FILE COPY

012407

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: November 26, 1997

MEMORANDUM

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

FROM: Jess Rowland 11/26/97
Branch Senior Scientist,
Science Analysis Branch, Health Effects Division (7509C)

THROUGH: K. Clark Swentzel 11/26/97
Chairman, Hazard Identification Assessment Review Committee
Toxicology Branch II, Health Effects Division (7509C)

TO: Donna Davis
Chief, Registration Action Branch, Health Effects Division (7509C)

and

Elizabeth Haeberer
Product Manger
Registration Action Branch, Registration Division (7508W)

PC Code: 129099

On September 11, 1997, the Health Effects Division's Hazard Identification Review select toxicological endpoints for acute dietary as well as occupational and residential exposure risk assessments and determined the uncertainty factors for use in acute and chronic dietary as risk assessments. The Committee's decisions were provided in the "Report of the Hazard Identification Assessment Committee" (Memorandum: J. Rowland, HED to E. Haeberer, RD, dated September 22, 1997). However, further clarification was requested regarding the Margin of Exposure (MOE) recommended for the acute and chronic dietary risk assessments. This Memorandum provides clarification on the recommended MOEs for these risk assessments.

I. BACKGROUND

1. Acute Dietary Risk Assessment

The Hazard ID Report (Page 13) stated that the additional 10 x factor to account for enhanced sensitivity of infants and children (as required by FQPA) should be reduced to 3 x for a total UF of 300 (10 x for each for inter-and intra-species variation and 3 x for FQPA). A 300 MOE was recommended because the dose identified for this risk assessment was based on the LOEL and not a NOEL.

Confusion: This apparently caused some confusion and presented a picture as if a total UF 1000 (10 x for inter-species, 10 x for intra-species, 3 x for FQPA and 3 x for a lack of NOEL) was required.

Clarification: The Committee determined that the 3 x factor covers both the FQPA and the lack of a NOEL and therefore only a MOE of 300 is required.

Rationale: A total MOE of 300 was judged to be adequate based on the following factors:

1) Developmental toxicity studies showed no increases sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

2) A two generation reproduction toxicity study in rats showed no increased sensitivity in pups as compared to adults and offspring.

3) The toxicology data base is complete and there are no data gaps.

4) The endpoint (decrease in motor activity) used for risk assessment was seen in adult female rats following a single oral dose in an acute neurotoxicity study.

5) The same effects (i.e, decrease in motor activity) was not seen in rats following repeated dosing in a subchronic neurotoxicity study.

Thus the 3 x factor should provide adequate protection for all population subgroups including infants and children.

2.Chronic Dietary Risk Assessment

The Hazard ID report (Page 14) listed the following three factors to support the requirement of a MOE of 300.

(I) Concern for structure activity relationship. Imidacloprid, a chloronicotinyl compound, is an analog to nicotine and studies in the published literature suggests that nicotine, when administered causes developmental toxicity, including functional deficits, in animals and/or humans that are exposed *in utero.*

(ii) Imidacloprid administration resulted in evidence of functional neurotoxicity in the acute toxicity study in rats. Dose-related decreases in motor activity was seen in females given a single oral dose. Significant alterations to brain weight were noted in the 2-year carcinogenicity study in rats.

(iii Need of a developmental neurotoxicity study for assessment of potential alterations on functional development (i.e., data gap).

Confusion Factor (ii)- when an acute study is used as a rationale for requiring a chronic MOE of 300, then why is this study not used in the rationale for acute risk assessment.

Clarification: The acute neurotoxicity study discussed in factor (ii) for chronic dietary risk assessment is the same study used for selecting the dose and the endpoint for acute dietary risk assessment

Error: Factor (iii) - The need for a developmental neurotoxicity is listed as a "data gap". This study is not a part of the Subdivision F Guideline requirement and therefore is not a data gap. HED has not used an Uncertainty Factor of 3 for risk assessment of other chemicals based solely on the request/need for this study.