

10/10/85

Caswell No(s):: 849 A

To: Henry Jacoby, PM No 21

Registration No(s):: 618-75 (Mertect 340-F)

Pesticide Petition No(s):: 563258

Chemical(s): Thiabendazole 2-(4-thiazolyl)
benzimidazole

Requested Action(s): Mertect, Sharp and Dohme requests a temporary tolerance for the use of Thiabendazole fungicide to treat Aspergillus spp. and Penicillium spp. on stored corn grain at 20 ppm.

Recommendation: Toxicology Branch has sufficient toxicity data in support for the safety to this residue level on corn grain, but defer to RCB regarding secondary residues in meat, fat and meat by products resulting from this use.

Inert(s) cleared 180.1001: Yes

% of ADI occupied: Existing: 46.92 Resulting: 51.92

Resulting % increase in TMRC: 10.7%

Data considered in setting the ADI: Please, see attached summary of toxicity data considered in setting this action. Refer to the enclosed ADI printout.

Attached (?): ADI printout: (YES/NO); TOX "one-liner": YES/NO; DER: YES/NO

Existing regulatory actions against registration: None

PAR status: None

New Data: None

Data gaps: Sensitization study

Comments: The established 0.4ppm milk tolerance will be adequate to cover TBZ residues from proposed use (RCB, Lung Cheng, 9/10/85).

Reviewer: Carol A. Rodriguez Date: 10/4/85

Section Head: Jane C. Harris 10/4/85 Branch Chief: W. H. B. 10/8/85

Toxicity Data Considered in Setting This Action:

- ° Acute oral LD50 (male rat) = 3.97 g/kg
(95% Conf. = 2.92 - 2.40 g/kg)
- ° Acute oral LD50 (female rat) = 3.54 g/kg
(95% Conf. = 2.14 - 5.85 g/kg)
- ° Acute oral LD50 (mouse) = 3.8 g/kg
- ° 2-Year rat feeding: Systemic NOEL = 10 mg/kg/day.
Systemic LEL = 40 mg/kg (growth depression)
Oncogenic potential - negative at 160
mg/kg/day (highest dose tested)
Dose levels tested: 10, 40 and 160 mg/kg/day.
- ° 2-Year dog feeding: Systemic NOEL = 50 mg/kg/day;
Systemic LEL = 125 mg/kg/day (decreased
body weight).
Dose levels tested: 20, 50 and 125 mg/kg/day.
- ° Lifetime oncogenic (mouse feeding) - Oncogenic NOEL >
5,330 ppm or 800 mg/kg/day (highest
level tested)
Systemic NOEL = 600 ppm or 100 mg/kg/day
Systemic ~~NOEL~~^{LEL} = 2000 ppm or 300 mg/kg/day -
lower weight gain. ✓
Dose levels tested 660 ppm (100 mg/kg/day),
2000 ppm (300 mg/kg/day), 5,330 ppm
(800 mg/kg/day).
- ° Rat Teratology: Teratogenic NOEL > 80 mg/kg/day (given
by gavage, single dose tested)
Maternal NOEL - < 80 mg/kg (only dose tested)
- lower mean implantation sites.
- ° Rabbit teratology: Teratogenic NOEL > 800 mg/kg/day.
(highest dose tested).
Dose levels tested: 100, 200, 400 and
800 mg/kg/day.
Maternal NOEL: 100 mg/kg
LOEL: 200 mg/kg - weight loss.
- ° 3-Generation reproduction (rat) - Reproductive NOEL =
20 mg/kg, reproductive LOEL = 40 mg/kg -
decreased viability index of Fla.
Dose levels tested: 20, 40 and 80 mg/kg.
- ° Mutagenicity Studies:
 1. Microbial (S. typhimurium) negative for induced revertants.
 2. Microbial (E. coli) negative for induced revertants.
 3. Host-mediated - negative
 4. In vivo Bone marrow - negative for chromosomal damage.
 5. Primary Bacterial DNA damage/repair - negative.

6. In vitro cytogenetics - negative - no increase in chromosome breakage in human embryonic fibroblast cultures.

- Metabolism, absorption, distribution and excretion in man, dog, rat, sheep, goat, cattle and swine:

Rapidly metabolized in man. Radioactive agent in animal species in many respects were similar to those found in man. Tissues from laboratory animals were virtually free of radioactivity.

File last updated 2/21/85

ACCEPTABLE DAILY INTAKE DATA

DRAFT

ADI, Dose	NOEL	S.F.	ADI	MPI
mg/kg	ppm		mg/kg/day	mg/day (60kg)
10.000	200.00	100	0.1000	6.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Apples(2)	10.000	2.53	0.37950
Citrus Fruits(33)	10.000	3.81	0.57179
Pears(116)	10.000	0.26	0.03832
Bananas(7)	0.400	1.42	0.00852
Squash(191)	1.000	0.11	0.00165
Sugar, cane&beet(154)	0.250	3.64	0.01364
Milk&Dairy Products(93)	0.100	28.62	0.04292
Sweet Potatoes(157)	0.020	0.40	0.00012
Soybeans (oil)(148)	0.100	0.92	0.00138
Cattle(26)	0.100	7.18	0.01078
Goats(62)	0.100	0.03	0.00005
Hogs(69)	0.100	3.43	0.00515
Horses(208)	0.100	0.03	0.00005
Sheep(145)	0.100	0.19	0.00029
Rice(137)	3.000	0.55	0.02483
Carrots(24)	10.000	0.48	0.07205
Eggs(54)	0.100	2.77	0.00416
Poultry(128)	0.100	2.94	0.00441
Papayas(109)	5.000	0.03	0.00225
Avocados(6)	10.000	0.03	0.00450
Mangoes(88)	10.000	0.03	0.00450
Potatoes(127)	3.000	5.43	0.24420
Wheat(170)	0.200	10.36	0.03109

MPI	THRC	% ADI
6.0000 mg/day (60kg)	1.4662 mg/day (1.5kg)	24.44

Unpublished, Tox Approved 1E2542, 2F2603, 2E2736, 3F2882, 3F2883, 4F2975

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Grapes, not raisins(67)	10.000	0.45	0.06745
Wheat(170)	2.800	10.36	0.43524
Milk&Dairy Products(93)	0.300	28.62	0.12877
Cantaloupe(23)	12.000	0.52	0.09382
Strawberries(152)	5.000	0.10	0.01380
Tomatoes(163)	0.500	2.87	0.02156
Potatoes(127)	7.000	5.43	0.56980
Peas(37)	40.000	0.03	0.01800
Beans, dry edible(10)	0.100	0.11	0.00347

MPI	THRC	% ADI
6.0000 mg/day (60kg)	2.8151 mg/day (1.5kg)	46.92

Current Action 5G3258

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Corn, grain(68)	20.000	1.00	0.30000

MPI	TRRC	% ADI
6.0000 mg/day(60kg)	3.1151 mg/day(1.5kg)	51.92
