

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

February 12, 1997

MEMORANDUM

Subject: EPA File Symbol: 10182-URA / ICIA5504 80WG
DP Barcode: D224546
Case No: 046875

From: Ian Blackwell, Biologist
Precautionary Review Section
Registration Support Branch
Registration Division (7505W)

ILB

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

Applicant: Zeneca Inc.
Agricultural Products
1800 Concord Pike
Wilmington, DE 19850-5458

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
azoxystrobin	80
<u>Inert Ingredient(s):</u>	<u>20</u>
Total:	100%

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BACKGROUND: Zeneca Ag Products has submitted a complete set of acute toxicity studies in support of "ICIA5504 50WG Fungicide". The studies were conducted by Zeneca's Central Toxicology Laboratory. The MRID numbers are 439354-02 through 439354-07.

RECOMMENDATIONS:

Each of the studies is acceptable to support the registration of the product.

The acute toxicity profile for file symbol 10182-URA is currently:

acute oral toxicity	III	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity	IV	acceptable
primary eye irritation	III	acceptable
primary skin irritation	IV	acceptable
dermal sensitization	nonsensitizer	acceptable

LABELING:

ID #: 010182-00416 ICIA5504 80WG

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 and chemical resistant footwear and waterproof gloves.

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Wear long-sleeved shirt and long pants, socks and shoes and waterproof gloves. Wash thoroughly with soap and water after handling.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

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IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. If person is unconscious, do not give anything by mouth and do not induce vomiting.

OR

IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger, or if available by administering syrup of ipecac. If person is unconscious, do not give anything by mouth and do not induce vomiting.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: 22
MRID No.: 439354-02

Reviewer: Ian Blackwell
Study Completion Date: 8/25/95
Report No.: CTL/P/4709

Testing Laboratory: Zeneca Central Toxicology Laboratory
Author: L. Bugg, H.J. Connolly

Quality Assurance (40 CFR §160.12): Included

Test Material: ICIA5504; "brown solid"; EPA file symbol 10182-URA

Species: Wistar, albino rats
Weight: males = 219-251 g; females = 200-206 g
Source: Barrired Animal Unit
Age: young adult

Summary:

- LD₅₀ (mg/kg):** Males > 2000
Females > 2000
Combined > 2000
- The estimated LD₅₀ is greater than 2000 mg/kg.
- Tox. Category:** III **Classification:** acceptable

Procedure (Deviation From §81-2):

Results:

Reported Mortality

DOSAGE	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000 mg/kg	0/5	0/5	0/10

Observations: No significant signs of toxicity.

Gross Necropsy Findings: Red and pale areas on the lungs of one pale rat. This is considered to be normal for this species.

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: 22
MRID No.: 439354-04

Reviewer: I. Blackwell
Study Completion Date: 7/27/95
Report No.: CTL/P/4738

Testing Laboratory: Zeneca Central Toxicology Laboratory
Author: N.C. Rattray

Quality Assurance (40 CFR §160.12): Included

Test Material: ICIA5504; solid"
Concentration: (nose-only exposure)

Species: rat
Weight: males = 267-308 g; females = 216-240 g
Source: Alderly Park
Age: young adult

Summary:

- LC₅₀ (mg/L):** Males = 3.62 mg/L
Females = 2.69 mg/L
Combined = not reported
- Tox. Category:** IV **Classification:** acceptable

Procedure (Deviation From §81-3):

Results:

Reported Mortality

Exposure Concentration	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
1.16 mg/L	0/5	0/5	0/10
2.52 mg/L	0/5	2/5	2/10
5.18 mg/L	5/5	5/5	10/10

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Chamber Atmosphere		
Dose Level	MMAD	GSD
1.12 mg/L	1.71 um	1.94
2.52 mg/L	2.28 um	1.88
5.18 mg/L	2.65 um	2.18

Chamber Environment	
Chamber Volume	27.61 liters
Airflow	15, 16, and 18 lpm
Temperature	20.3-22.2 ° C
Relative Humidity	51-75%

Clinical Observations: Activity decrease, breathing depth, irregular breathing rate, abnormal respiration with or without noise, gasping, scabbing, shaking, chromodacryorrhea, hunched posture, piloerection, ptosis, "snuffles", splayed gait, stains around nose, mucous secretion from nose, wet fur, sides pinched in.

Gross Necropsy Findings: Dark lungs, mottled lungs, pale areas on lungs.

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

Product Manager: 22
MRID No.: 439354-05

Reviewer: Ian Blackwell
Study Completion Date: 8/3/95
Report No.: CTL/P/4676

Testing Laboratory: Zeneca Central Toxicology Laboratory
Author(s): L. Bugg, H.J. Connolly

Quality Assurance (40 CFR §160.12): Included

Test Material: ICIA5504; "light brown solid"

Dosage: 100 mg

Species: New Zealand White rabbits

Sex: six females

Weight: 3005-3762 g

Age: young adult

Source: Charles River, UK

Summary:

1. **Toxicity Category:** III
2. **Classification:** acceptable

Procedure (Deviations From §81-4):

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal Opacity	2/6	5/6	2/6	0/6	0/6	0/6	---	---
Iris	3/6	2/6	0/6	0/6	0/6	0/6	---	---
Conjunctivae								
Redness	6/6	6/6	2/6	0/6	0/6	0/6	---	---
Chemosis	1/6	0/6	0/6	0/6	0/6	0/6	---	---
Discharge	6/6	1/6	0/6	0/6	0/6	0/6	---	---

--- = no observations at this point

Additional Observations: Erythema on eyelids of one animal, eyelids thickened, eye held closed, eyelids convoluted.

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DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: 22
MRID No.: 439354-06

Reviewer: Ian Blackwell
Study Completion Date: 8/25/95
Report No.: CTL/P/4701

Testing Laboratory: Zeneca Central Toxicology Laboratory
Author: L. Bugg, H.J. Connolly

Quality Assurance (40 CFR §160.12): Included

Test Material: ICIA5504

Dosage: 0.5 g moistened with 0.5-0.6 mL

Species: New Zealand White rabbit

Age: young adult

Sex: six females

Weight: 3561-4559 g

Source: Charles River, UK

Summary:

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

Procedure (Deviations From §81-5):

Results: Well-defined erythema was observed in 1/6, very slight erythema in 2/6 animals and very slight in 2/6 edema at 1 hour after the four hour exposure. Well-defined erythema was observed in 1/6; very slight erythema in 1/6 animals and very slight edema in 1/6 at 24 hours. On day 2, 1/6 animals displayed very slight erythema.

Special Comments:

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DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6)

Product Manager: 22
MRID No.: 439354-07

Reviewer: I. Blackwell
Study Completion Date: 8/30/95
Report No.: CTL/P/4713

Testing Laboratory: Zeneca Central Toxicology Laboratory
Author: A.M. Leah and L. Bugg

Quality Assurance (40 CFR §160.12): Included

Test Material: ICIA5504; "brown solid"
Positive Control Material: hexylcinnamaldehyde

Species: guinea pig
Weight: males = 245-315 g; females = 304-382 g
Source: Charles River, UK
Age: young adults

Method: Buehler Method

Summary:

1. **This Product is not a dermal sensitizer.**
2. **Classification:** acceptable

Procedure (Deviation From §81-6):

*The animals were challenged with a 30% dilution of test material although 75% was the highest non-irritating concentration.

Procedure: The test material was screened at 75%, 30%, 10% and 3% -- no irritation was observed at any concentration. The animals were induced with a 75% concentration (0.4 mL to the scapular region) and challenged with 75% and 30% concentrations (flanks) of test material.

Results: No irritation was observed in any of the test material-induced animals following any of the 3 induction treatments with the 75% test material. No erythematous responses were observed in the test material-induced animals following challenge with 30% test material. Following challenge with 75% test material, 16/19 (1/20 died) of the test animals challenged with 75% test material displayed scattered mild redness while 6/10 naive control animals challenged with 75% test material also displayed scattered mild redness.

Following challenge of the positive control animals with undiluted

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ACUTE TOX ONE-LINER

1. PC CODE: 128810
2. CURRENT DATE: February 11, 1997
3. TEST MATERIAL: azoxystrobin ... 80%; EPA file symbol 10182-URA

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat	Core Grade
acute oral toxicity / rat / Zeneca Central Tox. Lab / CTL/P/4708 / 8-25-95	439354-02	LD ₅₀ >2000 mg/kg	III	A
acute dermal toxicity / rat / Zeneca Central Tox. Lab / CTL/P/4709 / 8-25-95	439354-03	LD ₅₀ > 2000 mg/kg	III	A
acute inhalation toxicity / rat / Zeneca Central Tox. Lab / CTL/P/4738 / 7-27-95	439354-04	LC ₅₀ males = 3.62 mg/L females = 2.69 mg/L	IV	A
primary eye irritation / rabbit / Zeneca Central Tox. Lab / CTL/P/4776 / 8-3-95	439354-05	At 24 hours, opacity in 5/6, iritis in 2/6, redness in 6/6. No irritation by day 3.	III	A
primary skin irritation / rabbit / Zeneca Central Tox. Lab / CTL/P/4701 / 8-25-95	439354-06	Well-defined erythema in 1/6, very slight erythema and edema in 2/6 edema at 1 hour .	IV	A
dermal sensitization / guinea pig Zeneca Central Tox. Lab / CTL/P/4713 / 8-30-95	439354-07	non-sensitizer	---	A

Core Grade Key:

- A = Acceptable
- S = Supplementary (upgradeable)
- U = Unacceptable
- V = self-Validated

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