



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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

April 24, 2002

MEMORANDUM

Product Name: CLINCHER CA
EPA File Symbol: 62719-GLA
DP Barcode: D282260
Case No: 069854
Submission: S604177
Chemical: 082583 Cyhalofop-butyl

From: Byron T. Backus, Ph.D., Toxicologist /s/ **DMcCall**
Technical Review Branch for **Byron Backus**
Registration Division (7505C) **4-24-02**

To: Dianne Morgan/Joanne Miller, PM 23
Herbicide Branch
Registration Division (7505C)

Registrant: Dow AgroSciences LLC

ACTION REQUESTED: "The registrant has submitted two end-use formulations for a pending new chemical registration for cyhalofop-butyl. The registrant has submitted a letter (attached) stating that these formulations are identical to Clincher (62719-GGU), which was being supported by data from the technical product 62719-GGL, that was reviewed in HED. The new chemical is targeted for registration in mid/late May, therefore a letter requesting an expedited review is being forwarded separately. Please review the attached data for acceptability: MRID Nos. 45000236 - 45000242 and 45000401 - 45000408..."

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BACKGROUND: According to the label received by TRB, this product [CLINCHER CA] has the following ingredient declaration:

Active Ingredient:

Cyhalofop: 2-[4-(4-cyano-2-fluorophenoxy) phenoxy] propanoic acid, butyl ester, (R).....29.6%
Inert Ingredients:.....70.4%

As part of this package, TRB has received the following acute toxicity studies [conducted on a formulation designated as FOE 5043 SC 04402/0096 (Fluthiamide proposed c.n.); described as a beige white liquid suspension containing 504.1g(active)/L. From information in MRID 45522805 the specific gravity is reported as

COMMENTS AND RECOMMENDATIONS:

1. The material in this package includes the following acute toxicity studies which were conducted on a formulation identified as XRM-5151 Lot No. C0187-48 (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer], a liquid with a specific gravity of 0.96. TRB's interpretation is that the formulation used in these studies is identical or substantially similar to that proposed for EPA File Symbol 62719-GLA CLINCHER CA with a label claim of 29.6% Cyhalofop: 2-[4-(4-cyano-2-fluorophenoxy) phenoxy] propanoic acid, butyl ester, (R): Acute oral toxicity (rat) [MRID 45000239]; Acute dermal toxicity (rabbit) [MRID 45000242]; Acute inhalation toxicity (rat) [MRID 45000402]; Primary eye irritation (rabbit) [MRID 45000404]; Primary dermal irritation (rabbit) [MRID 45000406]; and dermal sensitization (guinea pig) [MRID 45000408]. These studies have all been classified as acceptable.

2. Based on the results of the reviewed acute toxicity studies, the following is the acute toxicity profile for EPA File Symbol 62719-GLA CLINCHER CA (label claim: 29.6% Cyhalofop):

Acute Oral LD50	Acceptable	Tox. Cat. III (MRID 45000239)
Acute Dermal LD50	Acceptable	Tox. Cat. IV (MRID 45000242)
Acute Inhalation LC50	Acceptable	Tox. Cat. IV (MRID 45000402)
Primary Eye Irritation	Acceptable	Tox. Cat. II (MRID 45000404)
Primary Dermal Irritation	Acceptable	Tox. Cat. III (MRID 45000406)
Dermal Sensitization	Acceptable	Negative (MRID 45000408)

3. Based on the acute toxicity profile given above and based on the proposed label use directions, the following is the appropriate precautionary labeling for this product, as obtained from the Label Review System:

NOTE TO PM: This product meets the criteria for a Restricted Use Pesticide, as laid out in 40 CFR 152.170(b)(iv) - Corneal involvement or irritation persisting for more than 7 days. It is your decision to make this a Restricted Use Pesticide. See 40 CFR156.10(j)(2) and PR Notice 93-1 for label requirements.

Label Review System

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

Keep Out of Reach of Children

WARNING AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.

If you do not understand the label, find someone to explain it to you in detail.)

Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear protective eyewear (goggles or face shield). Harmful if swallowed. Avoid contact with skin. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

Personal Protective Equipment (PPE)

Applicators and Handlers of this concentrated product must wear:

Long sleeved shirt and long pants

Protective eyewear (goggles or faceshield)

Chemical resistant (such as nitrile or butyl) gloves

Shoes and socks

USER SAFETY REQUIREMENTS

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.

When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS.

USER SAFETY RECOMMENDATIONS

Wash thoroughly with soap and water after handling. Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.

Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

Remove PPE immediately after handling this product. Wash the outside of gloves before

removing. As soon as possible, wash thoroughly and change into clean clothing.

FIRST AID

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15 to 20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eyes. Call a poison control center for treatment advice.

IF SWALLOWED: Immediately call a poison control center or doctor. Do not induce vomiting unless told to do so by a poison control center or doctor. Do not give any liquid to the person. Do not give anything by mouth to an unconscious person.

IF ON SKIN OR CLOTHING: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 to 20 minutes. Call a poison control center or doctor for treatment advice.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

This product is required to have a "Note to Physicians". It should include the following statements and information:

NOTE TO PHYSICIAN:

- **Contains petroleum distillate - vomiting may cause aspiration pneumonia**
- Technical information on symptoms;
- Use of supportive treatments to maintain life functions;
- Medicine that will counteract the specific physiological effects of the pesticide;
- Company telephone number to specific medical personnel who can provide specialized medical advice.

4. The following acute toxicity studies were apparently conducted on the technical active (designated as XRD-537, XRD-537 BE, and DE-537 in different studies, with percentage of active ranging from 95.8% to 99.5%): Acute oral toxicity (rat) [MRID 45000237]; Acute oral toxicity (mouse) [MRID 45000238]; Acute dermal toxicity (rat) [MRID 45000241]; Acute dermal toxicity (rat) [MRID 45000240]; Acute inhalation toxicity (rat) [MRID 45000401]; Primary eye irritation (rabbit) [MRID 45000403]; Primary dermal irritation (rabbit) [MRID 45000405]; and Dermal sensitization (guinea pig) [MRID 45000407]. All of these studies have been classified as acceptable.
5. Based on the results of the reviewed acute toxicity studies, the following is the acute toxicity profile for the technical.

Acute Oral LD50(rat)	Acceptable	Tox. Cat. IV (MRID 45000237)
Acute Oral LD50(mouse)	Acceptable	Tox. Cat. IV (MRID 45000238)
Acute Dermal LD50(rat)	Acceptable	Tox. Cat. IV (MRID 45000241)
Acute Dermal LD50(rat)	Acceptable	Tox. Cat. III ^a (MRID 45000240) ^a
Acute Inhalation LC50(rat)	Acceptable	Tox. Cat. IV (MRID 45000401)
Primary Eye Irritation	Acceptable	Tox. Cat. IV (MRID 45000403)
Primary Dermal Irritation	Acceptable	Tox. Cat. III (MRID 45000405)
Dermal Sensitization	Acceptable	Negative (MRID 45000407)

6. This package also contains an additional study, an Acute oral toxicity (rat) [MRID 45000236] which was conducted on material identified as XRD-537 Methyl Ester (99.8%±0.2% propanoic acid: 2-(4-(4-cyano-2-fluorophenoxy) phenoxy)-, methyl ester, (R(+))-. This study has been classified as acceptable, although its relevance as supporting data is not immediately clear from the information provided to TRB. The following is a partial acute toxicity profile for XRD-537 Methyl Ester:

Acute Oral LD50(rat)	Acceptable	Tox. Cat. IV (MRID 45000236)
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DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1)

Product Manager: 23
MRID No.: 45000239

Reviewer: Byron T. Backus, Ph.D.

CITATION: Bonnette, K.L. XRM-5151: An Acute Oral Toxicity Study in Fischer 344 Rats Amended Final Report. SLI Study No. 3504.4; Dow Study No. 990111. Unpublished study prepared by Springborn Laboratories Inc. (SLI), Spencerville, OH 45887. Amended Study Completion Date: October 12, 1999. MRID 45000239.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRM-5151; TSN 101724; Lot No. C0187-48; a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient.

SPECIES: Rat, Fischer 344

AGE(at dosing): Males: approximately 9-11 weeks; Females: approximately 9-10 weeks

WEIGHT (fasted): Males: 152-204 g; Females: 116-126 g

SOURCE: Harlan Sprague Dawley Inc., Indianapolis, IN

EXECUTIVE SUMMARY: *In an acute oral toxicity study (MRID 45000239), fasted (overnight) young adult (9-11 weeks old) Fischer 344 rats (5 males and/or 5 females/dose level) were orally gavaged with 500 (males only), 2000 or 5000 mg/kg XRM-5151 Lot No. C0187-48 (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]). The test material (a liquid with a specific gravity of 0.96) was administered as received from the sponsor.*

Symptoms included breathing difficulties, decreased defecation, rough haircoat, urine stain, dark material around the face and moderate to pronounced decreases in resistance to removal from the cage. Hand-held observations showed decreases in extensor-thrust response, decreases in reaction to handling, and increased lacrimation. Open-field observations included a slight to exaggerated gait. Animals which subsequently died also showed apparent hypothermia, hunched posture, decreases in muscle tone and a decrease in responsiveness to touch. There were no mortalities in males dosed at 500 mg/kg or females dosed at 2000 mg/kg, but 3/5 males died following dosage at 2000 mg/kg and all (5/5 females, 5/5 males) died following dosage at 5000 mg/kg. Deaths occurred by study day 4.

Gross pathological findings in the rats which died included abnormal contents of intestines and/or stomach and foci in the stomach. There were no significant gross pathological findings in rat which survived to terminal sacrifice.

Oral LD50 Male = 1611.7 (95% c.i. = 975.4-2663.1) mg/kg

Oral LD50 Females > 2000, <5000 mg/kg

XRM-5151 Lot No. C0187-48 (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]) is in toxicity category III in terms of oral toxicity.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 4), and No

Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1100): "On day 0, the test article was administered orally as a single dose using a ball tipped stainless steel gavage needle attached to a syringe... Individual doses were calculated based on the animal's fasted (day 0) body weight. Animals were returned to *ad libitum* feed after dosing... The animals were observed for clinical abnormalities...three times on day 0 (post-dose) and daily thereafter... Clinical abnormalities included, but were not limited to, changes in the skin, autonomic and central nervous systems, including tremors and convulsions, changes in level of activity, gait and posture, reactivity to handling or sensory stimuli, altered strength and stereotypies or bizarre behavior..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Total
500	0/5	-	0/5
2000	3/5	0/5	3/10
5000	5/5	5/5	10/10

Observations: "All animals given 5000 mg/kg died by study day 2 and 3/5 males given 2000 mg/kg died by study day 4... The most notable clinical abnormalities were observed at the 2000 mg/kg and 5000 mg/kg levels... " [One male at 500 mg/kg showed congested breathing following dosage; this was gone on day 1]. Symptoms included breathing difficulties, decreased defecation, rough haircoat, urine stain, dark material around the face and moderate to pronounced decreases in resistance to removal from the cage. Hand-held observations showed decreases in extensor-thrust response, decreases in reaction to handling, and increased lacrimation. Open-field observations included a slight to exaggerated gait. Animals which subsequently died also showed apparent hypothermia, hunched posture, decreases in muscle tone and a decrease in responsiveness to touch.

Gross Necropsy: Gross pathological findings in the rats which died included abnormal contents of intestines and/or stomach and foci in the stomach. There were no significant gross pathological findings in rat which survived to terminal sacrifice.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200, formerly §81-2)

Product Manager: 23
MRID No.: 45000242

Reviewer: Byron T. Backus, Ph.D.

CITATION: Bonnette, K.L. XRM-5151: An Acute Dermal Toxicity Study in New Zealand White Rabbits Final Report. SLI Study No. 3504.5; Dow Study No. 990114. Unpublished study prepared by Springborn Laboratories Inc. (SLI), Spencerville, OH 45887. Study Completion Date: October 12, 1999. MRID 45000242.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRM-5151; TSN 101724; Lot No. C0187-48; a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient.

SPECIES: Rabbit, New Zealand White

AGE: Adult

WEIGHT: Males: 2815 - 3418 g; Females: 2628 - 3307 g

SOURCE: Myrtle's Rabbitry, Thompson Station, TN

EXECUTIVE SUMMARY: *In an acute dermal toxicity study (MRID 45000242), a group of 5M & 5F adult New Zealand White rabbits received a 24-hour occluded exposure to 5000 mg/kg XRM-5151 Lot No. C0187-148, a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient.*

There was no mortality; occurrences of "isolated and transient incidences of decreased responsiveness to touch, increased reactivity to handling, fecal staining..." are reported as being not directly attributable to XRM-5151 "due to their transient nature, infrequent occurrences and both increase and decrease in responsiveness." There was dermal irritation at the application site of all rabbits which persisted to the end of the 14-day observation period.

There were no significant pathological findings observed following post-sacrifice necropsy.

Dermal LD50 Males > 5000 mg/kg (0/5 died at this dose level)

Dermal LD50 Females > 5000 mg/kg (0/5 died at this dose level)

Combined > 5000 mg/kg (0/10 rabbits died at this dose level)

XRM-5151 Lot No. C0187-148, a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) is in toxicity category IV in terms of dermal toxicity.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 4), and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1200): “On day -1, the fur was removed from the dorsal trunk area of the animals chosen for the limit test using an animal clipper... On the following day (day 0), the test article was administered dermally to approximately 10% of the body surface area. The four corners of this area were delineated in the clipped area with an indelible marker. The test article was then spread evenly over the delineated test area and held in contact with the skin with an appropriately sized 6-ply porous gauze dressing backed with a plastic wrap which was placed over the gauze dressing (occlusive binding). Removal and ingestion of the test article was prevented by placing an elastic wrap over the trunk and test area. The elastic wrap was further secured with adhesive tape around the trunk at the cranial and caudal ends... Individual doses were calculated based on the animal’s day 0 body weight. After dosing, collars were placed on the animals and remained in place until removal on study day 3. After an approximate 24-hour exposure period, the gauze dressing, plastic and elastic wrap were removed. Residual test article was removed using gauze moistened with deionized water followed by dry gauze.”

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000 ^a	0/5	0/5	0/10

^aDose volume was 5.21 mL/kg (corresponding to a density of 0.96 g/mL).

Observations: There was no mortality. According to information on p. 13 of MRID45000242: “Clinical abnormalities observed during the study included isolated and transient incidences of decreased responsiveness to touch, increased reactivity to handling, fecal staining and mechanical injury (nictitating membrane). These findings were not directly attributed to XRM-5151 due to their transient nature, infrequent occurrences and both increase and decrease in responsiveness. Dermal irritation consisting of erythema, edema, eschar, desquamation and/or superficial lightening were noted at the test site throughout the study in all animals.”

Gross Necropsy: “No significant [test material related] gross internal findings were observed at necropsy on day 14.”

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (870.1300, formerly §81-3)

Product Manager: 23
MRID No.: 45000402

Reviewer: Byron T. Backus, Ph.D.

CITATION: Clements, C.M. Cyhalofop-Butyl EC (XRM-5151): Acute Aerosol Inhalation Toxicity Study in Fischer 344 Rats. Laboratory Project Study ID 991080. Unpublished study prepared by Health & Environmental Research Laboratories, The Dow Chemical Company, Midland, MI 48674. Study Completion Date: May 26, 1999. MRID 45000402.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: Cyhalofop-Butyl EC (XRM-5151) (Lot No. C0187-48, TSN 101724); containing 29.3% cyhalofop N-butyl ester R-isomer as the active ingredient.

SPECIES: Rat, Fischer 344

AGE(at exposure): approximately 10 weeks old

WEIGHT (at exposure): Males: 210.3 - 225.9 g; Females: 132.1 - 141.9 g;

SOURCE: Charles River Laboratories, Raleigh, NC

EXECUTIVE SUMMARY: *In an acute inhalation toxicity study (MRID 45000402), a group of 5 male and 5 female young adult (approximately 10 weeks old) Fischer 344 rats received a 4-hour nose-only exposure to a mean time-weighted average concentration of 5.19 mg/L of the test material (Cyhalofop-Butyl EC, XRM-5151, Lot No. C0187-48, TSN 101724, containing 29.3% cyhalofop N-butyl ester R-isomer as the active ingredient). The mean MMAD was 1.78 μ m and the mean GSD was 2.28.*

There were no mortalities. Following exposure symptoms included extensive body soiling, perinasal soiling, perineal soiling (urine and/or fecal), nosy respiration, slow respiration, deep respiration and decreased activity. By day 4 5/5 males and 4/5 females were normal; the remaining female was normal by day 7. Hand-held and open-field observations were non-specific, although possibly related to the decreased activity. All rats had lost weight by day 4, but all had weight gains (from their day 1 values) by day 11.

There were no significant pathological findings observed in 5/5 males and 4/5 females following post-sacrifice necropsy. The remaining female had a liver hernia, a finding that was interpreted as not being associated with exposure to the test material.

Inhalation LC50 Males > 5.19 mg/L (0/5 died)

Inhalation LC50 Females > 5.19 mg/L (0/5 died)

Combined LC50 > 5.19 mg/L (0/10 rats died)

The test material, Cyhalofop-Butyl EC, XRM-5151, Lot No. C0187-48, TSN 101724, containing 29.3% cyhalofop N-butyl ester R-isomer as the active ingredient, is in toxicity category IV in terms of acute inhalation toxicity, based on the LC50 > 5.19 mg/L.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 4) and No Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.1300): Exposure was nose-only. A liquid aerosol was generated by metering the test material with a FMI pump into a stainless steel spray nozzle. The test material was mixed with compressed air in the spray nozzle and aerosol was sprayed into the chamber. "The mass concentration of aerosol present in the chamber was determined gravimetrically 4 times during the exposure period... The time-weighted average (TWA) exposure concentration was calculated from the gravimetric measurements. A substantial portion of the exposure atmosphere consisted of vapor (primarily the solvent vehicle), therefore, vapor samples were collected using sorbent tube(s) in-line with the Teflon filter... The aerodynamic particle size was determined twice during the exposure period through a six-stage cascade impactor by drawing samples, at a set rate using a Sierra series 110 constant flow air sampler..."

"Animals were weighed and examined prior to exposure to the test material. All animals were observed at least every 30 minutes during the exposure period and each workday during the two-week post-exposure period. The observations included an evaluation of the fur, eyes, mucous membranes and respiration. Behavior pattern and nervous system activity were assessed by specific observation for tremors, convulsions, salivation, lacrimation and diarrhea, as well as lethargy and other signs of altered central nervous system function..."

"A detailed clinical observation (DCO) was conducted daily (except on weekends and holidays) during the two-week post exposure period on all animals exposed. Hand-held and open-field observations included a careful physical examination and sensory evaluation according to an established format... Open-field observations and sensory evaluations were made in a small clear plastic box (50 cm x 50 cm)..."

Mean Exposure Concentration mg/L (Gravimetrically Determined) ^a	Number of Deaths/Number Tested		
	Males	Females	Combined
5.19	0/5	0/5	0/10

^aFour concentration measurements were made during exposure; values were 5.44 mg/L (20 minutes); 5.02 mg/L (104 minutes); 5.08 mg/L (165 minutes); and 5.24 mg/L (205 minutes).

The nominal concentration was 9.37 mg/L.

Clinical Observations: There were no mortalities. The only observation noted during exposure was urine-soiled fur in one female. Subsequently, 3/5 males and 4/5 females showed perineal soiling (usually just urine, but one female also showed fecal soiling). Other symptoms included were abnormalities in respiration (slow, deep and/or noisy) and decreased activity. All rats were normal by day 7. 2/3 males on study day 3 and again on day 12 showed minimal responsiveness to touch. All rats had reduced body weights on day 2, with some recovery by day 4 (although body weights for all were still below their day 1 values). All rats had gained weight relative to day 1 by day 11, and all continued to gain weight through day 15. [From p. 15 of MRID 45000402: "The mean body weight for the male and female rats were decreased by approximately 11 and 10% respectively, on test day two and exceeded the test day one mean weight by test day eleven..."]

Gross Necropsy: There were no visible lesions in 5/5 males and 4/5 females. One female rat had a liver hernia which was interpreted as an incidental finding unrelated to exposure.

Chamber Atmosphere

Grav. Conc. (mg/L)	Mean MMAD (μm)	Mean GSD
5.19	1.78	2.28

Particle Size Distribution: A mean of 34.5% of the particles by mass were less than 1.3 μm , and a mean of 75.4% were less than 3 μm .

Chamber Environment	
Internal Chamber Volume	42 L
Mean Chamber Airflow	30 LPM
Mean Temperature	20.0°C
Mean Relative Humidity	0%

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (870.2400, formerly §81-4)

Product Manager: 23
MRID No.: 45000404

Reviewer: Byron T. Backus, Ph.D.

CITATION: Bonnette, K.L. XRM-5151: A Primary Eye Irritation Study in New Zealand White Rabbits Final Report. SLI Study No. 3504.6; Dow Study No. 990113. Unpublished study prepared by Springborn Laboratories Inc. (SLI), Spencerville, OH 45887. Study Completion Date: October 6, 1999. MRID 45000404.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRM-5151; TSN 101724; Lot No. C0187-48; a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient.

SPECIES: Rabbit, New Zealand White

AGE: Adult

WEIGHT: Males: 3.720 - 4.041 kg

SOURCE: Myrtle's Rabbitry, Thompson Station, TN

EXECUTIVE SUMMARY: *In a primary eye irritation study (MRID 45000404), 0.1 mL of XRM-5151, Lot No. C0187-48, a clear amber liquid (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]) was instilled into the conjunctival sac of one eye of each of 3 New Zealand white rabbits.*

There was corneal opacity and iritis in all 3 eyes, with the corneal opacity persisting through day 7 but clearing by day 10. All eyes were positive for conjunctival redness through 72 hours.

The test material, XRM-5151, Lot No. C0187-48 (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]) is in toxicity category II in terms of primary eye irritation potential, based on the presence of corneal opacity in 3/3 eyes on day 7, which cleared by day 21.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 4) and No Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.2400): 0.1 mL of the test article was instilled into the conjunctival sac of the right eye of each of three rabbits after gently pulling the lower lid away from the eye. The eyelids were gently held together for approximately one second after instillation to limit loss of the test material. Following macroscopic observations at the 24-hour scoring interval, the eyes were examined using fluorescein sodium dye. If any positive fluorescein findings were noted at 24 hours, a fluorescein examination was conducted on the test eyes at each subsequent scoring interval until a negative response was obtained.

Results:

Observations	Number "positive"/number tested							
	1 hr	24 hrs ^a	48 hrs	72 hrs	7 days	10 days	14 days	21 days
Corneal Opacity	3/3	3/3 ^a	3/3	3/3	3/3	0/3	0/3	0/3
Iritis	3/3	3/3	3/3	3/3	1/3	0/3	0/3	0/3
Conjunctivae:								
Redness ^b	3/3	3/3	3/3	3/3	0/3	0/3	0/3	0/3
Chemosis ^b	3/3	3/3	2/3	2/3	1/3	0/3	0/3	0/3
Discharge ^b	3/3	3/3	2/3	0/3	0/3	0/3	0/3	0/3

^aSodium fluorescein used in the examination at 24 hours and at each subsequent reading until a negative response was obtained.

^bScore of 2 or more considered positive.

"Exposure to the test article produced corneal opacity in 3/3 test eyes at the 1-hour scoring interval. The corneal injury was confirmed by positive fluorescein dye retention at the 24-hour scoring interval. The corneal opacity resolved in all test eyes by study day 10. Iritis was observed in 3/3 test eyes by the 1-hour scoring interval and resolved completely in all test eyes by study day 10. Conjunctivitis (redness, swelling and discharge) was noted in 3/3 test eyes at the 1-hour scoring interval. The conjunctival irritation resolved completely in all test eyes by study day 21. Additional ocular findings noted included corneal neovascularization (3/3 test eyes) and sloughing of the corneal epithelium (1/3 test eyes)."

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (870.2500, formerly §81-5))

Product Manager: 23
MRID No.: 45000406

Reviewer: Byron T. Backus, Ph.D.

CITATION: Bonnette, K.L. XRM-5151: A Primary Skin Irritation Study in New Zealand White Rabbits Final Report. SLI Study No. 3504.7; Dow Study No. 990112. Unpublished study prepared by Springborn Laboratories Inc. (SLI), Spencerville, OH 45887. Study Completion Date: October 7, 1999. MRID 45000406.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRM-5151; TSN 101724; Lot No. C0187-48; a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient.

SPECIES: Rabbit, New Zealand White

AGE: Adult

WEIGHT: Males: 2.725 - 2.979 kg

SOURCE: Myrtle's Rabbitry, Thompson Station, TN

EXECUTIVE SUMMARY: *In a primary dermal irritation study (MRID 45000406), 0.5 mL of XRM-5151, Lot No. C0187-48, a clear amber liquid (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]) was applied to an intact skin site on the back of each of 3 New Zealand white rabbits, with 4-hr semi-occluded exposure.*

At 1, 24, 48 and 72 hours scores for erythema ranged from 1 to 2 and scores for edema ranged from 1 to 2. On Day 7 all 3 rabbits scored 2 for erythema, and 1 or 2 for edema. At 21 days irritation had cleared in 2/3 rabbits, while the remaining rabbit scored 1 (very slight) for erythema and 1 (very slight) for edema. The PDIS (average of 1, 24, 48 and 72-hr scores) was 3.17. The test material, XRM-5151, Lot No. C0187-48, a clear amber liquid (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]) is in toxicity category III in terms of dermal irritation potential, based on the effects observed in this study.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 4) and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.2500): "On day -1, the animals chosen for use on the primary skin irritation study had the fur removed from the dorsal area of the trunk using an animal clipper. Care was taken to avoid abrading the skin during the clipping procedure... On the following day (day 0), the test article was applied to a small area of intact skin on each animal (approximately 1 inch x 1 inch)..." The test article was administered under a 1" x 1" 4-ply gauze patch that was held in contact with the skin at the cut edges with non-irritating tape. "Removal and ingestion of the test article was prevented by placing an elastic wrap over the trunk and test area (semi-occlusive binding). The elastic wrap was then further secured with adhesive tape around the trunk at the cranial and caudal ends. After dosing, collars were placed on each animal and remained in place until removal on day 3. After a four-hour exposure period, the elastic wrap and gauze patch were removed from each animal... Residual test article was removed using gauze moistened with deionized water followed by dry gauze.

Results: At 1, 24, 48 and 72 hours scores for erythema ranged from 1 to 2 and scores for edema ranged from 1 to 2. On Day 7 all 3 rabbits scored 2 for erythema, and 1 or 2 for edema. At 21 days irritation had cleared in 2/3 rabbits, while the remaining rabbit scored 1 (very slight) for erythema and 1 (very slight) for edema. The PDIS (average of 1, 24, 48 and 72-hr scores) was 3.17.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (870.2600, formerly §81-6)

Product Manager: 23
MRID No.: 45000408

Reviewer: Byron T. Backus, Ph.D.

CITATION: Bonnette, K.L. XRM-5151: A Dermal Sensitization Study in Hartley Albino Guinea Pigs Modified Buehler Design. Final Report. SLI Study No. 3504.8; Dow Study No. 990115. Unpublished study prepared by Springborn Laboratories Inc. (SLI), Spencerville, OH 45887. Study Completion Date: October 7, 1999. MRID 45000408.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRM-5151; TSN 101724; Lot No. C0187-48; a clear amber liquid with a density of 0.96 g/mL containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient.

SPECIES: Guinea Pig, Hartley-derived albino

AGE (main sensitization study): Males: approx. 8 weeks old; Females: approx. 10 weeks old

WEIGHT(at initiation of induction): Males: 353-410 g; Females: 338-385 g

SOURCE: Hilltop Lab Animals Inc., Scottdale, PA

EXECUTIVE SUMMARY: *In a dermal sensitization study (MRID 45000408) using a modified Buehler design, a group of 10 male and 10 female Hartley-derived albino guinea pigs received a total of three six-hour induction exposures at one week apart, to 0.3 mL of undiluted XRM-5151 Lot No. C0187-48, a clear amber liquid containing 29.3% cyhalofop N-butyl ester (R-isomer) as the active ingredient. A control group of 5 males and 5 females remained unexposed.*

Two weeks after the last induction dose, all guinea pigs were challenged with a six-hour exposure to 25% w/v XRM-5151 in deionized water at a previously unused dermal site.

On challenge, 24- and 48-hour irritation scores ranged from 0 to + in both previously exposed (induced) guinea pigs as well as the unexposed controls.

The report includes a positive control study which utilized 1-Chloro-2,4-Dinitrobenzene (0.3 mL of 0.1% w/v DNCB in acetone/ethanol for induction, two 0.3 mL aliquots of 0.05% and 0.1% w/v DNCB in acetone/ethanol for challenge) which was completed on July 17, 1999. In addition, there is a second positive control study which utilized alpha-Hexylcinnamaldehyde (0.3 mL of 5% w/v in ethanol for induction, two 0.3 mL aliquots of 1% and 2.5% w/v alpha-HCA in acetone for challenge) which was completed on June 24, 1999. Both positive control studies showed appropriate responses.

There were no indications that the test material, XRM-5151 Lot No. C0187-48, a clear amber liquid containing 29.3% cyhalofop N-butyl ester (R-isomer) is a dermal sensitizer.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 6) and No Data Confidentiality (p. 2) statements were provided.

Procedure: For induction: "On the day prior to each dose administration, the guinea pigs had the hair removed with a small animal clipper. Care was taken to avoid abrading the skin during

the clipping procedures... A dose of 0.3 mL of the test article was placed on a Hilltop chamber backed by adhesive tape (occlusive patch). The chambers were then applied to the clipped surface as quickly as possible... The induction procedure was repeated on study day 7 and on study day 14 so that a total of three consecutive exposures were made to the test animals."

For challenge: "On the day prior to challenge dose administration, the test and challenge control animals were weighed and the hair was removed from the right side of the animals." On the following day (day 28) chambers containing (presumably 0.3 mL) 25% w/v XRM-5151 in deionized water were applied to a previously unused dermal site on the 10 male and 10 female guinea pigs which had been previously exposed, as well as the group of 5 male and 5 female guinea pigs which were previously unexposed controls.

Results: At 24 hours 6/10 males and 7/10 females scored \pm ; at 48 hours 3/10 males and 2/10 females scored \pm . All other previously induced guinea pigs scored zero. At 24 hours 4/5 control males and 1/5 control females scored \pm ; at 48 hours 2/5 males and 0/5 females scored \pm . All other control guinea pigs scored zero.

The report includes two positive control studies. One utilized 1-Chloro-2,4-Dinitrobenzene (0.3 mL of 0.1% w/v DNCB in acetone/ethanol for induction, two 0.3 mL aliquots of 0.05% and 0.1% w/v DNCB in acetone/ethanol for challenge) and was completed on July 17, 1999. The second positive control study utilized alpha-Hexylcinnamaldehyde (0.3 mL of 5% w/v in ethanol for induction, two 0.3 mL aliquots of 1% and 2.5% w/v alpha-HCA in acetone for challenge) and was completed on June 24, 1999. Both positive control studies showed appropriate responses.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D282260
2. **PC CODE:** 082583 Cyhalofop-butyl
3. **CURRENT DATE:** April 24, 2002
4. **TEST MATERIAL:** XRM-5151 Lot No. C0187-48 (active ingredient: 29.3% cyhalofop N-butyl ester [R-isomer]), a liquid with a specific gravity of 0.96. This is being used to support EPA File Symbol: 62719-GLA CLINCHER CA with a label claim of 29.6% Cyhalofop: 2-[4-(4-cyano-2-fluorophenoxy) phenoxy] propanoic acid, butyl ester, (R)

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/ Springborn Labs Inc./SLI Study No. 3504.4/Oct. 12 1999	45000239	Fischer 344 rats used; LD ₅₀ (M) = 1611.7 (95% c.i. : 975.4-2663.1) mg/kg; LD ₅₀ (F) > 2000 mg/kg; < 5000 mg/kg (all survived at 2000 mg/kg; all died at 5000 mg/kg). Dose levels: 500 (M only), 2000 & 5000 mg/kg. Symptoms included breathing difficulties, decreased defecation, rough haircoat, urine stain, dark material around the face, moderate to pronounced decreases in resistance to removal from the cage, decreases in extensor-thrust response, decreases in reaction to handling, and increased lacrimation. Animals which died also had hypothermia, hunched posture, decreases in muscle tone and a decrease in responsiveness to touch.	III	A
Acute dermal toxicity/rabbit/ Springborn Labs Inc./SLI Study No. 3504.5/Oct. 12 1999	45000242	LD ₅₀ > 5000 mg/kg (males, females, combined) with 0/10 rabbits dying after dosage at this dose level. No definite indications of systemic toxicity, but dermal irritation at the application site persisted to the end of the 14-day observation period.	IV	A
Acute inhalation toxicity/rat/ Health & Environmental Research Labs Dow Chemical/Laboratory Project ID 991080/May 26 1999	45000402	LC ₅₀ > 5.19 mg/L (0/5 F, 0/5 M died at this exposure level). Nose-only exposure. The mean MMAD was 1.78 µm and the mean GSD was 2.28. Following exposure symptoms included extensive body soiling, perinasal soiling, perineal soiling (urine and/or fecal), respiration abnormalities and decreased activity. By day 4 5/5 males and 4/5 females were normal; with all normal by day 7. Hand-held and open-field observations were non-specific, possibly related to the decreased activity. All rats had lost weight by day 4, but all had weight gains (from day 1 values) by day 11.	IV	A
Primary eye irritation/rabbit/ Springborn Labs Inc./SLI Study No. 3504.6/Oct. 6 1999	45000404	Corneal opacity in 3/3 eyes on day 7, with all irritation clearing by day 10.	II	A

Primary dermal irritation/rabbit/ Springborn Labs Inc./SLI Study No. 3504.7/Oct. 7 1999	45000406	PDIS = 3.17. 3 rabbits used; at 1, 24, 48, 72 hrs & 7 days scores for erythema ranged from 1-2, scores for edema ranged from 1-2. On day 21 irritation had cleared in 2/3 rabbits, while remaining rabbit scored 1 for erythema and 1 for edema.	III	A
Dermal sensitization/guinea pig/ Springborn Labs Inc./SLI Study No. 3504.8/Oct. 7 1999	45000408	Modified Buehler design: six-hour induction exposures at one week apart, to 0.3 mL of undiluted XRM-5151. A control group remained unexposed. Two weeks after the last induction dose, all guinea pigs were challenged with a six-hour exposure to 25% w/v XRM-5151 in deionized water at a previously unused dermal site. Challenge, 24- and 48-hour irritation scores ranged from 0 to \pm in both previously exposed (induced) guinea pigs as well as the unexposed controls.	No	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1)

Product Manager: 23
MRID No.: 45000237

Reviewer: Byron T. Backus, Ph.D.

CITATION: Kosaka, T. XRD-537: Acute Oral Toxicity Study in Rats. Laboratory Study No. GHF-R 260. Unpublished study prepared by Kodaira Laboratories, The Institute of Environmental Toxicology, Tokyo 187, Japan. Study Completion Date: January 13, 1992. MRID 45000237.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRD-537, Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; an off-white powder with a purity of 97.1%.

SPECIES: Rat, SD (Crj:CD), pathogen free

AGE(at dosing): 6 weeks

WEIGHT (fasted): Males: 157-170 g; Females: 131-144 g

SOURCE: Charles River Japan, Inc. (Shimofurusawa, Atsugi-shi, Kanagawa)

EXECUTIVE SUMMARY: *In an acute oral toxicity study (MRID 45000237), fasted (overnight) young adult (6 weeks old) SD (Crj:CD) rats (5 males and 5 females) were orally gavaged with 5000 mg/kg of XRD-537, Lot No. AGR-295713 (purity: 97.1%), administered as a suspension (257 mg/mL) in 1% Tween 80 aqueous solution. The dosing solution was administered at a constant volume of 20 mL/kg.*

There was no mortality. No symptoms were observed. All rats showed good body weight gains in the periods from day 0 to day 7 and from day 7 to day 14.

No abnormalities were found on gross pathological examination following terminal sacrifice.

Oral LD50 Male \geq 5000 mg/kg (no male rats died after being dosed at this level)

Oral LD50 Females \geq 5000 mg/kg (no female rats died after being dosed at this level)

Oral LD50 Combined \geq 5000 mg/kg (0/10 rats died after being dosed at this level)

XRD-537, Lot No. AGR-295713 (R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; purity 97.1%) is in toxicity category IV in terms of oral toxicity.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP Compliance (p. 3, 4), Quality Assurance (p. 6), and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1100): "A prescribed amount of the test substance was weighed and homogeneously suspended in 1% Tween 80 aqueous solution... The dosing solution was prepared to be administered at a constant volume of 20 mL/kg body weight. The concentration of the test substance in the test formulation was 257 mg/mL... Overnight fasting was conducted until the end of administration of the test substance to all animals. The test formulation was administered into the stomach by gavage using stomach tubes..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Total
5000	0/5	0/5	0/10

Observations: There were no mortalities. "No abnormal clinical signs were noted in any animals of both sexes." All rats showed good body weight gains in the periods from day 0 to day 7 and from day 7 to day 14.

Gross Necropsy: "There were no gross abnormalities at autopsy in any animals of both sexes 14 days after administration."

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1)

Product Manager: 23
MRID No.: 45000238

Reviewer: Byron T. Backus, Ph.D.

CITATION: Kosaka, T. XRD-537: Acute Oral Toxicity Study in Mice. Laboratory Study No. GHF-R 258. Unpublished study prepared by Kodaira Laboratories, The Institute of Environmental Toxicology, Tokyo 187, Japan. Study Completion Date: January 13, 1992. MRID 45000238.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRD-537, Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; an off-white powder with a purity of 97.1%.

SPECIES: Mouse, ICR (Crj:CD-1)

AGE(at dosing): 6 weeks

WEIGHT (fasted): Males: 30.8-35.2 g; Females: 21.7-25.3 g

SOURCE: Charles River Japan, Inc. (Shimofurusawa, Atsugi-shi, Kanagawa)

EXECUTIVE SUMMARY: *In an acute oral toxicity study (MRID 45000238), fasted (2 hour) young adult (6 weeks old) ICR (Crj:CD-1) mice (5 males and 5 females) were orally gavaged with 5000 mg/kg of XRD-537, Lot No. AGR-295713 (purity: 97.1%), administered as a suspension (257 mg/mL) in 1% Tween 80 aqueous solution. The dosing solution was administered at a constant volume of 20 mL/kg.*

There was no mortality. No symptoms were observed. All mice showed body weight gains in the periods from day 0 to day 7 and from day 7 to day 14.

No abnormalities were found on gross pathological examination following terminal sacrifice.

Oral LD50 Male \geq 5000 mg/kg (no male mice died after being dosed at this level)

Oral LD50 Females \geq 5000 mg/kg (no female mice died after being dosed at this level)

Oral LD50 Combined \geq 5000 mg/kg (0/10 mice died after being dosed at this level)

XRD-537, Lot No. AGR-295713 (R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; purity 97.1%) is in toxicity category IV in terms of oral toxicity.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP Compliance (p. 3, 4), Quality Assurance (p. 6), and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1100): "A prescribed amount of the test substance was weighed and homogeneously suspended in 1% Tween 80 aqueous solution... The dosing solution was prepared to be administered at a constant volume of 20 mL/kg body weight. The concentration of the test substance in the test formulation was 257 mg/mL... Animals were fasted from about 2 hours prior to the administration until the end of administration of the test substance to all animals. The test formulation was administered into the stomach by gavage using stomach tubes..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Total
5000	0/5	0/5	0/10

Observations: There were no mortalities. "No abnormal clinical signs were noted in any animals of both sexes." All mice showed body weight gains in the periods from day 0 to day 7 and from day 7 to day 14.

Gross Necropsy: "There were no gross abnormalities at autopsy in any animals of both sexes 14 days after administration."

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200, formerly §81-2)

Product Manager: 23
MRID No.: 45000241

Reviewer: Byron T. Backus, Ph.D.

CITATION: Stebbins, K.E. and K.J. Brooks. DE-537 N-Butyl Ester: Acute Dermal Toxicity Study in Fischer 344 Rats. Laboratory Project Study ID 981083. Unpublished study prepared by Health & Environmental Research Laboratories, The Dow Chemical Company, Midland MI 48674. Study Completion Date: July 6, 1998. MRID 45000241.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: DE-537 n-butyl ester; Reference No. AGR295713; containing 96.4% DE-537 n-butyl ester (no physical description of the test material is given in MRID 45000241; however, from information in MRIDs 45000237 and 45000238 XRD-537, Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; is reported as an off-white powder).

SPECIES: Rat, Fischer 344

AGE: Young adult (approximately 10 weeks old when dosed)

WEIGHT: Males: 224.6 - 242.8 g; Females: 143.3 - 146.3 g

SOURCE: Charles River Laboratories Inc., Raleigh, NC

EXECUTIVE SUMMARY: *In an acute dermal toxicity study (MRID 45000241), a group of 5M & 5F young adult (approximately 10 weeks old) Fischer 344 rats received a 24-hour occluded exposure to 5000 mg/kg DE-537 n-butyl ester, Reference No. AGR295713, containing 96.4% DE-537 n-butyl ester.*

There was no mortality; two males had chromodacryorrhea on test day 2 which was interpreted to not be treatment-related. There was no dermal irritation at the application site. One male and all five females lost weight in the period from day 1 to day 8, but all rats gained weight in the period from day 1 to day 15.

On post-sacrifice necropsy, there were no gross abnormalities.

Dermal LD50 Males > 5000 mg/kg (0/5 died at this dose level)

Dermal LD50 Females > 5000 mg/kg (0/5 died at this dose level)

Combined > 5000 mg/kg (0/10 rats died at this dose level)

DE-537 n-butyl ester, Reference No. AGR295713, containing 96.4% DE-537 n-butyl ester, is in toxicity category IV in terms of dermal toxicity.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 4), and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1200): "The dorsal side of the trunk of each rat was clipped free of fur the day prior to application of the test material. Five male and five female rats were treated with 5000 mg of test material per kg body weight. A gauze patch with cotton backing was used to hold the test material in place on the back of the rat and the patch was held in place with an Vetrap® and elastic tape. The size of the gauze/cotton was approximately 3 by 3 cm (approximately 10% of the surface area of the rats). The wrappings were removed

after approximately a 24-hour exposure period and observations were recorded for irritation at the application site. The skin was wiped thoroughly with a water moistened soft disposable towel and dried with a soft disposable towel..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: There was no mortality. It is stated on p. 11 of MRID 45000241 that: "There were no clinical signs indicative of systemic toxicity, and none of the rats had dermal irritation at the application site. Two males had chromodacryorrhea on test day two, which was interpreted to not be treatment-related." One male and all five females lost weight in the period from day 1 to day 8, but all rats gained weight in the period from day 1 to day 15.

Gross Necropsy: "There were no treatment-related gross pathologic observations."

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200, formerly §81-2)

Product Manager: 23
MRID No.: 45000240

Reviewer: Byron T. Backus, Ph.D.

CITATION: Kosaka, T. XRD-537: Acute Dermal Toxicity Study in Rats. Laboratory Study ID GHF-R 259. Unpublished study prepared by Kodaira Laboratories, Institute of Environmental Toxicology, Japan. Study Completion Date: January 13, 1992. MRID 45000240.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRD-537, Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; an off-white powder with a purity of 97.1%.

SPECIES: Rat, SD (Crj:CD), pathogen free

AGE(at exposure): 8 weeks [reported: not consistent with body weights, below]

WEIGHT: Males: 308-353 g; Females: 199-216 g

SOURCE: Charles River Japan, Inc. (Shimofurusawa, Atsugi-shi, Kanagawa)

EXECUTIVE SUMMARY: *In an acute dermal toxicity study (MRID 45000240), a group of 5M & 5F young adult (ostensibly 8 weeks old) SD (Crj:CD) rats received a 24-hour occluded exposure to 2000 mg/kg XRD-537, Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate (purity: 97.1%) under a filter paper moistened with distilled water.*

There was no mortality nor indications of systemic toxicity. The report does not indicate whether or not there was any dermal irritation. All rats gained weight in the period from day 0 to day 7 and again from day 7 to day 14.

On post-sacrifice necropsy, there were no gross abnormalities.

Dermal LD50 Males > 2000 mg/kg (0/5 died at this dose level)

Dermal LD50 Females > 2000 mg/kg (0/5 died at this dose level)

Combined > 2000 mg/kg (0/10 rats died at this dose level)

XRD-537, Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate (purity: 97.1%) is no worse than toxicity category III in terms of dermal toxicity. It is noted that the same material is in toxicity category IV in terms of dermal toxicity in the study in MRID 45000241.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP Compliance (p. 3 & 4), Quality Assurance (p. 9), and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1200): "On the day before the administration the back region of each animal was clipped and shaved. On the day of administration, a prescribed amount of the test substance was applied to the shaved 4 x 5 cm skin site together with a filter paper moistened with distilled water by a closed patch for 24 hours. Following the exposure period, the test substance remaining in contact with the skin sites was washed off with lukewarm water and neutral soap..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: There was no mortality. It is stated on p. 17 of MRID 45000240 that: "No abnormal clinical signs were noted in any animals of both sexes" and that "No body weight losses were found in any animals 7 and 14 days after the administration when compared with their body weights on the day of treatment."

Gross Necropsy: "There were no gross abnormalities at autopsy in any animals of both sexes 14 days after the administration."

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (870.1300, formerly §81-3)

Product Manager: 23
MRID No.: 45000401

Reviewer: Byron T. Backus, Ph.D.

CITATION: Ebino, K. XRD-537 BE: Acute Inhalation Toxicity Study in Rats. Laboratory Study ID IET 90-0179. Unpublished study prepared by Mitsukaido Laboratories, The Institute of Environmental Toxicology, Japan. Study Completion Date: January 17, 1994. MRID 45000401.

SUBMITTER: Dow AgroSciences

TEST MATERIAL:XRD-537 BE technical. Chemical name: R-(+)-n-Butyl-2-(4-(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, Lot No. AGR 295713, purity 96.0%. Described as a sticky white powder, which becomes fine after addition of SiO₂.H₂O. For the purposes of this study a pulverized mixture of 80 parts XRD-537 BE and 20 parts (w/w) white carbon was used.

SPECIES: Rat, Fischer (F344/DuCrj)

AGE(at exposure): approximately 8 weeks old

WEIGHT (at exposure): Males: 205 - 225 g; Females: 132 - 150 g;

SOURCE: Charles River Japan, Inc. (Atsugi Breeding Center, Kanagawa, Japan)

EXECUTIVE SUMMARY: *In an acute inhalation toxicity study (MRID 45000401), a group of 5 male and 5 female young adult (approximately 8 weeks old) Fischer 344 rats received a 4-hour whole-body exposure to a mean concentration (measured by HPLC analysis) of 5.63 mg/L of XRD-537 BE technical (containing 96% R-(+)-n-Butyl-2-(4-(2-fluoro-4-cyanophenoxy) phenoxy) propanoate) mixed (4:1 w/w) with white carbon (rats were exposed to a mean concentration of 1.80 mg/L white carbon in this study). The mean MMAD was 5.2 µm and the mean GSD was 2.4. A control group of 5M & 5F rats was exposed to white carbon only (1.92 mg/L, with a mean MMAD of 2.7 µm and a mean GSD of 3.0).*

There were no mortalities. Following exposure symptoms (occurring in all rats exposed to XRD-537 BE) included bradypnea, abnormal respiratory sounds and reddish mucous material in the nasorostral region. Rats were normal by day 2. In the vehicle control group reddish mucous material in the nasorostral region was observed in 2/5 M and 5/5 F at termination of exposure, but this sign had disappeared 2 hours later. All animals (exposed and controls) showed body weight increases on days 7 and 14.

There were no abnormal findings observed in any of the rats following post-sacrifice necropsy.

Inhalation LC50 Males > 5.63 mg/L (0/5 died)

Inhalation LC50 Females > 5.63 mg/L (0/5 died)

Combined LC50 > 5.63 mg/L (0/10 rats died)

The test material, XRD-537 BE technical (containing 96% R-(+)-n-Butyl-2-(4-(2-fluoro-4-cyanophenoxy) phenoxy) propanoate) is in toxicity category IV in terms of acute inhalation toxicity, based on the LC50 > 5.63 mg/L.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP (p. 3), Quality Assurance (p. 10) and No Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.1300): Exposure was whole body for 4 hours. "A pulverized mixture of 80 parts of XRD-537 BE technical and 20 parts (w/w)...white carbon was supplied by the sponsor and used as the test substance. The addition of the white carbon was necessary to enable pulverization to the required particle size... The test substance and the white carbon, which were pulverized by a jet air mill...were received and stored in an automatic desiccator...under dark, dry conditions at room temperature. The test substance and the white carbon were used for the study without further processing."

Two groups of rats were used. One was exposed to the test substance, and the other was exposed to a dust generated from the white carbon alone.

Mean Exposure Concentration mg/L (Analytically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0 ^a	0/5	0/5	0/10
5.63 ^b	0/5	0/5	0/10

^aRats were exposed to a mean atmospheric concentration of 1.92 mg/L white carbon; the nominal concentration of the white carbon was 6.60 mg/L

^bThe nominal concentration of XRD-537 BE was 19.98 mg/L; In addition rats were exposed to a mean concentration of 1.80 mg/L white carbon (total nominal concentration with white carbon: 25.42 mg/L).

Clinical Observations: There were no mortalities. Following exposure symptoms (occurring in all rats exposed to XRD-537 BE) included bradypnea, abnormal respiratory sounds and reddish mucous material in the nasorostral region. Rats were normal by day 2. In the vehicle control group reddish mucous material in the nasorostral region was observed in 2/5 M and 5/5 F at termination of exposure, but this sign had disappeared 2 hours later. All animals (exposed and controls) showed body weight increases on days 7 and 14.

Gross Necropsy: There were no abnormal findings observed in any of the rats following post-sacrifice necropsy.

Chamber Atmosphere		
Conc. (mg/L)	Mean MMAD (µm)	Mean GSD
0 ^a	2.7	3.0
5.63	5.2	2.4

^aRats were exposed to a mean atmospheric concentration of 1.92 mg/L white carbon

Chamber Environment^a	
Internal Chamber Volume	380 L
Mean Chamber Airflow	100 LPM
Temperature	25-26°C
Relative Humidity	45-55%

^aDuring exposure to XRD-537 BE

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (870.2400, formerly §81-4)

Product Manager: 23
MRID No.: 45000403

Reviewer: Byron T. Backus, Ph.D.

CITATION: Jones, J.R. XRD-537 BE: Primary Eye Irritation Test in the Rabbit. Laboratory Study ID 413/9. Unpublished study prepared by Safeparm Laboratories Ltd., Derby, U.K. Study Completion Date: October 20, 1993. MRID 45000403.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRD-537 BE, Batch No. DECO-26-42T; chemical name: R-(+)-n-Butyl-2-(4(2-fluoro-4-cyanophenoxy) phenoxy) propanoate; an off-white powder with a purity of 95.8%.

SPECIES: Rabbit, New Zealand White

AGE: Adult (12-16 weeks old)

WEIGHT: 2.46 - 2.96 kg

SOURCE: David Percival Ltd., Cheshire, UK

EXECUTIVE SUMMARY: *In a primary eye irritation study (MRID 45000403), a volume of 0.1 mL (approximately 70 mg) of XRD-537 BE, Batch No. DECO-26-42T (chemical name: R-(+)-n-Butyl-2-(4(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, an off-white powder with a purity of 95.8%) was instilled into the conjunctival sac of one eye of each of 6 New Zealand white rabbits.*

At one hour, one eye showed iritis, and an additional eye was positive for both redness and chemosis. There was no corneal opacity. At 24 hours and subsequently none of the eyes was positive for irritation (two eyes scored "1" for conjunctival redness). At 48 and 72 hours all eyes had completely cleared (all scores zero).

The test material, XRD-537 BE, Batch No. DECO-26-42T (chemical name: R-(+)-n-Butyl-2-(4(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, an off-white powder with a purity of 95.8%) is in toxicity category IV in terms of primary eye irritation potential, based on the lack of positive irritation effects at 24 hours.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3 and 5), Quality Assurance (p. 4) and No Data Confidentiality (p. 2) statements are provided.

Procedure (including deviations from 870.2400): "One rabbit was initially treated. A volume of 0.1 mL of the test material, which was found to weight approximately 70 mg...was placed into the conjunctival sac of the right eye... The upper and lower eyelids were held together for about one second immediately after application, to prevent loss of the test material... After consideration of the ocular responses produced in the first treated animal, five additional animals were treated. In order to minimise pain on instillation of the test material, one drop of local anaesthetic "Ophthaine", 0.5% proxymetacaine hydrochloride...was instilled into both eyes of four of these animals 1 - 2 minutes before treatment."

Results:

Observations	Number "positive"/number tested			
	1 hr	24 hrs	48 hrs	72 hrs
Corneal Opacity	0/6	0/6	0/6	0/6
Iritis	1/6	0/6	0/6	0/6
Conjunctivae:				
Redness ^a	1/6	0/6	0/6	0/6
Chemosis ^a	1/6	0/6	0/6	0/6
Discharge ^a	3/6	0/6	0/6	0/6

^aScore of 2 or more considered positive.

There is no indication within this report that sodium fluorescein was used as part of the eye irritation assessment.

Results: Two animals are reported as having an initial pain reaction to administration of the test substance. "Residual test material was noted around the treated eye of all animals one hour after treatment... No corneal effects were noted during the study... Iridial inflammation was noted in one treated eye one hour after treatment. No other iridial effects were noted... Moderate conjunctival irritation was noted in all treated eyes one hour after treatment. Minimal conjunctival redness was noted in two treated eyes at the 24-hour observation. No other conjunctival effects were noted."

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (870.2500, formerly §81-5))

Product Manager: 23
MRID No.: 45000405

Reviewer: Byron T. Backus, Ph.D.

CITATION: Jones, J.R. XRD-537 BE: Primary Dermal Irritation Test in the Rabbit. Laboratory Study ID 413/8. Unpublished study prepared by Safeparm Laboratories Ltd., Derby, U.K. Study Completion Date: October 20, 1993. MRID 45000405.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRD-537 BE, Batch No. DECO-26-42T; chemical name: R-(+)-n-Butyl-2-(4(2-fluoro-4-cyanophenoxy) phenoxy) propanoate; an off-white powder with a purity of 95.8%.

SPECIES: Rabbit, New Zealand White
AGE: Adult (approximately 12-16 weeks old)
WEIGHT: 2.01 - 2.41 kg
SOURCE: David Percival Ltd., Cheshire, UK

EXECUTIVE SUMMARY: *In a primary dermal irritation study (MRID 45000405), 0.5 g of XRD-537 BE, Batch No. DECO-26-42T (R-(+)-n-Butyl-2-(4(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, an off-white powder with a purity of 95.8%) moistened with 0.5 mL distilled water was applied to an intact skin site on the back of each of 6 New Zealand white rabbits, with 4-hr semi-occluded exposure.*

At 1 hour 1/6 rabbits scored "1" for erythema; the remaining 5 scored zero. All scores for edema were zero. All scores at 24, 48 and 72 hours. The PDIS (average of 1, 24, 48 and 72-hr scores) was 0.04. The test material, XRD-537 BE, Batch No. DECO-26-42T (R-(+)-n-Butyl-2-(4(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, an off-white powder with a purity of 95.8%) is in toxicity category IV in terms of dermal irritation potential, based on the effects observed in this study.

Study Classification: *Acceptable*

COMPLIANCE: Signed and dated GLP (p. 3 and 5), Quality Assurance (p. 4) and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.2500): "On the day before the test each of a group of six rabbits was clipped free of fur from the dorsal/flank area using veterinary clippers... On the day of the test a suitable test site was selected on the back of each rabbit. A quantity of 0.5 g of the test material, moistened with 0.5 mL of distilled water, was introduced under a 2.5 cm x 2.5 cm gauze patch and placed in position on the shorn skin. The patch was secured in position with a strip of surgical adhesive tape (BLENDERM: approximate size 2.5 cm x 4.0 cm). To prevent the animals [from] interfering with the patches, the trunk of each rabbit was wrapped in an elasticated corset (TUBIGRIP)... Four hours after application the corset and patches were removed from each animal and any residual test material removed by gentle swabbing with cotton wool in distilled water."

Results: At 1 hour 1/6 rabbits scored "1" for erythema; the remaining 5 scored zero. All scores for edema were zero. All scores at 24, 48 and 72 hours. The PDIS (average of 1, 24, 48 and 72-hr scores) was 0.04.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (870.2600, formerly §81-6)

Product Manager: 23
MRID No.: 45000407

Reviewer: Byron T. Backus, Ph.D.

CITATION: Johnson, I.R. DE-537 N-Butyl Ester: Delayed Contact Hypersensitivity Study in the Guinea Pig. Laboratory Study ID GHE-T-591. Unpublished study prepared by Huntingdon Life Sciences Ltd, Suffolk, England. Study Completion Date: January 11, 1996. MRID 45000407.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: DE-537 N-Butyl Ester; Batch No. AGR 276542; a light buff lumpy crystalline powder. According to information on p. 31 of MRID 45000407 the material assayed 99.5% w/w DE 537 N-Butyl

SPECIES: Guinea Pig, Dunkin-Hartley albino
AGE (main sensitization study): Males: 6-8 weeks old
WEIGHT(at initiation of induction): Males: 381-456 g
SOURCE: David Hall, Staffordshire, England

EXECUTIVE SUMMARY: *In a dermal sensitization study (MRID 45000407) using the Magnusson-Kligman Maximization Test, a group of 10 male Dunkin-Hartley albino guinea pigs received (on day 1) intradermal injections of Freund's Complete Adjuvant, 1% w/v DE-537 N-Butyl Ester, Batch No. AGR 276542 in propylene glycol and 1% w/v DE-537 N-Butyl Ester, Batch No. AGR 276542 in propylene glycol in the adjuvant. On day 7 the application site was treated with sodium lauryl sulphate, and on day 8 0.6 mL 50% w/v DE-537 in propylene glycol was applied topically with 48-hour occluded exposure. The same induction treatments using vehicle alone were conducted on a control group of 5 male guinea pigs.*

Two weeks after the last induction dose, all guinea pigs were challenged at three sites with 24-hour exposures to 0.03 mL vehicle, 0.03 mL 10% w/v DE-537 in propylene glycol, and 0.03 mL 50% w/v DE-537 in propylene glycol.

On challenge, the 50% w/v DE-537 in propylene glycol caused slight (grade 1) erythema in one test and one control animal at 24 hours only. The 10% w/v DE-537 did not cause any irritation response.

The report includes two positive control studies which utilized alpha-Hexylcinnamaldehyde; one of these studies was conducted in the period from May 4, 1995 to May 28, 1995 (according to the Quality Assurance Inspections - p. 6 of MRID 45000407 - the final report for the study with DE-537 was reviewed on October 17, 1995). This positive control study gave appropriate responses.

There were no indications that the test material, DE-537 N-Butyl Ester, Batch No. AGR 276542 is a dermal sensitizer.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP (p. 3 & 4), Quality Assurance (p. 6) and No Data Confidentiality (p. 2) statements were provided.

Procedure: For the first induction: "Three pairs of injections (0.1 mL) were made deep into the dermis, such that on either side of the dorsal median line there were three injection sites in a row parallel to the spinal column." At the anterior sites, injections were FCA (Freund's Complete Adjuvant); at the middle sites, injections were of test material in vehicle (1% w/v DE-537 in propylene glycol); at the posterior sites, injections were of test material in FCA (1% w/v DE-537 in FCA). For the second induction: "On Day 7, the clipped dorsa of all animals were subject to inunction with 0.5 mL w/v sodium lauryl sulphate in petrolatum... On Day 8, the dermal site overlying the scapulae were treated by topical application of 0.6 mL of a test material formulation to test animals, while controls received 0.6 mL of vehicle. Each dose was applied to a 4 x 2.5 cm absorbent patch (Whatman No. 3 filter paper) which was applied to the skin and covered by an occlusive dressing (Blenderm and Elastoplast) for 48 hours..."

For challenge: "Both flanks of all animals were clipped on Day 21. On Day 22 these areas were wet shaven to reveal a 5 x 5 cm area on the left flank and a 10 x 5 cm area on the right flank. Approximately one hour later the left site was treated by topical application of 0.03 mL of the vehicle while the right side received 0.03 mL of the maximum non-irritant concentration...[50%] to one site and a dilution [10%] to a second site. The doses were applied to 1 cm diameter absorbent patches...and covered by an occlusive dressing (Blenderm and Elastoplast) for 24 hours..."

Results: On challenge, the 50% w/v DE-537 in propylene glycol caused slight (grade 1) erythema in one test and one control animal at 24 hours only. The 10% w/v DE-537 did not cause any irritation response.

The report includes two positive control studies which utilized alpha-Hexylcinnamaldehyde; one of these studies was conducted in the period from May 4, 1995 to May 28, 1995 (according to the Quality Assurance Inspections - p. 6 of MRID 45000407 - the final report for the study with DE-537 was reviewed on October 17, 1995). This positive control study gave appropriate responses

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D282260
2. **PC CODE:** 082583 Cyhalofop-butyl
3. **CURRENT DATE:** April 24, 2002
4. **TEST MATERIAL:** XRD-537 Lot No. AGR-295713; R-(+)-n-butyl-2-[4-(2-fluoro-4-cyanophenoxy) phenoxy] propionate; an off-white powder with a purity of 97.1% (used for the studies in MRIDs 45000237, 45000238, 45000240); DE-537 n-Butyl Ester, Reference No. AGR295713 with a purity of 96.4% (used for the study in MRID 45000241); XRD-537 BE, Lot No. AFR 295713, chemical name: R-(+)-n-Butyl-2-(4-(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, purity 96.0% (used for the study in MRID 45000401); XRD-537 BE, Batch No. DECO-26-42T; chemical name: R-(+)-n-Butyl-2-(4-(2-fluoro-4-cyanophenoxy) phenoxy) propanoate, purity 95.8% (used for the studies in MRIDs 45000403 & 45000405); and DE 537 n-Butyl Ester, assaying 99.5% (used for the study in MRID 45000407).

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/Kodaira Labs Japan/Lab Study No. GHF-R-260/Jan. 13 1992	45000237	LD ₅₀ (M,F, combined) > 5000 mg/kg (0/10 rats died after dosage at this level). No symptoms observed, all rats had good body weight gains days 0-7, 7-14, no abnormalities on necropsy.	IV	A
Acute oral toxicity/mouse/Kodaira Labs Japan/Lab Study No. GHF-R-258/Jan. 13 1992	45000238	LD ₅₀ (M,F, combined) > 5000 mg/kg (0/10 mice died after dosage at this dose level). No symptoms observed, all mice had body weight gains days 0-7, 7-14. No abnormalities on necropsy.	IV	A
Acute dermal toxicity/rat/Kodaira Labs Japan/Lab Study No. GHF-R 259/Jan. 13 1992	45000240	LD ₅₀ (M,F, combined) > 2000 mg/kg (0/10 rats died after 24-hr dermal exposure to this dose level). No symptoms observed; no abnormalities following post-sacrifice necropsy.	III*	A
Acute dermal toxicity/rat/Health & Environmental Labs Dow Chemical/Lab Project Study ID 981083/July 6 1998	45000241	LD ₅₀ (M,F, combined) > 5000 mg/kg (0/10 rats died after 24-hr dermal exposure to this dose level). No definite symptoms observed; although 1M and 4F lost weight in the period from day 1 to day 8; no abnormalities following post-sacrifice necropsy.	IV	A
Acute inhalation toxicity/rat/Mitsukaido Laboratories Japan/Lab Study ID IET 90-0179/Jan. 17 1994	45000401	LC ₅₀ > 5.63 mg/L (0/5 F, 0/5 M died at this exposure level). Whole-body exposure. The mean MMAD was 5.2 µm and the mean GSD was 2.4. Following exposure symptoms included bradypnea, abnormal respiratory sounds and reddish mucous material around the nasorostral region. Rats were normal by day 2. No abnormal findings on post-sacrifice necropsy.	IV	A
Primary eye irritation/rabbit/Safepharm Labs Ltd. England/Lab Study ID 413/9 /Oct. 20 1993	45000403	At 1 hr 1/6 eyes was positive for iritis and 1/6 eyes was positive for conjunctival redness and chemosis. None of the eyes was positive for irritation on day 1.	IV	A

Primary dermal irritation/rabbit/ Safeparm Labs Ltd. England/ Lab Study ID 413/8 /Oct. 20 1993	45000405	PDIS = 0.04. 6 rabbits used; at 1 hr 1/6 scored "1" for erythema; all other rabbits scored zero. All rabbits scored zero for edema. All scores zero at 24, 48 & 72 hrs.	IV	A
Dermal sensitization/guinea pig/ Huntingdon Life Sciences Ltd. England/Laboratory Study ID GHE-T-591/Jan. 11 1996	45000407	Magnusson-Kligman Maximization Test: 10 Dunkin-Hartley albino males received 3 pairs of injections on day 1, including two of Freund's Complete Adjuvant, two of 1% w/v test material in propylene glycol and 1% w/v test material in propylene glycol in FCA. On day 7 application site was treated with sodium lauryl sulphate and on day 8 0.6 mL 50% w/v DE-537 in propylene glycol was applied with 48-hr exposure. Challenge was 24-hr exposure to 0.03 mL 50% DE-537 and 0.03 mL 10% DE-537 in propylene glycol. No indication of dermal sensitization.	No	A

Core Grade Key: **A** =Acceptable, **S** = Supplementary, **U** = Unacceptable, **V** = Self Validated

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100, formerly §81-1)

Product Manager: 23
MRID No.: 45000236

Reviewer: Byron T. Backus, Ph.D.

CITATION: Mizell, M.J., D.L. Eisenbrandt & J.E. Battjes. XRD-537 Methyl Ester: Acute Oral Toxicity Study in Sprague-Dawley Rats. Laboratory Project Study ID HET DR-0285-8062-001. Unpublished study prepared by Mammalian and Environmental Toxicology Research Laboratory, the Dow Chemical Company, Midland, MI 48674. Final Report Dated: September 26, 1988. MRID 45000236.

SUBMITTER: Dow AgroSciences

TEST MATERIAL: XRD-537 Methyl Ester; Sample Reference AGR 256056; a white solid with an average assay of $99.8 \pm 0.2\%$ propanoic acid: 2-(4-(4-cyano-2-fluorophenoxy) phenoxy)-, methyl ester, (R(+))-

SPECIES: Rat, Sprague-Dawley

AGE(at dosing): At least 9 weeks old

WEIGHT (fasted): Males: 267.3 - 282 g; Females: 170.7 - 174.0 g

SOURCE: Charles River Breeding Laboratories Inc., Kingston, NY

EXECUTIVE SUMMARY: *In an acute oral toxicity study (MRID 45000236), fasted (overnight) adult (at least 9 weeks old) Sprague-Dawley rats (5 males and 5 females) were orally gavaged with 5000 mg/kg of XRD-537 Methyl Ester (a white solid with an average assay of $99.8 \pm 0.2\%$ propanoic acid: 2-(4-(4-cyano-2-fluorophenoxy) phenoxy)-, methyl ester, (R(+))-. The XRD-537 Methyl Ester was administered as a 75% w/v suspension in corn oil:acetone (9:1).*

There was no mortality. The only symptom was lethargy, observed in two males at 2 hours post-dosage. All rats showed body weight gains in the periods from day 1 to day 7 and from day 7 to day 14.

No test-material related abnormalities were found on gross pathological examination following terminal sacrifice.

Oral LD50 Male ≥ 5000 mg/kg (no male rats died after being dosed at this level)

Oral LD50 Females ≥ 5000 mg/kg (no female rats died after being dosed at this level)

Oral LD50 Combined ≥ 5000 mg/kg (0/10 rats died after being dosed at this level)

XRD-537 Methyl Ester, Sample Reference AGR 256056; a white solid with an average assay of $99.8 \pm 0.2\%$ propanoic acid: 2-(4-(4-cyano-2-fluorophenoxy) phenoxy) - methyl ester, (R(+))-; is in toxicity category IV in terms of oral toxicity.

Study Classification: Acceptable

COMPLIANCE: Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 4), and No Data Confidentiality (p. 2) statements were provided.

Procedure (including deviations from 870.1100): "Five rats per sex received 5000 mg of the test material per kg body weight by single-dose gavage. The XRD-537 ME was administered as a 75% (w/v) suspension in corn oil:acetone (9:1). All animals were fasted the night before treatment..."

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Total
5000	0/5	0/5	0/10

Observations: There were no mortalities. "All animals were normal throughout the study, with the exception of two males which were lethargic two hours post-treatment... All animals gained weight throughout the observation period..."

Gross Necropsy: "One female rat had an incidental observation in the kidneys which was not treatment-related. All other tissues and animals were within normal limits at necropsy."

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D282260
2. **PC CODE:** 082583 Cyhalofop-butyl(? - but this was a study using methyl ester)
3. **CURRENT DATE:** April 24, 2002
4. **TEST MATERIAL:** XRD-537 Methyl Ester; Sample Reference AGR 256056; a white solid with an average assay of $99.8 \pm 0.2\%$ propanoic acid: 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)-, methyl ester, (R(+))-

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/ Mammalian & Environmental Toxicology Research Laboratory Dow Chemical/Lab Project Study ID HET DR-0285-8062-001/Sept. 26 1988	45000236	LD ₅₀ (M, F, combined) > 5000 mg/kg. No mortality among 5M, 5F rats receiving 5000 mg/kg. The only symptom was lethargy, observed in 2 males at 2 hours post-dosage. All rats showed body weight gains in the periods from day 1 to day 7 and from day 7 to day 14. No test-material related abnormalities were found on gross pathological examination following terminal sacrifice.	IV	A

Core Grade Key: **A = Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**