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

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DATE: October 20, 1997

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: ***IMIDACLOPRID*** - Addendum to the Report of the Hazard Identification Assessment Review Committee.

FROM: Jess Rowland, Branch Senior Scientist, Jess Rowland 10/20/97
Science Analysis Branch, Health Effects Division (7509C)

THROUGH: K. Clark Swentzel, Chairman, K. Clark Swentzel 10/20/97
Hazard Identification Assessment Review Committee
Toxicology Branch II, Health Effects Division (7509C)

TO: Richard Loranger, Branch Senior Scientist
Registration Action Branch, Health Effects Division (7509C)

On September 11, 1997, the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) met to evaluate the toxicology data base of Imidacloprid to select toxicological endpoints for acute dietary as well as occupational and residential exposure risk assessments. At that meeting the HIRC concluded that dermal risk assessment for occupational and residential exposures are not required based on the lack of dermal and systemic toxicity following single and repeated exposures to Imidacloprid in laboratory animals and thus, there is no concern for exposure via this route.

On September 15, 1997, the Risk Assessment Committee (RARC) during its review of the risk assessment document for Imidacloprid raised the concern as to why the neurotoxicity endpoint, which was identified for the Acute Dietary exposure was not selected for dermal occupational/residential risk assessments as well.

On October 16, 1997, HIARC met to clarify the above concern raised by RARC. The HIARC's conclusions are as follows:

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The HIARC concluded that the neurotoxicity endpoint, although applicable for Acute Dietary risk assessment is not appropriate for dermal risk assessments for the following reasons:

1). The clinical signs that manifested as increased motor activity in rats following a single oral dose at 42 mg/kg/day was observed only in the Acute Neurotoxicity Study (MRID No. 43170301 & 43285801) and was not substantiated in other studies via the oral or the dermal routes.

2) In a subchronic toxicity study, no neurotoxic clinical signs or neuropathology were seen in rats following repeated oral administrations at doses of 0, 10.5, 69.3, or 213 mg/kg/day for 13 weeks. For neurotoxicity, the NOEL was $\geq$ 213 mg/kg/day (MRID No. 43286401).

3) Although neurotoxic clinical signs observable via the oral route are also observable via the dermal route, no such neurotoxic clinical signs were observed either after a single dermal dose in the Acute Dermal LD50 study with rats (MRID No. 42055332) or after repeated dermal applications in the 21-Day Dermal Toxicity with rabbits (MRID No. 42256329).

4) The lack of dermal or systemic toxicity at the Limit-Dose (1000 mg/kg/day) in the 21-Day Dermal Toxicity indicate poor dermal absorption which was also substantiated by the lack of dermal or systemic toxicity in the Acute Dermal study where the LD50 was >5000 mg/kg/day (MRID Nos. 42055332 & 42256329)

5) Poor dermal absorption was also indicated by the ratio obtained when the oral NOEL of 24 mg/kg/day established in the developmental rabbit study was compared with the dermal NOEL of 1000 mg/kg/day established in the dermal study with the same species (rabbits) (Oral NOEL = 24 mg/kg/day / Dermal NOEL =1000 mg/kg/day x 100 = approximate dermal absorption = 2.4%).

6) In addition, if there is no systemic toxicity with the technical material which was used in the toxicity studies, exposure to the formulated products with lower technical active ingredients even lessens the risk in real-life situations.

7) Domestic animal safety studies conducted with cats and dogs following single or repeated dermal applications of Imidacloprid (10% formulation) showed no major treatment-related dermal, clinical signs, body weight effects or clinical chemistry alterations. These studies demonstrated that cats and dogs can tolerated 50 mg/kg without significant adverse reactions (MRID Nos. 43679501, 43679502, 43679607, 43679608).

Based on these observations, HIARC re-affirmed their earlier conclusion that occupational/ residential risk assessments are not required for dermal exposures to Imidacloprid.