

US EPA ARCHIVE DOCUMENT

3-5-90

375C

009279



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 F 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>90.0</u>
<u>(methylhexyl) alanine methyl ester</u>	
<u>Inert Ingredient(s):</u>	<u>10.0</u>
Total	100.0%

BEST AVAILABLE COPY

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 Toxic 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.

Wardlaw 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-EUR-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 - Care 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)
 MRID No.: 00034103
 Testing Laboratory: Ciba-Geigy, Basle, Switz.
 Author(s): L. Villmann
 Species: Rabbit, Russian strain
 Sex: 2M + 3F
 Source: not given
 Dosage: 0.1 g
 Test Material: J
 Quality Assurance (40 CFR §160.12):

Reviewer: ^{London} M. Waller
 Report Date: 3-1-70
 Report No. 5153-5285

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 treatment, 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 Opacity		3/3	3/3	2/3	0/3	0/3		
Iris		0/3	0/3	0/3	0/3	0/3		
Conjunctivae Redness		3/3	3/3	2/3	0/3	0/3		
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."

BEST AVAILABLE COPY 6