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

JUL 17 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCE

MEMORANDUM

DATE: July 17, 1981

SUBJECT: Tilt 3.6E/Pecans and Rice; ~~100-EUP-AO~~, 100-EUP-TN,
PP#1G2530 CASWELL#323EE Accession#070162

FROM: William Dykstra, Toxicologist
Toxicology Branch/HED (TS-769)

WBD for LDC 7/17/81

TO: Henry Jacoby (21)
Registration Division (TS-767)

Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Recommendations:

1. The EUP programs and temporary tolerances are not toxicologically supported. The statistically significant increase in mice with liver masses at the high dose of 2500 ppm in the interim report submitted may indicate a potential oncogenic effect at this dosage level. A final report of the mouse oncogenicity study is required to support the requested actions.

A. 100-EUP-TN; Pecans

1. EUP Program

STATES INVOLVED, QUANTITY OF PRODUCTS TO BE USED AND ACREAGE TO BE TREATED

State	1982 Season Approx. Acres	1982 Season Gals. Tilt 3.6E	1982 Season Lbs. ai	1983 Season Approx. Acres	1983 Season Gals. Tilt 3.6E	1983 Season Lbs. ai
Alabama	20	20	72	50	50	180
Arizona	10	10	36	30	30	108
Arkansas	10	10	36	30	30	108
Florida	10	10	36	30	30	108
Georgia	20	20	72	70	70	252
Louisiana	20	20	72	50	50	180
Mississippi	20	20	72	50	50	180
Missouri	10	10	36	30	30	108
New Mexico	10	10	36	30	30	108
Oklahoma	10	10	36	50	50	180
South Carolina	40	40	144	30	30	108
Texas	20	20	72	70	70	252
TOTAL:	200	200	720	520	520	1872

Totals for both seasons:

720 Acres
720 Gals. Tilt 3.6E
2592 Lbs. active ingredient

States to which product may be shipped for further distribution:

Tennessee

B. 100-EUP-AO; Rice

1. EUP Program

STATES INVOLVED, QUANTITY OF PRODUCTS TO BE USED AND ACREAGE TO BE TREATED

State	1982 Approx. Acres	1982 Gals. Tilt 3.6E	1982 Lbs. ai	1983 Approx. Acres	1983 Gals. Tilt 3.6E	1983 Lbs. ai
Arkansas	450	71	255.6	900	141	507.6
California	250	40	144.0	500	79	284.4
Louisiana	300	47	169.2	600	94	338.4
Mississippi	150	24	86.4	300	47	169.2
Texas	300	47	169.2	600	94	338.4
TOTAL:	1450	229	824.4	2900	455	1638.0

Totals FOR BOTH YEARS: 4350 Acres
684 Acres
2462.4 Lbs. Active Ingredient

States to which product may be shipped for further distribution:

Tennessee

C. Section F - Proposed Tolerances

Temporary tolerances are proposed for the combined residues of the fungicide CGA-64250 (1[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole and its metabolites determined as 2,4-dichlorobenzoic acid and expressed as the parent compound in or on the following raw agricultural commodities:

Commodity	PPM
Pecans	0.1
Rice	4.0

Review:

1. Previously Submitted Toxicology Studies:

   a. Memo of 4/30/81 from W. Dykstra to Henry Jacoby

   1. Studies with Tilt 3.6E

      °Acute rat oral LD_{50} = 1310 (1130-1520) mg/kg (both sexes)
      °Acute rabbit dermal LD_{50} = > 5010 mg/kg (no deaths)
      °Primary eye irritation - Rabbit: TOX II
      °Primary skin irritation - Rabbit: TOX III
      °Acute rat inhalation LC_{50}: > 2.45 mg/L/4 hours
      °Skin sensitization - Guinea Pig: positive

   2. Studies with CGA-64250 Technical

      °Acute rat oral LD_{50} = 1517 (958-2291) mg/kg (both sexes)
      °Acute mouse oral LD_{50} = 1490 (1138-1875) mg/kg (both sexes)
      °Acute chinese hamster oral LD_{50} = 3006 (2152-3943) mg/kg (both sexes)
      °Acute rabbit oral LD_{50} = 1344 (1062-1710) mg/kg (both sexes)
      °Acute I.P. LD_{50} - Rat = 508 (381-653) mg/kg (both sexes)
      °Acute dermal LD_{50} - Rat: > 4000 mg/kg (both sexes)
      °Primary eye irritation - Rabbit: TOX II
      °Primary skin irritation - Rabbit: TOX IV
      °Acute inhalation LC_{50} - Rat = 1263 (1075-1650) mg/m^3
      °Skin sensitization - Guinea Pig: negative
      °Salmonella/microsomal assay: negative
      °Mouse dominant lethal: negative
      °Chinese hamster nucleus anomaly: negative
      °Rat teratology: negative at 300 mg/kg; fetotoxic NOEL = 100 mg/kg
      °Rabbit teratology: negative at 180 mg/kg; fetotoxic NOEL = 180 mg/kg
      °90-day rat feeding study: NOEL is 240 ppm
      °90-day dog feeding study: NOEL is 50 ppm

2. Toxicity Data Submitted with this Petition

   a. Brief summary interim reports of the chronic/oncogenic rat feeding study and mouse oncogenicity study were submitted with little data.

      Of particular interest is the summary of the number of mice dying with liver massess during the period 52-84 weeks as shown below:

NUMBER OF MICE DYING WEEK 52 TO 84

	1o Control	2o 100 ppm	3o 500 ppm	4o 2500 ppm
Interim Kill (53)	11 (0)	11 (0)	11 (2)	9 (4)
53-56	2 (1)	2 (1)	1 (0)	0
57-60	2 (1)	3 (2)	0	1 (1)
61-64	3 (0)	2 (1)	5 (2)	1 (1)
65-68	0	1 (0)	0	2 (1)
69-72	3 (1)	1 (1)	1 (0)	7 (7)
73-76	1 (1)	2 (1)	1 (0)	1 (1)
77-80	0	1 (1)	2 (1)	5 (3)
81-84	4 (1)	4 (1)	0	2 (1)
Total minus interim kill	17 (5)	22 (8)	16 (3)	19 (15)
Total plus interim kill	28 (5)	22 (8)	27 (5)	38 (19)

In parentheses - number of mice dying with liver masses during the period

Statistical Analysis of the above data demonstrates that liver masses in mice occurred at a statistically significant increased level at the high dosage of 2500 ppm (statistics attached).

Conclusions and Recommendations:

The EUP programs and temporary tolerances are not toxicologically supported. The statistically significant increase in mice with liver masses at the high dose of 2500 ppm in the interim report submitted may indicate a potential oncogenic effect at this dosage level. A final report of the mouse oncogenicity study is required to support the requested actions.

Attachment

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