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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: Revised Risk Assessment on Monocrotophos (Azodrin)

To: Becky Cool
Special Review Branch
Registration Division (TS-767C)

From: Judith W. Hauswirth, Ph.D. Judith W. Hauswirth 1/20/88
Section Head, Section VI
Toxicology Branch/HED (TS-769C)

Thru: Theodore M. Farber, Ph.D., Chief
Toxicology Branch/HED (TS-769C)

Action Requested: Recalculate MOS's for cotton, peanut, and tobacco uses of azodrin using EAB's revised exposure assessment (memorandum dated Sept. 27, 1987), calculate MOS's for sugarcane uses and recalculate MOS's for the proposed use of azodrin on corn.

Background:

1. Proposed corn use: In a memorandum dated July 16, 1987, TB calculated the MOS's for the proposed use of azodrin on corn. A dermal penetration factor of 11% was used for these calculations. This number has since been raised to 15% after a complete and thorough review of the dermal penetration study, and therefore, the MOS's need to be revised.

2. Cotton, peanut, and tobacco uses: EAB has redone their exposure assessment for these uses (see memorandum dated Sept. 27, 1987) and therefore, the MOS's for these uses need to be revised.

3. Sugarcane use: In their memorandum of Sept. 27, 1987, EAB included an exposure assessment for sugarcane uses. MOS's have not been calculated for this use.

4. Toxicological effects used for calculating MOS's:
a. NOEL for teratogenicity was derived from a rabbit study. The NOEL for agenesis of the intermediate lobe of the lung was 1 mg/kg.

b. The lowest NOEL's for cholinesterase inhibition (including brain) are found in the rat and the dog and are as follows:

Dog: 13 week dog study NOEL = 0.5ppm or 0.0125 mg/kg/day; LEL = 1.5ppm (Core grade - supplementary)

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14 day dog study: NOEL = 0.5ppm or 0.0125 mg/kg/day; LEL = 1.5ppm (this study was not core graded)

2 yr. dog study: NOEL = 1.6ppm or 0.04 mg/kg/day; LEL = 16 ppm (Core grade minimum)

Rat: 13 week rat: NOEL = 0.5ppm or 0.025 mg/kg/day; LEL = 1.5ppm (Core grade minimum)

2 yr. rat: NOEL = 0.09ppm or 0.0045 mg/kg/day; LEL = 0.9ppm (Core grade minimum)

Note: The NOEL for this study was changed by the Toxicology Branch ADI Committee from 0.027 ppm to 0.09 ppm. The effects on cholinesterase seen at 0.027 were seen at only one time point during the study in both males and females and were not considered to be treatment related. The ADI was calculated based upon a NOEL of 0.0045 mg/kg/day and a safety factor of 100.

The NOEL chosen for calculating the MOS's for azodrin uses was that derived from the 13 week rat study. Although the NOEL was lower in the dog, as derived from the 14 day and 13 week studies; one of these studies was not core graded and the other was supplementary. In addition, the 2 yr. dog study, which was core minimum, had a higher NOEL for cholinesterase inhibition than either short term dog study and both of the rat studies. The rat was chosen as the most sensitive species and the subchronic rat NOEL was chosen for MOS calculations since the human exposure is not chronic but short term.

Calculations:

MOS's were calculated as follows: $\frac{\text{Appropriate NOEL (mg/kg/day)}}{\text{Exposure (mg/kg/day) x Dermal Penetration (\%)}}$

1. Ground Boom Application:

Mixer/Loader/Applicator:

Open pour

Teratogenicity:

Cotton: MOS = 22.2 (Range 16.7-31.7)

Tobacco: MOS = 44.4

Peanuts: MOS = 35

Corn: MOS = 8 (Range 7-8.6)

Cholinesterase:

Cotton: MOS = 0.55 (Range 0.41-0.8)

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Tobacco: MOS = 1.1

Peanuts: MOS = 0.88

Corn: MOS = 0.2

Closed System:

Teratogenicity:

Cotton: MOS = 148 (Range 111-215)

Tobacco: MOS = 256

Peanuts: MOS = 215

Corn: MOS = 88 (Range 20-312)

Cholinesterase:

Cotton: MOS = 3.7 (Range 2.8-5.4)

Tobacco: MOS = 6.4

Peanuts: MOS = 5.4

Corn: MOS = 2.4

2. Aerial Application:

Mixer/Loader (closed system):

Teratogenicity:

Cotton: MOS = 81 (Range 61-121)

Tobacco: MOS = 19600

Peanuts: MOS = 171

Sugarcane: MOS = 167

Corn: MOS = 108

Cholinesterase:

Cotton: MOS = 2.0 (Range 1.5-3)

Tobacco: MOS = 490

Peanuts: MOS = 4.3

Sugarcane: MOS = 4.2

Corn: MOS = 2.7

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Pilot:

Teratogenicity:

Cotton: MOS = 155 (Range 116-238)

Tobacco: MOS = 267

Peanuts: MOS = 247

Sugarcane: MOS = 267

Corn: MOS = 133

Cholinesterase:

Cotton: MOS = 3.9

Tobacco: MOS = 6.7

Peanuts: MOS = 6.2

Sugarcane: MOS = 6.7

Corn: MOS = 3.3

An acceptable MOS for teratogenicity is usually considered to be 100 and for cholinesterase 10.

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