



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

MEMORANDUM

DATE: DEC 15 1981

SUBJECT: Dimethoate on Cherries, PP No. 7E1949 (Caswell No. 358)?

FROM: George Z. Ghail, Ph.D.
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TO: P. Critchlow
Product Manager, No. 43
Registration Division (TS-767)

THRU: Christine F. Chaisson, Section Head *C. F. Chaisson*
Toxicology Branch, HED (TS-769) *W. Burnam*

William Burnam, Acting Branch Chief
Toxicology Branch, (TS-769)

Petitioner: The Interregional Research Project No. 4
Agricultural Experiment Station
Cook College
New Brunswick, N J 08903

Action Requested:

Establishment of a tolerance of 2.0 ppm of dimethoate residues on cherries.

Recommendations:

Toxicology Branch recommends for the establishment of the proposed tolerance on cherries.

Detailed Considerations:

1. The ADI was established on the basis of a NOEL of 8.00 ppm (0.2 mg/kg) for cholinesterase inhibition in human volunteers (14 to 57 days). The ADI was considered to be 0.02 mg/kg considering a safety factor of 10 fold.
2. Establishment of the proposed tolerance would contribute 0.00307 mg/day to the daily human diet or 0.26% of the ADI.
3. An adequate margin of safety (MOS) exists to cover any teratogenic risk that may arise from this additional use.

Toxicology Profile:

A. Technical Dimethoate:

(R. Coberly, 11/1/66 and 8/1/75; M. Quaife 8/21/75; D. Ritter 10/22/75)

1. Acute oral toxicity
Mouse LD₅₀ 60 mg/kg (female)
Rat LD₅₀ 185 (180-325) mg/kg and 240-336 mg/kg for male and female respectively.
Guinea pig LD₅₀ 350-400 mg/kg
2. Acute dermal toxicity
Rat LD₅₀ 1,550 (1,240-1,938) mg/kg.
Guinea pigs LD₅₀ > 2000 mg/kg
3. Acute inhalation toxicity
Rat one-hour LC₅₀ > 2 but < 200 mg/L.
4. Primary eye irritation
Rabbit, eye irritant, moderate opacity and slight conjunctival redness, chemosis and discharge.
5. Primary skin irritation
Rabbit, not irritant
6. Delayed neurotoxicity
Hen demyelination, NOEL 130 ppm of dimethoate, and 240 ppm of the dimethoate oxygen analog.
7. Subchronic feeding
Dog 90-day feeding, NOEL ChE inhibition 9 ppm for dimethoate
Rat 90-day feeding, NOEL ChE inhibition 32 ppm for dimethoate
Human volunteers, NOEL ChE inhibition 15 mg/day, LEL 30 mg/day
8. Subchronic dermal toxicity
No data are available.
9. Subchronic inhalation toxicity
No data are available.
10. Subchronic neurotoxicity
No data are available. However, from the acute neurotoxicity data it is concluded that dimethoate and its oxygen analog do not produce delayed neurotoxicity, therefore, subchronic testing is not required.

11. Chronic feeding
Rat 2-year, NOEL 1 ppm for brain, blood and plasma ChE inhibition

12. Oncogenicity

A report alleging carcinogenicity of dimethoate has appeared in the literature by Gibel et al (1973). Arch Geschwulstforsch. 41 (4): 311-328. (E. Germany).

A subsequent report summarized by the NCI in 1977 (DHEW Publication No. NIH 77-804) indicated that dimethoate treatment did not significantly increase the incidence of tumors in both rats and mice under the test conditions.

13. Teratogenicity

Data are available on Cygon 4E (a formulation containing 47.3% dimethoate) indicating that the chemical was a mild mutagenic agent in cats at 5.7 mg/kg per day (HDT). Mutagenic effects were manifested as polydactyly, and increase in the number of digits on either the front or the back paw.

In another study on rats using the same formulation, the chemical caused wavy ribs at the highest two doses (5.7 and 11.3 mg/kg).

The presence of unknown inerts in the test chemical makes the interpretation difficult.

The NOEL in both studies was considered to be 2.8 mg/kg per day.

The requirement for more teratogenic studies with the technical material had been waived by the Assistant Administrator. (RPAR Position Document 2/3).

14. Reproduction

Mouse, NOEL 50 ppm

15. Mutagenicity

A number of studies indicated that dimethoate is mutagenic in bacterial and mammalian systems (references may be found in the RPAR published in FR 42: 176, 9/12/77).

16. Metabolism

Some data are available to elucidate the metabolic aspects of dimethoate.

Data Gaps:

A second chronic feeding study in non-rodent.

B. Dimethoate Metabolites;

1. Acute oral toxicity
Acute oral LD₅₀ in rats 55 mg/kg for the oxygen analog, 1,500-2,000 mg/kg for the demethyl derivative and 2,500-3,000 mg/kg for the carboxy derivative.
2. Acute delayed neurotoxicity
Hen NOEL 240 ppm for the dimethoate oxygen analog.
3. Subchronic feeding
Dog 90-day feeding, NOEL ChE inhibition 1.6 ppm for the dimethoate oxygen analog.
Rat 30-day feeding, NOEL 0.8 ppm for the dimethoate oxygen analog.
Rat 33-day feeding, NOEL 330 ppm for dimethoate carboxy derivative.

File last updated 10/23/81

ACCEPTABLE DAILY INTAKE DATA

Human mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day (60kg)
0.200	8.00	10	0.0200	1.2000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Apples(2)	2.000	2.53	0.07590
Beans(9)	2.000	2.04	0.06120
Broccoli(19)	2.000	0.10	0.00307
Cabbage, sauerkraut(22)	2.000	0.74	0.02207
Cauliflower(27)	2.000	0.07	0.00215
Celery(28)	2.000	0.29	0.00858
Collards(37)	2.000	0.08	0.00245
Escarole/endive(56)	2.000	0.03	0.00090
Grapefruit(65)	2.000	0.99	0.02974
Kale(75)	2.000	0.03	0.00090
Lemons(82)	2.000	0.17	0.00521
Lettuce(84)	2.000	1.31	0.03924
Mustard Greens(99)	2.000	0.06	0.00184
Oranges(108)	2.000	2.17	0.06500
Pears(116)	2.000	0.26	0.00766
Peas(117)	2.000	0.69	0.02085
Peppers(120)	2.000	0.12	0.00368
Spinach(150)	2.000	0.05	0.00153
Swiss Chard(158)	2.000	0.03	0.00090
Tangerines(160)	2.000	0.03	0.00090
Tomatoes(163)	2.000	2.87	0.08624
Turnip Greens(166)	2.000	0.03	0.00090
Turnips(165)	2.000	0.05	0.00153
Grapes, inc raisins(66)	1.000	0.49	0.00736
Melons(92)	1.000	2.00	0.03005
Potatoes(127)	0.200	5.43	0.01628
Cottonseed (oil)(41)	0.100	0.15	0.00022
Pecans(118)	0.100	0.03	0.00005
Safflower(141)	0.100	0.03	0.00005
Sorghum(147)	0.100	0.03	0.00005
Corn, grain(68)	0.100	1.00	0.00150
Soybeans (oil)(148)	0.050	0.92	0.00069
wheat(170)	0.040	10.36	0.00622
Eggs(54)	0.020	2.77	0.00083
Meat, inc poultry(89)	0.020	13.85	0.00415
Milk&Dairy Products(93)	0.002	28.62	0.00086

MPI	TMRC	% ADI
1.2000 mg/day (60kg)	0.5108 mg/day (1.5kg)	42.56

Current Action PP# 7E1949

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Cherries(30)	2.000	0.10	0.00307

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MPI
1.2000 mg/day(60kg)

TMRC
0.5138 mg/day(1.5kg)

% ADI
42.82

File last updated 10/23/81

ACCEPTABLE DAILY INTAKE DATA

Human	NOEL	S.F.	ADI	MPI
mg/kg	ppm		mg/kg/day	mg/day (60kg)
0.000	8.00	10	0.0200	1.2000

Published tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Apples (2)	2.000	2.53	0.07590
Beans (9)	2.00	2.04	0.06120
Broccoli (19)	2.000	0.10	0.00307
Cabbage, sauerkraut (22)	2.000	0.74	0.02207
Cauliflower (27)	2.000	0.07	0.00215
Celery (28)	2.000	0.29	0.00858
Collards (37)	2.000	0.08	0.00245
Escarole/endive (56)	2.000	0.03	0.00090
Grapefruit (65)	2.000	0.99	0.02974
Kale (75)	2.000	0.03	0.00090
Lemons (82)	2.000	0.17	0.00521
Lettuce (84)	2.000	1.31	0.03924
Mustard Greens (99)	2.000	0.06	0.00184
Oranges (106)	2.000	2.17	0.06500
Pears (116)	2.000	0.26	0.00766
Peas (117)	2.000	0.69	0.02085
Peppers (120)	2.000	0.12	0.00368
Spinach (150)	2.000	0.05	0.00153
Swiss Chard (158)	2.000	0.03	0.00090
Tangerines (160)	2.000	0.03	0.00090
Tomatoes (163)	2.000	2.87	0.08624
Turnip Greens (166)	2.000	0.03	0.00090
Turnips (165)	2.000	0.05	0.00153
Grapes, inc raisins (66)	1.000	0.49	0.00736
Melons (92)	1.000	2.00	0.03005
Potatoes (127)	0.200	5.43	0.01628
Cottonseed (oil) (41)	0.100	0.15	0.00022
Pecans (118)	0.100	0.03	0.00005
Safflower (141)	0.100	0.03	0.00005
Sorghum (147)	0.100	0.03	0.00005
Corn, grain (68)	0.100	1.00	0.00150
Soybeans (oil) (148)	0.050	0.92	0.00069
wheat (170)	0.040	10.36	0.00622
Eggs (54)	0.020	2.77	0.00083
Heat, inc poultry (89)	0.020	13.85	0.00415
Milk & Dairy Products (93)	0.002	28.62	0.00086

MPI	THRC	% ADI
1.2000 mg/day (60kg)	0.5108 mg/day (1.5kg)	42.56

Current Action PP# 7E1949

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Cherries (30)	2.000	0.10	0.00307