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

MEMORANDUM

APR 30 1982 ... 28 1982

TO: Jay Ellenberger (12)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Larvin; EPA Reg.#264-GUE, 264-GUR; PP#0F2413, 0H5275;
Larvin in/on Cotton and Soybeans.
CASWELL#900AA Accession#070764

Recommendations:

1. The registration of Larvin Thiodicarb Insecticide 75 WP and Larvin 500 Thiodicarb Insecticide can be toxicologically supported. The waiver for the acute inhalation toxicity study of Larvin 500 Thiodicarb Insecticide is acceptable. The data indicate that the ratio of a nominal concentration to an analytical concentration (159:1) makes it impractical to generate respirable particles of this product. The risk of inhalation exposure to Larvin 500 is remote.

2. The requested permanent tolerances can be toxicologically supported.

Review:

1. Section F: Proposed Tolerance for the Pesticide Chemical

The petitioner proposes that the following Pesticide and Feed Additive tolerances be established for the combined residues of thiodicarb, Dimethyl N,N'-[thiobis[(methylimino)carbonyloxy]]bis [ethanimidothioate] in or on:

Pesticide Tolerances

cottonseed ------ 0.4 ppm
soybeans (seed) - 0.1 ppm
soybean straw --- 0.2 ppm

Feed Additive Tolerances

cottonseed hulls - 0.8 ppm
soybeans hulls -- 0.4 ppm

2. The formulations to be used are Larvin Thiodicarb 75 WP (EPA Reg.#264-GUR) and Larvin 500 Thiodicarb Insecticide (EPA Reg.#264-GUR). Inerts are cleared under 180.1001.

3. No regulatory actions are pending against the pesticide and no RPAR criteria have been exceeded.

4. No permanent tolerances have been published.

5. Toxicity Data Submitted with this Petition.

(a) Request of waiver for Acute Inhalation Study with Larvin 500 Thiodicarb Insecticide.

The waiver request is acceptable. The data indicate that the ratio of a nominal concentration to an analytical concentration (159:1) make it impractical to generate respirable particles of the product. The risk of inhalation exposure to Larvin 500 is remote.

(b) Three-generation Rat Reproduction Study.

The submitted pathology data are acceptable. There were no compound-related effects. The NOEL for the study is 10.0 mg/kg/day (HDT). The study is acceptable as Core-Minimum Data.

(c) Mouse Oncogenicity Study.

The submitted pathology data are acceptable. There were no compound-related oncogenic effects. The oncogenic potential is negative at 10 mg/kg/day (HDT). The study is acceptable as Core-Minimum Data.

(d) Rat Chronic/Oncogenic Feeding Study.

The submitted pathology data, and organ weight data are acceptable. Relative to the issue of hepatic hyperplasia and neoplastic nodules, the submitted data demonstrate that no treatment-related effect was present. The NOEL for cholinesterase inhibition is 10.0 mg/kg/day. The NOEL for chronic toxicity is 3.0 mg/kg/day. The LEL for chronic toxicity is 10.0 mg/kg/day and the effect is decreased body weight in both sexes (HDT). The oncogenic potential is negative at 10 mg/kg/day (HDT). The study is acceptable as Core-Minimum Data.

2

(e) Effects of Larvin (US51762) on Cholinesterase Activity in a 28-Day Dietary Inclusion Study in rats (Busy Run Research Center; Project#45-19; 4/6/82)

Groups of 10 male and 10 female Fischer 344 rats were fed dietary levels of 0, 1.0, 3.0, 10.0 and 30.0 mg/kg/day of Larvin in the diet for 28 days. Body weight and food consumption were measured weekly. Parameters measured at 7, 14 and 28 days included packed cell volume, total plasma protein, plasma and erythrocyte cholinesterase activity. Brain cholinesterase was determined after 28 days.

Results:

Plasma and RBC cholinesterase was significantly decreased in male rats at the 30 mg/kg/day dosage level at 7 and 14 days. In female rats, RBC cholinesterase was significantly decreased at 7, 14 and 28 days. Plasma cholinesterase was significantly decreased in females at 14 days. Food consumption and body weight gain were significantly decreased at 30 and 10 mg/kg/day during the study in female rats.

Conclusion:

The NOEL for cholinesterase inhibition is 10 mg/kg/day.

Classification: Core-Minimum Data

6. Summary of Toxicity Data on the technical which supported the permanent tolerances.

- °Rat oral LD_{50} = 325 mg/kg
- °Rat teratology: negative at 30 mg/kg/day; fetotoxic NOEL = 3.0 mg/kg/day
- °Mouse teratolgy: negative at 200 mg/kg/day; fetotoxic NOEL = 200 mg/kg/day
- °Acute delayed neurotoxicity: negative at 660 mg/kg
- °Rat dominant lethal: negative at 10 mg/kg/day
- °Ames Samonella/Microsome Plate Test: negative
- °Micronucleus Test: negative
- °Reverse Mutation in Saccharomyces cerevisiae: negative
- °Mitotic Crossing Over in Saccharomyces cerevisiae: negative
- °Mitotic Gene Conversion in Saccharomyces cerevisiae: positive
- °Primary DNA Damage in Escherichia coli: negative
- °3-Generation Rat Reproduction: NOEL = 10 mg/kg/day (HDT)
- °Mouse Oncogencity: oncogenic potential: negative at 10 mg/kg/day (HDT)
- °Six-Month Dog Feeding: ChE NOEL = 15 mg/kg/day; Subchronic toxicity NOEL = 15 mg/kg/day
- °2-Year Chronic/Oncogenic Rat Feeding Study: ChE NOEL = 10 mg/kg/day; chronic toxicity NOEL = 3.0 mg/kg/day; oncogenic potential: negative at 10 mg/kg/day (HDT)

3

7. Calculation of the ADI

The ADI is based on the NOEL of 15.0 mg/kg/day in the 6-month dog feeding study. A 1000 fold safety factor was used to calculate the ADI.

$$ADI = 15.0 \text{ mg/kg/day} \times \frac{1}{1000}$$

$$ADI = 0.015 \text{ mg/kg/day}$$

The MPI for a 60 kg person is 0.9 mg/day

8. The permanent tolerances utilize 0.25% of the ADI (computer printout attached).

Conclusions and Recommendations:

The permanent tolerances can be toxicologically supported.

William Dykstra, Ph.D WDD
Toxicology Branch
Hazard Evaluation Division (TS-769) 4/30/82

Attachment

TS-769:th:TOX/HED:WDykstra:4-28-82:card 4

ACCEPTABLE DAILY INTAKE DATA

	Dog	NOEL	S.F.	ADI	MPI
	mg/kg	mg		mg/kg/day	mg/day(60kg)
	15.000	600.00	1000	0.0150	0.9000

Unpublished, Tox Approved 282581

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Cottonseed (oil)(41)	0.000	0.15	0.00000
Soybeans (oil)(148)	0.000	0.92	0.00000

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.0000 mg/day(1.5kg)	0.00

****

Current Action PP# 0F2413

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Cottonseed (oil)(41)	0.400	0.15	0.00090
Soybeans (oil)(148)	0.100	0.92	0.00138

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.0023 mg/day(1.5kg)	0.25

****