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

JAN 21 1987

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: CARBARYL; Company Response to Tox Br. Review of Metabolism Studies; TOX CHEM. NO. 160.

FROM: R. Bruce Jaeger, Head
Review Section #1
Toxicology Branch/HED (TS-769) 12/30/86

TO: Larry Schnaubelt, PM#12
Insecticide/Rodenticide Branch
Registration Division (TS-767)

Registrant: Union Carbide Agriculture Products Company
Letter of Nov. 11, 1986 (No. 265-86) 1/15/87

Registration No.: 264-324

The Registrant provided responses to concerns addressed in our 5/15/86 memorandum (R. Landolt) regarding the metabolism of carbaryl in rat and dog.

Response #1 :

TB requested characterization of the polar fraction in dog urine vs rat urine. The company states that mercapturic acid conjugates, as well as 1-naphthyl cysteine derivatives, were not found in either dog or rat urine. However, they noted that "side-by-side comparisons" of the same fractions (rat and dog) were qualitatively similar but quantitatively different. Nonetheless, they still have not determined exactly what the components are, only that they co-chromatograph in a similar manner. They conclude that metabolism of carbaryl was qualitatively similar between rat and human. Tox. Branch is unable to draw the same conclusion on the basis of such limited information in humans.

Response #2 :

TB observed that the quantitative difference in metabolism between dog and rat were probably the result of differences in absorption of orally administered carbaryl based on the physical form and the vehicle used (i.e. capsule vs corn oil). Clarification of these differences was requested. The company has responded by noting this difference is due to 1) "true species differences in kinetics" and 2) "incomplete absorption of crystalline carbaryl administered in capsules to dogs".

Response #3 :

TB observed that the rat study using female rats did not permit a quantitative comparison beteen rat and dog since only one sex was used. The company has noted no difference between male and female dogs and therefore, separate evaluation in male rats is unnecessary. While TB intuitively agrees, there are obvious quantitative, if not qualitative, differences between the sexes as pointed out in our 5/15/86 review (pg 6). These noted differences demonstrate possible differences in preferential or major routes of absorption, elimination and excretion which we encourage the Registrant to address. No additional data seem necessary, however, at this time.

TB takes issue with the Registrant's statement that "we (TB, RD, UC) agreed that all metabolism questions had been resolved". As noted in our 5/15/86 review and our brief comments above, TB does not consider "all metabolism questions to be resolved", since approximately 27-53% of highly polar metabolites in the urines of rats and dogs, respectively, remain unidentified. Also, in dogs, approximately 78-86% of the fecal metabolites comprise conjugated or unextractable moieties. While more is known about fecal metabolites in rats, approximately 10% remain unextractable or unidentified conjugates.