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

002319

29-NOV-1982

MEMORANDUM

TO: Franklin Gee, Product Manager #17
Registration Division (TS-767)

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

THRU: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

Budd 11/29/82

SUBJECT: Ectrin® Insecticide 10% Water Dispersible Liquid. Livestock and Premise Spray. EPA File No. 677-UUT. Accession No. 247363.

TOX Chem. No. 77A

The Toxicology Branch (TB) has received 7 acute studies conducted either on the formulation (EPA File No. 677-UUT) or on the 1:200 use dilution of the formulation. All studies have been reviewed, classified and categorized for toxicity category. The TB has also reviewed acute inhalation studies conducted on a 15% WP formulation of fenvalerate and WL-43775 (fenvalerate) EC FX 3368.

TB objects to the registration of this product. TB is not able to evaluate the potential hazard resulting from the use of the product until the Residue Chemistry Branch (RCB) problems are resolved (see RCB review by A. Rathman dated July 26, 1982).

The TB is also requesting that the petitioner add the following statement to the precautionary labeling, Avoid breathing vapors and spray mist.

Important Note:

The TB in a previous review (see attached) of this formulation requested an acute dermal LD50 study on the 10% WDL as well as a primary skin irritation study on the 10% WDL. The request for these 2 studies arose as a result of misinterpretation of production batch codes (8-8-23-1DLH and 8-8-23-2DLH) for product test codes.

This misinterpretation has now been resolved through a telephone conversation (November 23, 1982) between this reviewer and Mr. Robert Shoup of Diamond Shamrock (Ph. 216-694-4666). The acute dermal LD50 and primary skin irritation studies previously requested for the 10% WDL had been submitted and now have been correctly identified and reviewed. Mr. Shoup will follow up on this telephone conversation with a letter of clarification.

1 of 39

The request for the conduct of these 2 studies is therefore negated.

The confidential formula for this product is as follows:

CONFIDENTIAL

Chemical	Percent
Technical fenvalerate	11.15

CBI removed

CONFIDENTIAL

Albin B. Kocialski, Ph.D. 12/3/82
Toxicology Branch
Hazard Evaluation Divison (TS-769)

OPP:HED:TOX:A.K.:sb 11/10/82 X77395 Rm 820 #m18

CONFIDENTIAL

Subject: Acute Oral LD50 of SD-43775 (8-8-23-1DLH), a 10.5% w/v Water Dispersible Liquid, in the Male and Female Rat.

Formulation Composition:

SD-43775	10.5% w/v

CBI removed

CONFIDENTIAL

EPA File Number: 677-UUT

Product: Ectrin® Insecticide 10% WDL

Accession Number: 247363

Testing Facility: Shell Development Company
Modesto, California

Study Number: TIR 74-098-76

Testing Period: 1976

Report Submitted to Sponsor: 1976

Materials and Methods:

Twenty adult male (165-200 g) and 20 adult female (148-162 g) Sprgue-Dawley rats (purchased from Simonsen, Gilroy, California) were individually housed and were fasted overnite with free access to water for 16-18 hours. Animals were assigned to 4 treatment groups with 5 males and 5 females comprising each group. No control group was employed. The 10.5% WDL formulation was administered undiluted by the oral route. Doses administered were as follows:

ml/kg	mg a.i./kg
0.56	59
1.00	105
1.80	189
3.20	336

Several observations were made for onset and duration of pharmacotoxic signs and time of lethality during the first day. Daily observations were then made for the 14-day holding period. Body weights were recorded on day 0 and at 7 and 14 days. A gross organ necropsy was conducted on all animals dying acutely and sacrificed (carbon dioxide or Diabutal®) at termination.

Results:

Signs observed at the lowest dose level administered (59 mg a.i./kg) were hypoactivity, salivation, exophthalmos lacrimation, ataxia and tremors. Signs generally began 2 hours after drug administration. Animals were recovered by 24 hours. No animals died at this lowest dose level. Increased dose resulted in decreased onset, increased severity and duration of signs seen at the low dose as well as these new signs: frequent rubbing of the nose with forepaws or on the cage floor, hypersensitivity, coarse generalized tremors, piloerection, dyspnea, hunched posture, intermittent to clonic convulsions and death.

Some decreased body weight gain appeared evident with increased dose.

Necropsies performed on survivors revealed a mottled appearance of the kidneys. It could not be determined whether or not this observation was compound related as no control group was employed. Necropsies of the animals dying acutely in the two highest dosed groups showed inflammation of the lungs.

The AOLD50 for this 10% WDL formulation for both males and females combined was determined (method of Finney) to be as follows:

1512.0 mg/kg with 95% C.L. of 1210-2011 mg/kg

Classification: Core-Guideline

Category of Toxicity: 3

Subject: Acute Oral Toxicity of the Use Dilution of SD-43775 (Batch No. 8-8-23-2DLH) in the Rat. A 1:200 Dilution of Ectrin® Insecticide 10% WDL.

Formulation Composition: The formulation composition is identical to EPA File No. 677-UUT. Ectrin® Insecticide 10% WDL diluted 1:200.

Accession Number: 247363

Testing Facility: Shell Development Company
Modesto, California

Study Number: TIR 74-136-76

Testing Period: 1976

Report Submitted to Sponsor: 1976

Materials and Methods:

Ten male Sprague Dawley rats (Simonsen, Gilroy, California) were fasted overnight (fasted weight: 230-262 grams), identified and administered orally a 16 g/kg dose of a 1:200 use dilution of SD-43775. Close observations were made for onset and duration of toxic effects and lethality at 1/2, 1, 2, 4, 6 and 24 hours following administration and daily thereafter excepting weekends for 14 days. Food was returned 2 hours after treatment, and water was available ad libitum. Individual body weights were obtained initially and at 6 and 14 days. The test was terminated at 14 days. Necropsies were not performed.

Results:

No signs of toxicosis or lethality occurred. No significant body weight change was evident at 6 and 14 days.

Conclusion:

The AOLD50 for a 1:200 dilution of the Ectrin® Insecticide 10.5% WDL is greater than 16.0 g/kg.

Classification: Core-Minimum

Category of Toxicity: IV

Subject: Primary Skin Irritation Test with SD-43775, Code No 8-8-23-2DLH. Ectrin® Insecticide 10% WDL, in Male Albino Rabbits.

Formulation Composition: Ectrin® Insecticide 10% WDL

Accession Number: 247363

Testing Facility: Industrial Bio-Test Laboratory, Inc.

Study Number: IBT No. 8530-09587

Testing Period: September, 1976

Report Submitted to Sponsor: September, 1976

Materials and Methods:

(Note: The test procedure was modeled after that of Draize.) The hair was clipped from the back and flanks each of six New Zealand strain rabbits. Two test sites located lateral to the midline of the back approximately 10 centimeters apart were selected. One of the two sites was abraded by making 4 epidermal incisions, 2 perpendicular to the other 2 while the other test site remained intact.

The test material was applied to each of the test sites on each rabbit and occluded with gauze patches which were secured with masking tape. The trunk of each animal was then wrapped with impervious plastic sheeting. Direct exposure to the test material was for 24 hours after which the plastic wrapping, gauze and all residual test material were removed. The intact and abraded test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. The sites were again examined and scored after 72 hours. Values were calculated to determine the primary irritation score.

Results and Conclusions:

The primary irritation score was calculated to be 1.7 out of a possible maximum of 8.0. The formulation is mildly irritating.

Classification: Core-Guideline

Category of Toxicity: 3

See also attached memo dated August 11, 1981, Marcia Williams to Doug Campt entitled - IBT Program Review of Acute Studies.

Aug. 11, 1981

SUBJECT: IBT Program Review of Acute Studies

FROM: Marcia Williams
Director
Special Pesticide Review Division

·002319

THRU: Edwin L. Johnson
Deputy Assistant Administrator
for Pesticide Programs

TO: Doug Campt
Director
Registration Division

As you know, the IBT review program was established four years ago to review the pivotal studies for chemicals with tolerances. Because the original list of studies sent to registrants inadvertently included some acute studies, registrants assumed that acute studies were to be included in the special IBT review program. Of the approximately 1300 studies which have now been identified by registrants as IBT studies, about 700 of them are acutes. Those studies have now almost completed review and were done by a group of graduate students and consultants working in SPRD. Those students and consultants are now gone, and acutes are being reviewed by Clement Associates along with the chronic studies.

In the last two months, 24 acute studies supporting a pending registration action on carbofuran and 11 acute studies supporting a pending action on Ethion have been submitted to the IBT program for review. We usually put studies supporting pending actions in a high priority category. However, we are hesitant to move the review of acute studies ahead of the review of chronic studies. We are also concerned about adding a significant number of new studies to Clement's workload since this task already extends beyond the expiration date for the contract.

Therefore, we have decided to return these acutes studies to you for review through normal RD/HED channels. We ask that, in the future, RD transmit only chronic studies to SPRD for inclusion in the IBT review.

Do use your own judgement

CONCURRENCES								
SYMBOL	TS-791	TS-791						
SURNAME	[illegible]	DICKINSON						
DATE	8/10/81	8-11-81						

EPA Form 1320-1 (12-70) OFFICIAL FILE C

We strongly urge that scientists asked to review these studies be advised that the studies were generated at IBT and that acute studies conducted at IBT have been found invalid in 32% of the cases.

We also want to point out to RD that reliance on acute studies which have already been considered valid through the IBT program review should be used with caution. Some U.S. determinations (only those by: on acutes were based on whether the LD_{50} was calculated correctly and not on whether the study was done correctly. Therefore, these studies should be evaluated in the context of other studies on the chemical conducted at other facilities. When only IBT data are available, you may want to require additional studies to confirm the results from the IBT studies. All Canadian reviews (and those done by TB/H considered the conduct of the study as well as the LD_{50} calculation and, therefore, should be useful by themselves for regulatory determinations.

Please note!

cc: Chris Chaisson
Larry Chitlik

CM-791:JLA:Ruby Whiters:9/6/81:MEMLOC43/42
Revisions per JLA:aw:9/10/81:MEMLOC 42/43

Subject: Acute Dermal Toxicity Study with SD-43775, Code No 8-8-23-2DLH, Ectrin® Insecticide 10% WDL, in Male and Female Rabbits.

Formulation Composition: Ectrin® Insecticide 10% WDL

Accession Number: 247363

Testing Facility: Industrial Bio-Test Laboratory, Inc.

Study Number: IBT No. 8530-09587

Testing Period: September, 1976

Report Submitted to Sponsor: September, 1976

Materials and Methods:

Young adult male and female (4 M, 4F) New Zealand strain rabbits were acclimated to laboratory conditions 7 days prior to testing. Animals were housed individually and observed for general health. Food and water were offered ad libitum.

The backs of the rabbits were shaved free of hair 24 hours prior to dermal applications of the test substance. The shaved area of each animal constituted about 30 percent of the total body surface. A 24 hour waiting period followed to allow healing of any micropscopic abrasions produced as a consequence of shaving.

The test material was applied at a dose level of 2,000 mg/kg. The test site was covered by wrapping the trunk of the animal with imprevious plastic sheeting which was securely taped in place. A light weight flexible plastic collar was placed on each animal to preclude ingestion. The test material remained in contact with the skin for 24 hours. The plastic sheeting and all residual test material was removed after 24 hours.

The test sites were examined for local skin reactions and the animals were returned to their cages. Observations for mortality, local skin reactions, and behavioral abnormalities were continued for a total of 14 days following the skin applications. Body weights were recorded on days 0, 7 and 14. Necropsy was conducted on all animals.

Results:

Seven of 8 animals survived the experiment. One male rabbit died on day 4.

It was reported that the test material was severely irritating to the skin of the animals. Skin changes at 24 hours were characterized by red, well-defined erythema, severe edema and second degree burns. Escharosis was present at the test sites at 7 and 14 days.

Body weight losses and some slight weight gains were reported.

Necropsy revealed pale kidneys in one male and enlarged gall bladders and depletion of body fat stores in two females.

Conclusion:

ADLD50 is greater than 2,000 mg/kg.

Classification: Core-Guideline

Category of Toxicity: 3

NOTE: Animals were not abraded. However, the low toxicity and the large area shaved would seem to indicate that the study need not be repeated as the toxicity category would in all probability remain unchanged at 3.

See also attached memorandum from Marcia Williams to Doug Campt thru Edwin Johnson. Memo dated August 11, 1981 and entitled - IBT Program Review of Acute Studies.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Aug. 11, 1981

002319

SUBJECT: IBT Program Review of Acute Studies

FROM: Marcia Williams
Director
Special Pesticide Review Division

THRU: Edwin L. Johnson
Deputy Assistant Administrator
for Pesticide Programs

TO: Doug Campt
Director
Registration Division

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So use your own judgment

BEST AVAILABLE COPY

CONCURRENCES								
SYMBOL	TS-791	TS-791						
SURNAME	Quadrani	DICKINSON						
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Read note!

cc: Chris Chaisson
Larry Chitlik

TB-791:JLA:Ruby Whiters:8/6/81:MEMLOC43/42
Revisions per JLA:aw:8/10/81:MEMLOC 42/43

Subject: Determination of Eye Irritant Effects of SD-43775 (Code No 8-8-23-1DLH) in the Rabbit.

Formulation Composition: Ectrin® Insecticide 10% WDL. EPA File No. 677-UUT (see review of AOLD50 of EPA File 677-UUT for formulation composition).

Accession Number: 247363

Testing Facility: Shell Development Company
Modesto, California

Study Number: TIR 74-100-76

Testing Period: September, 1976

Report Submitted to Sponsor: September, 1976

Materials and Methods:

Nine New Zealand strain young rabbits weighing between 2.6 and 3.6 kg were used in the study. All animals were housed individually and allowed free access to food and water. All rabbits were determined to be clinically healthy prior to the test. The eyes of all test rabbits were also examined for test suitability using a fluorescein dye and observing the eyes under UV illumination.

The method of Draize and the procedure as defined for the FHSA were used to test the irritancy of the preparation.

One-tenth of a milliliter (0.1 ml) of the preparation has placed into the conjunctival sac of one of the eyes of each of 6 rabbits. The eyes of these rabbits remained unwashed. Three other rabbits were treated in a similar manner but had their eyes irrigated with a saline solution 4 seconds after instillation of the test perparation.

Eye examinations were conducted at 1, 24, 48 and 72 hours and at 7 and 14 days. A fluorescein test was repeated at 24, 48 and 72 hours and at 7 and 14 days to verify the presence or absence of corneal damage.

Results:

The cornea and iris showed no response to the test preparation in all nine animals. All animals manifiested redness, chemosis and discharge (conjunctival envolvement). Irritancy peaked in unwashed eyes at the 24 hour reading (average score of 11 out of possible 20) and then trended downward. Signs of irritancy were absent at 7 days. Animals whose eyes were rinsed attained the maximum score of 2 for redness, chemosis, aned discharge (score of 2 out of a possible maximum score of 20) at the 24 hour reading. The eyes which received a rinse were clear at 48 hours.

Conclusion:

Rinsing the eyes was beneficial in reducing the degree of conjunctival inflammation. The preparation (10% WDL Ectrin® Insecticide, EPA Reg. No. 677-UUT) is irritating to the eye.

Classification: Core-Guideline

Category of Toxicity: 3

Subject: Determination of Eye Irritant Effects of a 1:200 Aqueous Dilution of SD-43775 (Code No 8-8-23-2DLH) in the Rabbit.

Formulation Composition: Ectrin® Insecticide 10% WDL. (EPA File No. 677-UUT diluted 1:200).

Accession Number: 247363

Testing Facility: Shell Development Company Modesto, California

Study Number: TIR 74-132-76

Testing Period: September, 1976

Report Submitted to Sponsor: September, 1976

Materials and Methods:

The study generally follows the procedures previously reported for the Determination of Eye Irritant Effects of SD-43775 (Code No. 8-8-23-1DLH) in the Rabbit. Accession No. 247363. Study No. TIR-100-76.

The slight variations in this study (TIR 74-132-76) such as animal body weights and a longer contact time (20 seconds) between the test preparation and the eye prior to irrigation are not of a sufficient magnitude to re-write the procedures for this reported study (i.e., TIR 74-132-76).

Results:

The test preparation, a 1:200 dilution of Ectrin® Insecticide 10% WDL, EPA File No.677-UUT, is essentially non-irritating under test conditions.

Classification: Core-Guideline

Category of Toxicity: 4

Subject: Acute Vapor Inhalation Study in Rats

Test Compound: SD-43775 (8-8-23-1DLH). Ectrin® Insecticide 10% WDL

Accession Number: 247363

Testing Facility: Industrial Bio-Test Laboratories, Inc.

Study Number: IBT No. 8562-09588

Testing Period: September, 1976

Report Submitted to Sponsor: September, 1976

Comments by Toxicology Branch:

Attached is a xeroxed copy of the one page report submitted by IBT to the Shell Chemical Company with regard to this study.

The Shell Chemical Company states that this study was audited by them and was declared invalid for the following reasons:

- inadequate control of the conduct of the experiment,
- poor documentation of test conditions,
- and poor documentation of reported observations.

Conclusion:

This reviewer accepts Shell's conclusion that the study is invalid. This reviewer also points out that,

- this study is not necessary to support the registration of Ectrin® Insecticide 10% WDL EPA File No. 677-UUT,
- an acute inhalation toxicity study has been conducted on the Ectrin® Insecticide 10% WDL by Hazleton Labs and will be reviewed.

CONFIDENTIAL

002319

REPORT TO SHELL CHEMICAL COMPANY

ACUTE VAPOR INHALATION TOXICITY STUDY IN RATS

Test Material: SD 43775
Code No. 8-8-23-2DLH
Form Administered: Vapor
Acute LC_{50}: > 22.55 mg/l air

Strain: Charles River Rats
Exposure Time: 1 hour
Observation Period: 14 days
IBT No. 8562-09583
Protocol RA241

Generation of Test Material:

Vapor was generated by passing a stream of clean, dry air (-40°C dew-point) through the undiluted test material contained in a gas washing bottle. The resulting air-vapor mixture was then introduced into the exposure chamber

Chamber Conditions

Group No.	Size (liters)	Pressure (inches Hg)	Temperature (°C)	Air Flow (l/min)
Test	80	30.06	23	4.08

Results

Group No.	Total Number of Animals Male/Female	Nominal Concentration	Mortality Male-Female	Weight Gain Male-Female (grams) 7-Day	Final
Test	5/5	22.55 mg/l air	0/5 - 0/5	50-21	88-26

Remarks

There were no deaths or untoward reactions noted during the exposure or the 14-day observation period which followed. Body weight gains at 7 and 14-days were within the normal limits. Necropsy, performed on all rats at the end of the observation period, did not reveal any gross pathologic alterations that were attributable to the effects of the test material.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Prepared by: Lori Zabel
Lori Zabel, B.A.
Assistant Toxicologist
Inhalation Toxicity

Approved by: John W. Goode
John W. Goode, Ph. D.
Manager
Decatur Research Laborat

mk.

9/10/76

Subject: Toxicity Studies on the Pyrethroid Insecticide WL-43775, Emulsifiable Concentrate FX 3368. Acute Inhalation Exposure of Rats to an Aqueous Spray. (See note at end of review.)

Test Compound: Emulsifiable Concentrate FX 3368 diluted with with water to give a dispersion containing 3 grams per liter of WL-43774. (Note: WL-43775 is synonymous fenvalerate.)

Accession Number: 247363

Testing Facility: Tunstall Laboratory
Sittingbourne, England

Study Number: TLGR. 0097-75

Testing Period: December, 1975

Report Submitted to Sponsor: December, 1975

Materials and Methods:

The emulsifiable concentrate FX 3368 was diluted with water to give a dispersion containing 3 grams per liter of WL-43775. This dispersion was dilivered into the chamber at a rate of 50 mls/min. The air flow through the chamber was 0.7 m^3 per minute. The volume median diameter was 77 um with a geometric standard deviation of 1.4. The 25% and 75% volume diameters were 60 and 96 microns respectively. The atmospheric concentration of the aqueous spray in the vicinity of the animals was calculated to be 1.3 mg per liter.

Four male and 4 female seven week old rats of the CD strain (COBS) (supplied by Charles River [UK] Ltd., Manston, Kent) were exposed continuously for 4 hours. Each animal was restrained in a holder to minimize dermal contact and ingestion thru grooming. After exposure the rats were washed in clean water, dried and kept under observation for 14 days.

Results and Discussion:

The test chamber atmosphere consisted mainly of droplets too large to be inhaled by animals or man. However, the size of the droplets (77 um) produced in the chamber were slightly smaller than droplets which would be formed under actual field application conditions. Spraying devices normally used in the field produce droplets in the 100 to 400 micron range (Note: this reviewer notes here that particle sizes greater than 10 microns are almost completely removed in the nasal passages).

Immediately after exposure three of the female rats showed an abnormal gait manifested by walking with their hindquarters held clear of the ground and with hind legs more widely spaced than normal. Two of the rats reverted to normal after 2 days and the third after 3 days. No other signs were observed during the period of exposure or during the 14 day observation period. This effect, which was reported to be typical of pyrethroid intoxication, was attributed to dermal exposure and absorbtion of the test material. It was reported that although rats were partly protected by the holders the animals became thoroughly soaked with spray during the exposure.

Conclusion:

AILC50 for 4 hours is greater than 3 grams per liter.

Classification: Supplementary

Category of Toxicity: 4

Note: This study was previously reviewed and reported by Reto Engler, Ph.D. formerly of the Toxicology Branch. The study was not at that time classified by the core system of classification.

Subject: Acute Inhalation Toxicity Study in Rats with Ectrin® 15% Wettable Powder Formulation

Test Compound: Ectrin® 15% Wettable Powder Formulation (Note: active ingredient in the formulation is fenvalerate) T-139-1

Accession Number: 247363

Testing Facility: Hazleton Laboratories America, Inc.

Study Number: Hazleton Project No. 200-238

Testing Period: October 1-16, 1981

Report Submitted to Sponsor: January, 1982

Material and Methods:

Sprague-Dawley descended CD-Crl rats obtained from the Charles River Breeding Laboratories were quaratined for 14 days under environmentally controlled conditions. Ten males and 10 females in good health were divided into two groups of 5 males and 5 females per group. One group (Group I), served as the control group. All animals were individually housed and uniquely coded.

All animals were simultaneously placed into separate 100-L exposure chambers for 4 hours. Chamber environment closely resembled pre-test quarantine conditions. The test material was generated directly into the experimental chamber using a Wright Dust Feed mechanism. Four particle size distribution samples were obtained approximately every 60 minutes. Airflow for both chambers was monitored every 30 minutes and maintained at 16.7 L/minutes. The control group was exposed to filtered air after it was rehumidified to simulate Group 2 conditions. The behavior and appearance of all animals were observed at 30 minute intervals during exposure and hourly for 4 hours post-exposure. Animals were observed twice daily during the remainder of the 14 day observation period.

Animals were also weighed on day 0 and on days 2, 3, 4, 7 and 14 post-exposure. Body weights and body weight changes were analyzed statistically.

All animals were exsanguinated on day 15 post-exposure. Necropsy followed with special attention paid to the lungs and upper respiratory tract. Lungs, liver and kidneys and any other organs exhibiting gross pathological changes were preserved for possible future examination.

Results:

Nominal air conncentrations was determined to be 5.48 mg/L. The mean gravimetric concentration was determined to be 0.75 mg/L at the breathing zone of the animals. The mass median airodynamic diameter was determined to be 4.05 microns.

No animmals died during the 14 day experiment. All animals in the control group appeared normal for the duration of the experiment. Male and female test animals showed nearly identical signs from a qualitative and quantitative aspect. Signs appeared to follow a normal distribution. Signs which appeared with increased exposure were, sluggishness, squinting, nasal discharge, lacrimation, labored breathing and a bloody crust formation of the eyes, nose, and mouth. All signs generally disappeared 4 hours after termination of the exposure, and all animals (except 1) appeared normal 14 days post-exposure.

Male body weight in the group receiving the test compound was comparable to the control group at all time intervals. Females receiving the test compound showed an initial body weight loss followed by a gain greater than that shown by controls. Body weight gain for females between groups was comparable for all time periods after day 3 post-exposure.

Gross pathological findings in the treated groups, when present, were not different from the control group.

Conclusion:

Exposure to the 15% wettable powder at a nominal concentration of 5.48 mg/L (0.75 mg/L gravimetric) of air for 4 hours via the inhalation route produced (during the period of exposure) pharmacologic transitory effects as manfested by irritation to mucous membranes, lethargy (sluggishness), labored respiration and weight gain suppression (females only). No deaths were observed.

The 4 hour AILC50 for the 15% wettable powder is greater than 0.75 mg/L (gravimetric concentration).

Classification: Core-Guideline

Category of Toxicity: 2

FRONT PANEL

Federal
Draft 1

002319

Diamond Shamrock

ECTRIN™ INSECTICIDE 10% WATER DISPERSIBLE LIQUID

LIVESTOCK AND PREMISE SPRAY

Active Ingredient:

Cyano (3-phenoxyphenyl) methyl-4-chloro-alpha-(1-methylethyl) benzeneacetate	10%*
Inert Ingredients	90%
TOTAL	100%

*This product contains 0.8 lbs of Ectrin Insecticide per gallon

EPA Reg. No. 677-------- EPA Est. No.--------

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Side Panel for Precautionary Statements

Net Contents: One Quart (32 fl. ozs.)

Diamond Shamrock Corporation
Animal Health Division
1100 Superior Ave.
Cleveland, Ohio 44114

4/82

22

SIDE PANEL

Statement of Practical Treatment

002319

If swallowed - Drink 1 to 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person. Call a physician or Poison Control Center immediately.

If on skin - Wash affected area with plenty of soap and water. Get medical attention if irritation persists.

If in eyes - Flush eyes with plenty of water. Call a physician.

Precautionary Statements
Hazards to Humans

Do not breathe vapors (?)

CAUTION: Harmful if swallowed or absorbed through skin. Do not get in eyes or on skin. Wear goggles, protective clothing and gloves while handling. Remove and wash contaminated clothing before reuse.

Environmental Hazards

This product is highly toxic to fish. Keep out of any body of water. Do not apply when weather conditions favor drift from treated areas. Do not contaminate water by cleaning of equipment or disposal of wastes. Apply this product only as specified on this label.

This product is highly toxic to bees. Do not allow drift on crops or weeds where bees are actively foraging. Use only as directed.

Storage and Disposal

Do not contaminate water, food or feed by storage or disposal.

Storage: Store in a secure, dry and temperate area above 32°F.

Pesticide disposal: Pesticide, spray mixture or rinsate that cannot be used according to label instructions must be disposed of according to applicable Federal, State or local procedures.

Container disposal: Triple rinse (or equivalent) and dispose of in a sanitary landfill or by incineration if allowed by State and Local authorities.

Warranty and Limitation of Damages

Seller warrants that this material conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use and Buyer assumes the risk of any use contrary to such directions. SELLER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR OF MERCHANTABILITY, AND NO AGENT OR SELLER IS AUTHORIZED TO DO SO EXCEPT IN WRITING AND WITH SPECIFIC REFERENCE TO THIS WARRANTY. In no event shall Seller's liability for any breach of warranty exceed the purchase price of the material as to which a claim is made.

SIDE PANEL

DIRECTION FOR USE

002319

It is a violation of Federal Law to use this product in a manner inconsistent with the labeling.

GENERAL DIRECTIONS

Ectrin Insecticide WDL is suitable for use in conventional power or low pressure knapsack sprayers and in power misters. Follow the USE DIRECTIONS to select the recommended solution for a specific insect use. Then, refer to the DILUTION TABLE for mixing directions to obtain the percent solution recommended. There is no withholding period from last application to slaughter.

Do not use in milk or egg storage rooms. Do not allow spray to drift on waterers or feeds. Do not allow Premise Spray solutions to drift onto livestock. Do not apply as a larvicide. Apply only as directed. For full benefit of fly control use proper manure management to reduce sources of fly breeding.

LIVESTOCK USE DIRECTIONS

ANIMAL	INSECT	USE	% SOLUTION	REMARKS
Beef and Non-lactating Cattle	Horn, Face, House, Stable Flies, Lice, and Ticks	Spray	0.05%	Apply to wet all animals thoroughly. Use up to 1/2 gallon of spray per animal depending on size and hair coat. Pay particular attention to the legs (Stable Flies) and to the head and neck (Face Flies). Do not repeat more often than once each 2 weeks.
	Horn Fly	Spray	0.01%	Apply to wet all animals thoroughly. Use up to 1/2 gallon of spray per animal
		Pour-on	0.1%	Apply 4 fl. ozs./head down midline of back.
Dairy Cattle (including lactating)	Horn, Face, House & Stable Flies, Lice, Ticks	Spray	0.25%	Apply 2-3 fl. oz per anima with attention to head, neck, legs, and down backline. Do not apply more frequently than every 4 days.
		Spray	0.05%	Apply 1-2 pints per animal with attention as above. Do not apply more frequently than weekly.

SIDE PANEL CONTINUED

LIVESTOCK USE DIRECTIONS (CON'T)

002319

ANIMAL	INSECT	USE	% SOLUTION	REMARKS
Swine	House Flies and lice	Spray	0.05%	Apply up to 1 pint thoroughly per animal with particular attention to neck and ears. Retreat in 30 days if necessary.
Angora Goats (Mohair production only)	Lice	Spray	0.025%	Apply 1-2 pints of spray per animal off shears for best results. Repeat when necessary.
Horses	Horn, Face, House, and Stable Flies	Spray	0.1%	Apply about 8 fl. ozs. as light spray with attention to face, head, and legs. Do not treat animals intended for slaughter.

PREMISE USE DIRECTIONS

INSECT	PROBLEM AREAS	% SOLUTION	REMARKS*
House flies, stable flies, Fannia.	Livestock confinement areas including horse stalls, poultry houses, beef and dairy barns, calf pens, sheep sheds, swine buildings, animal hospital pens and kennels.	0.25%	Do not treat animals with this concentration. Remove livestock from area prior to spraying. Return when surfaces have dried. Spray thoroughly to point of run-off. Nonabsorptive surfaces will use less spray while absorptive surface will use more. For dry unpainted wood, cement blocks and similar absorptive surfaces apply 1 gal. solution/ 500 sq. ft. For galvanized sheet, masonite, painted surface and other hard nonabsorptive surfaces apply about 1/2 gallon/ 1000 sq. ft. Do not contaminate feed or water.
	Feedlots (exposed area), exterior walls of farm buildings, feed storage areas, feeders, corrals, and paddocks.	0.25%	Do not treat animals with this concentration. Spray thoroughly to the point of run-off. Apply about 1 gal/500 sq. ft. of sprayable surface-walls, and other fly gathering places. Apply with a pressure power sprayer.

*Repeat application when flies again reach a nuisance level but not more frequently than every 3 weeks. Surfaces exposed to rain, dirt or strong sunlight require the most frequent applications.

SIDE PANEL CONTINUED

002319

DILUTION TABLE

AMOUNT OF ECTRIN 10% WDL	AMOUNT OF WATER (GALLONS)				
	0.01%	0.025%	0.05%	0.1%*	0.25%
2 fl. ozs.**	15	6	3	1.5	5 pints
4 fl. ozs.	30	12.5	6	3.0	1.25
1 Pint	125	50	25	12.5	5
1 Quart	250	100	50	25	10

*For pour-on mixture add 2 fl. ozs. of a wetting agent per 5 gallons of water. A household detergent such as Joy or Ivory can be used.

**1 fluid ounce is equivalent of 2 tablespoons.

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

002319

MEMORANDUM NOV 2

TO: Franklin Gee, Product Manager #17
Registration Division (TS-767)

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

THRU: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Ectrin™ Insecticide Livestock and Premise Spray. A 10% Water Dispersible Liquid (WDL). EPA File No. 677-UUT (EPA Reg. No. 677-447).
TOX Chem No. 77A

Diammond Shamrock Corporation is seeking to register this product for use as a direct animal spray and for use in animal premises.

Toxicology Branch (TB) objects to the registration of this product. TB is not able to evaluate the potential hazard resulting from the use of this product until:

- The RCB problems are resolved (see RCB review by A. Rathman dated July 26, 1982).

- The following two acute studies are submitted on the formulation:

  i. Acute Dermal LD50
  ii. Primary skin irritation

The same objections were raised in our previous review of this product.

The petitioner has also asked for the deletion of the sentence "Do not treat animals intended for slaughter." which appears in the remarks column for horses. TB believes this deletion at this time would be objectionable to RCB and therefore suggests that Registration Division obtain an RCB opinion with respect to this request by Diamond Shamrock.

The TB has reviewed, classified and categorized for purpose of toxicity the submitted 4.0 hour AILC50 study.

The confidential formula for this product is as follows:

27

2 [duplicate DER of the one in TXR # 0002254]

CONFIDENTIAL

CONFIDENTIAL

Chemical	Percent (%)
Technical fenvalerate	11.15

CBI removed

The inerts are cleared under Section 180.1001(e).

Subject: Acute Inhalation Toxicity Study in Rats with Ectrin™ 10% WDL Formulation.

Test Compound: Ectrin™ - 10% WDL Formulation (active ingredient is fenvalerate)

Accession Number: Not given, EPA File Symbol No 677-UUT

Testing Facility: Hazleton Laboratories America Inc.

Study Number: Project No. 200-252

Testing Period: March 18, 1982 - April 9, 1982

Report Submitted to Sponsor: July 22, 1982

Materials and Methods:

Sprague-Dawley descended CD-Crl rats obtained from the Charles River Breeding Laboratories (Kingston, New York) were quarantined for 7 days under environmentally controlled conditions. Fifteen males and 15 females in good health were divided into 3 groups of 5 males and 5 females per group. One group (Group 1) served as the control group and received air alone. Groups 2 and 3 received a total actual concentration of between 2.3 to 4.7 of* aerosolized test material. All groups were exposed for a period of 4 hours in 100-L exposure chambers. Airflow was maintained at 16.7 liters/minute. Chamber environment was monitored every 30 minutes during exposure and closely resembled conditions of the quarantine period.

The actual total concentration of exposure for each group was calculated. Gravimetric chamber concentrations were also determined. Samples were collected at approximate hourly intervals during exposures. Four particle size distribution samples were also obtained during exposure approximately every 60 minutes.

The behavior and appearance of all animals were observed at 30 minute intervals during the exposures, hourly for 4 hours following the exposures and twice daily during the remainder of the 14 day post-exposure period.

28

* mg/L

Animals were weighed 5 times prior to termination and at termination. Body weights were analyzed statistically.

Animals were exsanguinated at termination and necropsied. Lungs, liver, kidneys and any organ exhibiting gross changes were preserved in 10% neutral buffered formalin for possible future examination.

Results:

The total acutal concentration for groups 2 and 3 was between 2.3 to 4.7 mg/L. The gravimetric concentration data for groups 2 and 3 was 32.6 and 93.7 ug/L respectively. The mean aerodynamic diameter and geometric S.D. for Group 2 was 3.59 u and 1.48 respectively. The mean aerodynamic diameter for Group 3 could not be determined because the MMAD was greater than 4.7 u. However, at least 43% of the respirable aerosal was less than 4.7 u.

No animals died during the study.

Exposure - related observations noted in the treatment groups during and/or immediately following the exposure included rapid respiration, clear discharge from the nose and mouth, lacrimation, reddish-brown discharge from the nose and sluggishness of movement and labored respiration. All group 2 and 3 animals appeared normal by Day 1 and throughout the 14-day post-exposure period.

Statistically significant and possibly exposure related reductions of mean body weight gains were apparent only in Group 3 males and females.

No consistent exposure-related trend was apparent in any of the gross pathology observations.

Conclusion:

Exposure to the 10% WDL formulation at a total actual concentration of between 2.3 to 4.7 mg/L for 4 hours produced transitory effects manifested by irritation to the mucous membranes, lethargy, respiratory distress and weight gain fluctuation. No deaths were observed.

The 4 hour AILC50 for the 10% WDL is greater than 2.3 mg/L (total actual concentration).

Conclusion: Core-Guideline

Category of Toxicity: III

NOTE.

See also AILC50 study with Ectrin™ 15% Wettable Powder. Accession No. 247363. Hazleton Project No. 200-238. The results of this study (10% WDL) generally confirm the signs observed in the study conducted on the 15% WP as well as the AILC50 for 4 hours.

Albin B. Kocialski, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

OPP:HED:TOX:A.KOCIALSKI:sb 10/29/82 X77395 Rm. 820 #m18

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

002319

JUL 26 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: EPA Registration No. 667-UUT. Pydrin* direct animal use. Evaluation of analytical methods and residue data

FROM: A. Rathman, Chemist
Residue Chemistry Branch
Hazard Evaluation Division

R. J. Hummel for

THRU: Charles Trichilo, Chief
Residue Chemsitry Branch

CT

TO: Franklin D. R. Gee
Product Manager (17)

and

Toxicology Branch

*Diamond Shamrock Corporation is seeking to register their product Ectrin (continuing 10% fenvalerate as a water dispersible liquid) for use as a direct animal spray and for use in animal premises.

Currently there are tolerances for residues of fenvalerate in the meat, fat, and meat byproducts of cattle, hogs, horses and, sheep at 1 ppm and in milk fat at 2 ppm. These tolerances have been established to cover secondary residues which may result from use of the chemical on r.a.c.s that are animal feed items.

Conclusions

1. The manufacturing process (and impurities in the technical material) is different than the process Shell states they are using. However, the technical material is the Shell

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*The names fenvalerate, SD 43775, Pydrin, and Ectrin are used throughout this review and are synonymous.

product according to the confidential formula. We need to know which process Shell is actually using.

2. We do not consider the fate of fenvalerate in animals adequately defined when considering direct dermal uses. We need a metabolism study reflecting dermal treatment with residue characterization in meat and milk. We also need a letter of authorization from Shell to use the oral metabolism data that are available.

3. An adequate method for fenvalerate per se is available for enforcement purposes. Depending upon the results of the metabolism study requested in 2 above, additional methodology may be needed.

4a. We can make no final conclusion on the level of residues that are likely to result in milk and beef tissues until 2 above is resolved. However, the submitted residue studies are deficient in that no plateau was ever reached and the studies do not reflect residues likely to result when the animal is both treated dermally and exposed to treated premises.

4b. We can make no final conclusion on the level of residues likely to result in swine tissues until 2 above is resolved and until we know the exact application rate in terms of amount of ai/animal/treatment.

4c. Since, in general, it is not practical to remove poultry when premise treatments are made, this use should either be removed from the label or data to support such a use should be submitted.

4d. Since use on Angora goats raised for mohair production and horses not intended for salughter would not result in residues in food for consumption by man or animal, we have no objections to these uses.

Recommendation

We recommend against the proposed uses on beef and dairy cattle and swine as well as the premise uses because of Conclusions 2, 3, 4(a), 4(b), and 4(c). We have no objections to the proposed uses on Angora goats and horses. The Company should be requested to obtain the correct manufacturing process from Shell since the process included in this submission is different than what we understand Shell's process to be.

Detailed Considerations

Formulation

The Company notes in the Confidential Statement of Formula that the technical material is obtained from Shell. However, the manufacturing process (and impurities in the technical product) is different than the process detailed in PP# 7F2013. Shell's petition, PP# 7G1926, listed two different manufacturing processes (including the one presented in this submission) and the impurities listed are the same as appear in this submission. It is not clear which process is actually being used and this information should be obtained from Shell.

The product is to be formulated as Ectrin Insecticide are 10% water dispersible liquid containing 11.15% technical fenvalerate, [redacted] The inerts are cleared under Section 180.1001(e).

Proposed Uses

The product is used to control various insects and ectoparasites. Spray concentrations range from 0.01-0.25%, applications are to be made by conventional power or low pressure knapsack sprayers or power misters. No pre-slaughter intervals are proposed. The table below lists the direct animal uses with minimum repeat treatment intervals where specified.

Livestock Uses:

Animal	Spray Concentration	Remarks
Beef and Non-Lactating Cattle	0.05%	Use up to 1/2 gal spray/animal (1 gm a.i.). Treatments may be made every 2 weeks.
	0.01%	Use up to 1/2 gal spray/animal (0.2 gm a.i.). No restriction on repeat treatments.
	0.1%	Use 4 fl ozs/animal (0.11 gm a.i.) as a pour-on down mid line of back. No restriction on repeat treatments.

Inert ingredient information may be entitled to confidential treatment

Dairy Cattle	0.25%	2-3 fl oz/animal (0.2 gm a.i.). Repeat applications at weekly intervals.
	0.05%	1-2 pts/animal (0.5 gram a.i.). Repeat applications at weekly intervals.
Swine	0.05%	1 pt/animal (0.25 gram a.i.). Repeat in 30 days if necessary.

Premise Use: A 0.25% solution is to be applied at the rate of 1 gal/500 sq. ft. (or at 1/2 gal./1000 sq. ft. to non-absorptive surfaces) to livestock confinement areas including horse stalls, poultry houses, beef, and dairy barns, calf pens, sheep sheds, swine buildings, animal hospital pens and kennels. Animals are to be removed prior to spraying and returned when surfaces have dried. Repeat applications are not to be made more frequently than every three weeks. Additionally, feed lots (exposed area), exterior walls of farm buildings, feed storage areas, feeders, corrals, and paddocks may be treated with the 0.25% solution at the rate of 1 gal/500 sq. ft.

Other Uses

There are treatments recommended for lice and fly control on horses and Angora goats; these uses are not considered in this review, since only horses not intended for slaughter and goats raised for mohair production are included.

It should be noted that the removal of poultry from poultry houses before premise treatment would be impractical on most farms.

Nature of the Residue

No animal metabolism data have been included in this submission. While the Company states that it can rely on Shell's data, we have no letter of authorization from Shell. In addition to authorization from Shell, we will also need metabolism data reflecting dermal use so that we can determine if the metabolic route is the same from oral and dermal exposure.

Analytical Methods

The method proposed for enforcement purposes is Shell's method MMS-R-447-2 entitled "Determination of SD 43775 Residues in Animal Tissues, Milk, Milk Fat, Cream, Hair, Eggs, and Gauze Patches."

For tissues, fenvolerate is extracted with hexane, partitioned into acetonitrile. The acetonitrile is exchanged to hexane and cleaned-up on a Florisil column. The residue is determined by ECGC.

Data were obtained using either the above method or methods similar to the above method. Samples of milk, milk fat and various tissues were fortified with fenvalerate at levels ranging from 0.001-0.1 ppm with recoveries ranging overall from 54-135% with most in the range of 80-120%. Blanks were <0.01-0.02 ppm with the exception of two samples, one of cream at 0.36 ppm and one of meat fat at 0.38 ppm.

The method was subjected to a method trial with milk samples fortified at 0.02 and 0.04 ppm and found acceptable (J. Onley, memo of 7/24/78; PP# 7F2013). We consider this method suitable for obtaining data and for enforcement purposes.

Residue Data

A total of six studies reflecting dermal treatments were submitted (five on cattle and one on swine).

In considering the maximum level of residues that may result in meat and milk, three combined avenues must be considered: (1) the dietary burden possible from crops that are feed items that currently have fenvalerate tolerances, (2) additional dietary burden from animals licking treated premises or other treated animals and (3) direct application.

CATTLE: None of the available data reflect the maximum possible combined exposure from these avenues, although a number of the studies reflect exaggerated dermal treatment rates both with regard to amount applied and frequency.

A study was conducted utilizing 10 lactating Holsteins, which were treated 3 times at weekly intevals with an EC formulation at the rate of 2 grams a.i./animal/treatment. Only a single animal was available for control purposes. This study was designed to reveal the time required for residues of the parent compound to reach a maximum, and the levels involved. The sampling intervals were 1, 7, 14, 28, and 56 days after the last treatment.

The data indicate that residues of SD 43775 per se in brain, kidney and liver were all non-detectable (<0.01 ppm). Muscle samples all showed <0.01 or 0.01 ppm (including the control), regardless of sampling interval. Residues appeared to predominate in the fat; unfortunately, the data are of litte value, since the single control animal had an apparent SD 43775 residue of 0.38 ppm in renal fat. This compares with residues ranging from 0.07-0.42 ppm in the treated animals. The 0.42 ppm high value reflects sacrifice 7 days subsequent to the last treatment. At the 56 day post-treat interval, residues of 0.10-0.12 ppm were reported. Subcutaneous fat analyses showed residues of 0.09 ppm for the control animal, and a 0.03-0.22 ppm range for the treated animals. Again, the high values were noted in the animals sampled 7 days after the last treatment. At the 56 day interval, SD 43775 residues had declined to the 0.04-0.05 ppm level in subcutaneous fat.

Milk and cream analyses for these same animals showed SD 43775 residues reaching a maximum 3 days after the last treatment. The residues ranged from 0.02-0.04 ppm in milk and from 0.06-0.23 ppm in cream. Twenty-eight days post-treatment all samples were reported at <0.01 ppm. As in tissues, the residue levels reported for the control milk and cream of 0.02 and 0.36 ppm, respectively, cast doubt on the validity of the study and render the study valueless. (The control cream value is reported at a level >0.1 ppm higher than the maximum value seen in the treated animals).

Additional tissue, milk, and cream analyses were conducted on a Holstein administered 200 mg SD 43775 orally (ca. 10 ppm dietary) each day for a total of 7 days. The treated and control animal were sacrificed after the morning milking on the last day of the treatment period. All tissues showed <0.01 ppm SD 43775 in the control, and all save fat in the treated animal. Renal and subcutaneous fat are reported at the 0.14 and 0.02 ppm levels, respectively. The daily milk and cream analysis indicate that a residue plateau was not reached in the 7 days of feeding; the final cream samples showed a range of 0.18-0.38 ppm SD 43775 residues. This study has some utility in assesssing the possible burden of SD 43775 per se in tissues from animals licking treated premises or other treated animals, although the fact that a residue plateau was not attained reduces its value. It is noteworthy that the observed range of SD 43775 residues in the cream of the dermally-treated cows discussed above. The showing of up to ca. 80 mg/sq. ft. SD 43775 (acetone extraction) in the hair (thoracic region-4 sites) one day after the third treatment suggests that "lickers" could possibly ingest a substantial portion of the 200 mg/day that is representative of the 10 ppm dietary level. (The study below shows up to ca. 120 mg/sq. ft. hair surface).

In another study utilizing an emulsifiable concentrate, three lactating cows were treated with ca. 2 grams a.i. three times at weekly intervals. Milk was sampled daily throughout the treatment period and up to one week after the last treatment; all samples (whole milk basis) showed no detectable residues (<0.01 ppm) of SD 43775. Tissues were sampled at sacrifice, which was 1, 3 and 7 days after the last treatment. Unlike the previously described study, the control animal showed no detectable residues (<0.01 ppm) of SD 43775 in fat or a[illegible]f the tissues sampled. The treated animals also showed <0.01 ppm in muscle, liver, kidney, and brain and up to 0.20 ppm in renal fat 7 days after the last treatment. The various fat samples (subcutaneous, renal, and back) show an increase with time; the study was terminated before a plateau was reached.

In the third study, employing a water dispersible liquid, a single treatment at 2 grams a.i. was administered to each of two lactating cows. Unlike the previously described study, the control animal was housed in a separate pasture, and thus yielded all tissue and milk (fat basis) values at <0.01 ppm. Milk was sampled for 24 days post treatment; the animals were then sacrificed. Residues of SD 43775 peaked in milk fat 6 days post-treatment at 0.64 ppm in one animal and at 3 days and 1.1 ppm in the other. By the 24th day, the 0.01 ppm level was attained in the milk fat of both animals. Tissue residues for both animals at the 24 hour sacrifice interval were 0.02 and 0.03 ppm for renal subcutaneous fat, respectively; all other tissues were reported at <0.01 ppm.

Given the limitation of the above study, the results substantiate those discussed previously, considering that cream averages ca. 20% milk fat. The 1.1 ppm figure above could thus be 0.22 ppm expressed on the cream basis. This compares to 0.36 ppm maximum in cream from the 3 treatment 2 gram a.i. dose study. Since the proposed use indicates biweekly treatments, this study is of value to demonstrate the additive residue effects of multiple treatments; more than 3 weeks between treatments would be required for residues of SD 43775 per se to fully dissipate. The study also serves to demonstrate that oral or dermal contact between treated cows is probably a significant source of residues that is, the "segregated" control animal of this study displayed no detectable residues, while the control animal of the 10 cow/3 treatment study showed residues approximating those of the treated animals.

In the fourth study, two cows were treated once with an E.C. at the rate of 2 gm a.i./animal. The study also contained a control animal. Each animal was housed in one of the three separate pastures; the two treated cows were fitted with

restraining straps so that animals could not lick themselves but could still browse and get up and down without difficulty.

Samples of milk were taken for 14 days after the treatment. Maximum residues of SD 43775 were seen after two or 3 days post-treatment at a level of 0.17 ppm. At 14 days post-treatment milk fat from one animal contained 0.02 ppm and the other animal contained no detectable residues (<0.02 ppm). The animals were sacrificed 14 days post-treatment with residues detected only in the fat (0.03 ppm in renal fat). All other tissues contained <0.01 ppm apparent SD 43775.

In the fifth study, a total of 20 beef cattle were used (16 treated and 4 controls). The animals were treated with two quarts of either a WP or a water dispersible liquid made up to concentrations of 0.05% (1 gm a.i./animal). The cattle were given either one treatment with sacrifice at 3 and 7 days post-treatment or two treatments at a 21-day interval with sacrifice either 3 or 7 days after the second treatment. Maximum residues resulted in the fat at 7 days post-treatment (regardless of the number of treatments made). After one treatment the maximum SD 43775 residue in fat was 0.055 ppm, after two treatments, the maximum detected residues was 0.094 ppm.

No final conclusion can be made until the animal metabolism question is resolved. However, these studes are all deficient in that no plateau was ever reached and the studies do not reflect the residues likely to result when the animal is treated dermally and exposed to treated premises (exposure through feeding can be determined by data submitted by Shell). Therefore, we are unable to determine if the established fenvalerate meat and milk tolerances are adequate to allow for these added uses.

SWINE: A single study was submitted reflecting application to swine. In this study a total of twenty pigs were used. The pigs were treated with either on EC or a water dispersible liquid at the rate of 50 mg/sq. ft. (we have no way of calculating the total amount of a.i. applied per animal per treatment). The pigs were treated either 1, 2, or 3 times with biopsy samples taken at 1 and 2 week intervals after each treatment (or at 1, 2, 3, and 4 week intervals after the last treatment). Applications were made at 2-week intervals with some animals sacrificed at 2 weeks post-treatment from a single treatment, from 2 treatments or from all three treatments. Some animals were sacrificed 5 weeks after the third treatment.

It should be noted that residues of SD 43775 were only detectable in fat with other tissues containing no detectable

(<0.01 ppm) residues. Residues in the fat increased with the number of treatments and showed a maximum of 0.2 ppm after three treatments (2 week post-treatment interval). With the 5-week interval (after three applications), residues in fat had declined to 0.05 ppm.

We can make no final conclusion until the metabolism question is resolved and until we know the exact application rate in terms of amount of a.i./animal/treatment.

POULTRY: No data have been submitted for poultry. The label for premise use in poultry houses directs to remove "livestock" from the area prior to spraying. This, in general, is not practical with poultry. Therefore, either the poultry house use most be removed or we must have data to support such a use.

GOATS and HORSES: Since the uses direct application to goats for mohair production only and horses not intended for slaughter, we have no objections to these uses.

TS-769:RCB:ARRATHMAN:X77324:CM#2,RM810:07/26/82
cc:R.F., Circu, Reviewer, S.F. Amended Use File
RDI:R.J.Hummel, 7/23/82;R.D.Schmitt, 7/23/82