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

SEP 24 1984

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: OF2413/0H5275/3F2793/3H5378 Thiodicarb/Larvin-Toxicology Evaluation of "Sensitivity of Method" for Acetamide

TO: Jay Ellenberger
Product Manager (12)
and

Dennis Edwards
Registration Division (TS-767)

FROM: Christine F. Chaisson C.F. Chaisson
Head, Section Review IV
Toxicology Branch
Hazard Evaluation Division (TS-769) 9/24/84

Background:

Union Carbide has proposed that EPA establish feed additive tolerances for thiodicarb residues in/or on hulls of cottonseed and soybean seed using FDA's Sensitivity of Methods (SOM) policy. The interest is in a metabolite, acetamide, which was tested in rats, and found to be carcinogenic. ("Carcinogenesis Bioassay of Acetamide, Hexanamide, Adipamide, Urea and P-Tolylurea in Mice and Rats", V.R. Fleishman et.al., J. Env. Path. Tox. 3:149-170, 1980). This report was evaluated and found to be faulty in many respects (Litt., 5/24/83). However, because of the Delaney Clause of FFDCA, and the absence of any better study, this study was used to calculate a geometric mean of the Q_1^* (Litt, 2/8/83).

For the purpose of addressing Union Carbide's proposal, in concert with the latest FDA guidelines on risk assessment, the FDA food factors and assessment methodology was used. For the target tissues listed below, a residue was calculated, below which risk is expected to be less than 1×10^{-6}. If the analytical procedures proposed by Union Carbide are at or below these levels, the SOM may be acceptable. The values given below should be considered by the Residue Chemistry Branch.

Target Tissue	FDA food factor (% of diet)	Residue associated with 1 X 10^{-6} risk (ppb)	Residue level for SOM Calculated by U.C. (ppb)
Milk	100	36	22.2
Eggs	33	108	66.7
Meat	33	108	66.7
(Liver)	*	(1836)	1134

*For acetamide, the anticipated met residue liver residue ratio is 1/17, and the consumption factor is assumed to be part of "meat". Therefore, the SOM residue is assumed to be a function of the 17 fold increase in detectability.

These residue levels should be compared to the LLRM as determined by Residue Chemistry. In all cases, the residue levels calculated here are higher than that submitted as the theoretical calculation by Union Carbide. Union Carbide "corrected" their estimates for a total overall diet, which resulted in a decrease in the required level of sensitivity. The Toxicolgy Branch accepts the unadjusted FDA food factors as adequate for the risk assessment.

Other toxicology and risk assessment methodologies presented by Union Carbide appear to meet the new FDA guidelines, and therefore are acceptable.

cc: Anne Barton
(Caswell file) #900AA
Richard Schmitt, RCB

TS-769:CChaisson:tmr:9/21/84 Code Mis. 1

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