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

AUG 8 1989

007415

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: 9H5577/10182-EIE. Commodore 10WP (Lambdacyhalothrin). Petition for Food Additive Tolerance and Application for Registration for Use in Food Handling Establishments (New Use)

Tox. Chem. No. 725C
Project Nos. 9-1119A; 9-1278

TO: George LaRocca, PM Team # 15
Insecticide-Rodenticide Branch
Registration Division (H7505C)

FROM: Pamela M. Hurley Ph.D., Toxicologist Pamela M Hurley 6/22/89
Section I, Toxicology Branch I
Insecticide, Rodenticide Support
Health Effects Division (H7509C)

THRU: Robert Zendzian Ph.D., Pharmacologist
Acting Section Head
Section I, Toxicology Branch I
Insecticide, Rodenticide Support
Health Effects Division (H7509C)

Record No(s). 241891/237127

Background and Request:

ICI Americas Inc. has submitted a petition for a food additive tolerance of lambda cyhalothrin on food. The formulation that is to be used will be Commodore 10WP, a 10% formulation containing lambda cyhalothrin as the active ingredient. The requested use is for residual pest control in and on buildings and structures and their immediate surroundings and on modes of transport. Permitted areas of use will include but are not limited to industrial buildings, houses, apartment buildings, laboratories, busses, greenhouses, and nonfood/feed areas of stores, warehouses, vessels, railcars, trucks, trailers, aircraft, schools, nursing homes, hospitals, restaurants, hotels and food manufacturing, processing and servicing establishments. Intended uses will also include outdoor use, and barrier treatments. The insecticide is intended for dilution with water for spray application and will be used for control of ants, centipedes, cockroaches, crickets, carpet beetles, firebrats, flies, lesser grain borers, millipedes, pillbugs, red flower beetles, rice weevils, silverfish, sowbugs, bees, spiders, and wasps.

The requested tolerance is for 0.03 ppm in or on food commodities exposed to the insecticide during treatment of food-handling establishments where food and food products are held, processed, prepared or served.

The Toxicology Branch (TB-I) has been requested to examine the available toxicity data on this insecticide and determine whether or not the data supports this new-use petition and tolerance.

The substance identification and technical data for lambdacyhalothrin (PP321) are given in a previous Experimental Use Permit Petition (10182-EUP-UR), memorandum to G. LaRocca from P. Hurley, dated May 8, 1986.

Comments and Response:

The following toxicity studies are required to be submitted in support of the tolerance petition and for registration of the product (ref. Fed. Reg. 40 CFR Part 158, October 24, 1984).

Technical Product	Required	Satisfied
Acute oral LD_{50}	Yes	Yes
Acute dermal LD_{50}	Yes	Yes
Acute inhalation LC_{50}	Yes	(comment 1)
90-day feeding studies		
rodent	Yes	Yes
nonrodent	Yes	Yes (comment 2)
21-day dermal	Yes	Yes (comment 3)
21-day inhalation	Yes	No (comment 4)
Chronic feeding		
rodent	Yes	Yes (comment 3)
nonrodent	Yes	Yes
Oncogenicity		
rat	Yes	Yes (comment 3)
mouse	Yes	Yes (comment 3)
Teratogenicity (2 species)	Yes	Yes (comment 3)
Reproduction (2-generation)	Yes	Yes (comment 3)
Mutagenicity		
Gene mutation	Yes	Yes
Struct. Chrom. Aberration	Yes	Yes
Other genotoxic effects	Yes	Yes

End Use Product

Acute oral LD_{50}	Yes	Yes
Acute dermal LD_{50}	Yes	Yes
Acute inhalation LD_{50}	Yes	Yes
Primary eye irritation	Yes	Yes
Primary dermal irritation	Yes	Yes
Dermal sensitization	Yes	Yes

Pure Active Ingredient

General metabolism	Yes	Yes (comments 3,5)

1. Although the acute inhalation study on the technical product is required for the petitioned uses, TB will waive this requirement because an adequate acute inhalation study on the formulation has been submitted and because the expected inhalation exposure will be on a diluted version of the formulation (0.03-0.06% a.i. as opposed to 10% a.i. in formulation tested in inhalation study).

2. The requirement for a nonrodent subchronic feeding study has been fulfilled by the availability of an adequate chronic dog study (1-year) on technical lambdacyhalothrin.

3. The long term studies conducted on cyhalothrin have been used in partial fulfillment of the toxicity data requirements for lambdacyhalothrin. Lambdacyhalothrin consists of 2 of the 4 enantiomers of cyhalothrin. On the basis of structural considerations and metabolism and subchronic data on both lambdacyhalothrin and cyhalothrin, TB has previously accepted the long term data on cyhalothrin in partial fulfillment of the toxicity study requirements for lambdacyhalothrin (see original tolerance request for cotton, memorandum from P. Hurley to G. LaRocca, dated 7/20/86).

4. The label on the proposed product states that this formulated product may be used in a wide variety of places, including industrial buildings, houses, apartment buildings, laboratories, busses, greenhouses, and nonfood/feed areas of stores, warehouses, vessels, railcars, trucks, trailers, aircraft, schools, nursing homes, hospitals, restaurants, hotels and food manufacturing, processing and servicing establishments. TB is concerned that for such a wide variety of application sites, use conditions and human exposure scenarios, inhalation exposure may be significant for some persons, particularly for the greenhouse use and use in other enclosed places where persons are likely to remain for long periods of time (e.g. nursing homes,

hospitals, hotels, houses, apartments, schools, etc.). Therefore, we are requiring a 21-day inhalation study. In addition, based on consideration of the physical characteristics of the technical product and of the proposed uses, TB recommends that this study be conducted on the formulated product (Commodore 10WP) rather than the technical product. This requirement parallels a previous requirement for a 21-day inhalation study to be conducted on PP321 1E Insecticide (13.1% lambdacyhalothrin) which was proposed for nearly identical uses (see memoranda from P. Hurley to G. LaRocca dated 8/27/87 and 4/27/88).

5. Extensive metabolism studies have been conducted on the purified form of cyhalothrin. A comparative study between cyhalothrin and lambdacyhalothrin has indicated that their absorption, distribution, metabolism and excretion patterns are identical following a single 1 mg/kg dose in the male rat. Therefore, TB has previously accepted the metabolism studies conducted on cyhalothrin along with the comparison study mentioned above in fulfillment of the metabolism studies required for the present petition (see memorandum from P. Hurley to G. LaRocca, dated 7/20/86).

6. Clearance of the inerts is to be addressed by the Registration Division.

7. The draft label is acceptable as written. A copy is attached.

8. A copy of the proposed tolerance (Section F) is attached.

9. The Toxicology Branch cannot recommend granting the currently proposed petition until the requirement for a 21-day inhalation study is fulfilled.

10. An 8-point document is attached.

Studies Reviewed

.....10% WP Formulation.....

Study	Results	Core Classification
Acute oral LD_{50} - rat	LD_{50}'s: 190 mg/kg (male); 157 mg/kg (female)	Guideline
Acute dermal LD_{50} - rat	LD_{50}'s: >2000 mg/kg (both sexes)	Guideline
Acute inhalation LC_{50} - rat	LC_{50}'s: 642 ug/l (male); 855 ug/l (female)	Guideline
Primary eye irritation - rabbit	PIS=22.5. Mildly irritating	Guideline
Primary dermal irritation - rabbit	PIS=3.33. Moderately irritating	Guideline
Dermal sensitization - Guinea pig	Not a sensitizer	Guideline

8-Point Review

[Prepared for 9H5577, lambdacyhalothrin on food, June 22, 1989]

1. Toxicity data with technical grade lambdacyhalothrin and with technical grade cyhalothrin (justification given in point #8 of this document) considered in support of this tolerance (selected studies).

Acute oral LD_{50}, rats	79 mg/kg in males 56 mg/kg in females
90-day feeding, rats lambdacyhalothrin	NOEL 50 ppm, LOEL 250 ppm based on reduced body wt gain
26-week oral, dogs cyhalothrin	NOEL 1 mg/kg/day LOEL 2.5 mg/kg/day (liquid feces)
Chronic feeding, rat cyhalothrin	NOEL 50 ppm, LOEL 250 ppm (reduced body wt gain. No onco. effects)
Chronic oral, dog lambdacyhalothrin	NOEL 0.5 mg/kg/day, LOEL 3.5 mg/kg/day (clinical signs of neurotoxicity)
Chronic/Onco, mouse cyhalothrin	NOEL 100 ppm, LOEL 500 ppm (decreased body wt gain. No onco. effects)
Teratology, rabbit cyhalothrin	NOEL maternal tox. 10 mg/kg/day, LOEL 30 mg/kg/d, (decreased body wt gain). NOEL fetotox. 30 mg/kg/d Not teratogenic.
Teratology, rat cyhalothrin	NOEL maternal tox. 10 mg/kg/day, LOEL 15 mg/kg/d (reduced body wt). NOEL embryo-leth. & fetotox. 15 mg/kg/d. Not tera-togenic.

Reproduction - 3 gen., rat cyhalothrin	NOEL parental tox. 10 ppm, LOEL 30 ppm (decr. bw gain). Offspring: NOEL 10 ppm, LOEL 30 ppm (decr. body wt gain.).
Metabolism, rats cyhalothrin and lambdacyhalothrin	55% oral absorption. Extensively metabolized when absorbed; cleavage of ester to cyclopropyl-carboxylic acid & phen-oxybenzyl derivatives. Accumulation of un-changed cmpd. in fat upon chronic admini-stration.
Mutagenicity - Ames gene mutation lambdacyhalothrin	Not mutagenic
Mutagenicity - Chrom. Aberr. in rodents lambdacyhalothrin	Did not induce micro-nuclei.
Mutagenicity - Gene mutation in Lymphoma cells, lambdacyhalothrin	Not mutagenic
Mutagenicity - In vitro cytogenetics lambdacyhalothrin	Not a clastogen in human lymphocytes.

2. Additional toxicity data considered desireable: None.

3. Not applicable.

4. A tolerance on cotton has been published (0.01 ppm for each of the following commodities: fat, meat, and meat by-products of cattle, goats, hogs, sheep and horses, cottonseed, and milk). Tolerances on soybeans, wheat grain, corn, sunflower and animal products have either already been published or are still pending.

5. The relationship of these tolerances on the contribution to the diet and the MPI must be addressed by the Dietary Exposure Branch and the TAS system.

6. The 3-generation reproduction study on cyhalothrin in the rat with a safety factor of 100 was used to calculate the

ADI. The NOEL was 0.5 mg/kg/day (10 ppm). The ADI is calculated to be 0.0050 mg/kg/day and the MPI is 0.3000 mg/day (60 kg).

7. There are no pending regulatory actions against registration of this pesticide.

8. The Registrant has requested that the long term studies conducted on cyhalothrin be used in partial fulfillment of the toxicity data required for the tolerance petition for lambdacyhalothrin. Lambdacyhalothrin consists of 2 of the 4 enantiomers of cyhalothrin. On the basis of structural considerations, metabolism and subchronic data on both lambdacyhalothrin and cyhalothrin, and on the fact that data from the chronic dog study conducted on lambdacyhalothrin does not conflict with the data from the 6-month dog study conducted on cyhalothrin, the Toxicology Branch (TB-I) has accepted the long term data on cyhalothrin as partial fulfillment of the toxicity studies required for the tolerance petition on lambdacyhalothrin. TB had also previously decided the both cyhalothrin and lambdacyhalothrin will be considered to be the same chemical for the purpose of establishing the ADI and TMRC (see previous memorandum from P. Hurley to G. LaRocca, dated 7/20/87). Any future tolerance petitions for either cyhalothrin, lambdacyhalothrin or any other mixtures of the 16 possible isomers of the chemical structure (provided that the appropriate toxicological data are previded) will be treated as if they are the same chemical and the proposed tolerances will be added to the percent ADI calculated for lambdacyhalothrin in this action.

SECTION F

PROPOSED FOOD ADDITIVE TOLERANCE

It is proposed that 21 CFR be amended by the establishment of a food additive tolerance for residues of lambda cyhalothrin [[1-alpha(S*),3-alpha(Z)]-(±)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate] in or on the following commodities:

0.03 ppm in or on food commodities

exposed to the insecticide during treatment of food-handling establishments where food and food products are held, processed, prepared or served.

LAMBDA - CYHALOTHRIN 128897

Page _____ is not included in this copy.

Pages 10 through 15 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

X A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

_____ 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.

Reviewed By: Pamela Hurley, Ph.D. Pamela McHurley 6/22/89 007415
Section I, Tox. Branch, IRE (H7509C)
Secondary Reviewer: Robert Zendzian, Ph.D. 6/22/89
Section I, Tox. Branch, IRE (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute oral - rat (81-1)

TOX. CHEM. NO.: 725C

ACCESSION NUMBER/MRID NO.: 409422-02

TEST MATERIAL: Lambda cyhalothrin 10WP

SYNONYMS: Karate, Commodore 10 WP, PP321

STUDY NUMBER(S): AR4624

REPORT NUMBER: CTL/P/2179

SPONSOR: ICI Americas Inc., Agricultural Products, Wilmington, Delaware 19897

TESTING FACILITY: ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK

TITLE OF REPORT: Lambdacyhalothrin: Acute Oral Toxicity to the Rat of a 100 g/kg WP Formulation

AUTHOR(S): Patricia Mannion

REPORT ISSUED: 8/01/88

CONCLUSION: Male and female rats were administered one oral dose of a 100 g/kg WP formulation of Karate (either 100, 150 or 200 mg/kg) and observed for 15 days. The acute oral LD_{50}'s were calculated as follows: 139 (approximate lower 95% confidence limit 150) mg formulation/kg for males and 157 (approximate 95% confidence limits 150, 200) mg formulation/kg for females.

Toxicity Category: II

Classification: Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: [1 alpha (S*), 3 alpha (Z)]-(+-)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate

Description: fine off-white powder
Batch #(s), Other #(s): 247/69, formulation reference GFU 595; CTL reference # YG2537/100/001
Purity: 10.79%
Source: ICI
Vehicle (if applicable): deionized water

2. Test Animals and/or Other Test System (if applicable):

Species and Strain (sexes): Male and female SPF Wistar-derived albino rats (Alpk:APfSD strain)

Age: Not given
Weight(s): 245-331 g (males), 175-239 g (females)
Source(s): Animal Breeding Unit, ICI Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, UK

3. Procedure:

a. Basis For Selection of Dose Levels: Preliminary oral study in which a range of dose levels were tested.

c. Animal Assignment and Dose Levels:

Test Group	Dose Administered mg/kg*	Number of Animals male	female
Contr.	0	5	5
1	100	5	5
2	150	5	5
3	200	5	5

* mg/kg formulation suspended in deionized water at a volume of 10 ml/kg and administered by gavage

d. Clinical Observations and Mortality: Observed for signs of toxicity once between 30 and 90 minutes after dosing, at approximately 2 1/2 hours, and between 4-6 hours after dosing; and once daily up to day 15.

d. Body Weight Determinations: On the day before dosing (day -1), the day of dosing (day 1), and on days 3, 6, 8, and 15. The animals dosed at 150 mg formulation/kg were not weighed on day 6.

e. Gross Pathology: Animals found in extremis and those surviving at the end of the study were killed by halothane BP followed by cervical dislocation and examined by necropsy for any macroscopic abnormalities.

f. Statistical Analyses: The report stated that "The acute oral median lethal dose and the 95% confidence limits were calculated from the mortality data (including animals killed in extremis) by the probit method (Finney 1971) using nominal dose values. Approximate confidence limits, where appropriate, are given by the highest dose with no mortalities and the lowest dose with 100% mortality."

B. RESULTS:

1. Clinical Observations and Mortality: Four of 5 males and 5/5 females either died or were killed in extremis following a dose of 200 mg/kg. At 150 mg/kg, 1/5 females was killed in extremis. The rest of the females and all the males at both this dose level and at 100 mg/kg survived until the end of the study. All deaths occurred on day 1 of the study. The acute oral LD_{50}'s were calculated as follows: 130 (approximate lower 95% confidence limit 150) mg formulation/kg for males and 157 (approximate 95% confidence limits 150, 200) mg formulation/kg for females. The report stated that "marked signs of toxicity were seen in all except one of the animals dosed at 100 mg/kg and all those dosed at 150 mg/kg. The signs included dehydration, breathing irregular, splayed gait, ataxia, salivation, staining around mouth and nose, upward curvature of spine and decreased activity. All surviving animals appeared normal by day 6. Extreme signs of toxicity were seen in the animals dosed at 200 mg/kg including convulsions, writhing, ataxia and irregular respiration. The one surviving male had recovered by day 6."

2. Body Weight Determinations: Initially, all animals lost weight due to fasting, but all surviving animals had gained weight by day 6 or 8.

3. Gross Pathology: No macroscopic abnormalities were observed in any of the treated animals at necropsy.

3. Quality Assurance Measures: Signed Good Laboratory Practice and Quality Assurance statements were provided.

7. DISCUSSION: This appears to be an adequately conducted study. It is classified Core Guideline.

LAMBDACYHALOTHRIN: ACUTE ORAL TOXICITY TO THE RAT
OF A 100g/kg WP FORMULATION

TABLE 1

MORTALITIES

Dose Levels mg/kg	Male		Female	
	Day No.	No. of Animals	Day No.	No. of Animals
100	0/5	0/5	0/5	0/5
150	0/5	0/5	1/5	1/5
200	1/5	4/5	1/5	5/5

There were 5 animals per sex per group.

Reviewed By: Pamela Hurley, Ph.D. Pamela M. Hurley 6/22/89
Section I, Tox. Branch, IRS (H7509C)
Secondary Reviewer: Robert Zendzian, Ph.D.
Section I, Tox. Branch, IRS (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute dermal - rat (81-2)

TOX. CHEM. NO.: 725C

ACCESSION NUMBER/MRID NO.: 409421-03

TEST MATERIAL: Commodore 10WP Insecticide

SYNONYMS: Karate, PP321, lambda cyhalothrin

STUDY NUMBER(S): CR2452

REPORT NUMBER: CTL/P/2169

SPONSOR: ICI Americas Inc., Agricultural Products, Wilmington, Delaware

TESTING FACILITY: ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK

TITLE OF REPORT: Lambdacyhalothrin: Acute Dermal Toxicity to the Rat of a 100 g/kg WP Formulation

AUTHOR(S): M. M. Leah

REPORT ISSUED: July 19, 1988

CONCLUSION: An acute dermal toxicity test using a 10% WP formulation of Karate was conducted on rats. A dose level of 2000 mg/kg was used (limit test). Although signs of clinical toxicity and irritation were observed, no mortalities were observed. Therefore, the acute dermal LD_{50} is greater than 2000 mg/kg.

Toxicity Category: III

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: (1 alpha (S*), 3 alpha (Z))-(+/-)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate

Description: fine off-white powder
Batch #(s): Other #(s): ref. 247/69, formulation reference BFU 633E: CTL ref. Y02537/100-301
Purity: 10.79%
Source: ICI Americas Inc., Goldsboro, NC
Vehicle (if applicable): deionized water

2. Test Animals and/or Other Test System (if applicable):

Species and Strain (sexes): male and female SPF Wistar-derived albino rats (Alpk:APfSD strain)

Age: Not given
Weight(s): 251-260 g (males); 159-183 g (females)
Source(s): Animal Breeding Unit, ICI Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, UK

3. Procedure:

a. Test Method: Five male and 5 female rats were used for the study. Hair was removed from an area of approximately 10 cm x 5 cm on the dorso-lumbar region of each animal 16-32 hours prior to application of the test substance. The main study was preceded by a preliminary study in which a range of dose levels were tested. Based on the results of the preliminary study, a single dose level of 2000 mg/kg (limit test) was selected for the main study. The formulation was made into a paste with deionized water prior to administration. The applied material was covered with a gauze patch which was in turn covered by a patch of plastic film and held in position using adhesive bandage and PCV tape wrapped around the animal. The animals were exposed to the test material for 24 hours. At the end of the 24-hour exposure period, the dressings were removed and any residual test material was removed with warm water.

b. Clinical Observations and Mortality: The animals were observed for clinical signs of toxicity once between 60-90 minutes after application (while dressings were still in place) and then once daily up to day 15.

c. Body Weight Determinations: The animals were weighed immediately prior to application of the test substance and on days 8, 4, 8 and 15.

d. Gross Necropsy: All animals were grossly examined for macroscopic abnormalities at termination of the study.

e. Statistical Analyses: The acute dermal median lethal dose was estimated using nominal dose values.

B. RESULTS:

1. Clinical Observations and Mortality: No animals died during the study. Therefore, the acute dermal median lethal dose was in excess of 2000 mg/kg for both male and female rats. Signs of slight systemic toxicity were seen in all except one animal. Clinical signs included diarrhea, urinary incontinence, downward curvature of the spine and upward curvature of the spine. The report stated that "most animals had recovered by Day 4 (although two females showed urinary incontinence until Days 11 or 15). The abnormalities [were] considered to be due to the presence of the bandage and/or the irritant effects." Signs of moderate irritation were observed in all animals and persisted throughout most of the observation period. These signs included cracking, desquamation, erythema, new skin, edema, scabbing and thickening. Two females were still showing signs of irritation by the end of the study.

2. Body Weight Determinations: The report stated that "initially most animals showed a decrease in bodyweight but all had regained their initial (Day 1) weight by Day 8 and continued to gain weight during the remainder of the study."

3. Gross Pathology: There were no macroscopic abnormalities at necropsy.

4. Quality Assurance Measures: Signed Quality Assurance and Good Laboratory Practice Statements were provided.

C. DISCUSSION: This is a limit test. Although clinical signs of toxicity and irritation were observed at 2000 mg/kg body weight, no mortalities were observed. Therefore, no further dose levels are required. The study is classified as Core Guideline.

LAMBDACYHALOTHRIN: ACUTE DERMAL TOXICITY TO THE RAT OF A 100g/kg WP FORMULATION
TABLE 1
CLINICAL OBSERVATION ANALYSIS BY GROUP

ANALYSIS FOR DAYS: 1 TO 15 SEX: MALES SYSTEMIC EFFECTS

CLINICAL OBSERVATION	GROUP 01 2000 MG/KG
KILLED TERMINATION	5- 5
SIGNS OF DIARRHOEA	3- 3
SIGNS OF URINARY INCONTIN	2- 2
PM EXAMINATION:NAD	5- 5
DOWNWD CURVATURE OF SPINE	1- 1
UPWARD CURV'URE OF SPINE	5- 4
NO. OF ANIMALS	5

LAMBDACYHALOTHRIN: ACUTE DERMAL TOXICITY TO THE RAT OF A 100g/kg WP FORMULATION
TABLE 1
CLINICAL OBSERVATION ANALYSIS BY GROUP

ANALYSIS FOR DAYS: 1 TO 15 SEX: FEMALES SYSTEMIC EFFECTS

CLINICAL OBSERVATION	GROUP 01 2000 MG/KG
KILLED TERMINATION	5- 5
SIGNS OF URINARY INCONTIN	22- 4
PM EXAMINATION:NAD	5- 5
UPWARD CURV'URE OF SPINE	7- 3
NO. OF ANIMALS	5

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LAMBDACYHALOTHRIN: ACUTE DERMAL TOXICITY TO THE RAT OF A 100g/kg WP FORMULATION
TABLE 1
CLINICAL OBSERVATION ANALYSIS BY GROUP

ANALYSIS FOR DAYS: 1 TO 15 SEX: MALES IRRITATION EFFECTS

CLINICAL OBSERVATION	GROUP 01 2000 MG/KG	
TEST SUBSTANCE APPLIED	5	5
CRACKING	3	1
CLIPPED	16	5
DESQUAMATION	41	5
APPLIC. AREA DECONT/MNTED	5	5
ERYTHEMA	18	5
NEW SKIN	5	1
OEDEMA	10	3
SCABBING	6	2
SCABS:FEW	2	1
SCABS:SMALL SCATTERED	18	3
THICKENING	4	1
NO. OF ANIMALS	5	

LAMBDACYHALOTHRIN: ACUTE DERMAL TOXICITY TO THE RAT OF A 100g/kg WP FORMULATION
TABLE 1
CLINICAL OBSERVATION ANALYSIS BY GROUP

ANALYSIS FOR DAYS: 1 TO 15 SEX: FEMALES IRRITATION EFFECTS

CLINICAL OBSERVATION	GROUP 01 2000 MG/KG
DRESSING OFF	1- 1
TEST SUBSTANCE APPLIED	5- 5
CLIPPED	11- 5
DESQUAMATION	48- 5
APPLIC. AREA DECONT/MNTED	5- 5
ERYTHEMA	16- 4
NEW SKIN	13- 2
NEW SKIN:SPARSE HAIR GRTH	3- 1
OEDEMA	12- 4
SCABBING	11- 2
SCAB LIFT MORE SCAB UNDER	3- 1
SCABS:SMALL SCATTERED	24- 4
THICKENING	6- 2
NO. OF ANIMALS	5

Reviewed By: Pamela Hurley, Ph.D. Pamela McHurley 6/22/89
Section I, Tox. Branch, IRS (H7509C)
Secondary Reviewer: Robert Zendzian, Ph.D. 6/23/89
Section I, Tox. Branch, IRS (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute inhalation - rat (81-3)

TOX. CHEM. NO.: 725C

ACCESSION NUMBER/MRID NO.: 409422-04

TEST MATERIAL: Commodore 10WP

SYNONYMS: Lambdacyhalothrin, Karate, PP321

STUDY NUMBER(S): HR0825

REPORT NUMBER: CTL/P/3264

SPONSOR: ICI Americas Inc., Agricultural Products, Wilmington, Delaware 19897

TESTING FACILITY: ICI Central Toxicology Laboratory, Alderley Park Macclesfield, Cheshire UK

TITLE OF REPORT: Lambdacyhalothrin: 4-Hour Acute Inhalation Toxicity Study in the Rat of a 100 g/kg WP Formulation

AUTHOR(S): P. M. Hext

REPORT ISSUED: August 15, 1988

CONCLUSION: Commodore 10WP was tested in a 4-hour inhalation study in rats at the following concentrations: 0, 20, 50 and 100 ug/l. Clinical signs of toxicity were observed in all treated groups and in the control group where the clinical signs appeared to be related to being restrained. The LC_{50}'s were calculated as follows: formulation - males: 641 (373-1134) ug/l, females: 855 (535-3080) ug/l; lambda-cyhalothrin - males: 63.0 (37.4-117) ug/l, females: 85.2 (53.1-30.9) ug/l.

Toxicity Category: III

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: [1 alpha (S*), 3 alpha (Z)]-(+/-)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate

Description: Off-white powder
Batch #(s), Other #(s): GFU 595
Purity: 10.79%
Source: ICI Agrochemicals, Fernhurst, Surrey, UK
Vehicle (if applicable): None

2. Test Animals and/or Other Test System (if applicable):

Species and Strain (sexes): Male and female SPF Alpk:APfSD (Wistar-derived) albino rats

Age: 7 weeks
Weight(s): 216-238 (males), 194-229 (females)
Source(s): Alderly Park, Cheshire, UK

3. Procedure:

a. Basis For Selection of Dose Levels: Dose levels were selected on the basis of the known inhalation toxicity of lambda-cyhalothrin.

b. Animal Assignment and Dose Levels:

Test Group	Dose Administered ug/l*	Number of Animals male	female
Contr.	0	5	5
1	20	5	5
2	50	5	5
3	100	5	5

* 4-hour exposure period

c. Atmosphere Generation: Trial atmosphere generations were carried out prior to the start of the study. Each atmosphere was generated using a Wright dust-feed mechanism. Clean, dry air was passed through the dust-feed at flow rates of either 10 or 13 litres/min. Air flow rates were measured using flowmeters and were altered as necessary.

d. Measurement of Aerodynamic Particle Size: The particle sizes were measured by means of a Marple Cascade Impactor. The mean weight of aerosol in each size range was then used to calculate the aerodynamic particle size distribution of the aerosol. The mass median aerodynamic diameter and geometric standard deviation were calculated.

e. Analysis of Atmospheric Concentration: The atmospheric concentration of lambda-cyhalothrin was determined by dissolving the formulation deposited on the VM-1 filters and the stages of the Cascade Impactor in hexane. The resultant solutions were then analysed by gas chromatography to calculate the atmospheric concentrations of the test chemical.

f. Exposure System: The animals were exposed nose-only in restraining tubes. Temperature and relative humidity within each chamber were measured during exposure.

g. Clinical Observations and Mortality: All animals were clinically examined prior to exposure, at the end of the exposure period, and daily thereafter for up to 14 days. They were also observed frequently for signs of toxicity during the 4-hour exposure period.

h. Body Weight Determinations: All rats were weighed on days -1, 1, 2, 3, 8 and 15.

i. Gross Necropsy: All rats were subjected to a macroscopic post mortem examination with particular attention being given to abdominal and thoracic viscera. Lungs, trachea and liver were removed and weighed and were preserved for future examination along with any abnormal tissues. The animals that were killed in extremis were examined in the same manner, except that organ weights were not recorded since there were no concurrent controls.

j. Statistical Analyses: Where appropriate, test and control data were compared using a two-sided Student's t-test. The median lethal concentration and slope of the regression line were estimated by logistic regression and the confidence limits were calculated using a likelihood ratio interval. An approximate lower 95% confidence limit was represented by the highest dose with no morta[illegible]ty

and the upper 95% confidence limit was represented by the lowest dose with 100% mortality.

B. RESULTS:

1. Atmosphere Analysis:

Particulate Concentration: The mean measured particulate concentrations in ug/l were as follows: target - 20 ug/l active ingredient (a.i.), measured - 177.6 +/- 9.3 ug/l formulation (17.76 ug/l a.i.); target - 50 ug/l a.i., measured - 555.4 +/- 48.8 ug/l formulation (55.54 ug/l a.i.); and target - 100 ug/l a.i., measured - 973.9 +/- 61.8 ug/l formulation (97.39 ug/l a.i.).

Chemically Analyzed Atmospheric Concentration: The atmospheric concentrations of the test chemical determined by chemical analysis were as follows: target - 20 ug/l a.i., measured - 19.0 +/- 0.93 ug/l a.i.; target - 50 ug/l a.i., measured - 53.5 +/- 4.23 ug/l a.i.; and target - 100 ug/l a.i., measured - 98.0 +/- 6.05 ug/l a.i.

Aerodynamic Particle Size Distribution: The following table, taken from the text of the report, summarizes the aerodynamic particle size distributions of the total particulate:

Group	Formulation Concentration (ug/l)	Median Size D_{50} um	Geometric Standard Deviation	% By Weight "Respirable" (= 2.5 um AED	"Inhalable" (=15um AED
20 ug/l	177.3	1.79	4.14	59.68	92.29
50 ug/l	555.4	2.18	4.26	53.86	90.07
100 ug/l	973.9	2.88	4.95	46.36	84.69

AED - aerodynamic equivalent diameter

2. Clinical Observations and Mortality: There were no deaths in the low dose group. Two males and 1 female were killed in extremis in the mid-dose group on day 1; and 3 males and 2 females were killed in extremis on day 1. 1 male died during exposure, and 1 female died following exposure in the high dose group.

Clinical observations included the following: abnormalities generally associated with restraint seen in all groups, including controls, but the severity was greater in the treated animals - stains around the

snout, hunched posture, piloerection, wet fur and chromodacryorrhea); reduction in response to sound; tail lashing; gasping; tonic convulsions; and head and paw flicking.

The LC_{50}'s were calculated as follows: formulation - males: 642 (373-1184) ug/l, females: 855 (535-3080) ug/l; lambda-cyhalothrin - males: 68.0 (37.4-117) ug/l, females: 85.2 (53.1-30.9) ug/l.

3. Body Weight Determinations: The report stated that "there was a statistically significant, treatment related body weight loss on Day 2 which was of a similar severity in all test groups. However, surviving animals in these groups gained weight at a greater rate than the controls during the first 3 days after exposure, so that by Day 15 the group mean body weights were similar."

4. Gross Pathology: The report stated the following: "discolored areas were seen on the lungs of animals which died or were killed *in extremis* on Day 1. One male in the 973.9 ug/l [high dose] group had a dark red area on the liver and froth in the trachea (indicating pulmonary edema."

"Animals killed on Day 15 showed no gross abnormalities at *post mortem* examination which were related to treatment."

5. Organ Weights: Both the relative and absolute lung weights of the 1 surviving male in the high dose group were significantly higher than the control group. The relative and absolute liver weights of females in the low and high dose groups were also greater than the controls.

6. Quality Assurance Measures: Both a quality assurance statement and a good laboratory practice statement were provided in the report.

DISCUSSION: This appears to be a well-conducted study. A sufficient number of particles were small enough to be respirable. The LC_{50}'s are similar to the ones for the 13.1% formulation (175-315 ug/l - liquid). This study is Core Guideline.

LAMBDA - CYHALOTHRIN 128897

Page _____ is not included in this copy.

Pages 33 through 37 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product 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.

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Reviewed By: Pamela Hurley, Ph.D. Pamela M Hurley 6/22/89
Section I, Tox. Branch, IRS (H7509C)
Secondary Reviewer: Robert Zendzian, Ph.D. [signature] 6/22/89
Section I, Tox. Branch, IRS (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Eye Irritation - Rabbit (81-4)

TOX. CHEM. NO.: 725C

ACCESSION NUMBER/MRID NO.: 409422-05

TEST MATERIAL: Commodore 10WP Insecticide

SYNONYMS: Karate, PP321, lambda-cyhalothrin

Laboratory Project ID No.: CTL/P/2170

SPONSOR: ICI Americas Inc., Agricultural Products, Wilmington, Delaware

TESTING FACILITY: ICI Central Toxicology Laboratory, Alderley Park Macclesfield, Cheshire UK

TITLE OF REPORT: Lambdacyhalothrin: Eye Irritation to the Rabbit of a 100 g/kg WP Formulation

AUTHOR(S): C. Henderson

REPORT ISSUED: July 7, 1988

CONCLUSION: Lambdacyhalothrin 10WP was tested for potential to produce eye irritation in rabbits using a modification of the Draize test. The highest mean total score was 22.5 at day 1. By 7 days, the total mean score was 0. Therefore, lambdacyhalothrin WP10 is classified as mildly irritating to the rabbit eye.

Toxicity Category: III

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: [1 alpha (S*), 3 alpha (Z)]-(+/-)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate

Description: Off-white powder
Batch #(s), Other #(s): Preparation reference 247/69, formulation reference GFU 595
Purity: 10.79%
Source: ICI Americas Inc, Goldsboro, North Carolina

2. Test Animals and/or Other Test System (if applicable):

Species and Strain (sexes): Male New Zealand White albino rabbits

Age: Not given
Weight(s): 2209-3109 g
Source(s): Mellor Rabbits, Chadderton Heights, Chadderton, Nr Oldham, Greater Manchester, UK

3. Procedure: Both eyes of each rabbit were examined with the aid of fluorescein within 24 hours prior to the study. Six males were chosen for the study. Approximately 100 mg was applied into the conjunctival sac of the left eye of each animal and the lids were held together for 1-2 seconds. The other eye was left untreated. The initial pain reaction was recorded on a 5-point scale. The eyes were examined, using the Draize scoring method at 1 hour and 1, 2, 3, 4 and 7 days after application of the test substance. Fluorescein staining was used at the 1-4 and 7 day readings and a modified form of the Kay and Calandra system was used to classify and interpret the scores.

B. RESULTS: The report stated that due to the low density of the formulation, it was not possible to apply 100 mg into the rabbit eye. After each application of the formulation, any remaining residue was weighed and the weight was recorded. The amount of formulation which was applied ranged from 47 - 75 mg (see table 3). Following administration of the test substance, a slight initial pain was observed in 5 animals and moderate initial pain was seen in 1 animal.

The report stated that "1-2 hours following application, moderate conjunctival redness, mild chemosis and severe discharge was seen in all 6 animals. All these conjunctival

effects had disappeared in all 6 animals 7 days after application. In addition, slight or mild corneal opacity was seen in all 6 rabbits and slight iritis in 4 rabbits. Again, these effects had disappeared 7 days after instillation...

Additional signs of eye irritation seen during the study included slight to moderate Harderian discharge, slight to moderate erythema on the eyelids, slight convolutions on the eyelids, dried secretions on periorbital skin and slight vesicular pannus. All of these additional signs of irritation had disappeared 7 days after application."

The highest mean total score was 22.5 at day 1. By 7 days, the total mean score was 0. Therefore, Lambdacyhalothrin WP10 is classified as mildly irritating to the rabbit eye. The toxicity category is III.

Quality Assurance Measures: Signed Good Laboratory Practice and Quality Assurance Statements were provided.

C. DISCUSSION: This is an acceptable eye irritation study. It is classified as Core Guideline.

LAMBDACYHALOTHRIN: EYE IRRITATION TO THE RABBIT OF A 100g/kg WP FORMULATION

TABLE 1

EYE IRRITATION: MEAN SCORES FOR RABBIT EYES

Time After Application	Mean Scores			
	Cornea (max 80)	Iris (max 10)	Conjunctiva (max 20)	Mean Total Score (max 110)
1-2 hr	5.8	2.5	14.0	22.3
1 day	10.8	1.7	10.0	22.5
2 days	7.5	1.7	7.7	16.8
3 days	3.3	0.0	5.0	8.3
4 days	3.3	0.0	3.3	6.7
7 days	0.0	0.0	0.0	0.0

Means based on 6 animals and rounded to one decimal place.
Individual animal data are given in Table 2.

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Secondary Reviewer: Robert Zendzian, Ph.D.
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DATA EVALUATION REPORT

STUDY TYPE: Primary Dermal Irritation - rabbit (81-5)

TOX. CHEM. NO.: 725C

ACCESSION NUMBER/MRID NO.: 409422-06

TEST MATERIAL: Commodore 10WP

SYNONYMS: Karate, PP321, lambda-cyhalothrin

STUDY NUMBER(S): EB3496

REPORT NUMBER: CTL/P/2165

SPONSOR: ICI Agrochemicals, ICI Americas Inc., Agricultural Products, Wilmington, Del. 19897

TESTING FACILITY: ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire UK

TITLE OF REPORT: Lambdacyhalothrin: Skin Irritation to the Rabbit of a 100 g/kg WP Formulation

AUTHOR(S): J.C. Barber

REPORT ISSUED: July 4, 1988

CONCLUSION: Lambda cyhalothrin 10WP was tested for dermal irritation potential in the rabbit. The highest mean Primary Irritation Index score was 3.33, which corresponds to a rating of moderately irritating.

Toxicity Category: IV

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: (1 alpha (S*), 3 alpha (Z))-(+/-)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate

Description: off-white powder
Batch #(s), Other #(s): Prep. ref. 247/89, formulation reference GFU595, CTL reference Y02537/100/001
Purity: 10.79%
Source: ICI Americas Inc., Goldsboro, North Carolina
Vehicle (if applicable): Deionized water

2. Test Animals and/or Other Test System (if applicable):

Species and Strain (sexes): Male New Zealand White albino rabbits

Age: Not given
Weight(s): 3235-4296 g
Source(s): Mellor Rabbits, Chadderton Heights, Nr Oldham, Greater Manchester, UK

3. Procedure: Six rabbits were used for the study. Twenty-fours prior to the start of the study, the hair was clipped from the back of each animal (an area of approximately 7 cm x 13 cm), one flank per animal. Approximately 500 mg of the test material was applied to the test site as a paste, using deionized water as the vehicle. The treated area was covered with gauze and secured with surgical tape and impermeable rubber sheeting which was in turn secured with adhesive impermeable polyethylene tape. The dressing was left in position for 4 hours and then removed. The remaining test material was wiped off with cotton wool and warm water. Irritation was measured using the Draize scale at approximately 30-60 minutes, and 1, 2, 3 (only 5 animals at this point), 4 and 7 days. One animal was also examined at 6 days. The mean erythema score was calculated by adding together the erythema scores of all 6 animals at the 1 and 2-day readings and the erythema scores of 5 animals at the 3-day readings and dividing the total by 17 (1 site on each of 6 rabbits scored 1, 2 and 3 days after treatment). A mean edema score was calculated in a similar manner.

B. RESULTS: The report stated that "signs of slight to moderate irritation were seen following a single four-hour application of the formulation to rabbit skin. Within the first 24 hours following application, very slight to moderate erythema was seen in all 6 rabbits and very slight to severe edema was present in 5 of the rabbits." All erythema and edema had disappeared in 3/6 rabbits after 3 days and in the remainder of the rabbits by 7 days. Slight desquamation was observed in 1 animal on days 6 and 7 following application. The highest mean Primary Irritation Index score was 3.33, which corresponds to a rating of moderately irritating. The Toxicity Category is IV.

Quality Assurance Measures: Signed Good Laboratory Practice and Quality Assurance Statements were provided.

C. DISCUSSION: This is an acceptable study. It is classified as Core Guideline.

LAMBDACYHALOTHRIN: SKIN IRRITATION TO THE RABBIT OF A 100g/kg WP FORMULATION

TABLE 1

SKIN IRRITATION TO THE RABBIT: ERYTHEMA AND OEDEMA SCORES

Animal Number	Erythema								Oedema							
	Time after decontamination								Time after decontamination							
	30-60 Min	1 Day	2 Days	3 Days	4 Days	6 Days	7 Days	10 Days	30-60 Min	1 Day	2 Days	3 Days	4 Days	6 Days	7 Days	10 Days
4	3	2	2	-	2	1	0	0	4	4	4	-	4	0	0	0
5	0	1	1	1	-	-	0	-	0	2	2	1	-	-	0	-
6	0	2	1	0	-	-	0	-	0	2	1	0	-	-	0	-
7	0	1	0	0	-	-	0	-	0	1	1	0	-	-	0	-
8	0	1	1	0	-	-	0	-	0	0	0	0	-	-	0	-
9	0	2	2	1	-	-	0	-	0	2	1	0	-	-	0	-

- no observation made.
Assessments were made using the Draize scale (Appendix B).

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Secondary Reviewer: Robert Zendzian, Ph.D. [illegible] 6/21/89
Section I, Tox. Branch, IRS (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization - Guinea pig (81-6)

TOX. CHEM. NO.: 725C

ACCESSION NUMBER/MRID NO.: 409422-07

TEST MATERIAL: Commodore 10WP

SYNONYMS: Lambdacyhalothrin, Karate, PP321

STUDY NUMBER(S): GG4303

REPORT NUMBER: CTL/P/2305

SPONSOR: ICI Americas Inc. Agricultural Products, Wilmington, Delaware 19897

TESTING FACILITY: ICI Central Toxicology Laboratory, Alderley Park Macclesfield, Cheshire, UK

TITLE OF REPORT: Lambdacyhalothrin: Skin Sensitization to the Guinea Pig of a 100 g/kg WP Formulation

AUTHOR(S): A.M. Leah

REPORT ISSUED: July 29, 1988

CONCLUSION: Lambdacyhalothrin 10WP was tested in a dermal sensitization study in Guinea Pigs. It was not a skin sensitizer under the conditions of the study.

Classification: Core Guideline

A. MATERIALS AND METHODS:

1. Test Compound(s):

Chemical Name: [1 alpha (S*), 3 alpha (Z)]-(+/-)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate

Description: Fine, off-white powder
Batch #(s), Other #(s): ref. 247/69, formulation ref. GFU 595, CTL ref. Y02537/100/001
Purity: 10.79%
Source: ICI Americas Inc, Goldsboro, North Carolina
Vehicle (if applicable): deionized water
Positive Control(s) (if applicable): Formaldehyde

2. Test Animals and/or Other Test System (if applicable):

Species and Strain (sexes): Male Alpk:Dunkin Hartley guinea pigs
Age: Not given
Weight(s): 346-449 g (main study) or 313-451 g (positive control study).
Source(s): Animal Breeding Unit, ICI Pharmaceuticals, Alderly Park, Macclesfield, Cheshire, UK

3. Procedure:

Basis For Selection or Dose Levels: Dose levels were selected on the basis of a sighting study.

Sighting Study:

Challenge Stage: 3, 10, 30, and 75% w/v preparations in deionized water was applied to each of 2 male guinea pigs as will be described in the challenge phase of the main study. An additional 4 males were also challenged 1 week later with 75% and 30% w/v preparations. On the basis of the results, the 75% and 30% preparations were selected for challenge phase of the main study.

Induction Stage: A 75% preparation was applied to each of 2 male animals as described in the main study, except that the preparation was applied to the flanks, not the scapular region. Since no irritation was noted, this dose was used for the main study.

Main Study:

Induction: Thirty male guinea pigs were used in the study, 20 test animals and 10 controls. Each animal was clipped free of hair on the scapular region (5 cm x 5 cm area) and treated with a topical application of approximately 330 mg of a 75% (w/v) preparation of the formulation in deionized water. The preparation was applied to a lint pad which was covered with adhesive tape, an adhesive elastic bandage and PVC tape. The controls received water in the same manner. The occlusive dressing was left in place for approximately 6 hours. The induction procedure was repeated at the same site, during the next 2 weeks, for a total of 3 six-hour exposures. The interval between each exposure was 7 days. The irritation response was noted 24 hours after the removal of each patch and before application of the next patch. The animals were left untreated for 2 weeks after the final induction exposure, prior to the challenge.

Challenge: Each animal was clipped free of hair on both flanks (15 cm x 5 cm). The 75% preparation was applied to 1 flank and the 30% preparation was applied to the other flank via the use of lint pads as above. The lint pads had been stitched to rubber sheeting which was in turn held in place by adhesive impermeable polyethylene tape. The patches were held in place for 6 hours. The dressings were removed and the erythematous reactions were quantified and recorded, using the 4-point scale shown below, approximately 24 and 48 hours after the removal of the dressings.

Scale:-

0 - no reaction
1 - scattered mild redness
2 - moderate diffuse redness
3 - intense redness and swelling

The response was classified by subtracting the percentage of the control animals that responded from the percentage of the treated animals that responded and comparing the net response with the following scheme:

% net response	description
0	not a sensitizer
>0-8	weak sensitizer
>8-28	mild sensitizer
>28-64	moderate sensitizer
>64-80	strong sensitizer
>80-100	extreme sensitizer

Positive Control: The sensitizing potential of formaldehyde solution was assessed using the method described above. A 30% dilution of solution in deionized water was applied for both the inductions and the challenge.

E. RESULTS: During the induction phase, 2/20 animals had a slight irritation response after the first and/or the second application. The controls had no response. After the challenge phase, neither controls nor treated animals had any response. The positive controls elicited a strong skin sensitization response.

Quality Assurance Measures: Signed Quality Assurance and Good Laboratory Practice statements were provided.

F. DISCUSSION: This appears to be an acceptable study. It is classified as Core Guideline.

LAMBDACYHALOTHRIN: SKIN SENSITISATION TO THE GUINEA PIG OF A 100g/kg WP FORMULATION

TABLE 1

OBSERVATIONS RECORDED DURING THE INDUCTION PHASE

Induction concentrations:- 1st; 75% (w/v) in deionised water
2nd; 75% (w/v) in deionised water
3rd; 75% (w/v) in deionised water

TEST ANIMALS Study No: GG4303

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
1	NAD	NAD	NAD	NAD	NAD
2	NAD	NAD	NAD	NAD	NAD
3	NAD	NAD	NAD	NAD	NAD
4	NAD	NAD	NAD	NAD	NAD
5	NAD	NAD	NAD	NAD	NAD
6	NAD	NAD	NAD	NAD	NAD
7	NAD	NAD	NAD	NAD	NAD
8	NAD	NAD	NAD	NAD	NAD
9	NAD	NAD	NAD	NAD	NAD
10	NAD	NAD	NAD	NAD	NAD

LAMBDACYHALOTHRIN: SKIN SENSITISATION TO THE GUINEA PIG OF A 100g/kg WP FORMULATION

TABLE 1 - continued

OBSERVATIONS RECORDED DURING THE INDUCTION PHASE

Induction concentrations:- 1st; 75% (w/v) in deionised water
2nd; 75% (w/v) in deionised water
3rd; 75% (w/v) in deionised water

TEST ANIMALS Study No: GG4303

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
11	ME	SD, SF	SD, SSS	NAD	NAD
12	NAD	NAD	NAD	NAD	NAD*
13	NAD	NAD	NAD	NAD	NAD
14	NAD	NAD	NAD	NAD	NAD
15	NAD	NAD	NAD	NAD	NAD
16	NAD	NAD	NAD	NAD	NAD
17	SE	NAD	NAD	NAD	NAD
18	NAD	NAD	NAD	NAD	NAD
19	NAD	NAD	NAD	NAD	NAD
20	NAD	NAD	NAD	NAD	NAD

* Killed prior to challenge due to prolapse.

LAMBDACYHALOTHRIN: SKIN SENSITISATION TO THE GUINEA PIG OF A 100g/kg WP FORMULATION

TABLE 1 - continued

OBSERVATIONS RECORDED DURING THE INDUCTION PHASE

Induction concentrations:- 1st; Water and Bandage only
2nd; Water and Bandage only
3rd; Water and Bandage only

CONTROL ANIMALS Study No: GG4303

Animal Number	24 Hours After 1st Induction	Immediately Prior to 2nd Induction	24 Hours After 2nd Induction	Immediately Prior to 3rd Induction	24 Hours After 3rd Induction
21	NAD	NAD	NAD	NAD	NAD
22	NAD	NAD	NAD	NAD	NAD
23	NAD	NAD	NAD	NAD	NAD
24	NAD	NAD	NAD	NAD	NAD
25	NAD	NAD	NAD	NAD	NAD
26	NAD	NAD	NAD	NAD	NAD
27	NAD	NAD	NAD	NAD	NAD
28	NAD	NAD	NAD	NAD	NAD
29	NAD	NAD	NAD	NAD	NAD
30	NAD	NAD	NAD	NAD	NAD

LAMBDACYHALOTHRIN: SKIN SENSITISATION TO THE GUINEA PIG OF A 100g/kg WP FORMULATION

TABLE 2

ERYTHEMA SCORES

Challenge concentrations: 75% and 30% (w/v) in deionised water Study No: GG4303

Animal Number	Test Animals			
	75% (w/v)		30% (w/v)	
	24 Hr	48 Hr	24 Hr	48 Hr
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
5	0	0	0	0
6	0	0	0	0
7	0	0	0	0
8	0	0	0	0
9	0	0	0	0
10	0	0	0	0
11	0	0	0	0
12	-	-	-	-
13	0	0	0	0
14	0	0	0	0
15	0	0	0	0
16	0	0	0	0
17	0	0	0	0
18	0	0	0	0
19	0	0	0	0
20	0	0	0	0

The scale used for scoring erythema is given on page 5.
- animal died prior to challenge.