8-30-94

MEMORANDUM

SUBJECT: Imazalil. Laying Hen and Lactating Goat Metabolism. The Metabolism Committee Meeting Held on August 18, 1994.

FROM: Leung Cheng, Chemist
Special Review Section I
Chemistry Branch - Reregistration Support
Health Effects Division (7509C)

THROUGH: Edward Zager, Chief
Chemistry Branch - Reregistration Support
Health Effects Division (7509C)

TO: The HED Metabolism Committee

Results of the metabolism of imazalil in hen and lactating goat were presented to the HED Metabolism Committee on August 18, 1994 (see the memorandum dated 8/4/94, L. Cheng, for details). Imazalil was extensively metabolized in hen and goat. Only six metabolites out of about twenty identified were found in both hen and goat. Residue levels in hen eggs and tissues were <0.01 ppm (except 0.028 ppm in liver) when the exaggerated dose was taken into consideration. When normalized to expected dietary burden, residue levels in goat ranged from 0.015 ppm to 3.3 ppm in milk and tissues. Members of the Committee were asked whether the current tolerance expression for animal commodities should remain unchanged or separate tolerance expressions be set for poultry and ruminant? Which metabolites require regulation in each case?

The Committee concluded that, in the absence of information to the contrary, any metabolite containing the 2,4-dichlorophenyl moiety is of toxicological concern and must be included in the dietary risk assessment. The Committee concluded that CBRS should define a list of metabolites containing this moiety which should be analyzed in animal feeding studies and explicitly included in the tolerance expression. These metabolites together with the parent compound should serve as marker compounds which should, using metabolite ratios found in the metabolism studies, be used to determine residue values for dietary risk assessment. It would be assumed that only metabolites identified in the metabolism study as having the 2,4-dichlorophenyl moiety constitute the residue to be included in risk assessment.

A. Individuals in Attendance:

1. Metabolism Committee: (Signatures indicate concurrence unless

otherwise stated)

Reto Engler _____

Richard Schmitt _____

Richard Loranger _____

Michael Metzger _____

Alberto Protzel _____

Karl Baetcke _____

George Ghali _____

Charles Frick _____

2. Scientists: (Non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report)

Leung Cheng _____

Henry Spencer _____

3. Metabolism Committee Members in Absentia: (Committee members who were unable to attend the discussion; signatures indicate concurrence with the overall conclusions of the Committee) - NONE

B. Material Reviewed:

Discussed were two studies that are entitled "Imazalil: Distribution, Metabolism (Nature of the Residue) and Excretion Study in the Laying Hen", Janssen Report No. 93/JST006/0615, 12/17/93, and "14C-Imazalil: Distribution, Degradation, Metabolism and Excretion After Repeated Oral Administration to a Lactating Goat", Janssen Report No. R23979/FK1206, 7/22/92, and supplements.

cc:Circ, SF, List B File, Cheng, Metabolism Committee File
RDI:ARRathman:8/23/94:MSMetzger:8/23/94
7509C:LCheng:CBRS:CM2:Rm804D:8/22/94:■3:IMAZALIL\RENGLER