6-15-90

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 241-GGR
Pursuit Plus EC

FROM: Sheila A. Moats
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

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.
003I Fmazethapyr	2.10
454BB Pendimethalin	30.13
Inert Ingredient(s):	67.77
Total	100.0%

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188

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/PRS.

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.

7

008838

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

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 - 201g. Exposure): (14); other ( )
Source: Charles River Labs. Inc. Wilmington MA.
Test Material: PURSUIT Plus EC.
Quality Assurance (40 CFR §160.12): Adequate.

Conclusion:

1. LD_{50} (mg/kg): Males = 3821 mg/kg (no calculable range); Females = 3247 (2073-4264) mg/kg. Combined = 3506 (2949-4045) mg/kg.
2. The estimated LD_{50} is
3. 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 the 5000 mg/kg level, additional levels of 3750, 2500 & 1,250 mg 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.

Symptomology & Gross Necropsy Findings:

The toxic signs ranged from salivation, diuresis, decr 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 bladders, yellow staining of fur & fat, & blood around the nose, eyes & mouth. Surviving animals had yellow staining fur around the ano-genital area. 3

008838

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

Product Manager: (25) Reviewer: S. Moats
MRID No.: 413981-04 Report Date: 6/5/90
Testing Laboratory: American Cyanamid Report No.: T-0163
Author(s): Lowe, Carolyn. A.
Species: New Zealand Whites - albino.
Sex: ♂s + ♀s. Wt.: 2.190 - 3.270 kg.
Test Material: Pursuit plus EC.
Quality Assurance (40 CFR §160.12): Adequate.

Summary:

1. LD_{50} (mg/kg): Males = ; Females = ; Combined = > 2000 mg/kg;
2. The estimated LD_{50} is
3. Tox. Category: III. Classification: Guidelines.

Procedure (~~Deviations from §81-2~~): ♂s + ♀s rabbits were dosed dermally with 2000 mg/kg. body wt. of the test substance. The test site was occluded with an plastic 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 sizes, dry flaking skin at dosing site, decreased activity, anorexia, & depression.

008838

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

Product Manager: (25)
MRID No.: 413981-05
Testing Laboratory: Biosearch Inc.
Author(s): Hershman, Richard. J.
Species: Sprague Dawley - rats.
Sex: ♂s + ♀s. Weight: 209 - 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. 89-6690A

Summary:

1. LC_{50} (mg/kg): Males = ____; Females = ____; Combined = 75.54 mg/L.
2. The estimated LC_{50} is ____
3. Mean Concentration: ____
4. Tox. Category: IV. Classification: Guidelines

Procedure (Deviations From §81-2): 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 thru a dessicant prior to being passed thru 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.

Reported Mortality

Exposure Concentration (mg/L)	(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:

Approx: 58% of the collected particulates at the various exposure levels were 2.1 um or smaller.
All animals appeared normal throughout the 4-hr. exposure. Gross necropsy findings showed no abnormalities, except for dark red patches in lung areas & stained fur.

Dose	Hour	Stage	Size Range um	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

MMAD = 5.54 ± 0.47.

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: 6 ♂s. Weight:
Source: Skippack Farms, Pennsylvania.
Dosage: 0.1 g.
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 (-4hrs) 1 hr, 24 hrs, 48 hrs, 72 hrs, 4 days + 7 days. Draize scale for evaluation of eye irritation was used for scoring.

Results:

	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.

008838

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

Product Manager: (25)
MRID No.: 413981-07
Testing Laboratory: American Cyanamid Co.
Author(s): Lowe, Carolyn A.
Species: New Zealand Whites - rabbits.
Age: Young adults
Sex: ♂s.
Weight:
Dosage: 0.5 ml.
Test Material: Pursuit plus E.C.
Quality Assurance (40 CFR §160.12): Adequate

Reviewer: S. Moats
Report Date: 6/6/90
Report No. T-0162

Summary:

The Primary Irritation Index = 0.96

Toxicity Category: IV

Classification: Guidelines.

Procedure (Deviations From §81-5): Six ♂ animals were used for th 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 afte 4-hour exposure. The animals were examined for irri 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:

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

Product Manager: (25) Reviewer: S. Moats
MRID No.: 413981-08 Report Date: 6/6/90
Testing Laboratory: Dawson Research Corp Report No. DRC-4915
Author(s): Murchison, Thomas E.
Species: Harlan Sprague Dawley - Guinea Pigs.
Sex: males Weight: 332-473g.
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 50% concentration of the test material was selected for dosing. 35 guinea pigs were used for induction + challenge phases. The mid-dorsal region of each animal was clipped of hair + ~4 ml of the test material formulation was applied to a gauze patch + placed on application site. The test sites were occluded + approx. 6 hours later, the occlusive wraps + patches were removed + residual material rinsed off. The application sites were examined + scored for erythema + edema at 24 + 48 hrs 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 treated 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 used for the challenge phase since it was the highest non-irritating conc. Foll. the final dose on Day +19, the animals remained untreated for 2 wks. On Day 33 + challenge dose of the test material was administered to each animal in the test + naive control gps. The positive control + naive positive control gps. were given a single applic. of the DNCB as in the induct. phase. After the 48-hr. obsc. all the animals were euthanized + discarded.

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

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