

6-15-90



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

008838

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCESMEMORANDUMSUBJECT: EPA Reg. No./File Symbol 241-GGRPursuit Plus EC

FROM: Sheila A. Moats ^{NY 6/6/90}
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C) ^{E 5/15/90}

TO: Taylor / Allen (PM 25)
Fungicide-Herbicide Branch
Registration Division (H75-05C)

APPLICANT: American Cyanamid Company
Agricultural Research Division
P.O. Box 400
Princeton, N.J. 08540

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
003 I <u>Imazethapyr</u>	<u>2.10</u>
454BB <u>pendimethalin</u>	<u>30.13</u>
Inert Ingredient(s):	<u>67.77</u>
Total	100.0%

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Background

The American Cyanamid Company submitted acute oral, dermal, inhalation, primary eye, + skin irritation and dermal sensitization studies to support registration of Pursuit Plus EC herbicide.

MRID nos used were 413981-03-08.

Recommendations

1. The acute toxicity studies submitted by American Cyanamid company are acceptable to RSB/JPRS.

2. No further acute toxicity tests are required.

Labeling

1. The "CAUTION" signal word is acceptable.

2. The Precautionary Statements are acceptable.

3. The Statement of Practical Treatment must also include the following additional information

"IF in Eyes": Flush eyes with plenty of water. Call a physician if irritation persists.

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

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Product Manager: (25) Reviewer: S. Moats
 MRID No.: 413981-03 Report Date: 6/5/90
 Testing Facility: American Cyanamid Co. Report No. T-0169
 Author(s): Lowe, Carolyn A.
 Species: Sprague Dawley strain - albino rats
 Age: 7-8 weeks Observation Days (Post
 Weight: 150 - 201 g. Exposure): (14); other ()
 Source: Charles River Labs. Inc. Wilmington MA.
 Test Material: PURSUIT PLUS.EC.
 Quality Assurance (40 CFR §160.12): Adequate.

Conclusion:

- LD₅₀ (mg/kg): Males = 3821 mg/kg (no calculable range); Females = 3247 (2073-4264) mg/kg. Combined = 3506 (2949-4045) mg/kg
- The estimated LD₅₀ is 3506 mg/kg
- Tox. Category: III. Classification: Guidelines

Procedure (Deviations From §81-1): Young adult ♂ + ♀ rats were administered an initial dose of 5000 mg/kg of the test material. Due to mortality at a 5000 mg/kg level, additional levels of 3750, 2500, & 1250 mg/kg were tested to define the LD₅₀. The test material was administered by oral gavage.

Results:

Reported Mortality

DOSAGE (mg./kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
5000	5/5	5/5	10/10
3750	2/5	3/5	5/10
2500	0/5	1/5	1/10
1250	0/5	0/5	0/10

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Symptomology & Gross Necropsy Findings:

The toxic signs ranged from salivation, diuresis, decreased activity, diuresis prostration, etc. Signs of toxicity generally occurred during the 1st, 24 & 48 hrs. following dosing. Recovery in the surviving animals was complete by day-3 following dosing. Gross necropsy findings ranged from congestion of the liver, lungs, & kidneys, hemorrhage & gas filled intestines, dark fluid filled urinary bladder, yellow staining of fur & fat, & blood around the nose, eyes & mouth. Surviving animals had yellow staining fur around the ano-genital area. 3

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

Product Manager: (25)
 MRID No.: 413981-04
 Testing Laboratory: American Cyanamid
 Author(s): Lowe, Carolyn A.
 Species: New Zealand Whites - albino
 Sex: ♂s + ♀s Wt.: 2190 - 3.270 kg.
 Test Material: Pursuit plus EC.
 Quality Assurance (40 CFR §160.12): Adequate.

Reviewer: S. Moats
 Report Date: 6/5/90
 Report No.: T-0163

Summary:

- LD₅₀ (mg/kg): Males = _____; Females = _____; Combined = > 2000 mg/kg;
- The estimated LD₅₀ is _____
- Tox. Category: III. Classification: Guidelines.

Procedure (Deviations from §81-2): ♂ + ♀ rabbits were dosed dermally with 2000 mg/kg. body wt. of the test substance. The test site was occluded with an elastic wrap + test material left in contact with the skin for 24 hrs. The occlusive wrap + remaining test material were removed at the end of the 24-hr. exposure period. The animals were observed for overt toxicity signs during the 14-day test period. Necropsies were performed on all the animals.

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

All test animals survived the 14-day observation period. Overt signs of toxicity included yellow staining, erythema, edema, atonia, small sores, dry flaking skin at dosing site, decreased activity, anorexia, + depression.

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (S81-3)

Product Manager: (25)
 MRID No.: 413981-05
 Testing Laboratory: Biosearch Inc.
 Author(s): Hershman, Richard J.
 Species: Sprague Dawley - rats
 Sex: ♂s + ♀s Weight: 208 - 301 g.
 Source: Buckshire Corp. Perkasie, PA.
 Test Material: Pursuit plus EC.
 Quality Assurance (40 CFR §160.12): Adequate.

Reviewer: S. Moats
 Report Date: 6/5/90
 Report No. 89-6696 A

Summary:

1. LC₅₀ (mg/kg): Males = _____; Females = _____; Combined = 75.54 mg/L.
2. The estimated LC₅₀ is _____
3. Mean Concentration: _____
4. Tox. Category: IV. Classification: Guidelines

Procedure (Deviations From S81-2): The test animals were housed individually in cages with a 230 L chamber + were exposed to the test article for 4 hr. The test article was administered as an aerosol generated by a nebulizer fed by a syringe pump. The air was passed through a dessicant prior to being passed through the test article. The rate of airflow, temp., + humidity were monitored + recorded every 30 min. Four dose levels were administered to determine the LC-50. Particle size was determined using an Andersen Sampler cascade impactor. Following the 4-hr exposure, the animals were returned to their cages + observed for a 14-day period.

Exposure Concentration (mg/L)	Reported Mortality (NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
4.55 mg/L.	0/10	1/10	1/20
4.58 mg/L.	1/10	0/10	1/10
4.87 mg/L.	1/10	0/10	1/10
5.54 mg/L.	2/10	1/10	3/10

Symptomology & Gross Necropsy Findings:

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Approx: 58% of the collected particulates at the various exposure levels were 2.1 µm or smaller.

All animals appeared normal throughout the 4-hr. exp.

Gross necropsy findings showed no abnormalities, except for dark red patches in lung areas + stained f.

Dose	Hour	Stage	Size Range µm.	Cumulative %
5.54 mg/L.	2	a	0.7 - 1.1	17.32
		b	1.1 - 2.1	62.12
	3	a	0.7 - 1.1	17.14
		b	1.1 - 2.1	59.73

$$MMA D = 5.54 \pm 0.47.$$

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DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (25) Reviewer: S. Moats
 MRID No.: 413981-06 Report Date: 6/6/90
 Testing Laboratory: American Cyanamid Co Report No. T-0161
 Author(s): Lowe, Carolyn A.
 Species: New Zealand Whites - Rabbits
 Sex: 8's Weight:
 Source: Skippack Farms, Pennsylvania
 Dosage: 0.4g
 Test Material: Pursuit Plus E.C.
 Quality Assurance (40 CFR §160.12): Adequate

Summary:

Tox. Category: III Classification: Guidelines.

Procedure (Deviation From §81-4): A dose of 0.1ml of test material was instilled into the conjunctival sac of the left eye of each of 6 rabbits. The right eye served as the untreated control. The eyes were examined at the following intervals: pre-treatment (-4 hrs) 1 hr, 24 hrs, 48 hrs, 72 hrs, 4 days & 7 days. Draize scale for evaluation of eye irritation was used for Results: scoring.

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	6/6	5/6	5/6	4/6	0/6		
Iris	0/6	0/6	0/6	0/6	0/6	0/6		
Conjunctivae Redness	0/6	5/6	5/6	5/6	4/6	0/6		
Chemosis	6/6	5/6	5/6	5/6	4/6	0/6		
Discharge	6/6	3/6	1/6	1/6	0/6	0/6		

Comments: Corneal involvement or irritation cleared in 7 days or less.

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DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: (25) Reviewer: S. Moats
 MRID No.: 413981-07 Report Date: 6/6/90
 Testing Laboratory: American Cyanamid Report No. T-0162
 Author(s): Lowe, Carolyn A. Co.
 Species: New Zealand Whites - rabbits.
 Age: Young adults
 Sex: M.
 Weight: _____
 Dosage: 0.5 ml.
 Test Material: Pursuit plus E.C.
 Quality Assurance (40 CFR §160.12): Adequate

Summary:

The Primary Irritation Index = 0.96

Toxicity Category: IV

Classification: Guidelines.

Procedure (Deviations From §81-5): Six animals were used for the study. The test site was prep on each animal by clipping the trunk free of hair. Two test: one control + one treated were selected on opposite side the dorsal mid-line. 0.5 ml of the test material was applied a 1" square gauze patch + placed on the intact skin. The patches were wrapped + the wraps were removed after 4-hour exposure. The animals were examined for irritation as follows: 4, 24, 48, 72 hrs, 4, 7, 10, 15, 17 + 21 days.

Results:

No overt signs of toxicity were observed during the study period. + all animals survived the 21-day observation period.

The calculated primary irritation index was 0.96 — The test material causes mild or slight irritation to rabbits.

Special Comments:

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DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (25)
 MRID No.: 413981-08
 Testing Laboratory: Dawson Research Corp
 Author(s): Murchison, Thomas E.
 Species: Harlan Sprague Dawley - Guinea Pigs
 Sex: males Weight: 332-473 g.
 Source: Harlan Sprague Dawley, Haslett, Michigan
 Test Material: Pursuit Plus 3EC
 Positive Control Material: Dinitro chlorobenzene (DNCB)
 Quality Assurance (40 CFR §160.12): Adequate
 Method: Open Epicutaneous.

Summary:

1. This product is / is not a dermal sensitizer.
2. Classification: Guidelines

Procedure (Deviation From §81-6): Based on a dose range study
 material was selected for dosing. 50% concentration of the test
 induction + challenge phases. 35 guinea pigs were used
 each animal was clipped of hair + 0.4 ml of the test mate
 formulation was applied to a gauze patch + placed on
 application site. The test sites were occluded + approx.
 hours later, the occlusive wraps + patches were remo
 + residual material rinsed off. The application sites were
 examined + scored for erythema + edema at 24 + 4
 after dosing (1) Test Group. 10 ♂s were treated with 0.4 ml
 of the test article formulation.
 (2) Positive Control Gp. 10 ♂s were trea
 with 0.4 ml of 0.1 DNCB in 50% ethanol. (3) Naive Control

10 ♂s were untreated + unclipped until Day + 32.
 (4) Naive Positive Control Gp. Five ♂s were untreated
 + unclipped until Day + 32. A 25% concentration of Pursuit was us
 for the challenge phase since it was the highest non-irritating
 Foll: the final dose on Day + 19, the animals remained
 untreated for 2 wks. On Day 33 + a challenge dose
 of the test material was administered to each anima
 in the test + naive control gps. The positive control +
 naive positive control gps. were given a single applic
 of the DNCB as in the induce phase. After the 48-hr. obs
 all the animals were euthanized + discarded.

Results. A 50% concentration of Pursuit caused
 irreversible skin damage, + the concentration was lower
 to 25%. The 25% concentration did not produce derm
 sensitiz in any guinea pig.

The positive control DNCB is a skin sensitiz
 in guinea pigs.

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