10-29-81 RCB

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File petition

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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE: OCT 29 1981

SUBJECT: Chlorothalonil Tolerance on Dry Beans (PP No. 8E2065, Acc. No. 099906, Caswell No. 215 B).

FROM: George Z. Ghail, Ph.D.
Toxicology Branch, HED (TS-769)
G. Ghali

TO: Clinton L. Fletcher
Product Manager No. 43
Registration Division (TS-767)

THRU: Christine F. Chaisson, Section Head
Toxicology Branch, HED (TS-769)
C F Chaisson 10/29/81

Petitioner:

Interregional Research Project No. 4
State Agricultural Experimental Station
Rutgers University
New Brunswick, N.J. 08903

Action Requested:

Establishment of tolerance of 0.1 ppm for chlorothalonil and its 4-OH metabolite in/on dry beans.

Background:

A petition was submitted on March 3, 1978 to establish a tolerance of 0.3 ppm for combined residue of the fungicide chlorothalonil and its 4-hydroxy metabolite in/on dry beans. Toxicology Branch recommended against the establishment of such a tolerance (memo by D. Ritter, July 28, 1978).

On January 19, 1981, the petitioner submitted an amended petition proposing a tolerance of 0.1 ppm to be established.

Conclusions and Recommendations:

1. Toxicology Branch recommends for the establishment of the proposed tolerance of 0.1 ppm for combined residue of chlorothalonil and its 4-OH metabolite in/on dry beans.

2. Toxicology Branch defers to the Residue Chemistry Branch the question of whether a transfere of residues to meat, milk, poultry and eggs is possible as a result of this use, and whether tolerances for these food commodities are required.

Detailed Considerations:

1. The ADI is based on a NOEL of 60 ppm from 2-year dog study and is considered to be 0.015 mg/kg/day.

2. Tolerances for the combined residues of chlorothalonil and its 4-OH metabolite have been established under 40 CFR 180.275 for a variety of raw agricultural commodities. These tolerances are supported by acute, subacute, chronic and mutagenicity studies.

3. Dietary residues would not be significantly increased by the addition of the proposed tolerance since it constitutes only 0.00047 mg/day over the existing TMRC or 0.05% of the ADI. This increase is considered toxicologically insignificant.

4. The TMRC from tolerances existing in the CFR 180.275 totalled 0.7012 mg/day per a 60 kg person. This represents a cancer risk of 10^{-6} to 10^{-5}. The addition of 0.00047 mg/day as a result of the establishment of the proposed tolerance does not significantly add to this risk and is considered an acceptable increase in exposure (see Cancer Risk Analysis, memo by D. Ritter to C. Fletcher dated January 14, 1980).

Established Tolerances:

Tolerances for chlorothalonil and its 4-OH metabolite have been established under 40 CFR 180.275 for a variety of raw agricultural commodities (See computer printout attached).

Toxicology Profile:

A. Technical Chlorothalonil:

(Memo by R. Coberly 10/6/77, 11/8/77, also memo by D. Ritter 3/1/81).

1. Acute oral toxicity 163.81-1

   Rat LD_{50} > 10,000 mg/kg
   Dog LD_{50} > 5,000 mg/kg

2. Acute dermal toxicity 163.81-2
   Rabbit LD_{50} >10,000 mg/kg

3. Acute inhalation toxicity 163.81-3
   Rabbit LC_{50} > 4.7 mg/l

4. Primary eye irritation 163.81-4
   Rabbit, severe irritation. Tox. Category I.

5. Subchronic oral toxicity 163.82-1

16-week dog feeding, NOEL < 250 ppm
4-month rat feeding, NOEL < 250 ppm

6. Chronic feeding 163.83-1

2-year dog feeding, NOEL < 1500 ppm
2-year dog feeding, NOEL 60 ppm
2-year rat feeding, NOEL < 5000 ppm
2-year rat feeding, NOEL < 60 ppm
18-month rat feeding, NOEL < 500 ppm

7. Oncogenicity 163.83-2

A report by the National Cancer Institute indicated that chlorothalonil was carcinogenic in male and female Osborne-Mendel rats, but not in B6C3F1 mice.

8. Teratogenicity 163.83-3

Rabbit, NOEL 62.5 mg/kg (HDT).
Rabbit, negative at 5.0 mg/kg/day.

9. Reproduction 163.83-4

3-generation, rat, NOEL 5000 ppm
3-generation, rat, NOEL for lactation 1500 ppm, NOEL for reproduction 15,000 ppm.

10. Mutagenicity 163.84 - 1 thru - 4

A variety of mutagenicity tests were available to assess the mutagenic potential of chlorothalonil. These tests included; host-mediated assay (negative), in vivo cytogenetic in mice (negative), cell transformation in rats (negative), Ames assay (negative), microbial DNA repair in S. typhimurium and B. subtilis (negative in both species, except for a positive response of a suggestive nature in strain TA 1978 of the Salmonella), and in vitro point mutation in V-79 hamster cells and BALB/3T3 mouse fibroblasts (negative).

11. Metabolism 163.85-1

The metabolism of the radiolabeled chlorothalonil was investigated in rats. After 96 hours, 70 and 8% of the orally administered dose were excreted in the feces and urine respectively. The bulk of the remaining 15% was recovered in the blood, muscle, gut and fat.

B. 4-OH Metabolite

(Memo by D. Ritter, March 18, 1981)

1. Acute oral toxicity 163.81-1

Rat LD_{50} 422 mg/kg (male), 242 mg/kg (female).
Rat LD_{50} 332 mg/kg
Dog LD_{50} 100 mg/kg

2. Subchronic oral toxicity 163.82-1

4-month rat feeding, NOEL 100 ppm
90-day dog feeding, NOEL < 50 ppm

3. Reproduction 163.83-4

3-generation reproduction in rat, NOEL not established.

C. BRAVO 500:

A formulation of chlorothalonil contains 40.76% of the active ingredient. (memo by C. A. Rodriguez November 30, 1978).

1. Acute oral toxicity 163.81-1
Rat LD_{50} 4.2 (2.9-6.1) g/kg

2. Acute dermal toxicity 163.81-2
Rabbit LD_{50} > 20.0 g/kg

3. Acute inhalation toxicity 163.81-3
Rat 4-hour LC_{50} > 7.16 mg/L

4. Primary eye irritation 163.81-4
Severe eye irritation in rabbits, Tox. Category I

Primary dermal irritation 163.81-5
The primary dermal irritation index found to be 1.3 in rabbits and considered slightly irritating and non-corrosive. Tox Category IV.

CFR 180.27[illegible] Chlorothalonil 9/30/81

File last updated 9/30/81

ACCEPTABLE DAILY INTAKE DATA

Dog mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day(60kg)
1.500	60.00	100	0.0150	0.9000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Celery(28)	15.000	0.29	0.06438
Broccoli(19)	5.000	0.10	0.00766
Brussel Sprouts(20)	5.000	0.03	0.00225
Cabbage,sauerkraut(22)	5.000	0.74	0.05519
Cauliflower(27)	5.000	0.07	0.00537
Cucumbers,inc pickl(46)	5.000	0.73	0.05442
Melons(92)	5.000	2.00	0.15023
Onions,green(107)	5.000	0.11	0.00843
Pumpkin,inc squash(131)	5.000	0.11	0.00843
Beans,snap(12)	5.000	0.98	0.07358
Summer Squash(155)	5.000	0.03	0.00225
Tomatoes(163)	5.000	2.87	0.21561
Passion fruit(112)	3.000	0.03	0.00135
Carrots(24)	1.000	0.48	0.00720
Corn,sweet(40)	1.000	1.43	0.02145
Onion(dry bulb)(106)	0.500	0.72	0.00537
Peanuts(115)	0.300	0.36	0.00161
Potatoes(127)	0.100	5.43	0.00814
Papayas(109)	15.000	0.03	0.00675
Bananas(7)	0.050	1.42	0.00107
Parsnips(111)	1.000	0.03	0.00045

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.7012 mg/day(1.5kg)	77.91

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Unpublished,Tox Approved PP# 6E1841,7E1887,8E2037,0F22405,1G2471

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Mustard Greens(99)	15.000	0.06	0.01380
Turnip Greens(166)	15.000	0.03	0.00675
Escarole/endive(56)	6.000	0.03	0.00270
Chicory(32)	6.000	0.03	0.00270
Beets(14)	1.000	0.17	0.00261
Turnips(165)	1.000	0.05	0.00077
Spinach(150)	42.000	0.05	0.03219
Citrus Fruits(33)	0.010	3.81	0.00057
Almonds(1)	0.030	0.03	0.00001

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.7633 mg/day(1.5kg)	84.81

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Current Action PP# 8E2065

CROP	Tolerance	Food Factor	mg/day(1.5kg)

Beans,dry edible(10)	0.100	0.31	0.00047

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.7638 mg/day(1.5kg)	84.86

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Other Pending Tolerances PP 6F1749,6G1813/6H5136,6F1799

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Cherries(30)	15.000	0.10	0.02299
Peaches(114)	25.000	0.90	0.33725
Soybeans(148)	0.200	0.92	0.00275

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	1.1268 mg/day(1.5kg)	125.19

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