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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

13/MAR/2001

MEMORANDUM

Subject:	EPA Reg. No./ File Symbol:	264-ATE	Charter brand PB Fungicide
	DP Barcode:	D272014	
	Case No:	068199	
	PC Code:	125620, 079801	
From:	Eugenia McAndrew, Biologist Technical Review Branch Registration Division (7505C)		
To:	Summer Gardner-Jenkins, PM Team 21 Fungicide Branch Registration Division (7505C)		
Applicant:	Aventis CropScience 2 T.W. Alexander Drive Research Triangle Park, NC 27709		

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
125620	Triticonazole	1.25
079801	Thiram	12.50
	Inert Ingredient(s):	86.25
	Total:	100.00%

ACTION REQUESTED: PM requests review of acute toxicity data for EPA File Symbol 264-ATE, Charter brand PB Fungicide.

BACKGROUND: Aventis CropScience has submitted a six pack of acute toxicity studies in support of registration of EPA File Symbol 264-ATE, a new product known as Charter brand PB Fungicide. MRID # are 450428-02 to -07. The studies were conducted at WIL Research Laboratories, Inc., Ashland, Ohio. The product contains two active ingredients - triticonazole and thiram. The triticonazole is pending registration.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable.

The acute toxicity profile for EPA File Symbol 264-ATE is as follows:

acute oral toxicity	III	Acceptable	MRID 45042802
acute dermal toxicity	III	Acceptable	MRID 45042803
acute inhalation toxicity	II	Acceptable	MRID 45042804
primary eye irritation	IV	Acceptable	MRID 45042805
primary skin irritation	IV	Acceptable	MRID 45042806
dermal sensitization	Yes	Acceptable	MRID 45042807

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System.

ID #: 000264-00672 Charter brand PB Fungicide

AGRICULTURAL USE REQUIREMENTS:

DIRECTIONS FOR USE:

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, wear: coveralls over long-sleeved shirt and long pants, socks, shoes and waterproof gloves.

SIGNAL WORD: WARNING AVISO

PRECAUTIONARY STATEMENTS:

May be fatal if inhaled. Harmful if swallowed or absorbed through skin. Avoid contact with eyes, skin or clothing. Do not breathe spray mist. For handling activities during [insert applicable terms based on direction for use: airblast mistpower, pressure greater than 40 p.s.i. with fine droplets, smoke, mist, fog, aerosol or direct overhead] exposures, wear either a respirator with an organic vapor (OV) cartridge, or a canister with any N, P, R, or HE prefilter. For

all other exposures, wear a dust/mist/filtering respirator (MSHA/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N, P, R, or HE prefilter. Wear long-sleeved shirt and long pants, socks, shoes and waterproof gloves. Prolonged or frequently repeated skin contact may cause allergic reaction in some individuals. Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing and wash clothing before reuse.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

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 by mouth to an unconscious person.

IF ON SKIN OR CLOTHING: 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 INHALED: Move person to fresh air. If person is not breathing, cali 911 or ambulance, then give artificial respiration, preferably mouth-to-mouth, if possible. Call a poison control center or doctor for further treatment advice

USER SAFETY RECOMMENDATIONS:

Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing and wash clothing before reuse.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100)

Product Manager: 21
MRID No.: 45042802

Reviewer: Eugenia McAndrew
Study Completion Date: October 15, 1999
Study No.: WIL-21187

Testing Facility: WIL Research Laboratories, Inc.
Author: Tom G. Kern, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid
Species: Rat; albino; Crl:CD(SD)IGS BR
Age: 8 to 10 weeks
Weight (fasted): Males: 273-299 g; Females: 198-227 g
Source: Charles River Laboratories, Raleigh, NC
Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 2000 mg/kg
   Females: > 2000 mg/kg
   Combined: > 2000 mg/kg
2. **The estimated LD_{50} is** > 2000 mg/kg
3. **Tox. Category:** III **Classification:** Acceptable

Procedure (Deviations from 870.1100): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: All animals survived and gained weight during the 14-day observation period. Clinical signs included hypoactivity and clear ocular discharge in all animals and decreased defecation in one male on day 3. All animals appeared normal by day 4.

Gross Necropsy: No gross findings.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200)

Product Manager: 21
MRID No.: 45042803

Reviewer: Eugenia McAndrew
Study Completion Date: October 15, 1999
Study No.: WIL-21188

Testing Facility: WIL Research Laboratories, Inc.
Author: Tom G. Kern, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid
Species: Rat; albino; Crl:CD(SD)IGS BR
Age: 9 to 11 weeks
Weight (fasted): Males: 268-337 g; Females: 222-258 g
Source: Charles River Laboratories, Raleigh, NC

Dermal LD_{50} Testing:

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 2000 mg/kg
   Females: > 2000 mg/kg
   Combined: > 2000 mg/kg
2. **The estimated LD_{50} is** > 2000 mg/kg
3. **Tox. Category:** III **Classification:** Acceptable

Procedure (Deviations from 870.1200): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: All animals survived and gained weight during the 14-day observation period. All animals had pink staining at the dose sites. Clinical signs included desquamation at 8/10 test sites and focal eschar at 6/10 sites persisting through the end of the study in three animals.

Gross Necropsy: No gross findings.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (870.1300)

Product Manager: 21
MRID No.: 45042804

Reviewer: Eugenia McAndrew
Study Completion Date: November 30, 1999
Study No.: WIL-21186

Testing Facility: WIL Research Laboratories, Inc.
Author: Charles E. Ulrich. B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid administered as a liquid droplet aerosol

Species: Rat; albino; Crl:CD(SD)IGS BR
Age: 8 to 10 weeks
Weight (fasted): Males: 278-282 g; Females: 240-246 g
Source: Charles River Laboratories, Kingston, NY

Conclusion:

1. **LC_{50} (mg/L):**
   Males: > 0.4 mg/L
   Females: > 0.4 mg/L
   Combined: > 0.4 mg/L
2. **The estimated LC_{50} is** > 0.4 mg/L
3. **Tox. Category:** II **Classification**: Acceptable

Procedure (Deviations from 870.1300): None

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0.4[a]	0/5	0/5	0/10

[a] "The 0.4 mg/L concentration was the maximum obtainable concentration with the test article while maintaining a respirable aerosol particle size."

Clinical Observations: All animals survived the 4-hour exposure. Three animals lost weight during the first three days after exposure but eventually gained weight by the end of the 14-day observation period. "No clinical signs of toxicity were observed immediately following exposure or during the 14-day exposure period."

Necropsy Findings: One male had dark red areas on the lungs.

Chamber Atmosphere		
Gravimetric conc.	**MMAD**	**GSD**
0.4 mg/L	3.7 μm	3.21

Chamber Environment[a]	
Chamber Volume	7.5 L
Airflow	9.7 LPM
Temperature	21°C
Relative Humidity	59%

[a] Nose only

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (870.2400)

Product Manager: 21
MRID No.: 45042805

Reviewer: Eugenia McAndrew
Study Completion Date: October 15, 1999
Study No.: WIL-21190

Testing Facility: WIL Research Laboratories, Inc.
Author: Tom G. Kern, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid
Dosage: 0.1 mL
Species: Rabbit; albino; New Zealand White
Age: Young adult
Sex: 1 male and 2 females
Weight: 2.6 - 2.9 kg
Source: Covance Research Products, Inc., Denver, PA
Conclusion:

1. **Toxicity Category:** IV
2. **Classification**: Acceptable

Procedure (Deviations from 870.2400): None

Unwashed eyes:

Observations	Number "positive"/number tested					
	Hours				Days	
	1	24	48	72	4	7
Corneal Opacity	0/3	0/3	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3	0/3	0/3
Conjunctivae:						
Redness*	0/3	1/3	1/3	0/3	0/3	0/3
Chemosis*	3/3	3/3	1/3	0/3	0/3	0/3
Discharge*	0/3	0/3	0/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

Summary: Conjunctivitis (chemosis and redness) was observed in 3/3 eyes one hour after installation of test material resolving by 72 hours.

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (870.2500)

Product Manager: 21
MRID No.: 45042806

Reviewer: Eugenia McAndrew
Study Completion Date: October 15, 1999
Study No.: WIL-21189

Testing Facility: WIL Research Laboratories, Inc.
Author: Tom G. Kern, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid
Dosage: 0.5 mL
Species: Rabbit; albino; New Zealand White
Age: Young adult
Sex: 2 males and 1 female
Weight: 3.3 - 3.5 kg
Source: Covance Research Products, Inc., Denver, PA

Conclusion:

1. **Toxicity Category:** IV
2. **Classification**: Acceptable

Procedure (Deviations from 870.2500): None

Results: Primary Dermal Irritation Index = 0.3 Very slight erythema was noted at the three test sites one hour after patch removal. No other irritation was observed.

Special Comments: Length of exposure was 4 hours. Application sites were evaluated at 30-60 minutes and 24, 48 and 72 hours after patch removal.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (870.2600)

Product Manager: 21
MRID No.: 45042807

Reviewer: Eugenia McAndrew
Study Completion Date: November 17, 1999
Study No.: WIL-21191

Testing Facility: WIL Research Laboratories, Inc.
Author: Tom G. Kern, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid
Positive Control Material: Hexylcinnamaldehyde (HCA)
Species: Guinea pig; albino; [Crl:(HA)BR]
Age: Young adult
Weight: Males: 368-428 g; Females: 333-421 g
Source: Charles River Laboratories, Portage, MI
Method: Buehler

Conclusion:

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

Procedure (Deviations from 870.2600): None

Procedure: Preliminary irritation testing was conducted to determine the correct concentrations for induction and challenge. For the induction, 0.4 mL of undiluted test substance was applied to 20 test animals under occlusion for a period of six hours. The procedure was repeated once a week for three weeks for a total of three applications. Reactions were scored 24 and 48 hours after each induction. The animals rested for two weeks. For the challenge, 0.4 mL of undiluted test substance was applied to a naive site on each animal and to 10 naive control animals using the same procedures. Two weeks after the initial challenge, a rechallenge was performed in which the test article was administered to previously unexposed sites on the test and naive control animals. Reactions were scored 24 and 48 hours after the challenge and rechallenge applications. A positive control study using HCA was conducted concurrently with the main study.

Results: Very slight erythema was noted at 10/20 test animal sites during the induction phase. Following the challenge, very slight erythema was noted at 6/20 test animal sites and slight erythema (grade 1) at one site at the 24-hour observation. At 48 hours, very slight erythema remained at two sites and slight erythema at the one site. In the naive control group, 1/10 sites had very slight erythema at 24 hours. Following the rechallenge, 3/20 test animals had slight erythema and 11/20 had very slight erythema at the 24-hour observation. At 48 hours, one moderate (grade 2), four slight and 11 very slight reactions were noted. In the naive control group, one very slight dermal reaction was noted at 24 hours. No dermal reactions were noted at 48 hours. Based on these results, the test article was sensitizing to guinea pigs under the conditions of this study. The results for the HCA positive control study were appropriate.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D272014
2. **PC CODE:** 125620, 079801
3. **CURRENT DATE:** 13/MAR/2001
4. **TEST MATERIAL:** EXP 81096A; Lot Number 16STGX62; 12.92% thiram and 1.29% triticonazole; bright pink, opaque liquid

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat WIL Research Laboratories, Inc. WIL-21187/10-15-99	45042802	LD_{50} > 2000 mg/kg (males females combined)	III	A
Acute dermal toxicity/rat WIL Research Laboratories, Inc. WIL-21188/10-15-99	45042803	LD_{50} > 2000 mg/kg (males females combined)	III	A
Acute inhalation toxicity/rat WIL Research Laboratories, Inc. WIL-21186/11-30-99	45042804	LC_{50} > 0.4 mg/L (males females combined)	II	A
Primary eye irritation/rabbit WIL Research Laboratories, Inc. WIL-21190/10-15-99	45042805	Conjunctivitis in 3/3 eyes resolving by 72 hours.	IV	A
Primary dermal irritation/rabbit WIL Research Laboratories, Inc. WIL-21189/10-15-99	45042806	PDIS = 0.3 No irritation at 72 hours.	IV	A
Dermal sensitization/guinea pig WIL Research Laboratories, Inc. WIL-21191/11-17-99	45042807	A sensitizer	--	A

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