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SCIENTIFIC DATA REVIEWS
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: **Indoxacarb: ID# 8F04948, 000352-LOU**: Toxicology Disciplinary Chapter for Registration: Evaluation of the Existing and New Toxicity Data Base for: 1) Requested Registration and Tolerances, 2) DuPont's Response to the Previous HIARC Report (24-JUN-1999). Also Evaluate the Memorandum of Discussion Dated 3-AUG-1999 from Meeting Dated 24-JUN-1999.

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From: Marion Copley, D.V.M., D.A.B.T. Marion Copley 7/18/00
Registration Action Branch I
Health Effects Division (7509C)

To: Dan Peacock/Tina Levine (PM 4)
Registration Division (7505C)

Through: George J. Herndon, B.S.S. George Jeffrey Herndon 7/18/00
Registration Action Branch I
Health Effects Division (7509C)

I. CONCLUSIONS

The toxicity data base is complete (with the exceptions noted below) and supports conditional registration and the associated tolerances for **indoxacarb** (DPX-MP062) as an insecticide for use on apples, brassicas, cotton, lettuce, fruiting vegetables and corn. The submitted studies and DuPont's response to the first Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) meeting are all acceptable. However, a 90-day inhalation toxicity study is required based on the respiratory signs of toxicity observed in the acute inhalation studies and based on the presence of neurotoxicity in several studies in both rats and mice, a developmental neurotoxicity study is also required.

HED agrees in general with the **Memorandum of Discussion: EPA and DuPont Concerning HED Issues for DPX-MP062 (Indoxacarb)**. It should be pointed out however, that there were no binding commitments made on the part of HED at that meeting, only suggestions that DuPont follow-up the meeting with a formal submission of the information they presented.

II. ACTION REQUESTED

Registration Action Branch 1 (RAB1) received new toxicity data for evaluation relating to registration of **indoxacarb** as an insecticide for use on apples, brassicas, cotton, lettuce, fruiting vegetables and corn. Items submitted for review included several special mechanistic studies, a 28-day rat dermal study and responses to the HIARC report (document dated 24-JUN-1999, HED. Doc. No. 013528) (MRIDs 44879801 - 03, 44910801 - 03, 44983901). Five new DERs for these studies and 11 revised DERs are attached to this updated **Toxicology Disciplinary Chapter for Registration**. This Toxicology Chapter supersedes all previous toxicology chapters for **indoxacarb**.

HED was also requested (D262559) to evaluate the **Memorandum of Discussion** dated 3-AUG-1999 from a meeting between DuPont and OPP held 24-JUN-1999 (see statement in the conclusion section above).

III. BACKGROUND

Indoxacarb (DPX-MP062) is a new insecticide. It is comprised of 2 enantiomers (75% DPX-KN128, 25% IN-KN127). The DPX-KN128 enantiomer is considered to be the insecticidally active portion and acts by blocking the sodium channels in the insect's nervous system. The Registrant has conducted most of their long term studies with the racemic chemical—**JW062 (DPX-JW062)**—which is 50% DPX-KN128 and 50% IN-KN127. The Registrant has requested that the Agency use toxicity data generated with **JW062** to satisfy Section 3 registration and tolerance toxicity data requirements for **indoxacarb**. Although both **indoxacarb** and **JW062** are soluble in polyethylene glycol (PEG), it appears that **JW062** is less soluble in corn oil than **indoxacarb**. **JW062** also forms a suspension in methyl cellulose.

HED previously evaluated the data base for **indoxacarb** (HIARC #1: 24-JUN-1999, HED Doc. No. 013528, and Tox. Chapter: 8-JUL-1999, HED Doc. No. 013557) and determined that it did not support registration. The HIARC (HIARC #2 document dated July 17, 2000, HED Doc. No. 014241) reviewed the revised data base for **indoxacarb (DPX-MP062),** with regard to the acute and chronic Reference Doses (RfDs) and the toxicological endpoint selection for use, as appropriate, in occupational/residential exposure risk assessments. The potential for increased susceptibility of infants and children from exposure to **indoxacarb** was also evaluated as required by the Food Quality Protection Act (FQPA) of 1996. In addition, the HIARC re-addressed the issues evaluated previously: (1) use of the **JW062 (DPX-JW062)** toxicology data base to support registration of **indoxacarb**; and (2) several hazard issues.

cc: Caswell file, Copley (RAB1), Sarah Levy (RAB1), George Kramer (RAB1)