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DATA EVALUATION REPORT

Tetramethrin

Study Type: Subchronic Inhalation Toxicity in Rats

Prepared for:

Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031-1207

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Principal Author _____ Date 1/27/92
Carrie Rabe, Ph.D.

Reviewer _____ Date 1-29-92
Wayne Reichardt, Ph.D.

QA/QC Manager _____ Date 1/29/92
Sharon Segal, Ph.D.

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Project Officer: James E. Scott

Guideline Series 82-4: Subchronic Inhalation Toxicity in the Rat

EPA Reviewer: William Dykstra, Ph.D., DABT
Review Section I, Toxicology Branch I
Health Effects Division
Signature: William Dykstra
Date: 8/11/92

EPA Section Head: Roger Gardner, M.S.
Review Section I, Toxicology Branch I
Health Effects Division
Signature: Roger Gardner
Date: 8/11/92

DATA EVALUATION REPORT

STUDY TYPE: Subchronic inhalation toxicity

TEST MATERIAL: Tetramethrin

Tox Chem. Number: 844

SYNONYMS: Neo-Pynamin

STUDY NUMBER: 2279

MRID Number: 419950-03

SPONSOR: Agricultural Chemicals
Sumitomo Chemical Co., Ltd.

TESTING FACILITY: Environmental Health Science Laboratory
Sumitomo Chemical Co., Ltd.
1-98, 3-Chome, Kasugade-naka
Konohana-ku, Osaka
Japan

TITLE OF REPORT: Three-month Inhalation Toxicity Study of Neo-Pynamin in Rats (Determination of the No Observed Effect Level)

AUTHORS: Shinobu Kawaguchi

REPORT ISSUED: Study completed August 9, 1991

CONCLUSIONS: Tetramethrin was administered to Sprague-Dawley rats by inhalation for 13½ weeks, 5 days/week, for 6 hours/day. The actual (measured) exposure concentrations were 1.9, 4.4, and 19.8 mg/m^3. The following treatment-related effects were observed at these exposure levels:

1.9 mg/m^3 -- No effects

4.4 mg/m^3 -- No effects

19.8 mg/m^3 -- An 8.7% increase in the relative liver weight was observed in females. This supports a similar finding in both males and females at 20.3 mg/m^3 in a related study (MRID # 42012101).

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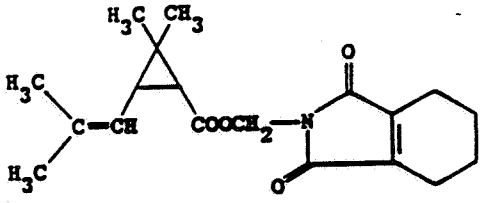
CORE CLASSIFICATION: This study is classified as Core Supplementary because exposure atmospheres were characterized on only 2 out of 5 days per week.

A. MATERIALS, METHODS, AND RESULTS

1. Test Article Description

Name: Tetramethrin

Formula: $C_{19}H_{25}NO_4$; 2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylic acid (1,3,4,5,6,7-hexahydro-1,3-dioxo-2H-isoindol-2-yl)methyl ester



Lot number: 90304

Purity: 95.3%; impurities not identified

Physical property: White crystalline solid; molecular weight, 331.42; melting point, 65-80°C

Stability: Not reported

Storage: Dark at 2-4°C

Vehicle: Corn oil

2. Test Article Analyses for Purity and Stability

No information was provided regarding analysis of the test article for purity and stability. However, samples of the test atmosphere at each exposure level were collected on silica gel sampling tubes for 5 minutes, twice per exposure, 2 days per week, and analyzed for test material concentration. According to Guideline 82-4, actual exposure concentrations should be determined at each exposure.

Following extraction with acetone, tetramethrin content was quantitated by gas chromatography utilizing flame ionization detection. According to the study protocol, the highest exposure concentration was intended to be 20.3 mg/m^3, equal to the lowest exposure concentration producing adverse effects in a previous study (study # 2189, MRID # 42012101).

The actual mean concentrations of tetramethrin measured in the breathing zone were as follows (taken from study # 2279, Table 4):

Group 3: 1.9 ± 0.19 mg/m^3
Group 4: 4.4 ± 0.60 mg/m^3
Group 5: 19.8 ± 1.16 mg/m^3

The test material was prepared as a 0.08% (Group 3), 0.24% (Group 4), or 0.8% (Group 5) solution in corn oil. Vehicle control atmospheres were generated using the same injection rate (ml/min) as the test atmospheres. The aerosol droplets that were generated were in the respirable range (see Table 1 for MMAD and LSD data). No information was provided regarding the actual concentration of corn oil in the tetramethrin-containing or vehicle control atmospheres. The nominal concentration of corn oil in the vehicle control atmosphere was determined daily during exposure, and the mean is presented in Table 1.

3. Exposure Conditions

Exposures (6 hours/day, 5 days/week, for 13½ weeks) were conducted using whole body exposure chambers (0.56 m^3 inner volume, Clea Japan Inc.) into which wire-mesh cages of individually penned animals were placed. The number of exposure chambers used and the number of animals introduced into each exposure chamber were not specified in the report; however, assuming that all of the rats at any given exposure level (10 males and 10 females) were exposed simultaneously in one chamber, the total volume of animals in each exposure chamber would not exceed 5% of the chamber volume (estimated by the reviewer).

Vehicle control and test atmospheres were generated by automatically injecting corn oil or 0.08%, 0,24%, or 0.8% solutions of tetramethrin in corn oil into an atomizer. The injection rate was 1.8 ml/min for both the vehicle control and test atmospheres. The aerosols generated were immediately directed into the exposure chamber. A diagram of the mist generator and exposure system are attached as Figure 1.

The nominal corn oil and tetramethrin concentrations were calculated by dividing the total amount of corn oil or tetramethrin injected into the atomizer by the total air flow through the chamber. As described above under "Test Article Analysis for Purity and Stability," actual aerial concentrations were determined 2 times per exposure, 2 exposure days per week, by collecting the aerosol on powdered silica gel in a glass tube for 5 minutes at a rate of 20 l/min and analyzing the samples by gas chromatography. The recommended frequency of analysis of the actual exposure concentration is at least once per exposure (Guideline 82-4). The nominal concentrations used and the actual concentrations achieved in the breathing zones of the test animals are presented in Table 1.

Air flow through the chamber was maintained at 0.12 m^3/min (12.9 air changes per hour). Air flow, temperature, relative humidity, and air pressure in the chamber were monitored continuously with an Intelligent Recorder (Model PGH, Fuji Electric Co., Ltd., Tokyo) and confirmed at 0, 2, 4, and 6 hours after initiation of exposure. Temperature was maintained at 24°C ± 2°C, which is above the recommended temperature of 22°C ± 2°C (Guideline 82-4), but well within the normal physiological tolerance range of the animals. Data for temperature and humidity are summarized in Table 1. No information was provided regarding oxygen content of the exposure atmospheres; however, air flow through the chamber (12.9 air changes per hour) should have been sufficient to maintain adequate oxygen levels.

Particle size distribution was determined at each exposure concentration 5 times per run, 2 days per week, using a Model SA-M1D Microscopic Sedimentation Analyzer (Shimadzu Corp.). The mass median aerodynamic diameter of the aerosol particles fell between 0.67 and 0.97 µm at each exposure level, and the log-standard geometric deviation ranged from 1.35 to 2.28 µm. The twice-weekly analysis of particle size in this study is less than the recommended analysis frequency of at least 1 time per exposure.

4. Animals

Five-week old Crj:CD (Sprague-Dawley) rats (SPF) were purchased from Charles River Japan, Inc., 11 days prior to the first exposure. Following a quarantine period of 7 days and "preliminary breeding for 4 days," 50 healthy males (224-257 g) and 50 healthy females (169-203 g) were selected for the study and randomly assigned to study groups (5 groups; 10 rats/sex/group) such that there were no statistically significant differences in mean body weights between the groups. The purpose of the preliminary breeding period is unclear, as is its timing in relation to study animal selection. However, judging by the absence of any evidence to the contrary, it is assumed that the study animals met the Guideline (82-4) requirement that females be nulliparous and non-pregnant.

Rats were caged in pairs segregated by sex and study group in suspended aluminum cages with wire mesh floors. Cages were changed weekly. Both before and after exposure, animals were housed in a room with a temperature of 24°C ± 2°C, relative humidity of 55% ± 10%, ventilation of 10-20 air changes per hour, and a 12-hour light/dark cycle. Food (Type CRF-1, Oriental Yeast Co., Ltd., Tokyo) and purified, filtered tap water were available to the animals ad libitum, except during exposures.

5. Statistical Analyses

Body weight, food and water consumption, hematology, blood biochemistry, and organ weight were analyzed using a one-way analysis of variance. If the difference was significant ($p < 0.05$), the least significant difference (LSD) method was also used to analyze for differences between the vehicle control group and the other study groups.

Urinalysis data were analyzed by the Kruskal-Wallis test. If the difference was significant ($p < 0.05$), the Scheffe's rank sum test was used to analyze for differences between the vehicle control group and the other study groups.

6. General Observations

(a) Mortality/moribundity/survival

Animals were observed daily for mortality/moribundity. On exposure days they were observed before, during, and 1 hour after exposure, and on nonexposure days they were observed once for animal survival. No mortality was observed prior to the terminal sacrifice on days 94 (males) and 95 (females) of the study.

(b) Clinical observations

Animals were observed daily for adverse clinical signs. On exposure days they were observed before exposure, 2, 4, and 6 hours after initiation of exposure, and 1 hour after termination of exposure. On nonexposure days they were observed once per day. Both summary and individual data were provided in the study report.

Irregular respiration was noted during exposure in some animals of both sexes in all of the study groups except the air controls. This effect was limited to the first week of exposure, and the incidence was not concentration-related. Other sporadic observations included loss of hair, conjunctival discharge, and wounds and scabs on the skin of the head, face, back, and paws. However, the incidence of these findings was not concentration related, and the majority of these signs probably resulted from fighting during the non-exposure intervals when rats were caged in pairs.

Wet fur and rough coats were noted in every animal exposed to the aerosol, including the vehicle controls. These effects are attributable to the accumulation of the aerosol on the animals. This accumulation of the aerosol is of concern because it introduces the possibility of dermal and oral exposure through grooming.

(c) Body weights/food consumption/water consumption

Body weights--Individual body weights were determined immediately prior to the first exposure and twice per week throughout the study. Final body weights of exsanguinated animals were determined at termination. Both summary and individual data were provided in the study report. No treatment-related effects on body weight gain were observed.

Food consumption--Food consumption was determined for each cage of two animals over two consecutive days once per week. Both summary and individual "per cage" data were provided. However, because animals were caged in pairs, individual (per animal) data could not be determined.

No effects on food consumption were observed in males or females that could be attributed to exposure to tetramethrin (Table 2). Females in the 1.9-mg/m^3 exposure group showed a statistically significant increase in food consumption over vehicle controls during week 8, but this change was incidental in nature and not related to any trend. Females in both the vehicle control group and all of the tetramethrin-treated groups tended to consume less than air controls, and statistically significant differences were noted between air and vehicle controls at weeks 5, 8, 9, and 13.

Water consumption--Water consumption was determined for each cage over two consecutive days once per week. Both summary and individual "per cage" data were provided. However, because animals were caged in pairs, individual (per animal) data could not be determined.

No treatment-related effects on water consumption were observed in females; however, there appeared to be a concentration-related increase in water consumption in tetramethrin-treated males relative to both the air and vehicle controls (Table 3). These data were not analyzed by the submitter for trends, but at the low, mid, and high exposure levels, water consumption increased by averages of 10.3%, 15.4%, and 20.5%, respectively, relative to the vehicle controls. The water consumption of the males at the highest exposure level was not, however, statistically significantly different from either the air or vehicle controls.

(d) Ophthalmoscopic examination

Apparently no ophthalmological examinations were performed in this study, although the Pesticide Assessment Guidelines (82-4) recommend that eye examinations be performed on at least the high-concentration and control animals prior to the first day of exposure and at the termination of the study. In the companion study (study # 2189, MRID # 42012101), no effect on the eye was observed by ophthalmological examination when animals were exposed to higher concentrations.

7. Clinical Pathology

All hematology and clinical chemistry parameters marked with an "X" below were examined in all animals using blood samples collected after the animals had been fasted for approximately 17 hours following the final exposure. The blood samples were drawn from the abdominal aorta in all cases. Both summary and individual data were provided for all of the groups.

(a) Hematology

X Hematocrit (HCT)*
X Hemoglobin (HGB)*
X Leukocyte count (WBC)*
X Erythrocyte count (RBC)*
X Platelet count*
X Reticulocyte count (RETIC)
X Red cell morphology
X Fibrinogen
X Leukocyte differential count*
X Mean corpuscular HGB (MCH)
X Mean corpuscular HGB concentration (MCHC)
X Mean corpuscular volume (MCV)
X Coagulation: prothrombin time (PT); activated partial thromboplastin time (APTT)

* = Recommended by Subdivision F (November 1984) Guidelines

There were no changes observed in any hematology parameters that were attributable to exposure to tetramethrin. A decrease in neutrophil count was observed in females at the 4.4-mg/m^3 exposure level when compared to the vehicle controls; however, this effect was incidental in nature. A number of differences between air and vehicle controls were observed, including statistically significant differences in hemoglobin and fibrinogen concentrations in males, and white blood cell and neutrophil counts in females.

(b) Blood (clinical) chemistry

Electrolytes

X Calcium*
X Chloride*
Magnesium
X Phosphorus*
X Potassium*
X Sodium*

Enzymes

X Alkaline phosphatase (ALP)
X Serum Cholinesterase
Red Blood Cell Cholinesterase
Brain Cholinesterase
X Creatinine phosphokinase
X Lactic acid dehydrogenase
X Serum alanine aminotransferase (SGPT)*
X Serum aspartate aminotransferase (SGOT)
X Gamma glutamyl transferase (GGT)

Other

X Albumin*
X Albumin/globulin ratio
X Blood creatinine*
X Blood urea nitrogen*
X Cholesterol
X Globulins
X Glucose*
X Total bilirubin*
Direct bilirubin
X Total protein*
X Triglycerides
X Phospholipids

X Leucine aminopeptidase (LAP)

* Recommended by Subdivision F (November 1984) Guidelines

There were no apparent concentration-related changes in any clinical chemistry parameters. Statistically significant, but incidental, decreases were observed in gamma globulin fraction in both sexes at the 1.9-mg/m^3 exposure level and in females at the 4.4-mg/m^3 level when compared to vehicle controls. A slightly decreased blood creatinine level was noted in males exposed to 19.8 mg/m^3, but this was an incidental decrease. As with hematology, a number of differences between air and vehicle controls were observed in males and/or females, including statistically significant changes in total protein, beta globulin, gamma globulin, serum alanine aminotransferase, alkaline phosphatase, albumin fraction, alpha 1 globulin, and the albumin-globulin ratio.

(c) Urinalysis

Urine samples were collected from all animals during week 13 and analyzed for the parameters indicated by an "X" in the list below:

X Appearance	Sediment (microscopic)	X Bilirubin
Volume	X Protein	X Blood
Specific gravity	X Glucose	Nitrate
X pH	X Ketones	X Urobilinogen

There were no treatment-related changes in any of the parameters examined.

8. Sacrifice and Pathology

Immediately following the collection of blood samples, all of the animals were sacrificed and subjected to gross necropsy. According to the study protocol, this included external examination as well as observation of the contents of the cranial, thoracic, abdominal, and pelvic cavities. However, the study report does not include a complete listing of all tissues and organs examined; the report includes only those in which an abnormality was observed. Although the study protocol states that kidneys were embedded in paraffin, sectioned, and stained with hematoxylin and eosin, and that all organs and tissues were preserved in 10% neutral buffered formalin, there is no listing of these organs and tissues, and there are no histopathologic data provided. The kidneys and liver are double-checked (XX) below, indicating that they were dissected and weighed.

Respiratory	Cardiovascular/	Neurologic

9

Nasopharyngeal tissues*
Trachea*
Lungs (perfused)*

Digestive System
Salivary glands*
Esophagus*
Stomach*
Duodenum*
Jejunum*
Ileum*
Cecum*
Colon*
Rectum*
XX Liver*
Pancreas*

Hematologic
Heart*
Bone marrow*
Thymus*
Aorta*
Lymph node*
Spleen*

Urogenital System
XX Kidneys*
Urinary Bladder*
Testes*
Uterus*

Brain*
Peripheral nerve*
Pituitary*
Eye & optic nerve*
Spinal cord
(3 levels)

Glandular
Adrenals*
Thyroid*
Parathyroids*

Other
Bone (sternum*)
Tissues with gross lesions*

* Recommended by Subdivision F (November 1984) Guidelines

(a) Macroscopic

The incidence of gross lesions was low overall, and none of the effects appeared to be treatment related. In the urinary bladders of one or two males from all groups except for the air control, there was an unidentified white substance. This effect may have been due to exposure to the test vehicle.

(b) Organ weights and organ-to-body weight ratios

Organ weight data were obtained for only the liver and kidneys in this study. A slight (8.7%) but statistically significant increase in relative liver weight was observed in females at the 19.8-mg/m^3 exposure level when compared to vehicle controls. There was no corresponding significant increase in the relative and absolute liver weights of males. However, it is likely that 19.8 mg/m^3 is approximately the threshold level for observable effects on the liver since a concentration-related increase in liver weight was observed in both males and females at 20.3 mg/m^3 in a previous study (study # 2189, MRID # 42012101).

The mean absolute and relative liver weights of all vehicle-exposed males were significantly higher than those of the air controls. This most likely represents a vehicle effect.

No treatment-related effects on kidney weight were observed.

The Pesticide Assessment Guidelines (82-4) recommend that in addition to the liver and kidneys, the lungs and testes should be weighed, and the SEP for inhalation toxicity testing recommends that the adrenals also be weighed.

(c) Microscopic Examination

Although the study protocol states that all tissues and organs were preserved and that kidneys were embedded in paraffin, sectioned, and stained, there are no histopathologic data provided in the report. The Pesticide Assessment Guidelines (82-4) recommend performing histopathology on all organs and tissues of the control and high-concentration groups, as well as on the lungs and target organs (liver and kidneys) of all animals. The SEP for inhalation toxicity testing recommends that the heart also be examined in all animals.

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The reviewers have no other comments regarding the materials and methods sections.

A description of the statistical analysis employed was included in the report.

A signed Good Laboratory Practice Compliance Statement, a signed Quality Assurance Statement, and a list of Quality Assurance Inspections were included.

B. DISCUSSION

This study (study # 2279, MRID # 419950-03) was designed as a follow-up of a previous study (study # 2189, MRID # 42012101) in which the lowest exposure level tested caused increased relative liver weights in both males and females. At the mid and high exposure levels in the previous study, hepatic lesions were also observed in both males and females and renal lesions were observed in males. The highest exposure level used in the current study (19.8 mg/m^3) was approximately equal to the lowest exposure level tested in the previous study (20.3 mg/m^3).

There were no treatment-related changes observed in mortality, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, or gross pathology under the conditions of this study. A very slight decrease in blood creatinine levels was observed in males at the high dose level but was judged to be incidental in nature. Data for food and water consumption were available only for paired animals.

The only treatment-related effect observed in the current study was an increase in the liver-to-body weight ratio of the high-concentration females. No statistically significant differences were observed between any treatment group and the vehicle controls with respect to water consumption, but an apparent concentration-related trend was observed by the reviewer in the water consumption of exposed males. Without appropriate statistical analysis for trends, this cannot be asserted with certainty.

No microscopic examination of tissues or ophthalmologic examinations were performed and only limited organ weight data were obtained in the current study. However, ophthalmologic and organ weight data and histopathologic

data for the liver and kidneys were available in the companion study for the group exposed to 20.3 mg/m^3. This data should closely approximate the results for the 19.8 mg/m^3 group in the current study.

The increase in the relative liver weights of high-dose females in this study is the basis for establishing 19.8 mg/m^3 as the LOEL for subchronic inhalation exposure. The NOEL observed under the conditions of this study is 4.4 mg/m^3 for females.

Although the data were reported adequately, and the summary data were supported by the data from individual animals, limitations to this study require it to be classified as Core Supplementary. These included minimal description of the exposure chamber employed and characterization of exposure atmospheres on only 2 out of 5 days per week.

TABLE 1. Characteristics of Exposure Atmospheres[a]

	Vehicle Control	Air Control	Low Level	Mid Level	High Level
Percent Solution	0.00	Not Applicable	0.08	0.24	0.80
Nominal Concentration[b] (mg/m^3)	13,900±420 (corn oil)	Not Applicable	12±0.4	36±1.0	120±3.4
Actual Concentration[b] (mg/m^3)	No Data	Not Applicable	1.9±0.19	4.4±0.60	19.8±1.16
Median Particle Size (μm)					
Minimum	0.67	Not Applicable	0.69	0.68	0.68
Maximum	0.95		0.97	0.94	0.96
Logarithmic Standard Geometric Deviation					
Minimum	1.39		1.39	1.40	1.40
Maximum	2.02		2.08	1.99	2.28
Chamber Temperature[b]					
Minimum	24.8±0.26	24.4±0.25	24.4±0.28	24.9±0.32	24.8±0.37
Maximum	25.6±0.17	25.3±0.18	25.1±0.14	25.7±0.15	25.5±0.18
Relative Humidity[b]					
Minimum	53±2.2	53±0.7	56±1.4	50±1.5	54±1.8
Maximum	57±2.2	56±1.0	59±1.6	53±1.5	54±1.9

[a]Data extracted from Study No. 2279, Tables 1, 3, 4, 5, 6, and 7
[b]Mean ± Standard Deviation

TABLE 2. Food Consumption at Selected Intervals from Rats Exposed to Tetramethrin-Containing Atmospheres[a,b]

Exposure Group	Mean Food Consumption (g/rat/day) at Study Week: 1	3	5	7	8	9	11	13	Average[c]
				Males					
Air Control	26±1.8	25±1.5	26±1.9	26±1.3	26±2.0	25±1.1	25±1.5	25±0.9	25±0.5
Vehicle Control	24±2.3	25±3.4	26±2.3	25±2.4	26±2.5	25±1.8	24±2.2	25.±1.6	25±0.8
1.9 mg/m^3	24±1.1	24±0.9	26±0.9	25±0.9	25±2.2	26±1.1	24±0.8	25±0.9	25±0.8
4.4 mg/m^3	23±1.3	25±1.6	26±2.4	26±2.3	26±3.0	27±1.9	26±2.1	25±1.9	26±1.1
19.8 mg/m^3	23±2.8	24±0.4	25±0.8	26±1.9	25±2.1	25±1.2	25±1.3	25±1.1	24±1.0
				Females					
Air Control	17±1.3	18±1.3	20±1.5**	18±0.5	19±1.9*	20±2.2[d]**	17±2.3	19±1.3[d]**	19±1.1
Vehicle Control	16±1.1	18±2.6	18±1.0	18±2.9	17±1.3	17±1.3	16±1.8	16±1.7	17±0.9
1.9 mg/m^3	17±0.7	18±1.9	19±1.8	18±1.8	19±1.8*	18±1.4	17±1.6	17±1.3	18±0.8
4.4 mg/m^3	16±0.5	18±0.9	18±0.4	18±0.8	17±0.8	17±1.4	17±1.3	15±1.3	17±1.1
19.8 mg/m^3	15±2.1	18±1.9	18±0.8	18±1.1	17±0.8	17±0.9	17±1.0	17±1.3	17±1.0

[a]Data extraceted from Study No. 2279, Table 10
[b]Mean ± standard deviation
[c]Calculated by reviewer from all reported daily means
[d]Based on 4 cages

* Significantly different from vehicle control; $p \leq 0.05$
** Significantly different from vehicle control; $p \leq 0.01$

TABLE 3. Water Consumption at Selected Intervals from Rats Exposed to Tetramethrin-Containing Atmospheres[a,b]

Exposure Group	Mean Water Consumption (g/rat/day) at Study Week: 1	3	5	7	9	11	13	Average[c]
				Males				
Air Control	36±2.4 (2.9)[d]	39±6.1 (2.6)	42±6.7 (2.4)	42±6.4 (2.4)	42±2.6 (0.0)	38±5.4 (2.7)	41±4.4 (13.9)	40±2.3 (2.6)
Vehicle Control	35±3.1	38±4.5	41±4.9	41±3.8	42±5.9	37±4.5	36±4.8	39±2.2
1.9 mg/m^3	38±5.2 (8.6)	41±6.4 (7.9)	44±8.0 (7.3)	45±7.3 (9.8)	45±11.1 (7.1)	43±12.2 (16.2)	42±11.2 (16.7)	43±2.5 (10.3)
4.4 mg/m^3	37±3.3 (5.7)	43±4.4 (13.2)	46±6.6 (12.2)	49±5.0 (19.5)	50±5.3 (19.0)	44±5.2 (18.9)	42±5.1 (16.7)	45±3.7 (15.4)
19.8 mg/m^3	41±5.4 (17.1)	44±5.1 (15.8)	48±9.3 (17.1)	52±10.3 (26.8)	50±11.4 (19.0)	48±13.1 (29.7)	47±13.0 (30.1)	47±3.7 (20.5)
				Females				
Air Control	27±4.8 (0.0)	28±2.0 (-9.7)	32±1.8 (0.0)	29±0.7 (-14.7)	32±2.4 (3.2)	27±2.3 (-12.9)	31±1.1 (3.3)	29.5±1.8 (-3.2)
Vehicle Control	27±1.8	31±4.1	32±3.5	34±3.6	31±6.3	31±6.4	30±6.1	31.0±1.7
1.9 mg/m^3	30±2.3 (11.1)	35±1.8 (12.9)	38±4.5 (18.8)	37±3.6 (8.8)	36±2.5 (16.1)	36±3.2 (16.1)	35±1.9 (16.7)	35.2±2.2 (12.9)
4.4 mg/m^3	28±2.2 (3.7)	32±3.1 (3.2)	35±4.7 (9.4)	37±5.5 (8.8)	33±4.5 (6.4)	34±8.6 (9.7)	31±5.0 (3.3)	33.2±2.6 (6.4)
19.8 mg/m^3	26±5.4 (-3.7)	32±4.1 (3.2)	35±5.3 (9.4)	34±5.9 (0.0)	31±2.6 (0.0)	32±1.6 (3.2)	31±4.7 (3.3)	32.2±2.7 (3.2)

[a]Data extracted from Study No. 2279, Table 11
[b]Mean ± standard deviation
[c]Calculated by reviewer from all reported daily means
[d]Percent increase from vehicle control; calculated by reviewer

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TABLE 4. Absolute and Relative Organ Weights of Rats Exposed to Tetramethrin-Containing Atmospheres for Three Months[a,b]

Exposure Group	Absolute Organ Weight		Organ to Body Weight Ratio	
	Liver	Kidneys	Liver	Kidneys
		Males		
Air Control	12.51 ± 1.226** (-13.6)[c]	3.30 ± 0.173 (-3.8)	2.39 ± 0.176** (-11.2)	0.63 ± 0.065 (-1.6)
Vehicle Control	14.48 ± 2.109	3.43 ± 0.253	2.69 ± 0.266	0.64 ± 0.045
1.9 mg/m^3	14.25 ± 1.671 (-1.6)	3.41 ± 0.356 (-0.6)	2.66 ± 0.198 (-1.1)	0.64 ± 0.056 (0.0)
4.4 mg/m^3	14.84 ± 1.441 (2.5)	3.56 ± 0.344 (3.8)	2.79 ± 0.177 (3.7)	0.67 ± 0.051 (4.7)
19.8 mg/m^3	14.30 ± 1.502 (-1.2)	3.44 ± 0.314 (0.3)	2.78 ± 0.093 (3.3)	0.67 ± 0.053 (4.7)
		Females		
Air Control	7.81 ± 0.699 (1.2)	2.07 ± 0.168 (5.1)	2.45 ± 0.156 (-3.1)	0.65 ± 0.042 (0.0)
Vehicle Control	7.72 ± 0.906	1.97 ± 0.187	2.54 ± 0.109	0.65 ± 0.045
1.9 mg/m^3	8.31 ± 0.669 (7.6)	2.05 ± 0.196 (4.1)	2.59 ± 0.135 (2.0)	0.64 ± 0.074 (-1.5)
4.4 mg/m^3	7.38 ± 0.677 (-4.4)	1.96 ± 0.142 (-0.5)	2.48 ± 0.145 (-2.4)	0.66 ± 0.030 (1.5)
19.8 mg/m^3	8.27 ± 1.169 (7.1)	2.08 ± 0.188 (5.6)	2.76 ± 0.272** (8.7)	0.70 ± 0.047 (7.7)

[a]Data extracted from Study No. 2279, Tables 16 and 17
[b]Mean ± standard deviation
[c]Percent increase from vehicle control; calculated by reviewer

** Significantly different from vehicle control; $p \leq 0.01$

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Figure 1. Schematic of the Exposure System Used