
553	186.	202.	220.	231.	236.	243.	261.	270.	276.	-M-b
554	203.	222.	239.	268.	283.	292.	308.	315.	332.	338.
555	187.	209.	215.	230.	237.	245.	250.	257.	270.	-M-b
556	201.	215.	230.	243.	254.	261.	281.	281.	288.	293.
557	199.	211.	217.	219.	238.	248.	252.	254.	269.	275.
558	190.	213.	221.	224.	243.	249.	267.	271.	281.	289.
559	199.	213.	225.	238.	252.	259.	272.	281.	290.	290.
560	189.	213.	236.	240.	257.	270.	273.	288.	292.	293.
561	223.	232.	250.	263.	268.	289.	295.	300.	305.	312.
562	204.	217.	232.	235.	263.	271.	285.	285.	307.	310.
563	185.	189.	189.	208.	209.	227.	234.	235.	250.	250.
564	211.	229.	248.	266.	280.	297.	309.	311.	325.	-M-b
GROUP AVERAGES	198.2	213.2	227.7	239.3	251.5	262.8	274.1	278.3	290.1	296.7
STANDARD ERRORS	2.9	2.9	3.9	4.5	4.9	5.0	5.4	5.5	5.5	6.4

BEST COPY AVAILABLE

	WEEK 10	WEEK 11	WEEK 12	WEEK 13	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
150	255.	254.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
151	338.	350.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	-M-b	[illegible]
152	294.	295.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
153	300.	300.	312.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
154	262.	272.	278.	278.	[illegible]	[illegible]	[illegible]	[illegible]	-M-b	[illegible]
155	309.	315.	326.	324.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
156	318.	329.	348.	326.	332.	334.	[illegible]	[illegible]	-M-b	[illegible]
157	342.	340.	343.	350.	[illegible]	[illegible]	[illegible]	[illegible]	-M-b	[illegible]
158	251.	251.	259.	262.	268.	268.	278.	[illegible]	275.	[illegible]
159	284.	299.	-M-a	292.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
160	332.	333.	342.	331.	342.	348.	348.	[illegible]	-M-b	-M-
161	351.	361.	371.	361.	370.	371.	[illegible]	[illegible]	[illegible]	[illegible]
162	373.	385.	378.	388.	407.	415.	415.	425.	425.	442.
163	291.	314.	310.	332.	336.	311.	311.	[illegible]	[illegible]	[illegible]
164	309.	309.	310.	317.	314.	335.	321.	322.	327.	347.
GROUP AVERAGES	308.3	315.0	321.8	316.4	323.9	332.3	333.4	338.7	337.3	346.6
STANDARD ERRORS	8.8	9.1	9.7	9.2	10.5	10.8	9.8	10.2	14.8	14.7
450	268.	277.	279.	278.	279.	294.	299.	299.	-M-b	-M-
451	298.	312.	314.	310.	314.	312.	326.	320.	-M-b	-M-
452	299.	310.	311.	305.	315.	321.	332.	326.	326.	[illegible]
453	366.	370.	369.	368.	351.	374.	383.	405.	-M-b	-M-
454	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
455	352.	358.	367.	360.	367.	375.	384.	385.	397.	[illegible]
456	289.	294.	305.	294.	303.	306.	316.	322.	317.	[illegible]
457	275.	284.	294.	289.	312.	309.	312.	314.	331.	[illegible]
458	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
459	314.	324.	324.	333.	331.	347.	351.	366.	-M-b	-M-
460	308.	322.	321.	319.	332.	360.	343.	338.	342.	[illegible]
461	264.	264.	264.	266.	266.	278.	281.	281.	296.	[illegible]
462	352.	364.	358.	356.	367.	377.	386.	396.	432.	[illegible]
463	300.	311.	320.	308.	321.	326.	336.	337.	-M-b	-M-
464	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
GROUP AVERAGES	307.1	315.8	318.8	315.5	322.0	330.8	337.8	338.1	344.9	349.6
STANDARD ERRORS	9.7	9.9	9.5	9.5	9.4	9.9	9.9	12.0	15.5	15.6
550	315.	316.	323.	311.	320.	328.	331.	348.	-M-b	-M-
551	304.	304.	309.	311.	308.	321.	320.	327.	325.	[illegible]
552	301.	304.	312.	315.	314.	316.	328.	342.	342.	346.
553	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
554	335.	349.	357.	355.	362.	366.	377.	394.	425.	[illegible]
555	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
556	295.	303.	302.	309.	311.	315.	325.	320.	-M-b	-M-
557	270.	274.	286.	286.	291.	296.	298.	297.	296.	[illegible]
558	291.	302.	305.	304.	315.	320.	329.	326.	-M-b	-M-
559	303.	310.	311.	305.	314.	322.	319.	326.	-M-b	-M-
560	298.	296.	311.	306.	312.	312.	320.	325.	-M-b	-M-
561	320.	323.	322.	324.	330.	334.	341.	345.	347.	349.
562	311.	317.	331.	335.	337.	346.	357.	366.	363.	348.
563	273.	265.	276.	264.	271.	282.	291.	296.	282.	277.
564	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
GROUP AVERAGES	301.3	305.7	312.1	310.3	314.4	320.5	328.0	332.4	339.7	342.6
STANDARD ERRORS	5.3	6.4	6.0	6.5	6.7	6.6	6.7	8.1	14.8	15.8

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[illegible] INSEL-MAT-TOLUENE-DIEY WT-F [illegible]
[illegible] 1-CH 3 DOSED WITH NICKEL 15 15 15

	WEEK 20	WEEK 21	WEEK 22	WEEK 23	WEEK 24	WEEK 25	WEEK 26	WEEK 27	WEEK 28
152	311.	309.	318.	316.	329.	-M-c	321.	-M-b	-M-
151	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
152	320.	322.	329.	325.	351.	345.	340.	331.	333.
153	335.	330.	284.	261.	255.	246.	230.	325.	327.
154	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
155	360.	358.	369.	368.	374.	-M-c	363.	-M-b	-M-
156	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
157	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
158	278.	279.	279.	286.	298.	292.	294.	293.	293.
159	333.	331.	328.	324.	329.	-M-c	335.	340.	340.
160	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
161	397.	407.	405.	421.	426.	422.	432.	-M-b	-M-
162	436.	441.	446.	450.	469.	-M-c	462.	487.	501.
163	347.	351.	353.	356.	359.	355.	357.	-M-b	-M-
164	346.	344.	349.	352.	363.	-M-c	368.	367.	362.
GROUP AVERAGES	346.3	347.2	346.0	345.9	355.3	332.0	350.2	357.2	359.3
STANDARD ERRORS	14.0	14.8	16.3	18.2	19.2	29.8	20.7	27.7	29.8
450	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
451	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
452	344.	352.	350.	351.	362.	-M-c	343.	-M-b	-M-
453	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
454	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
455	400.	406.	400.	397.	412.	-M-c	399.	-M-b	-M-
456	322.	324.	329.	330.	337.	-M-c	329.	331.	337.
457	333.	336.	343.	342.	344.	350.	357.	383.	398.
458	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
459	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
460	367.	363.	370.	378.	382.	378.	385.	-M-b	-M-
461	299.	298.	293.	294.	298.	-M-c	296.	300.	301.
462	411.	415.	431.	433.	450.	-M-c	448.	-M-b	-M-
463	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
464	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
GROUP AVERAGES	353.7	356.3	359.4	360.7	369.3	364.0	365.3	338.0	345.3
STANDARD ERRORS	15.5	16.1	17.3	17.4	19.1	14.0	18.9	24.2	28.3
550	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
551	336.	339.	340.	336.	341.	-M-c	343.	-M-b	-M-
552	352.	359.	357.	362.	368.	375.	367.	375.	373.
553	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
554	438.	447.	448.	450.	467.	476.	481.	510.	524.
555	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
556	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
557	301.	304.	299.	302.	309.	-M-c	303.	312.	316.
558	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
559	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
560	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
561	352.	361.	357.	364.	373.	-M-c	363.	-M-b	-M-
562	371.	365.	372.	369.	368.	-M-c	371.	-M-b	-M-
563	310.	313.	307.	321.	345.	-M-c	340.	-M-b	-M-
564	-M-b	-M-	-M-	-M-	-M-	-M-	-M-	-M-	-M-
GROUP AVERAGES	351.4	355.4	354.3	357.7	367.3	426.0	366.9	399.0	404.3
STANDARD ERRORS	17.2	17.8	18.6	18.0	18.6	50.0	20.9	58.4	62.1

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Appendix E
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values

Data Preface

[a]Sample clotted, no value reported.
[b]Sample spun out of tube during centrifugation, no value reported.

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78-7234 26WK INHAL-TOLUENE-RAT-HEMAT-13M 7/ 9/79
RESPONSES 1- 5; 3 GROUPS WITH SIZES 10 10 10

	HGB G%	HCT %	RBC 10*6/MM3	CLOT X MIN	WBC 10*3/MM3
101	15.9	52.	9.02	3.5	9.6
102	-M-a	49.	-M-a	2.0	-M-a
103	15.7	51.	8.60	4.0	7.9
104	16.2	53.	9.00	3.5	11.1
105	15.8	52.	8.50	3.5	10.6
106	16.5	55.	8.66	3.5	9.1
108	15.2	53.	8.31	1.5	9.3
112	14.5	49.	7.76	2.5	5.7
113	14.6	46.	7.45	3.0	11.0
114	-M-a	52.	-M-a	2.0	-M-a
GROUP AVERAGES	15.55	51.2	8.412	2.90	9.29
STANDARD ERRORS	0.26	0.8	0.197	0.27	0.64
400	15.9	52.	8.31	4.0	9.6
401	-M-a	50.	-M-a	1.0	-M-a
402	14.7	49.	8.10	3.5	9.8
403	16.3	54.	7.98	2.0	8.2
404	14.9	47.	8.15	1.5	9.1
406	14.8	53.	7.11	2.0	8.0
407	16.6	56.	8.31	5.5	6.9
408	14.2	50.	7.97	3.0	7.4
413	14.9	51.	8.49	4.0	8.2
414	16.5	49.	8.31	1.0	11.7
GROUP AVERAGES	15.42	51.1	8.081	2.75	8.77
STANDARD ERRORS	0.30	0.8	0.134	0.47	0.49
501	14.8	49.	8.13	2.0	7.9
502	15.9	51.	8.69	3.5	11.6
503	15.9	49.	8.13	2.0	13.2
504	15.2	50.	8.19	1.0	7.9
506	12.5	49.	6.95	3.0	9.3
507	15.0	48.	7.91	1.5	7.5
509	14.2	49.	8.24	2.0	9.0
512	14.7	50.	8.31	5.5	8.2
513	13.5	48.	7.74	3.5	8.6
514	14.8	54.	8.65	2.0	7.5
GROUP AVERAGES	14.65	49.7	8.094	2.60	9.07
STANDARD ERRORS	0.33	0.6	0.157	0.41	0.60

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78-7234 26WK INHAL-TOLUENE-RAT-HEMAT-26M 10/8/79
RESPONSES 1- 5; 3 GROUPS WITH SIZES 5 5 5

	HGB G%	HCT %	RBC 10*6/MM3	CLOT X MIN	WBC 10*3/MM3
103	16.9	48.	7.64	2.5	15.4
106	16.9	50.	8.40	2.5	10.7
107	17.0	49.	7.93	4.5	13.6
108	16.5	46.	7.60	5.0	12.6
112	16.2	48.	7.10	3.0	6.9
GROUP AVERAGES	16.70	48.2	7.734	3.50	11.84
STANDARD ERRORS	0.15	0.7	0.213	0.52	1.45
400	17.1	50.	7.79	5.0	10.3
401	16.8	49.	7.67	3.0	9.9
407	17.7	-M-b	8.39	2.5	10.2
411	17.9	50.	8.15	4.5	12.5
413	17.1	49.	7.48	4.0	7.9
GROUP AVERAGES	17.32	49.5	7.896	3.80	10.16
STANDARD ERRORS	0.21	0.3	0.165	0.46	0.73
501	15.9	46.	7.15	4.0	11.3
502	16.8	49.	7.84	3.5	13.2
504	17.2	49.	7.66	2.0	12.6
505	16.2	45.	7.54	4.0	12.3
514	16.8	48.	8.41	2.5	8.1
GROUP AVERAGES	16.58	47.4	7.720	3.20	11.50
STANDARD ERRORS	0.23	0.8	0.206	0.41	0.90

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78-7234 26WK INHAL-TOLUENE-RAT-HEMAT-13F 7/ 9/79
RESPONSES 1- 5; 3 GROUPS WITH SIZES 10 10 10

	HGB G%	HCT %	RBC 10*6/MM3	CLOT X MIN	WBC 10*3/MM3
150	14.0	44.	6.86	3.5	8.5
152	16.1	45.	7.81	4.0	9.8
153	15.4	-M-a	7.05	2.5	9.9
156	16.2	48.	7.15	2.0	9.4
158	15.4	45.	6.98	4.0	7.3
159	15.0	38.	7.42	4.0	8.7
160	15.5	47.	7.29	2.0	9.8
161	15.3	-M-a	7.51	1.5	9.7
163	-M-a	-M-a	-M-a	0.5	-M-a
164	-M-a	48.	-M-a	2.0	-M-a
GROUP AVERAGES	15.36	45.0	7.259	2.60	9.14
STANDARD ERRORS	0.24	1.3	0.111	0.39	0.32
452	16.8	49.	7.19	2.5	10.3
453	16.1	47.	7.42	3.5	11.2
455	15.2	47.	7.27	1.0	9.3
456	15.4	44.	7.23	5.0	9.7
457	15.0	44.	7.25	2.0	8.6
459	14.6	45.	7.26	2.5	8.2
460	15.9	48.	7.50	2.0	8.1
461	15.4	48.	7.34	1.0	8.2
462	15.1	46.	7.28	2.0	9.8
463	16.0	50.	7.89	1.5	7.4
GROUP AVERAGES	15.55	46.8	7.363	2.30	9.08
STANDARD ERRORS	0.20	0.6	0.066	0.38	0.37
550	16.7	-M-a	7.98	1.0	11.8
551	16.0	47.	6.53	2.5	10.3
554	16.2	47.	7.34	5.0	11.1
556	16.3	50.	7.51	2.5	8.1
557	16.1	48.	7.75	5.0	8.1
558	16.7	50.	7.26	4.0	8.4
559	16.0	48.	8.09	2.5	5.7
560	16.3	50.	8.13	1.5	7.7
561	16.3	49.	7.98	2.5	11.8
562	15.2	48.	7.39	1.0	9.4
GROUP AVERAGES	16.18	48.6	7.596	2.75	9.24
STANDARD ERRORS	0.13	0.4	0.157	0.47	0.63

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78-7234 26WK INHAL-TOLUENE-RAT-HEMAT-26F 10/ 8/79
RESPONSES 1- 5; 3 GROUPS WITH SIZES 5 5 5

	HGB G%	HCT %	RBC 10*6/MM3	CLOT X MIN	WBC 10*3/MM3
150	14.4	43.	7.26	5.5	8.3
155	14.7	43.	7.17	3.5	10.1
159	15.2	43.	7.65	3.0	9.0
162	14.9	44.	7.08	3.0	7.1
164	15.1	49.	7.07	1.5	6.9
GROUP AVERAGES	14.86	44.4	7.246	3.30	8.28
STANDARD ERRORS	0.14	1.2	0.107	0.64	0.60
452	16.0	47.	7.21	1.5	7.9
455	-M-a	-M-a	-M-a	1.0	-M-a
456	14.2	45.	6.56	1.0	5.3
461	-M-a	46.	-M-a	1.0	-M-a
462	15.2	47.	7.20	2.0	6.9
GROUP AVERAGES	15.13	46.3	6.990	1.30	6.70
STANDARD ERRORS	0.52	0.5	0.215	0.20	0.76
551	15.1	46.	6.89	2.5	6.3
557	14.3	47.	6.52	5.0	7.9
561	15.8	46.	7.19	3.0	13.3
562	15.7	-M-b	7.19	2.0	9.5
563	15.2	46.	7.69	4.5	6.2
GROUP AVERAGES	15.22	46.3	7.096	3.40	8.64
STANDARD ERRORS	0.27	0.3	0.193	0.58	1.31

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Appendix E (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values
Total and Differential Leukocytes

Preface

The following cells are identified and counted:

Abbreviation	Type of cell
Lym	Lymphocyte
Seg	Mature (segmented) neutrophil

Remarkable erythocyte or leukocyte morphology and any other comments are noted under "Other". Abbreviations used are:

Abbreviation	Type of cell
Mon	Monocyte
Ban	Band cell
Eos	Mature (segmented) eosinophil
Bas	Mature (segmented) basophil
Hypo	Hypochromic

Differential leukocytes are expressed as percent total leukocytes.

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Appendix E (cont.)
A 25 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values
Total and Differential Leukocytes
Week 13 - Males

Group ppm	An. No.	WBC $10^3/mm^3$	LYM	Neutrophil SEG	Other
I 0	101	9.6	85	14	1 Mon
	102	a	77	20	2 Mon, 1 Eos
	103	7.9	90	9	1 Mon
	104	11.1	92	8	
	105	10.6	90	10	
	106	9.1	89	11	
	108	9.3	89	11	
	112	5.7	92	8	1+ Hypo
	113	11.0	79	20	1 Mon
	114	a	84	15	1 Eos
	Mean	9.3			
	S.E.	0.6			
	N	8			
IV 100	400	9.6	87	13	
	401	a	a	a	
	402	9.8	80	17	3 Eos
	403	8.2	83	16	1 Eos
	404	9.1	83	15	2 Eos
	406	8.0	86	13	1 Eos
	407	6.9	67	33	
	408	7.4	84	15	1 Eos
	413	8.2	78	21	1 Bas
	414	11.7	95	5	
	Mean	8.8			
	S.E.	0.5			
	N	9			

[a]Sample clotted, no value reported.

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Appendix E (cont.)
A 26 Week Inhalation Toxicity Study
of Tolu· · in the Rat

Individual Hematology Values
Total and Differential Leukocytes
Week 13 - Males (cont.)

Group ppm	An. No.	WBC $10^3/mm^3$	LYM	Neutrophil SEG	Other
V	501	7.9	83	16	1 Eos
1500	502	11.6	94	5	1 Eos
	503	13.2	85	14	1 Eos
	504	7.9	79	21	
	506	9.3	84	16	
	507	7.5	78	22	
	509	9.0	80	19	1 Eos
	512	8.2	87	13	
	513	8.6	84	14	2 Eos
	514	7.5	83	16	1 Mon
	Mean	9.1			
	S.E.	0.6			
	N	10			

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Appendix E (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values
Total and Differential Leukocytes
Week 26 - Males

Group ppm	An. No.	WBC $10^3/mm^3$	LYM	Neutrophil SEG	Other
I 0	103	15.4	95	4	1 Eos
	106	10.7	87	13	
	107	13.6	83	17	
	108	12.6	89	9	2 Eos
	112	6.9	83	15	2 Eos
	Mean	11.8			
	S.E.	1.5			
	N	5			
IV 100	400	10.3	87	12	1 Eos
	401	9.9	91	8	1 Eos
	407	10.2	76	22	2 Eos
	411	12.5	88	10	1 Mon, 1 Eos
	413	7.9	83	17	
	Mean	10.2			
	S.E.	0.7			
	N	5			
V 2000	501	11.3	88	12	
	502	13.2	80	16	1 Ban, 3 Eos
	504	12.6	91	7	2 Eos
	505	12.3	91	9	
	514	8.1	93	6	1 Eos
	Mean	11.5			
	S.E.	0.9			
	N	5			

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Appendix E (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values
Total and Differential Leukocytes
Week 13 - Females

Group ppm	An. No.	WBC $10^3/mm^3$	LYM	Neutrophil SEG	Other
I 0	150	8.5	92	6	1 Mon, 1 Eos
	152	9.8	87	10	3 Eos
	153	9.9	91	9	
	156	9.4	78	20	2 Eos
	158	7.3	85	12	2 Ban, 1 Eos
	159	8.7	71	27	2 Eos
	160	9.8	78	21	1 Eos
	161	9.7	90	10	
	163	a	73	24	1 Mon, 1 Ban, 1 Eos
	164	a	92	8	
	Mean	9.1			
	S.E.	0.3			
	N	8			
IV 100	452	10.3	85	14	1 Eos
	453	11.2	89	10	1 Eos
	455	9.3	77	20	3 Eos
	456	9.7	84	15	1 Eos
	457	8.6	86	11	2 Mon, 1 Ban
	459	8.2	86	13	1 Eos
	460	8.1	82	17	1 Eos
	461	8.2	88	4	8 Eos
	462	9.6	89	10	1 Eos
	463	7.4	83	17	
	Mean	9.1			
	S.E.	0.4			
	N	10			

[a]Sample clotted, no value reported.

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Appendix E (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values
Total and Differential Leukocytes
Week 13 - Females (cont.)

Group ppm	An. No.	WBC $10^3/mm^3$	LYM	Neutrophil SEG	Other
V	550	11.8	84	15	1 Eos
1500	551	10.3	83	14	3 Eos
	554	11.1	75	22	3 Eos
	556	8.1	87	11	1 Mon, 1 Eos
	557	8.1	87	13	
	558	8.4	86	14	
	559	5.7	85	15	
	560	7.7	79	20	1 Eos
	561	11.8	92	8	
	562	9.4	86	11	3 Eos
	Mean	9.2			
	S.E.	0.6			
	N	10			

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Appendix E (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Hematology Values
Total and Differential Leukocytes
Week 26 - Females

Group ppm	An. No.	WBC $10^3/mm^3$	LYM	Neutrophil SEG	Other
I 0	150	8.3	80	18	2 Eos
	155	10.1	74	25	1 Eos
	159	9.0	77	20	3 Eos
	162	7.1	82	15	3 Eos
	164	6.9	86	11	3 Eos
	Mean	8.3			
	S.E.	0.6			
	N	5			
IV 100	452	7.9	87	9	4 Eos
	455	a	80	20	
	456	5.3	84	14	2 Eos
	461	a	87	8	5 Eos
	462	6.9	80	15	5 Eos
	Mean	6.7			
	S.E.	0.8			
	N	3			
V 1500	551	6.3	78	22	
	557	7.9	73	26	1 Eos
	561	13.3	81	18	1 Eos
	562	9.5	81	19	
	563	6.2	88	9	3 Eos
	Mean	8.6			
	S.E.	1.3			
	N	5			

[a]Sample clotted, no value reported.

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Appendix F
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Clinical Chemistry Values

Data Preface

[a]Possible sample contamination, value excluded from the calculation of the mean.
[b]Sample destroyed, technician error.

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78-7234 26WK INH-TOLUENE-RAT-CLINCHEM13M 7/ 9/79
RESPONSES 1- 4; 3 GROUPS WITH SIZES 10 10 10

	SGPT IU	ALK PHOS IU	BUN MG/DL	GLU MG/DL
101	19.	103.	18.8	109.
102	21.	112.	13.8	128.
103	14.	89.	14.6	110.
104	19.	106.	14.7	112.
105	17.	81.	17.1	108.
106	21.	94.	14.2	96.
108	16.	98.	13.8	119.
112	33.	113.	15.9	106.
113	18.	78.	15.4	113.
114	16.	106.	17.2	116.
GROUP AVERAGES	19.4	98.0	15.55	112.7
STANDARD ERRORS	1.7	3.9	0.53	3.4
400	26.	104.	17.6	129.
401	46.	168.	17.7	192.
402	24.	128.	16.1	132.
403	20.	137.	18.6	137.
404	18.	115.	14.2	123.
406	17.	78.	14.4	129.
407	14.	83.	15.7	101.
408	18.	82.	15.2	96.
413	15.	96.	15.3	110.
414	17.	107.	20.4	152.
GROUP AVERAGES	21.5	109.8	16.52	130.1
STANDARD ERRORS	3.0	9.0	0.63	8.7
501	21.	115.	15.7	109.
502	21.	94.	14.9	83.
503	17.	59.	15.8	93.
504	13.	99.	14.9	128.
506	18.	109.	15.5	147.
507	20.	108.	13.6	97.
509	15.	93.	16.5	113.
512	17.	88.	17.1	119.
513	14.	103.	15.6	143.
514	13.	89.	16.5	109.
GROUP AVERAGES	16.9	95.7	15.61	114.1
STANDARD ERRORS	1.0	5.0	0.31	6.6

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78-7234 26WK INH-TOLUENE-RAT-CLINCHEM26M 10/ 8/79

RESPONSES 1 4; 2 GROUPS WITH SIZES 5 5 5

	SGPT IU	ALK PHOS IU	BUN MG/DL	GLU MG/DL
103	15.	89.	17.4	140.
106	29.	90.	17.2	128.
107	23.	87.	14.3	136.
108	19.	93.	18.2	170.
112	28.	102.	16.4	135.
GROUP AVERAGES	22.8	92.2	16.70	141.8
STANDARD ERRORS	2.7	2.6	0.66	7.3
400	28.	86.	19.0	147.
401	-M-(82)[a]	111.	17.5	123.
407	14.	73.	19.0	107.
411	25.	94.	19.4	126.
413	21.	87.	16.7	131.
GROUP AVERAGES	22.0	90.2	18.32	126.8
STANDARD ERRORS	3.0	6.2	0.52	6.5
501	26.	111.	15.6	112.
502	23.	86.	15.3	120.
504	13.	64.	12.2	111.
505	12.	62.	15.2	152.
514	19.	99.	16.0	136.
GROUP AVERAGES	18.6	34.4	14.86	126.2
STANDARD ERRORS	2.7	9.6	0.68	7.9

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78-7234 20WK INH-TOLUENE-RAT-CLINCHEM13F 7/ 9/79
RESPONSES 1- 4; 3 GROUPS WITH SIZES 10 10 10

	SGPT IU	ALK PHOS IU	BUN MG/DL	GLU MG/DL
150	8.	27.	18.1	137.
152	11.	36.	17.6	119.
153	27.	37.	12.2	111.
156	16.	63.	18.7	131.
158	10.	39.	17.3	118.
159	12.	21.	15.4	121.
160	14.	52.	14.1	118.
161	19.	61.	18.6	131.
163	11.	28.	14.8	118.
164	11.	32.	12.3	129.
GROUP AVERAGES	13.9	39.6	15.91	123.3
STANDARD ERRORS	1.8	4.6	0.79	2.6
452	12.	37.	15.7	89.
453	12.	43.	15.5	125.
455	10.	35.	17.1	163.
456	16.	41.	15.5	102.
457	8.	21.	13.9	115.
459	13.	21.	14.6	118.
460	22.	30.	17.9	107.
461	11.	34.	16.3	131.
462	14.	37.	20.4	122.
463	13.	27.	18.0	139.
GROUP AVERAGES	13.1	32.6	16.49	121.1
STANDARD ERRORS	1.2	2.4	0.60	6.5
550	13.	38.	14.9	128.
551	11.	52.	16.4	120.
554	10.	22.	20.4	110.
556	11.	58.	17.0	94.
557	11.	32.	16.9	113.
558	12.	42.	18.2	98.
559	13.	51.	16.2	115.
560	12.	50.	23.0	122.
561	15.	61.	20.8	106.
562	11.	29.	19.3	136.
GROUP AVERAGES	11.9	43.5	18.31	114.2
STANDARD ERRORS	0.5	4.1	0.80	4.1

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78-7234 26WK INH-TOLUENE-RAT-CLINCHEM26F 10/ 3/79
RESPONSES 1- 4; 3 GROUPS WITH SIZES 5 5 5

	SGPT IU	ALK PHOS IU	BUN MG/DL	GLU MG/DL
150	17.	28.	18.3	164.
155	15.	27.	18.4	139.
159	17.	21.	21.4	144.
162	14.	23.	10.6	154.
164	16.	28.	19.7	156.
GROUP AVERAGES	15.8	25.4	17.68	151.4
STANDARD ERRORS	0.6	1.4	1.86	4.4
452	28.	26.	16.1	139.
455	28.	27.	18.2	142.
456	-M-(140)[a]	27.	16.3	143.
461	21.	32.	19.4	143.
462	-M-b	-M-b	-M-b	-M-b
GROUP AVERAGES	25.7	28.0	17.50	141.8
STANDARD ERRORS	2.3	1.4	0.79	0.9
551	19.	45.	17.2	114.
557	17.	14.	17.6	126.
561	20.	43.	19.0	146.
562	14.	32.	17.7	126.
563	27.	16.	18.6	126.
GROUP AVERAGES	19.4	30.0	18.02	127.6
STANDARD ERRORS	2.2	6.5	0.34	5.2

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Appendix G
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Urinalysis Values

Key

Gross			Appearance		
Appear	=	Appearance	Cl	=	Clear
Sp.G.	=	Specific Gravity	Cy	=	Cloudy
pH	=	Acid-Base Determination	D	=	Dark
P	=	Protein	H	=	Hazy
GL	=	Glucose	L	=	Light
K	=	Ketones	NC	=	No Color
B	=	Bilirubin	St	=	Straw
OC	=	Occult Blood	Y	=	Yellow

Protein: Negative (N); Positive (P); Trace (Tr); 30 mg/dl (1+); 100 mg/dl (2+); 300 mg/dl (3+); over 1000 mg/dl, (4+).

When positive protein values of 2+ or greater were obtained with Bili-Labstix©, the original sample was centrifuged and tested with sulfosalicylic acid. The results are presented in parentheses: Negative = N; Positive = P.

Glucose: Negative (N); Trace (Tr); 1/4 g/dl (1+); 1/2 g/dl (2+); 1 g/dl (3+); 2 or more g/dl (4+).

Ketones: Negative (N); Small (1+); Moderate (2+); Large (3+).

Bilirubin: Negative (N), Small (1+); Moderate (2+); Large (3+).

Occult Blood: Negative (N), Small (1+); Moderate (2+); Large (3+).

Positive occult blood values were verified using a fresh Bili-Labstix©. All animals with positive occult blood values were checked for signs of external bleeding.

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Appendix G (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Urinalysis Values
Week 13 - Males

Group ppm	Animal Number	Appear	Sp.G.	pH	P	GL	K	B	OC
I 0	101	HLY	1.033	8.0	Tr	N	N	N	N
	102	HLSt	1.035	8.0	1+	N	N	N	N
	103	ClLY	1.035	8.0	1+	N	N	N	N
	104	ClLSt	1.028	8.0	1+	N	N	N	N
	105	ClLSt	1.020	8.0	Tr	N	N	N	N
	106	HLSt	1.030	7.5	1+	N	N	N	N
	108	HLY	1.030	8.0	1+	N	N	N	N
	112	HLY	1.038	8.0	Tr	N	N	N	N
	113	HLY	1.040	8.5	2+(P)	N	N	N	N
	114	ClLSt	1.010	8.0	N	N	N	N	N
IV 100	400	CyLY	1.045	8.5	1+	N	N	N	N
	401	HLY	1.062	7.5	1+	N	N	N	N
	402	CyLY	1.040	7.0	1+	N	N	N	N
	403	ClLSt	1.015	8.0	N	N	N	N	N
	404	HLY	1.047	8.0	1+	N	N	N	N
	406	ClLY	1.025	7.0	Tr	N	N	N	N
	407	HLSt	1.027	8.0	N	N	N	N	N
	408	HLY	1.022	7.5	Tr	N	N	N	N
	413	a	1.039	8.0	1+	N	N	N	N
	414	CyLY	1.034	8.5	1+	N	N	N	N
V 1500	501	ClLY	1.026	8.0	1+	N	N	N	N
	502	CyLSt	1.015	8.5	N	N	N	N	N
	503	HLY	1.044	8.0	1+	N	N	N	N
	504	HLY	1.042	8.5	1+	N	N	N	N
	506	HLY	1.043	8.0	3+(P)	N	N	N	N
	507	HLY	1.056	7.0	1+	N	N	N	N
	509	HLY	1.027	8.0	1+	N	N	N	N
	512	ClLY	1.030	7.0	Tr	N	N	N	N
	513	HLSt	1.036	8.5	2+(P)	N	N	N	N
	514	CyLY	1.037	9.0	2+(P)	N	N	N	N

[a]Appearance not recorded due to a technician error.

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Appendix G (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Urinalysis Values
Week 26 - Males

Group	Animal Number	Appear	Sp.G.	pH	P	GL	K	B	OC
ppm									
I	103	HLY	1.045	8.0	2+(P)	N	N	N	N
0	106	CyLSt	1.040	6.5	1+	N	N	N	N
	107	HLSt	1.026	8.0	1+	N	N	N	N
	108	HDY	1.060	6.0	2+(P)	N	N	N	N
	112	HLSt	1.020	8.0	1+	N	N	N	N
IV	400	HLSt	1.033	7.0	1+	N	N	N	N
100	401	HLY	1.064	7.0	1+	N	N	N	N
	407	HLSt	1.026	7.0	Tr	N	N	N	N
	411	ClLSt	1.033	7.5	1+	N	N	N	N
	413	HDY	1.072	8.0	2+(P)	N	N	N	N
V	501	ClLSt	1.022	8.0	Tr	N	N	N	N
1500	502	ClLY	1.056	8.0	Tr	N	N	N	N
	504	ClLNC	1.014	8.0	Tr	N	N	N	N
	505	HLY	1.045	7.0	2+(P)	N	N	N	N
	514	ClDY	1.098	7.5	2+(P)	N	N	N	N

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Appendix G (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Urinalysis Values
Week 13- Females

Group ppm	Animal Number	Appear	Sp.G.	pH	P	GL	K	B	OC
I 0	150	NC	1.030	8.0	N	N	N	N	N
	152	ClLY	1.030	8.0	Tr	N	N	N	N
	153	HDY	1.056	9.0	1+	N	N	N	N
	156	CyLSt	1.037	8.0	N	N	N	N	N
	158	ClLY	1.042	6.0	Tr	N	N	N	N
	159	HLY	1.049	8.0	Tr	N	N	N	N
	160	NC	1.016	9.0	N	N	N	N	N
	161	CyLSt	1.045	7.0	Tr	N	N	N	N
	163	ClLY	1.036	8.0	N	N	N	N	N
	164	CyLSt	1.022	8.5	N	N	N	N	N
IV 100	452	HLY	1.034	8.0	Tr	N	N	N	N
	453	HLSt	1.045	7.0	1+	N	N	N	N
	455	HLSt	1.041	8.5	Tr	N	N	N	N
	456	ClLY	1.033	6.0	2+(P)	N	N	N	N
	457	ClLY	1.060	6.5	2+(P)	N	N	N	N
	459	HLSt	1.030	9.0	Tr	N	N	N	N
	460	HLSt	1.046	8.0	1+	N	N	N	N
	461	CyDY	1.070	8.5	1+	N	N	N	N
	462	ClLY	1.041	8.5	N	N	N	N	N
	463	ClDY	1.066	8.0	1+	N	N	N	N
V 1500	550	HLSt	1.016	8.5	N	N	N	N	N
	551	CyLSt	1.050	8.0	1+	N	N	N	N
	554	CyLSt	1.028	8.5	Tr	N	N	N	N
	556	HLY	1.038	8.5	Tr	N	N	N	N
	557	HLY	1.037	9.0	1+	N	N	N	N
	558	HLSt	1.014	8.0	1+	N	N	N	N
	559	HLY	1.014	8.5	Tr	N	N	N	N
	560	HLSt	1.015	8.0	Tr	N	N	N	N
	561	ClDY	1.030	8.5	N	N	N	N	N
	562	CyLSt	1.020	8.5	N	N	N	N	N

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Appendix G (cont.)
A 26 Week Inhalation Toxicity Study
of Toluene in the Rat

Individual Urinalysis Values
Week 26- Females

Group	Animal Number	Appear	Sp.G.	pH	P	GL	K	B	OC
ppm									
I	150	ClLY	1.042	7.5	1+	N	N	N	N
0	155	ClLSt	1.023	8.0	Tr	N	N	N	N
	159	ClLY	1.060	5.5	1+	N	N	N	N
	162	ClLNC	1.020	7.0	1+	N	N	N	N
	164	ClLSt	1.015	6.0	N	N	N	N	N
IV	452	ClLY	1.066	6.5	2+(P)	N	1+	N	N
100	455	HLY	1.060	7.0	3+(P)	N	N	N	N
	456	HLY	1.070	5.5	3+(P)	N	N	N	N
	461	HLY	1.043	8.0	Tr	N	N	N	N
	462	ClLSt	1.044	7.0	3+(P)	N	N	N	N
V	551	ClLY	1.068	6.0	3+(P)	N	N	N	b
1500	557	ClLY	1.050	8.5	1+	N	N	N	b
	561	ClLSt	1.033	8.0	N	N	N	N	b
	562	ClLNC	1.010	8.5	N	N	N	N	b
	563	ClLY	1.034	8.5	N	N	N	N	b

[b]Occult blood values not recorded due to a technician error.

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ALBERT EINSTEIN COLLEGE OF MEDICINE
of Yeshiva University
1300 MORRIS PARK AVENUE, BRONX, N.Y. 10461

Institute of Nanotoxicology
(212) 430-2309

Executive and Scientific Director:
Peter S. Spencer, Ph.D.
Medical Director:
Herbert H. Schaumburg, M.D.

April 4, 1980

POOR QUALITY ORIGINAL

Charles Holdsworth, Ph.D.
American Petroleum Institute
2101 L Street, N.W.
Washington, D.C. 20037

Dear Dr. Holdsworth:

In accordance with the terms and conditions of the API/ION Contract of August 16, 1977, page 1 & 2, item 3, please find twelve (12) copies of the final report for the January 1, 1979 - December 31, 1979 Project: Whole Animal Bioassay: n-heptane & toluene.

If you should have any questions, please do not hesitate to contact me.

Sincerely,

Deborah J. Crow
Administrator

DJC:le

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Wistar Animals Discussion n-Hexane, Toluene

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Methods

Animals intoxicated by inhalation at Bio-dynamics, Inc. were received in four separate batches. They were sacrificed for morphological examination within 1 week of receipt. Each animal was anesthetized with sodium barbitone and heparin, the chest opened and perfused via the ascending aorta with 4% paraformaldehyde for 0.5 min followed by phosphate-buffered 5% glutaraldehyde for 10 to 15 min. Animals were then dissected to remove the brain, spinal cord and sciatic/tibial complex. Samples of these tissues were post-fixed in osmium tetroxide, dehydrated and embedded in epoxy resin for light-microscopic study of sections or for the examination of single teased nerve fibers. The following areas were sampled:

Central Nervous System:	Peripheral Nervous System:
Lumbar spinal cord	Dorsal root ganglion
Thoracic cord	Lumbar ventral roots
Cervical spinal cord	Lumbar dorsal roots
Medulla oblongata	Sciatic nerve at sciatic notch
Cerebellar vermis	Tibial nerve at knee
Optic nerve	Tibial nerve branches*
Lateral geniculate nucleus	

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At least one section from each site was examined by light microscopy and scored for pathological changes. All slides were re[illegible]. A total of approximately 1850 slides was examined.

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Data Collected

1. 24 rats (n-heptane - 3 male, 3 female, low dose; 3 male, 3 female, high dose; toluene - 3 male, 3 female, low; 3 male, 3 female, high), received June 19, 1979, were perfused with fixatives, the central and peripheral nervous systems examined and found to be free of toxin-related pathological changes.

2. 50 rats (n-heptane - 5 male, 5 female, low; 5 male, 5 female, high; toluene - 5 male, 5 female, low; 5 male, 5 female, high; control - 5 male, 5 female), received on August 13, were perfused, the central and peripheral nervous system examined and found to be free of toxin-related pathological changes.

3. 40 rats (n-heptane - 4 male, 4 female, low; 4 male, 4 female, high; toluene - 4 male, 4 female, low; 4 male, 4 female, high; control - 4 male, 4 female), received on October 12, were perfused, the central and peripheral nervous system examined and found to be free of toxin-related pathological changes.

4. 34 rats (n-heptane - 3 male, 2 female, low; 3 male, 2 female, high; toluene - 3 male, 3 female, low; 3 male, 3 female, high; control - 6 male, 6 female),

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[illegible] the central and peripheral nervous system examined and found to be free of toxin related pathological changes.

5. A number of pathological changes was found in the tissue examined. These were more prominent in the later than in the earlier groups received, and appeared to be associated with advancing age. There was considerable inter-animal variation in the frequency of these changes; they occurred in control as well as exposed animals, and there was no relationship to dose in the exposed animals. The changes consisted of isolated axonal swellings in the gracile nucleus and tract, isolated myelin bubbles in dorsal roots and rare segmental remyelination and Wallerian degeneration in the peripheral nerves. The incidence of myelin bubbling was higher in the dorsal roots of the heptane animals in groups 3 and 4 as compared with controls. No significance is attached to this finding because a similar incidence was found in the high and low dose animals and there was no progression of changes between groups 3 and 4. These myelin bubbles and the isolated axonal swellings in the gracile tract are known to be normal findings in aged animals. Control and exposed animals also displayed isolated examples of unilateral or bilateral optic nerve degeneration with or without changes in the lateral geniculate nucleus. Their causation is unknown. Optic nerve changes were seen with greatest frequency in the low heptane and high toluene groups, but then only in a few animals. They were also seen in some control animals. Such changes are believed to be unassociated with exposure to toluene or heptane and may possibly result from a traumatic episode or, conceivably from an unidentified retrobulbar mass.

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Rats exposed by Biodynamics, Inc. to 100 and 1,500 ppm of toluene or 400 and 2000 ppm of n-heptane for periods of 6h/d 5d/week for up to 6 months have been examined morphologically following perfusion with glutaraldehyde, and have been found to be free of toxin related neuropathological changes.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Barbara J. Price
Vice President
Health, Environment & Safety
Phillips Petroleum Company
Bartlesville, Oklahoma 74004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAY 0 8 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and **refer to the reverse side of this page for "EPA Information Requests"** .

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12577A

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Triage of 8(e) Submissions

Date sent to triage: 12/14/95

NON-CAP CAP

Submission number: 12577A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

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w/neur

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entire document: 0 1 2 **pages** 1 **pages** 1,2, tab

Notes:

Contractor reviewer : CPS **Date:** 4/14/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 - 12577 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Phillips Petroleum Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 08/24/92 OTS DATE: 09/02/92 CSRAD DATE: 03/07/95

CHEMICAL NAME: Toluene

CAS# 108-88-3

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL. TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA: NON-CBI INVENTORY
YES
CAS SR NO
INTERIM R. IN TRAMINI

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES: RAT

TOXICOLOGICAL CONCERN:
LOW
MED
HIGH

USE:

PRODUCTION:

COMMENTS: Rats were exposed via inhalation (6hrs/day, 5d/week) for 26 weeks at mean concentrations of 0, 100, 1481 ppm. Glucose levels in the females were decreased in a dose-related manner. Increased liver enzymes was also observed in females. No histopathology was provided.