

3-5-90



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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 00-601

Metalaxyl Technical

FROM: William S. Woodrow WSW 3-2-90
Precautionary Review Section
Registration Support Branch E 3/5/90
Registration Division (H7505C)

TO: Chambliss/Lewis (PM 21)
Fungicide - Herbicide Branch
Registration Division (H7505C)

APPLICANT: Ciba-Geigy Corp.
P.O. Box 18300
Greensboro, NC 27419

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt.
<u>Metalaxyl: N-(2,6-dimethylphenyl)-N-</u> <u>(methylhexyl) alanine methyl ester</u>		<u>90.0</u>
<u>Inert Ingredient(s):</u>		<u>10.0</u>
Total		100.0%

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1/16

BACKGROUND

A letter of April 4, 1989 from Karen Stumpf of Ciba-Geigy reported draft labeling changes for Ciba-Geigy METALAXYL TECHNICAL (EPA Reg. NO. 100-601), which were stated to be in accordance with the labeling requirements set fourth in the Metalaxyl Registration Standard Ciba-Geigy received Oct. 6, 1988.

Among the label changes made was revision of the signal word from WARNING to CAUTION "with accompanying changes in the Precautionary Statements and creation of a Statement of Practical Treatment. According to Ciba-Geigy, "this change is precipitated by a review of the existing studies which the Agency has deemed acceptable"; Metalaxyl was originally designated Tox Category III for eye irritation. The Co. states that this particular eye study, in fact, indicated minimal irritation clearing within 4 days with no corneal opacity.

Woodward obtained a copy of the

original eye study (# 00084108, Ciba-Geigy, Basle Switzerland - no study date), and reviewed this study.

Woodrow reviewed a battery of acute toxicity and genetic studies conducted using Technical CGA-48988 (Ridomil), EPA #100-ANR (Technical Metolaxyl), which contained a ^{second} primary eye-irritation study. Woodrow's reviews of 11-27-78 and 11-8-78 Concerned Petition #892121 and EPA #100-FUP-62, respectively. The CGA-48988 Technical chemical - EPA #100-ANR also refers to Ciba-Geigy submission; to register Ridomil.

RECOMMENDATION

- 1) Primary eye-irritation studies performed using N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester (Metolaxyl Technical):
 - a. Eye irritation study called "original" by Ciba-Geigy correspondence; # 00084108 - reviewed by Woodrow 3-1-90: (Lab. # S155 5388)

Results

Toxicity Category - III, Classification - Core Guidelines (Corneal involvement and irritation absent by day 4). First reviewed by Woodrow 5-13-76, and again 3-2-90.

b. Eye irritation study performed using CIBA-GEIGY CGA-48988 (Technical Metalaxyl), submitted in connection with Ridomil registration. Woodrow 11-8/27-1978:

Results

Toxicity Category II, Classification - Core Guidelines-

"6 unwashed eyes - Moderate corneal opacity and conjunctival redness with 5 recovered and one persisting by day 7. All injuries were reversed by day 10."

2) Based on the Ciba-Geigy primary eye irritation study conducted using the Metalaxyl technical chemical, reviewed by Woodrow 11-8/27-1978, the #100-601 product signal word must remain "WARNING".

LABELING

- 1) A WARNING signal word is appropriate.
- 2) Under Precautionary Statements, state the following:

"Causes eye injury. Do not get in eyes or on clothing. Wear goggles, face shield, or safety glasses."

- 3) The Statement of Practical Treatment section, e.g., "If swallowed... etc," should come under the heading "Statement of Practical Treatment".

ADDITIONAL RECOMMENDATION COMMENT:

- 3) Since we have two acceptable acute eye irritation Toxicity Categories, representing two separate acute eye studies, we must use the most restrictive signal word; in this case the word must be "WARNING".

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

009279

Product Manager: (21)

Reviewer: London
M. Waller

MRID No.: 00034103

Report Date: 3-1-70

Testing Laboratory: Ciba-Geigy, Basle, Switz.

Report No. 5153-5385

Author(s): L. Vilmann

Species: Rabbit, Russian strain

Sex: 3M + 3F

Weight: 1.5-2.0 kg.

Source: not given

Dosage: 0.1 g

Test Material: g

Quality Assurance (40 CFR §160.12):

Summary:

Tox. Category: III Classification: Guidelines

Procedure (~~Deviation From §81-4~~): 0.1 g test material placed in conjunctival sac (lax) of 3M+3F rabbits - 30 sec. after treat. inst. Treated eyes of 3 rabbits washed in 10ml water. Eye irritation scored on Days 1, 2, 3, 4 & 7, according to the Draize system.

Results:

3 unwashed eyes:

Observations

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

Total score
(calculated AL)

8.33

8.66

4.00

Comments: The treated, and washed eyes, of 3 rabbits, did not show any harmful effects; all irritation scores = zero. Unwashed: Corneal involvement absent by Day 4, irritation also absent by Day 4.

NOTE: This is the "original Metabaxyl Technical eye study."

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