

4-20-88



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

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OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: AZODRIN (Monocrotophos) - Addendum to Prior Review  
of the Rabbit Teratology Study Submitted under  
Accession No. 401023-01.  
EPA Registration No. 352-459

TB Project No.: 8-0063  
Caswell No.: 377

FROM: Irving Mauer, Ph.D.  
Toxicology Branch  
Hazard Evaluation Division (TS-769C)

*Irving Mauer* 04-20-88

TO: Rebecca Cool  
Special Review Branch  
Registration Division (TS-767C)

THRU: Judith W. Hauswirth, Ph.D., Head  
Section VI, Toxicology Branch  
Hazard Evaluation Division (TS-769C)

*Judith W. Hauswirth*  
4/21/88

On May 18, 1987, the review and evaluation (TB Document No. 005885) of the following study (submitted in response to reregistration data requirements) was sent to the Registration Division (William Miller/Gary Otakie):

Developmental Toxicity Study of AZODRIN®  
Insecticide (Technical) in New Zealand  
White (NZW) Rabbits, performed by Argus  
Research Laboratories, Horsham, PA, Argus  
Protocol No. 619-005/Haskell Lab. Report  
No. 014-87, dated January 12, 1987.

We concluded that the study was CORE-MINIMUM DATA, with the following parameters:

Maternal NOEL = 1 mg/kg/day  
Maternal LEL = 3 mg/kg/day (fecal disturbances)  
Developmental NOEL = 1 mg/kg/day

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Developmental LEL = 3 mg/kg/day (agenesis of  
intermediate lobe of the lung)  
A/D Ratio = 1.00  
(Doses tested = 0, 0.1, 1.0, 3.0, and 6.0 mg/kg/day)

The text of our review also discussed the reported occurrence in does treated at the highest dose tested (HDT), 6 mg/kg/day, of the statistically significant increase in maternal deaths, decreased weight gain, clinical signs of organophosphate toxicity and gross pathological lesions (multiple gastric as well as duodenal ulcerations, pulmonary edema, and enlarged gallbladders). As is also clearly evident in the study report, there was a dose-dependent trend for these effects which included the next lower dose level, 3 mg/kg/day, as well as the HDT (although the effects were not statistically significant at the lower dose). In addition, the investigators recorded three 3 mg/kg group rabbits with alopecia and/or soft/dried feces that delivered prematurely (Days 27 to 29 of the study). Such spontaneous delivery was suggested by the authors as a compound-related effect, despite the zero incidence at other dose levels (including the HDT), as well as in controls. (It was further suggested that the increased mortality at the HDT, namely, 13 of 20 animals, may have diminished the likelihood of observing prematurity.) Finally, only gastric ulcerations were found on necropsy in the three mid-dose does that delivered prematurely, in two of which enlarged gallbladders were also found.

Therefore, the "one-liner" description of maternal effects at 3 mg/kg/day (the LEL) should be enlarged to include the effects considered to be compound-related (additions underlined):

Maternal NOEL = 1 mg/kg/day  
Maternal LEL = 3 mg/kg/day (death of one dam,  
gastrointestinal ulceration,  
premature delivery, fecal  
disturbance)

Developmental NOEL = 1 mg/kg/day  
Developmental LEL = 3 mg/kg/day (agenesis of  
intermediate lobe of lung)  
A/D Ratio = 1.00  
(Doses tested = 0, 0.1, 1.0, 3.0, and 6.0 mg/kg/day)

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