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

MAR 31 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Goat Metabolism Study Submitted by CIEL in Response to Lindane Registration Standard Data Call-in. Deference to TOX on the Need for a More Adequate Identification of Residues in Goat Liver and Kidney

FROM: Cynthia Deyrup, Ph.D., Chemist CD
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Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
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TO: Toxicology Branch (Ed Budd/John Doherty)
Hazard Evaluation Division (TS-769)

and

George LaRocca, Product Manager # 15
Registration Division (TS-767)

TOX (J. Doherty) has suggested that deferences to them from RCB be addressed in a memorandum specifically delineating RCB's questions. (J. Onley of RCB also talked to E. Budd of TB on this issue-3/29/88).

CIEL (Centre International d'Etudes du Lindane) has submitted goat metabolism studies reflecting both topical and oral dosing. Oral dosing reflected an estimated 1X and 10X dosing (estimates because of incomplete residue data). Dermal livestock treatments are also permitted. Therefore the total expected residue levels from 1X treatments would be the sum of the burden from ingestion and dermal treatment.

The following levels of activity in goat liver and kidney were reported.

Matrix	Goat 1 OR-1X	Goat 2 OR-1X	Goat 3 OR-10X	Goat 4 DERM-0.25X	Goat 0 DERM-1X
Kidney					
TRR (ppm)*	0.731	0.734	5.995	0.197	0.730
% TRR Lindane		4.5	6.5	7.0	
% TRR identified		4.5	6.5	7.0	
Liver					
TRR (ppm)	3.824	4.094	19.506	0.497	2.808
% TRR Lindane			0.2-0.6	9.7	1.7
% TRR 1,3,5-trichlorobenzene			<0.1		
% TRR Identified			<0.3-<0.7	9.7	1.7

*TRR = Total Radioactive Residue

Even though ^{14}C residues in liver were almost 20 ppm (lindane equivalents) in the goat fed at a 10X rate, almost none of the TRR was identified. Consequently, there is no way of determining residue levels in liver, even though radioassay indicates that levels of metabolites far exceed the established tolerance of 7 ppm lindane in goat fat (there are no established tolerances for other tissues). A similarly confused metabolic picture exists in kidney tissue.

If TOX is concerned about the unidentified residues in liver and kidney, the registrant will need to carry out further work.

Although the residues in liver and kidney were not identified, the registrant has tentatively identified metabolites in other matrices such as urine, milk, and fat. These metabolites are listed below in order to assist TOX in determining whether residues in liver and kidney need to be identified.

Residues Tentatively Identified in Goat Matrices

1,2,4-Trichlorobenzene
1,2,3,4-tetrachlorobenzene
1,2,3,5-tetrachlorobenzene
Hexachlorocyclohexene
1,2,4,5-Tetrachlorobenzene
3,4-Dichlorophenol
2,6-Dichlorophenol
4-Chlorophenol
2,4- or 2,5-Dichlorophenol
2,3,6-Trichlorophenol
2,3,5-Trichlorophenol
2,3,5,6- or 2,3,4,6-Tetrachlorophenol
2,3,4,5-Tetrachlorophenol
2,4,5-Trichlorophenol
2,4,6-Trichlorophenol

cc: Lindane Reg. Std. File-W. Boodee, PMSD/ISB, RF, Reviewer-Deyrup, G. LaRocca-PM#15, Circu, Lindane Subject File
RDI: J.H. Onley:3/29/88:RDSchmitt:3/29/88
TS-769:RCB:CM#2:RM810:X7484:CDeyrup:cd:3/29/88