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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

September 18, 2002

MEMORANDUM

Product Name: HEADLINE EC FUNGICIDE
EPA File Symbol: 7969-RIA
DP Barcode: D285393
Case No: 068823
Submission: S621522
Chemical: 099100 Pyraclostrobin

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

To: Cynthia Giles-Parker, PM 22
Fungicide Branch
Registration Division (7505C)

Registrant: BASF Corporation

ACTION REQUESTED: "Please review rebuttal to acute tox review. The company has requested that the Agency change the signal word from DANGER to WARNING."

BACKGROUND:

According to information received by TRB, this product [EPA File Symbol 7969-RIA Headline EC Fungicide] has the following label ingredient declaration:

Active Ingredient:
Pyraclostrobin.....23.6%
Inert Ingredients.....76.4%

The proposed product was the subject of a previous TRB review (dated 30 July 2001). In that review TRB essentially did secondary reviews of the Canadian Pest Management Regulatory Agency (PMRA) primary reviews.

In the Canadian PMRA primary reviews the proposed product was placed in toxicity category I for eye irritation potential and in toxicity category II for dermal irritation potential on the basis of the findings in the studies in MRIDs 45118312 and 45118315, respectively. These categorizations were accepted in the TRB review of 30 July 2001.

The registrant has responded (letter dated August 21, 2002) with additional information regarding both studies, and is requesting that the product be placed in toxicity category II in terms of eye irritation potential and in toxicity category III in terms of dermal irritation potential.

COMMENTS AND RECOMMENDATIONS:

1. After an examination of the BASF response to the Acute Eye Irritation study (MRID 45118312) review, this reviewer concurs that the toxicity category by this exposure route should be revised from I to II. The only positive effect observed at 7 days was an iridial score of 1 in 1/6 rabbits, and all eyes had completely cleared (all scores zero) by day 14. Toxicity category II for eye irritation is defined in 40CFR (156.10) as "Corneal opacity reversible within 7 days, irritation persisting for 7 days." In the December 27, 1996 edition of the Label Review Manual, Toxicity Category I for eye irritation is defined as: "Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days." and Category II is defined as: "Corneal involvement or irritation clearing in 8-21 days."

   The following is a revised Executive Summary for MRID 45118312:

EXECUTIVE SUMMARY: ***In a primary eye irritation study (MRID 45118312), 0.1 mL of Headline EC (BAS 500 00 F, Lot/Batch # 97-2, 24.1% pyraclostrobin), a brown liquid, was instilled into the conjunctival sac of one eye of each of 6 New Zealand white rabbits.***

Corneal opacity was observed in all 6 eyes at 24, 48 and 72 hours. It had cleared in all eyes by day 7. All eyes were also positive for conjunctival effects at 24, 48 and 72 hours. All eyes were positive for iridial irritation at 24 and 48 hours, as were 3/6 eyes at 72 hours. All corneal opacity had cleared by day 7, and none of the eyes were positive for conjunctival effects (although all eyes scored 1 for redness and/or chemosis on this date). The only positive effect on day 7 was an iritis score of "1" in 1/6 eyes. All scores were zero by day 14.

The test material, Headline EC (BAS 500 00 F, Lot/Batch # 97-2, 24.1% pyraclostrobin), a brown liquid, is in toxicity category II in terms of primary eye irritation potential, based on the occurrence of corneal opacity which had cleared by day 7, as well as the persistence of iritis in 1/6 eyes which had cleared by day 14.

Study Classification: Acceptable

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2. After an examination of the BASF response to the Dermal Irritation study (MRID 45118315) review, this reviewer concludes that the formulation should remain in toxicity category II by this exposure route. At 72 hours 5/6 rabbits scored "3" for erythema (1/6 scored "2") while 4/6 rabbits scored "1" for edema (2/6 scored zero). The P.I.I. for 72 hours was 3.5. In the December 27, 1996 edition of the Label Review Manual, Toxicity Category II for dermal irritation is defined as "Severe irritation at 72 hours (severe erythema or edema." and Category III is defined as: "Moderate irritation at 72 hours (moderate erythema)." The scoring system for acute dermal irritation is somewhat equivocal (in OPPTS 870.2500 moderate to severe erythema is scored as "3"); the registrant's response of August 21, 2002 states, in part: "The main findings at 24, 48 and 72 hours after application, which are the time points to be used for evaluation, were moderate to marked erythema and very slight to slight edema..." "Marked" would be somewhat more than "moderate." This reviewer also notes that 5/6 of the sites still scored "2" (very slight to well-defined) for erythema on day 14, and this persistence suggests that toxicity category II labeling would be more appropriate for this exposure route.

3. The following would then be the revised acute toxicity profile for 7969-RIA:

Acute Oral LD50	Acceptable	Tox. Cat. II (MRID 45118303)
Acute Dermal LD50	Acceptable	Tox. Cat. III (MRID 45118306)
Acute Inhalation LC50	Acceptable	Tox. Cat. IV (MRID 45118309)
Primary Eye Irritation	Acceptable	Tox. Cat. II (MRID 45118312)
Primary Dermal Irritation	Acceptable	Tox. Cat. II (MRID 45118315)
Dermal Sensitization	Acceptable	Negative (MRID 45118318*)

*Note: the MRID # for the dermal sensitization study is given as 54118318 in the PMRA primary review, but that number is inconsistent with the other MRID numbers.

4. The appropriate signal word for this product would then be WARNING. The precautionary labeling below was generated using the Label Review System using the assumption that the product would fall under WPS, but as this reviewer did not have a CSF and a copy of the proposed label uses some of the statements (particularly those relating to WPS exposure and type of gloves) are probably incomplete:

PRODUCT ID #: **007969-00186**

PRODUCT NAME: HEADLINE EC FUNGICIDE

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

SPANISH SIGNAL WORD: 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.)

Hazards to Humans and Domestic Animals:

May be fatal if swallowed. Causes skin irritation. Causes substantial but temporary eye injury. Harmful if absorbed through skin. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Do not get on skin or on clothing. Wear long-sleeved shirt and long pants, socks, chemical-resistant footwear, and chemical-resistant gloves. Remove and wash contaminated clothing before reuse. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Avoid contact with skin, eyes or clothing. Wear long-sleeved shirt and long pants, socks, shoes, and chemical-resistant gloves.

When mixing and loading wear a chemical resistant apron.

First Aid:

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

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

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - 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.

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.