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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAR 18 1986

MEMORANDUM

SUBJECT: EPA File Symbol 241-EUP-RRR
PSPM61 Herbicide (Formulation A)

EPA File Symbol 241-EUP-RRR
PSPM61 Herbicide (Formulation B)

FPOM: Mary L. Waller
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

TC: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (TS-767C)

Applicant: American Cyanamid Company
Agricultural Research Division
P.O. Box 400
Princeton, NJ 08540

261404
262404

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Formulation A

ACTIVE INGREDIENTS:	
Imazaquin (Ammonium salt of 2-[4,5-dihydro-4-methyl-4-(3-methyl-5-oxo-1H-imidazol-2-yl)-3-quinolinecarboxylic acid]	4.0%
Pendimethalin (N-1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine	22.6%
INERT INGREDIENTS	73.4%

Formulation B

ACTIVE INGREDIENTS:	
Imazaquin (Ammonium salt of 2-[4,5-dihydro-4-methyl-4-(1-methyl-5-oxo-1H-imidazol-2-yl)-3-quinolinecarboxylic acid]	4.8%
Pendimethalin (N-1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine	29.0%
INERT INGREDIENTS	66.2%

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BACKGROUND:

The applicant has submitted two batteries of data consisting of an acute oral, acute dermal, primary skin irritation, and eye irritation studies for each product. The applicant has also requested a waiver of the acute inhalation and dermal sensitization studies for each product. The studies were conducted by American Cyanamid Company. The data Accession Number is 261404. The type of support was not indicated.

RECOMMENDATION:

FHB/TSS findings are as follows:

1. The acute oral, acute dermal, primary skin irritation and eye irritation studies submitted on each product (Formulation A & B) are acceptable to support registration.
2. FHB/TSS will not waive the requirement for an acute inhalation and dermal sensitization for each product, and the registrant must supply both studies for each product. The studies referenced to support the waivers were conducted on each active ingredient. In regard to the acute inhalation study, the Proposed Guidelines on Testing state that the end-use product shall be tested to support registration of an end-use product. In regard to the dermal sensitization study, since neither active ingredient is a sensitizer, the registrant must test each product (Formulation A and B).
3. The signal word for Formulation A is "DANGER" and the signal word for Formulation B is "WARNING."
4. The Product Manager should inform the registrant that when future primary eye irritation scores are conducted, individual eye irritation scores for redness, chemosis, and discharge should be provided.

NOTE TO PM

FHB/TSS considers the two formulations different products. Each product contains a different percentage of the two active ingredients and contains different inert ingredients. Therefore, if at a later date the registrant chooses to register both products under section 3, different registration numbers should be assigned to Formulation A and B.

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REVIEW: Formulation A

1. Acute Oral Toxicity Study: American Cyanamid Company; Report No. A86-1; January 13, 1986.

PROCEDURE:

Four groups of 5 male and 5 female Charles River rats were fasted for 18 hours and later were dosed with 25 to 75 percent w/v aqueous dispersion of test material as follows: 2500, 3750, 5000 and 7500 mg/kg. An additional 5 females were dosed at the 3750 mg/kg level. Animals were observed daily for 14 days and were weighed at start of study, on day 7 and at termination of study. Gross necropsy was performed on all animals.

RESULTS:

No deaths occurred at 2500 mg/kg. At 3750 mg/kg, 2/5 males and 7/10 females died. At 5000 mg/kg, 3/5 males and 3/5 females died. At 7500 mg/kg, all males and females died. The LD₅₀ for males was reported to be 4330 (3193-5872) mg/kg. The LD₅₀ for females was reported to be 3695 (2614-4744) mg/kg. The combined LD₅₀ was reported to be 3951 (3340-4638) mg/kg.

Toxic symptoms observed were decreased activity, ataxia, prostration, dyspnea, diuresis, and comatose condition. Gross necropsy revealed pale or dark or congested condition of liver, congested kidneys, hemorrhagic lungs, liquid-filled bladder, atrophic condition of testes, hemorrhagic condition of scrotal sac and intestines and gas-filled intestines. No abnormalities were noted in animals dosed at 2500 mg/kg.

STUDY CLASSIFICATION:

Core Guideline Data

TOXICITY CATEGORY:

Category III - CAUTION

2. Acute Dermal Toxicity Study: American Cyanamid Company, Report No. A86-1; January 13, 1986.

PROCEDURE:

Five male and five female albino rabbits were shaved and 24 hours later, 2000 mg/kg of test material was applied to

the test site under occlusive wrap. After 24 hours, the test site was wiped with a moistened pad. Animals were observed daily for 14 days to note toxic symptoms. All animals were submitted to gross necropsy.

RESULTS:

One male exhibited diarrhea and died on day 5. Cause of death was reported to be unrelated to treatment. No other toxic symptoms were noted. The LD₅₀ was reported to be > 2000 mg/kg. At gross necropsy, the animal that died during the study exhibited congested and gas-filled intestinal tract, hemorrhagic lungs, dark liver and congested kidneys. No abnormalities were noted in the other test animals.

STUDY CLASSIFICATION:

Core Guideline Data

TOXICITY CATEGORY:

Category III - CAUTION

3. Primary Dermal Irritation Study: American Cyanamid Company; Report No. A86-1; January 13, 1986.

PROCEDURE:

Six albino rabbits were shaved and 24 hours later 0.5 cm of test material/test site were applied under occlusive wrap to an abraded and an intact test site on each animal. After exposure, the test site was wiped clean. Skin irritation was scored at 24 and 72 hours.

RESULTS:

Skin irritation at the intact skin test sites were scored as follows: at 24 hours 5/6 animals exhibited slight erythema, 1/6 exhibited slight edema; and at 72 hours, 5/6 animals exhibited slight erythema. Skin irritation at the abraded skin test sites were scored as follows: at 24 hours, 3/6 animals exhibited slight erythema, 3/6 exhibited moderate erythema and 5/6 exhibited slight edema; and at 72 hours, 5/6 animals exhibited slight erythema and 1/6 exhibited slight edema. The primary irritation score was reported to be 1.29.

STUDY CLASSIFICATION:

Core Guideline Data

TOXICITY CATEGORY:

Category IV - CAUTION

4. Primary Eye Irritation: American Cyanamid Company;
Report A86-1; January 13, 1986.

PROCEDURE:

Six New Zealand White rabbits received 0.1 ml of test material instilled in the conjunctival sac of the right eye which was held shut for 5 seconds. The left eye served as control. After 24 hours of exposure, the treated eye was rinsed with tap water. Eye irritation was scored.

RESULTS:

Eye irritation was scored as follows: at 24 hours, corneal opacity (1/6 = 40, 1/6 = 20, 2/6 = 15, 2/6 = 5), conjunctivae irritation (cumulative score for redness, chemosis, and discharge) (4/6 = 16, 2/6 = 14); at day 7, corneal opacity (1/6 = 20), conjunctivae irritation (3/6 = 2); at 14 days, corneal opacity (1/6 = 10), conjunctivae irritation (1/6 = 4) and at day 23, corneal opacity (1/6 = 20) and 1 animal still exhibited moderate vascularization of the cornea.

STUDY CLASSIFICATION:

Core Minimum Data - See comments under Recommendation.

TOXICITY CATEGORY:

Category I - DANGER

REVIEW: Formulation B

1. Acute Oral Toxicity Study: American Cyanamid Company;
Report No. A86-2; January 13, 1986.

PROCEDURE:

Four groups of 5 male and 5 female Charles River rats were fasted for 18 hours and later were dosed with a 25 to 75 percent w/v aqueous dispersion of the test material as follows: 2500, 3750 and 5000 mg/kg. Two additional groups of

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5 males each were dosed with 3150 and 7500 mg/kg. One additional group of 5 females was dosed with 1250 mg/kg. Animals were observed daily for 14 days and weighed at start of study, on day 7 and at study termination. Gross necropsy was performed on all animals.

RESULTS:

At 7500 and 3750 mg/kg, 5/5 males died. At 5000 and 3750 mg/kg, 5/5 females died. At 5000 mg/kg, 4/5 males died. At 3150 mg/kg, 2/5 males died. At 2500 mg/kg, 2/5 males and 2/5 females died. At 1250 mg/kg no deaths occurred among the females. The LD₅₀ for males was reported to be 3132 (1828-3994) mg/kg. The LD₅₀ for females was reported to be 2679 (1908-3763) mg/kg. The combined LD₅₀ was reported to be 2901 (2288-3374) mg/kg.

Toxic symptoms observed were decreased activity, prostration, ataxia, diuresis, dyspnea and comatose condition. Gross necropsy revealed dark liver, congested kidney, hemorrhagic lungs, hemorrhagic areas of the stomach, and blood-filled bladder.

STUDY CLASSIFICATION:

Core Guideline Data

TOXICITY CATEGORY:

Category III - CAUTION

2. Acute Dermal Toxicity Study: American Cyanamid Company; Report No. A86-2; January 13, 1986.

PROCEDURE:

Five male and five female albino rabbits were shaved and 24 hours later, 2000 mg/kg of test material was applied to the test site under occlusive wrap. After 24 hours, the test site was wiped with a moistened pad. Animals were observed daily for 14 days to note toxic symptoms. All animals were submitted to gross necropsy.

RESULTS:

No deaths occurred. The LD₅₀ was reported to be > 2000 mg/kg. No toxic symptoms were noted. Gross necropsy revealed pale lungs in one male.

STUDY CLASSIFICATION:

Core Guideline Data

TOXICITY CATEGORY:

Category III - CAUTION

3. Primary Skin Irritation Study: American Cyanamid Company;
Report No. A86-2; January 13, 1986.

PROCEDURE:

Six albino rabbits were shaved and 24 hours later 0.5 gm of test material/test site were applied under occlusive wrap to an abraded and an intact test site on each animal. After exposure, the test site was wiped clean. Skin irritation was scored at 24 and 72 hours.

Results:

Skin irritation at the intact skin test sites were scored as follows: at 24 hours, 3/6 animals exhibited slight erythema; at 72 hours, 1/6 animals exhibited slight erythema. Skin irritation at the abraded skin test sites were scored as follows: at 24 hours, 5/6 animals exhibited slight erythema and 1/6 exhibited slight edema; at 72 hours, 1/6 animals exhibited slight erythema. The primary irritation score was reported to be 0.46.

STUDY CLASSIFICATION:

Core Guideline Data

TOXICITY CATEGORY:

Category IV - CAUTION

4. Primary Eye Irritation Study: American Cyanamid Company;
Report No. A86-1; January 13, 1986.

PROCEDURE:

Six New Zealand White rabbits received 0.1 ml of test material instilled in the conjunctival sac of the right eye which was held shut for 5 seconds. The left eye served as control. After 24 hours of exposure, the treated eye was rinsed with tap water. Eye irritation was scored.

RESULTS:

Eye irritation was scored as follows: at 24 hours, corneal opacity (6/6 = 20), conjunctivae irritation (cumulative score for redness, chemosis and discharge) (1/6 = 20, 4/6 = 18, 1/6 = 16); at day 7, corneal opacity (1/6 = 40, 4/6 = 10, 1/6 = 5), conjunctivae irritation (2/6 = 8, 2/6 = 6, 1/6 = 4); at day 21, all irritation had cleared.

STUDY CLASSIFICATION:

Core Minimum Data - See comment under Recommendation.

TOXICITY CATEGORY:

Category II - WARNING

LABELING:FORMULATION A

1. Change signal word to "DANGER."
2. Move statement of practical treatment for eye exposure to front panel and place near signal word and child hazard warning. Include the sentence "Call a physician."
3. Include the following sentence in the statement of practical treatment:

If swallowed, drink promptly a large quantity of milk, egg whites, gelatin solution, or, if these are not available, drink large quantities of water. Avoid alcohol.

4. Additional labeling comments may be necessary upon submission of acute inhalation and dermal sensitization data.
5. The subheading "STORAGE AND DISPOSAL" and information below the subheading should appear either at the end of the Directions for Use or under the violation statements which follows the heading "DIRECTIONS FOR USE."

FORMULATION B

1. The subheading "STORAGE AND DISPOSAL" and information below the subheading should appear either at the end of the Directions for Use or under the violation statements which follows the heading "DIRECTIONS FOR USE."
2. Additional labeling comments may be necessary upon submission of acute inhalation and dermal sensitization data.

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Pendimethalin/
Imazaquin toxicology review

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Pages 9 through 17 are not included in this copy.

The material not included contains the following type of information:

- Identity of product inert ingredients
 - Identity of product impurities
 - Description of the product manufacturing process
 - Description of product quality control procedures
 - Identity of the source of product ingredients
 - Sales or other commercial/financial information
 - A draft product label
 - The product confidential statement of formula
 - Information about a pending registration action
 - FIFRA registration data
 - The document is a duplicate of page(s) _____
 - The document is not responsive to the request
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• The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
