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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

30/MAY/2000

MEMORANDUM

Subject:	File Symbol/EPA Reg. No.:	100-618	CGA-64250 Technical
	DP Barcode:	D266154	
	Case No:	037683	
	PC Code:	122101	
From:	Eugenia McAndrew, Biologist Technical Review Branch Registration Division (7505C)		
To:	Mary Waller, PM Team 21 Fungicide Branch Registration Division (7505C)		
Applicant:	Novartis Crop Protection, Inc. P.O. Box 18300 Greensboro, NC 27419-8300		

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
122101	Propiconazole	95
	Inert Ingredient(s):	5
	Total:	100%

ACTION REQUESTED: PM requests review of a dermal sensitization study which has been reported under FIFRA Section 6 (a) (2).

BACKGROUND: Novartis Crop Protection, Inc. has submitted a dermal sensitization study for Agency review in accordance with the FIFRA 6 (a) (2) reporting requirements. The product is EPA Reg. No. 100-618, CGA-64250 Technical. MRID # is 44949501. The study was conducted at Toxicology, Novartis Crop Protection AG, Stein, Switzerland.

In a letter dated October 13, 1999, Dr. Ed Chow, Novartis toxicologist, wrote:

> In a recent skin sensitization study (test no. 993101 performed at the test laboratories of Novartis Crop Protection AG in Stein, Switzerland) conducted to satisfy regulatory requirements for the European Union, propiconazole technical was found to show a moderately positive response based on the study's grading criteria...
>
> The finding of potential sensitization...is considered of very limited relevance to human health...This compound is also not known to be associated with any sensitization in humans under actual conditions of handling and use in more than ten years of commercial application.

RECOMMENDATIONS: The dermal sensitization study has been reviewed and is classified as acceptable. The results of the study show that the product is considered to be a dermal sensitizer.

The acute toxicity profile for EPA Reg. No. 100-618 is revised to include:

dermal sensitization	A sensitizer	Acceptable

LABELING: Based on the results of this dermal sensitization study, the following precautionary statement should be added to the label for this product according to the Label Review System.

Date: 05/30/00 LABEL REVIEW SYSTEM

ID #: 000100-00618 CGA-64250 TECHNICAL

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENT:

Prolonged or frequently repeated skin contact may cause allergic reaction in some individuals.

2

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (870.2600)

Product Manager: 21
MRID No.: 44949501

Reviewer: Eugenia McAndrew
Study Completion Date: September 7, 1999
Study No.: 993101

Testing Facility: Toxicology, Novartis Crop Protection AG
Author: Dr. E. Sommer

Quality Assurance (40 CFR §160.12): Included

Test Material: CGA 64250 tech.; 92.4% Propiconazol; Batch No. OP.303011; clear, brownish viscous liquid
Positive Control Material: Mercaptobenzothiazole (MBT)
Species: Guinea pig; albino; Himalayan Spotted [GOHI Ibm: GOHI (SPF)]
Age: Young adult (approximately 1-2 months)
Weight: Males: 320-414 g Females: 337-431 g
Source: RCC Ltd., Biotechnology & Animal Breeding Division, Switzerland
Method: Maximization Test

Conclusion:

1. **This product is a dermal sensitizer.**
2. **Classification**: Acceptable

Procedure (Deviations from 870.2600): None

Procedure: Pre-tests were conducted to determine the correct intradermal and epidermal concentrations for induction and challenge. For the induction, 20 test and 10 control animals were first treated with 6 intradermal injections each. The test animals were exposed to 0.1 mL of 5.0% test substance and the control animals to 0.1 mL of peanut oil which served as the vehicle. On day 8, the animals were treated with one topical application with the test animals receiving 0.4 g of undiluted test substance and the control animals receiving 0.4 g of vaseline vehicle. The dressings were held in place for 48 hours and reactions were scored one hour after patch removal. For the challenge on day 21, animals of both groups were treated with 0.35 mL of 30% test material and 0.35 mL of vaseline vehicle applied topically to two different sites. Reactions were scored 24and 48 hours after patch removal.

Results: After epidermal induction, positive skin reactions were noted for all animals in the test substance group. There were no positive skin reactions in the vehicle control group. Following challenge, 6/20 test animals scored positive at 24 hours and 10/20 at the 48 hour examination. In addition, desquamation was seen in 6/20 at 48 hours. The vehicle control group had no positive reactions. A positive control study using MBT was conducted within six months of the main study to validate the test system. The results were appropriate.

3

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D266154
2. **PC CODE:** 122101
3. **CURRENT DATE:** 30/May/00
4. **TEST MATERIAL:** CGA 64250 tech.; 92.4% Propiconazol; Batch No. OP.303011; clear, brownish viscous liquid

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Dermal sensitization/guinea pig Toxicology, Novartis Crop Protection AG/993101/9-7-99	44949501	A sensitizer	–	A

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