

0316

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: November 1, 1978

SUBJECT: Requests to amend CFR 40, Section 180.111, Malathion; "From preharvest application: 50 ppm in or on almond hulls; and from post-harvest application: 50 ppm in or on almond shells". Petition #8E2114 ~~Gaswell #535~~

FROM: Carlos A. Rodriguez - *Carlos A. Rodriguez*
TOX/HED TS-769 *// - 3 - 78*

TO: C. Fletcher, Minor Uses
STS/RD TS-767 *C4*

Petitioner: George M. Markle
Interregional Research Project No. 4
Rutgers University

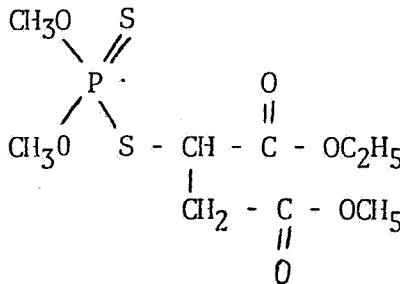
Recommendations:

The petitioned tolerance is toxicologically supported contingent upon a satisfactory Chemistry Branch review on the level and identity of the residues in/on almond shells.

Residue Chemistry Considerations:

A. Substance Identification:

1. Chemical name: 0,0-dimethyl dithiophosphate of diethyl mercaptosuccinate
2. Synonyms: malathion, eythion, emmats extra, fyfanon, Karbofos, Kop-thion, Kypfos, malaspray, malamar, MLT, Zithio, mercaptothion, carbofos, maldison.
3. Structure:



4. Physical/Chemical Data:

- a. Density = 10.25 lb/gal
- b. Color = clear liquid, may be colorless, yellow, amber or brown
- c. Melting point = 2.83°C
- d. Boiling point = 156-157°C at 0.7 mm Hg
- e. Vapor pressure = 0.00004 mm Hg at 30°C
- f. Specific gravity = 1.235 at 25°C
- g. Flash point = greater than 160°C
- h. Solubility = in water at 25°C, approximately 125 ppm. Completely soluble in most alcohols, esters, high aromatic solvents, ketones and vegetable oils. Poor solubility in aliphatic hydrocarbons.
- i. Chemical class = organophosphate, an irreversible acetylcholinesterase inhibitor.

B. Reference Petitions:

1. PP# 19
2. PP# 89
3. PP# 136
4. PP# 187
5. PP# 7E2001

C. Formulation

Cythion^R 57% E.L.

EPA Reg. No. 241-47

- | | |
|----------------------|------|
| 1. Active Ingredient | % |
| a. Malathion | 58.4 |
| 2. Inert Ingredients | |

[REDACTED]

Inert Ingredient
Information

9.4 Segment 9.4.1.1

100.00%

To treat 10,000 lbs. of almonds, use 4 fluid ounces in sufficient water as the almonds go into storage.

A. Toxicology - A summary of the toxicological properties of Malathion is given below:

<u>Species</u>	<u>LD₅₀ value (mg/kg)</u>
Rat	1,000 - 1,845
Mouse	700 - 3,321
Guinea pigs	570 - 815
Chickens	
Adult	>850
1 year old	150 - 200
3 to 4 weeks	200 - 400
2 to 2 weeks	370

Cat	> 500
Rabbit	> 900
Sheep	< 150
Cattle	200 - 560
Calves (dairy)	80

2. Toxicity of Malathion Via Routes Other Than Oral Value

Species	Route of entry	Measurement	Male	Female
Rat	Intraperitoneal	LD ₅₀ (mg/kg)	750	1,000
	Introvenous	LD ₅₀ (mg/kg)	50	50
	Subcutaneous	LD ₅₀ (mg/kg)	1,000	- - -
	Dermal	LD ₅₀ (mg/kg)	4,444	4,444
	Inhalation	LC ₅₀ 8 hr (mg/L)	> 60	> 60
Mice	Intraperitoneal	LD ₅₀ (mg/kg)	420 to 815	
	Inhalation	LC ₅₀ 8 hr (mg/m ³)	> 15	
Guinea pigs	Intraperitoneal	LD ₅₀ (mg/kg)	500	
	Dermal, 24 hr exposure	LD ₅₀ (mg/kg)	> 12,300	
	Inhalation, 5 ppm, 4 weeks		No effect	
Dogs	Intraperitoneal	LD ₅₀ (mg/kg)	1.51 mg/kg	
	Intravenous	LD ₅₀ (mg/kg)	> 430 to < 600	
	Inhalation, 5 ppm 4 weeks		Blood cholinesterase activity reduced	

o Single Dose Intraperitoneal Teratogenicity Study in Rats - NEL = 900 mg/kg

o¹ Rec-Assay Mutagenicity Study - negative

o² Reversion Assay Mutagenicity Study - negative

o³ Delayed Neurotoxicity Study in Chickens - negative

1&2) Shirasu, V., M. Moyiya, K. Kato, A. Furuhashi and T. Kada.
Mutagenicity screening of pesticides in the microbial system.
Mutation Research 40 (1976) 19-30.

3) Gaines, T.B. Acute toxicity of pesticides. TAP 14 (1969) 515-534.

3. Chronic Toxicity

Chronic Toxicity of Malathion to Rats

<u>Concentration of malathion in feed (ppm)</u>	<u>Duration of test (years)</u>	<u>Mortality (%)</u>	<u>Comments</u>
100, 1,000 5,000 Technical 65% as 25% wettable powder	2	0	No gross effects at 100 and 1,000 ppm. At 5,000 ppm food intake and weight gain were reduced. Significant depression of plasma, erythrocytes and brain cholinesterase activity at 1,000 and 5,000 ppm.
100, 1,000, 5,000 Technical 90% as 25% wettable powder	2	0	Growth rates and food intake not influenced. Significant depression of cholinesterase activity at all levels of exposure.
500, 1,000, 5,000, 20,000 Technical 99% as 25% wettable powder	2	0	Significant depression of cholinesterase activity of erythrocytes at all levels of exposure. Food intake and growth not affected at 500 and 1,000 ppm.

4. Human Studies

47-Day Human Feeding Study - NEL = 0.2 mg/kg/day ✓

B. Evaluation of the ADI

1. Prior tolerance under CFR 40. 180.111
2. Pending tolerances - none
3. Temporary tolerances - none
4. ADI Calculation

NEL (human) = 0.200 mg/kg/day

With the imposition of a 10 fold safety factor, the ADI is calculated to be:

$$0.2 \text{ mg/kg/day} \times 1/10 = 0.02 \text{ mg/kg/day} = \text{ADI}$$

5. Impact of the New Tolerance Request

There will be no increase of residues of malathion in the diet from this proposed use on animal feed since tolerances are already in existence for meat, milk, etc.

6. Total Tolerances Granted With Respect to the ADI

The ADI of 0.02 mg/kg/day would permit a maximum of 1.2 mg/day (MPI) in the 1500 gm diet of a 60 kg man. The tolerance in existence today are calculated to contribute 6.1307 mg to the daily human 1500 gm diet. Thus the MTRC exceeds the MPI by a factor of 5.11 or one may conclude that the ADI has theoretically been exceeded by a factor of 5.11.

It is to be noted that the latest total Diet Survey indicates that residues of malathion in the U.S. food supply do not actually exceed the WHO-ADI of 0.02 mg/kg/day. Their dietary intake for a 4 year average is 0.00013 mg/kg/day which is significantly below the ADI.

C. RPAR Criteria

No RPAR criteria have been exceeded.

D. Conclusions and Recommendations

Almond shells as proposed would comprise only a small percentage of the feed supplements for cattle, there is no reasonable expectation that finite residue will occur in meat or milk from animals consuming rations containing the treated almond shells and there will be no increase in residues contributed to the human diet resulting from the requested use of Malathion for post-harvest application of 50 ppm in or on almond shells.

TOX/HED:R.Engler:11/1/78:ssr

E. 11/3/78