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

009453

APR 20 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: EPA ID No.: 062499-00023 Orthene Technical (Acephate): One-Year Dog Feeding Study. EPA Guideline No.: 83-1

Reg. No.: 59639-41/62499-23
Submission No.: S393506
HED Project No.: 1-0912
Tox. Chem. No.: 002A

FROM: Krystyna K. Locke, Toxicologist
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THRU: Roger Gardner, Section Head
Section I, Toxicology Branch I
Health Effects Division (H7509C)
Roger Gardner 4-17-92
KB 4/17/92

Toxicology Branch I, Section I/HED has completed an evaluation of the following study:

One-Year Oral Toxicity Study in Dogs with Chevron Acephate Technical; D.W. Delgard, D.V.M.; Hazleton Washington, Vienna, VA; Study No.: HWA 2107-165; January 25,1991. MRID No.: 418120-01

NOEL, LEL and Classification were as follows:

NOEL: < 10 ppm, LDT; males (Inhibition of cholinesterase level in brain).

NOEL: 10 ppm; females.

LEL: 120 ppm; females (Cholinesterase inhibition in RBC and brain).

CLASSIFICATION: Core-Guideline

Groups of 5 male and 5 female beagle dogs received Acephate Technical (0, 10, 120 and 800 ppm) in the diet for one year. The primary treatment-related effect observed in this study was brain and erythrocyte cholinesterase inhibition. Brain cholinesterase levels were significantly inhibited in all male groups, and in the

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mid-dose and high-dose female groups. Erythrocyte cholinesterase levels were significantly inhibited in the mid-dose and high-dose groups of both sexes. Plasma cholinesterase levels were inhibited in the mid-dose and high-dose male groups and in all of the female groups, but the inhibitions were dose-unrelated and statistically insignificant. Despite severe cholinesterase inhibition in the brain of the mid-dose and high-dose groups of both sexes, symptoms usually associated with cholinesterase inhibition were not observed.

There was no outstanding data gap for a Pesticide Assessment Guideline 83-1 (chronic feeding in the nonrodent) with the U.S. EPA. This study was performed to fulfil the requirements of California's Birth Defects Prevention Act (SB-950) and the results were also sent to the U.S. EPA. However, the California's study, being recent and meeting the current acceptance criteria, is very useful to us. The 2-year dog feeding study which presently satisfies our Guideline 83-1 (nonrodent) requirement for Acephate Technical is an old IBT study (No.: C 8732; 12/28/72). Although the IBT study is valid and classified as Core-Minimum, it is not as scientifically sound as the California's study.

The currently submitted one-year dog feeding study does not affect the already established RfD for acephate (0.004 mg/kg/day). That RfD is based on the LEL of 2 ppm or 0.12 mg/kg (90-day rat feeding/cholinesterase study; No.: S-3068; 12/30/87) and an UF of 30. Using 10 ppm (0.25 mg/kg; current dog feeding study) as the LEL and an UF of 30, the new RFD would then be 0.008 mg/kg/day or higher than that already established.

MRID No.: 418120-01
Study No.: HWA 2107-165
Study date: 1/25/91

Subdivision F
Guideline Ref. No. 83-1
December 24, 1989

83-1 Chronic Feeding in the Rodent and Nonrodent (Dog)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. X Technical form of the active ingredient tested.
2. X At least 20 rodents or 4 nonrodents/sex/group (3 test groups and control group).
3. X Dosing duration in rodents minimum 12 month nonfood use, 24 months food use; in nonrodents minimum 12 months[1].
4. X Doses tested include signs of toxicity at high dose but no lethality in nonrodents or a limit dose if nontoxic (1,000 mg/kg).
5.* X Doses tested include a NOEL.
6.* X Analysis for test material stability, homogeneity and concentration in dosing medium
7. X Individual daily observations.
8. X Individual body weights.
9. X Individual or cage food consumption.
10.* X Opthalmoscopic examination (at least pertest and at term) control and high dose.
11. X Clinical pathology data for all nonrodents and at least 10 rodents/group consisting of 12, 13 & 14.
12. X Hematology at 6 month intervals consisting of at least;
    - X Erythrocyte count
    - X Hemoglobin
    - X Hematocrit
    - X Leucocyte count
    - *X Differential count
    - X Platelet count (or clotting measure)
13. X Clinical chemistry at 6 month intervals consisting of at least;
    - *X Alkaline phosphatase
    - X Aspartate aminotransferase
    - X Alanine aminotransferase
    - *X Creatinine kinase
    - *X Lactic dehydrogenase
    - X Glucose
    - X Bilirubin
    - *X Cholesterol
    - *X Creatinine
    - X Total Protein
    - X Albumin
    - X Urea nitrogen
    - X Inorganic phosphate
    - X Calcium
    - *X Potassium
    - X Sodium
    - *X Chloride

    X Plasma, RBC and brain cholinesterase levels
14. ___ Urinalysis at 6 month intervals consisting of at least;
    - X Blood
    - X Protein
    - X Ketone bodies
    - X Appearance
    - X Glucose
    - X Total bilirubin
    - *X Urobilirubin
    - X Sediment
    - X Specific gravity (osmolality)
    - *X Volume
15. X Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

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16. X Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

X aorta	X jejunum	X peripheral nerve
X eyes	X bone marrow	X kidneys†
X caecum	X liver†	X esophagus
X colon	X lung	X ovaries
X duodenum	X lymph nodes	___ oviduct
X brain†	X stomach	X pancreas
X skin	X mammary gland	X rectum
X heart	X spleen	X spinal cord (3x)
X testes†	X musculature	X thyroid / parathyroids
X pituitary	X epididymis	X salivary glands
X ileum	X adrenals	X thymus
X trachea	X urinary bladder	X accessory sex organs; uterus
X gall bladder		

† organs to be weighed

[1] In some cases, a six month study may be acceptable. Contact EPA to discuss the criteria for determining if such a study can be used to support reregistration.

Criteria marked with a * are supplemental and may not be required for every study.

009453

Primary review by: Krystyna K. Locke, Toxicologist
Section I, Toxicology Branch I/HED Krystyna K. Locke 4/27/92

Secondary Review by: Roger Gardner, Section Head
Section I, Toxicology Branch I/HED Roger Gardner 4-17-92

DATA EVALUATION RECORD

STUDY TYPE: 83-1. One-Year Feeding Study (Dog)

TOX. CHEM. NO.: 002A
MRID.NO.: 418120-01

TEST MATERIAL: CHEVRON Acephate Technical (Orthene); Lot No.:SX-1830; Purity: 99.9%; White powder with lumps, was stored under refrigeration protected from light; Stable below 180°F.

STUDY NUMBER: 2107-165

SPONSOR: Chevron Environmental Health Center. Inc., Richmond, California.

TESTING FACILITY: Hazleton Washington, Vienna, Virginia.

TITLE OF REPORT: One-Year Oral Toxicity Study in Dogs with Chevron Acephate Technical

AUTHOR: D.W. Dalgard, D.V.M.

REPORT ISSUED: January 25, 1991

CONCLUSIONS:

NOEL: < 10 ppm, LDT; males (cholinesterase inhibition in brain).
NOEL: 10 ppm; females

LEL: 120 ppm; females (cholinesterase inhibition in RBC and brain).

CLASSIFICATION: Core-Guideline

Groups of 5 male and 5 female beagle dogs received Orthene Technical (Acephate) in the diet for one year. The dose levels used were 0, 10, 120 and 800 ppm. Treatment-related effects included:

1. Inhibition of brain cholinesterase levels in all male groups , and in the mid-dose and high-dose female groups.

2. Inhibition of RBC cholinesterase levels in the mid-dose and high-dose groups of both sexes.

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3. Decrease in RBC, hemoglobin and hematocrit (mostly in the high-dose males).

4. Increase in activated partial thromboplastin time (APTT), mostly in the high-dose males.

5. Increase in the absolute and relative liver weight of the high-dose males and females.

6. Histopathological changes in the liver of the high-dose males and females (perivascular infiltration and pigment)

Acephate had no effect, in all groups, on the remaining parameters examined: body weight gain, food consumption and utilization, and necropsy findings.

Despite severe cholinesterase inhibition in the brain of the mid-dose and high-dose groups of both sexes, symptoms usually associated with cholinesterase inhibition were not observed.

EXPERIMENTAL PROCEDURES

Dosing was initiated on June 28, 1989 and the necropsy was completed on August 1, 1990.

Beagle dogs (5/sex/group) received acephate in diet for one year. The dose levels used were 0(Group 1), 10(Group 2), 120(Group 3) or 800(Group 4) ppm. The dose level for Group 3 started at 200 ppm and was lowered to 120 ppm during test week 2 at the Sponsor's request. The dogs received unlimited quantity of food (Purina Certified Canine Diet #5007) which was prepared twice weekly (Monday and Friday) and replaced four times weekly (Monday,Wednesday,Friday and Sunday). Between replacements, the diets were stored frozen. Water was provided ad libitum through an automatic watering system. The dose levels used in this study were based on the results of the preliminary study (No. 2107-164) in which, according to the testing laboratory, the doses of acephate used were 8, 20, 250, and 500 ppm. Other details on this 4-week study were not provided and the study was not submitted.

Dogs were selected for the one-year study on the basis of pretreatment physical examinations, hematology, serum chemistry, urinalysis, cholinesterase, and ophthalmoscopic examinations. The assignment of dogs to treatment groups was based on the individual mean values for erythrocytes cholinesterese levels, so that each group had similar mean values.

The dogs were:

1) Obtained from Hazleton Research Products, Inc., Cumberland, VA.;
2) Acclimated for 2 weeks;
3) Four to 4.5 months old and weighing 5.2-7.4 kg (males) and 4.9-7.2 kg (females) at the initiation of dosing;
4) Housed individually in elevated stainless-steel cages;
5) Were identified by ear tattoos.

The following parameters were examined for all dogs on the study:

1. Observations: twice daily , 6 hours apart, for general appearance, behavior, signs of toxicity and mortality.

2. Physical examinations: general, once a week; detailed, prior to initiating treatment and during 13, 26, 39, and 52 weeks.

3. Ophthalmoscopic examinations: during the acclimation period and at approximately 180 and 360 days after the initiation of treatment, using 1% Mydriacyl for pupil dilation and a binocular indirect ophthalmoscope.

4. Body weight: weekly during the acclimation period, on the day before the initiation of treatment, and weekly thereafter. Terminal body weights were recorded on the day that each dog was sacrificed and were used to calculate organ-to-body-weight ratios.

5. Food consumption: weekly (measured on Monday, Wednesday, Friday, and Sunday) throughout the study period. Using these data, food efficiency and compound (acephate) consumption were also calculated.

6. Hematology, clinical chemistry and urinalysis: hematology and clinical chemistry tests were performed on all dogs prior to the initiation of treatment (week -2) and during weeks 4, 13, 26, 39, and 52. Urinalysis were performed on all dogs prior to the initiation of treatment (week -2) and during weeks 26 and 52. Animals were food- and water-fasted overnight prior to the collection of samples. Blood was obtained by jagular venipuncture. Urine was collected via cagepan runoff.

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The following determinations were performed:

HEMATOLOGY

Absolute reticulocyte count
Activated partial thromboplastin time
Leukocyte differential count
Erythrocyte count
Corrected leukocyte count
Hematocrit
Hemoglobin concentration
Mean cell hemoglobin conc.
Mean cell volume
Plasma prothrombin time
Platelet count
Reticulocyte count
Leukocyte count
Cell morphology
Mean cell hemoglobin

CLINICAL CHEMISTRY

Alanine aminotransferase
Albumin
Albumin/globulin ratio
Alkaline phosphatase
Aspartate aminotransferase
Blood urea nitrogen
Blood urea nitrogen/creatinine ratio
Calcium
Chloride
Creatine kinase
Creatinine
Direct bilirubin
Gamma glutamyltransferase
Globulin
Glucose
Indirect bilirubin
Inorganic phosphorus
Lactate dehydrogenase
Potassium
Sodium
Total bilirubin
Total cholesterol
Total protein
Triglycerides
Uric acid

Erythrocyte (RBC-CHE) and plasma (PL-CHE-B) cholinesterase determinations were performed on all animals at three intervals during the quarantine period (weeks -3, -2 and -1) and during study weeks 4, 13, 26, and 52. The amount of hemolysis in the plasma was also determined. The erythrocyte cholinesterase levels were measured using acetylthiocholine as a substrate. Plasma cholinesterase levels were measured using butyrylthiocholine as a substrate. Brain cholinesterase (BR-CHE) was measured in all animals at the termination of the study using about one gram of tissue taken from the left half of the brain and acetylthiocholine as a substrate. Animals were not fasted prior to blood collection for cholinesterase determinations. An aliquot of plasma, erythrocytes, and brain tissue prepared for cholinesterase determination was stored frozen.

Procedures used for hematology and clinical chemistry determinations were referenced. For cholinesterase determination, four procedures were referenced (Attachment 1).

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URINALYSIS

Appearance
Bilirubin
Glucose
Ketones
Occult blood
Microscopic examination of sediment
Reducing substances
Specific gravity
Urobilinogen
Volume
pH
Protein

ANALYTICAL CHEMISTRY

Homogeneity Analyses - (9 samples/group) were performed for Group 4 on a pretest mix, for Group 2 on the second mix of Week 2, and for Group 3 on the second mix of Week 3.

Stability Analyses - were performed during Week 16 (second mix) for the low- and high-dose groups on fresh mixes, after 4 days under refrigeration, after 4 days at room temperature, and on samples refrigerated for 4 days followed by 3 days at room temperature.

Concentration Analyses - were performed on the second weekly mix during Weeks 1, 2, 5, 9, 13, 16, 21, 25, 29, 33, 37, 41, 45, 49, and 53. The samples were taken at the time of mixing, after two days of refrigeration following mixing, after two days in the feed hopper following mixing, and after two days of refrigeration followed by two days in the feed hopper following mixing(with the exception of Week 53).

7. Necropsy: was performed after 52 weeks of dosing under the direct supervision of a board-certified pathologist. At the scheduled sacrifice, the animals were anesthetized with sodium thiamylal and exsanguinated.

8. Organ weights: Absolute and relative (organ/terminal body weight and organ/brain weight ratios) weights were determined. The following organs were weighed:

Adrenals
Brain with brainstem
Heart
Kidneys
Liver with drained gallbladder
Lungs with mainstem bronchi
Ovaries
Pituitary
Spleen
Testes
Thyroids
Parathyroids

9. Histopathology: The following tissues were examined:

Adrenals
Aorta (thoracic)
Bone (rib)
Bone marrow (rib)
Brain with stem
Cecum
Colon
Duodenum
Epididymides
Esophagus
Eyes (2)
Gallbladder
Heart
Ileum
Jejunum
Kidneys (2)
Liver
Lungs with mainstem bronchi
Lymph node (mesent.)
Mammary gland (females)
Ovaries (2)
Gross lesions; tissue masses, and lymph nodes regional to each mass
Pancreas
Pituitary
Prostate
Rectum
Salivary gland (mandibular)
Sciatic nerve
Skeletal muscle (thigh)
Skin
Spinal cord (cervical, thoracic, and lumbar)
Spleen
Stomach
Testes (2)
Thymus
Thyroid lobes
Parathyroids
Trachea
Urinary bladder
Uterus (cervix, body and horns)

Sections from the above tissues, from all animals, were prepared and stained with hematoxylin and eosin. The sections were examined for microscopic changes by a veterinary pathologist. The brain was separated in two halves; the left half was used for cholinesterase determination and the right half, for histopathological examination.

STATISTICAL EVALUATIONS

Mean body weight gains, mean total food consumption, clinical pathology data (except cell morphology and urinalysis) and organ weights were analyzed statistically as is detailed in Attachment II.

RESULTS

Homogeneity, Stability and Concentration of the Test Material in Diets

The homogeneity analyses were all generally within 10 % (94.6 - 102 %) of the nominal dose levels.

With the exception of the 10 ppm level for samples that were stored at room temperature for 4 days, all stability analyses were within 10 % (92 - 112 %) of the nominal dose levels. Stability analyses for this level were 81.1 to 84.5 % of the nominal dose levels.

Concentration analyses were more variable than the homogeneity and stability analyses. At the 10 ppm level, about 52 % of the samples were between 90-110 % of the nominal dose level, and 33 % and 14% of the samples were between 80-90 % and 70-80 % of the nominal dose level, respectively. During Week 21, analytical results obtained on the fresh diet mix for the 10 ppm level indicated that the levels were 153 and 222 % (duplicate analyses) over the nominal level. These results were verified and suggested a mixing error. However, other samples analyzed from the same mix after refrigeration and after being in the hopper for 2 days were close to the nominal level. The reason for the high results were not determined.

At the 120 and 800 ppm levels, about 20 and 15 % of the samples, respectively, were between 80 and 90 % of the nominal level, whereas the remaining samples were between 90-110 % of the nominal level.

Mortality

One Group 3 (120 ppm) female was found dead during Week 49. The cause of death was not apparent upon microscopic examination of tissues. This dog had no prior history of illness. According to the report, it seemed unlikely that the death was treatment-related.

Clinical Observations

Treatment-unrelated findings included alopecia, lacrimation, sporadic emesis, sporadic soft/mucoid feces and sores on the ears.

Ophthalmological Examination

Opacity in the right eye was observed in one Group 2 (10 ppm) female at 6 month and at the termination of the study. No

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other abnormality was seen in this dog and no abnormalities were seen in the remaining dogs on the study.

Body Weight

Acephate had no effect on the mean body weight gain in this study. The total mean body weight gain (week 52 minus body weight just before the initiation of treatment) for the male dogs in the 0, 10, 120 and 800 ppm groups was 5.4, 5.7, 5.4 and 6.5 kg, respectively. The corresponding mean body weight gain for the female dogs was 4.3, 4.1, 3.8 and 4.8 kg, respectively.

Food Consumption

The mean weekly food consumption varied within each group, but was comparable for the control and the acephate-treated groups throughout the study. These data are summarized below.

Acephate (ppm)	Mean Weekly Food Consumption (g/dog) During Weeks 1 Through 52.	
	Males	Females
0	1422 - 2304	1179 - 1940
10	1569 - 2308	1361 - 2167
120	1372 - 2223	1039 - 1831
800	1479 - 2316	1372 - 2030

Efficiency of Food Utilization

Food efficiency (mean body weight gain per week x 100 / mean food consumption per week) was comparable for the control and the acephate-treated groups throughout the study.

Compound Consumption

Consumption of acephate was calculated for each treated dog and each group throughout the study. It was reported that the male and female dogs in Groups 2, 3 and 4 were exposed to acephate levels of approximately 0.27, 3.11 and 20.16 mg/kg/day, respectively. Based on TABLE 4D of the submission (Mean Compound Consumption, pages 90-94), the range of acephate consumption during test weeks 1-52 was as follows:

Acephate (ppm) Nominal Levels	Acephate (mg/kg/day)	
	Males	Females
10	0.19 - 0.42	0.19 - 0.43
120	2.01 - 7.86	1.90 - 8.06
800	12.84 -30.95	14.83 -34.61

Hematology

Statistically significant ($p<0.05$) hematological findings included decreases in erythrocyte count, hemoglobin concentration and hematocrit (mostly in the high-dose males), and increases in activated partial thromboplastin time (APTT), also in the high-dose males. These findings are summarized below.

Hematological Findings (Percent Reletive to Controls) in Dogs Fed Orthene (Acephate) Technical #

Acephate (ppm)		10	120	800
Decreases in:	Sampling Time(Week)	Males		
Erythrocytes	4	6.8	3.2	13.3 *
	13	15.5 *	7.4	25.6 *
	26	10.1 *	9.9 *	17.3 *
	39	5.6	7.6	17.6 *
	52	8.8	11.0 *	20.4 *
Hemoglobin	13	11.2 *	3.3	21.1 *
	26	3.9	6.5	14.3 *
	39	0.0	4.4	15.0 *
	52	3.7	7.3	17.7 *
Hematocrit ##	13	4.8 *	1.6	9.4 *
	26	2.2	2.8	6.0 *
	39	0.0	1.7	6.1 *
	52	1.5	3.3	7.5 *
Increases in:				
APTT	4	0.0	5.2	34.5 *
	13	0.0	1.7	36.4 *
	26	0.0	12.6 *	96.1 *
	39	0.0	13.1	56.6 *
	52	0.0	8.6	42.3 *

Acephate (ppm)		10	120	800
Decreases in:	Sampling Time(Week)	Females		
Erythrocytes	13	0.0	6.4	20.4 *
	26	5.5	11.3	21.1
	39	3.8	13.8	18.1
	52	4.4	4.7	7.6
Hemoglobin	13	0.0	5.8	16.1 *
	26	0.0	9.0	16.9
	39	0.0	12.3	14.1
	52	0.0	3.3	1.3
Hematocrit ##	13	0.0	2.5	14.9 ~~6.8~~ *
	26	4.0	8.2	16.2
	39	3.9	12.7	14.6
	52	2.6	2.9	1.2
Increases in:				
APTT	4	0.0	0.0	18.2
	13	0.0	0.0	14.7
	26	0.0	0.0	40.4
	39	0.0	16.1	32.1
	52	0.0	3.4	35.6

This table is based on TABLE 6 of the submission.
Calculated as follows: Hematocrit (%) in controls - hematocrit (%) in treated dogs = % increase over the control value.

Clinical Chemistry and Urinalysis

Acephate had no effect on any of these parameters examined.

Cholinesterase

Cholinesterase in erythrocytes (RBC) and plasma was reported as micromoles/mL and in brain, as micromoles/g of tissue. Treatment-related effect included a significant inhibition of RBC cholinesterase levels in the 120 and 800 ppm groups (both sexes), and of brain cholinesterase levels in all groups (males) and in the 120 and 800 ppm groups (females). RBC cholinesterase levels for the 10 ppm group were slightly higher than the controls for all sampling intervals in the males (3.7-9.7 % higher) and at 3 of 4 intervals in the females (8.5-16.3 % higher). Plasma cholinesterase levels were inhibited in the 120 and 800 ppm male groups and in all of the female groups, but the inhibitions were dose-unrelated and statistically insignificant. These data are summarized below.

Percent Inhibition of Cholinesterase Levels,Reletive to Controls,in RBC, Plasma and Brain #

Acephate (ppm)		10	120	800
	Sampling Time(Week)		Males	
RBC	4	0.0	42.1 *	76.9 *
	13	0.0	51.9 *	85.2 *
	26	0.0	50.5 *	86.0 *
	52	0.0	42.9 *	85.7 *
Plasma	4	0.0	18.3	9.6
	13	0.0	16.1	7.8
	26	1.6	16.4	5.8
	52	0.0	13.4	7.2
Brain	53	16.9 *	53.3 *	66.2 *
			Females	
RBC	4	4.3	44.1 *	76.4 *
	13	0.0	54.9 *	86.6 *
	26	0.0	50.6 *	86.8 *
	52	0.0	46.5 *	84.9 *
Plasma	4	27.7	28.1	30.2
	13	16.9	16.3	19.5
	26	20.3	21.2	18.4
	52	6.3	0.0	10.9
Brain	53	11.4	49.4 *	65.8 *

This table is based on TABLE 5 of the submission. For cholinesterase values, see Attachment III in this review.

* Significantly different from control, $p < 0.05$.

Necropsy

Nothing remarkable was observed in both sexes.

Organ Weights

These data were reported as absolute organ weight means (g), as organ-to-terminal body weight ratio means (%) and as organ-to-brain weight ratio means. The only treatment-related effect was an increase (statistically insignificant) in the absolute and

relative liver weights of the high-dose males and females. Relative to the control values, the absolute liver weight in the male and female dogs was increased by 28.8 and 16.8 %, respectively. The liver-to-terminal body weight ratios in the high-dose groups were as follows: males, 2.7 % (controls, 2.4 %) and females, 2.9 % (controls, 2.7 %).

Histopathology

Treatment-related changes were observed only in the liver of most high-dose dogs and in one mid-dose male, as follows:

> Perivascular pleocellular infiltration in the reticuloendothelial cells ----- in 1/5 mid-dose and 5/5 high-dose males, and in 3/5 high-dose females.
>
> Pigment in the reticuloendothelial cells ----- in 1/5 mid-dose and 4/5 high-dose males, and in 2/5 high-dose females.

COMMENTS

This study is well planned and reported in a very detailed manner, and it meets the December 24, 1989 EPA acceptance criteria. All analytical procedures used have been referenced and, in some instances, also described briefly. The following statements have been included in the submission:

Statement of No Data Confidentiality Claims.
Compliance with the Good Laboratory Practice Statement.
EPA Flagging Statement (This study neither meets nor exceeds any of the applicable criteria).
Quality Assurance Statement. This study -- protocol, in-life and final report -- were inspected many times during 7/25/89 and 1/25/91, when the final report was completed.

ACEPHATE

Page_____ is not included in this copy.

Pages 17 through 26 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

X FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.