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CURACRON, TOXICOLOGY PROFILE 11/1/78

from Dave Ritter (memo 11/2/78)

Background Information:

Curacron, a product of the Ciba-Geigy Corporation, P.O. Box 11422, Greensboro, N.C., 27409. The Company had submitted a tolerance petition (#PP 7G1888) proposing temporary tolerances for the combined residues for the insecticide O-(4-bromo-2-chlorophenyl)-O-ethyl S-propyl phosophorothioate and its metabolites in cotton seed at 3 ppm; eggs and the meat fat and meat by-products of cattle, goats, hogs, horses, poultry and sheep at 0.05 ppm; and milk at 0.01 ppm. Food additive tolerances in cotton seed hulls and soapstock hulls are likewise established however these are not human food items and will not further considered here. The following is a toxicology profile as you requested for the halogenated organophosphate Curacron in cotton.

ACUTE TOXICITY

Species	Substance	LD_{50}	Toxic Signs	Toxicity Category
Rat	Tech. Mat	400 mg/kg	sedation, dyspnea and tonic.clonic spasms	II
Rat	Formulation (4EC)	810 mg/kg	same as above	III
Rabbit Acute Dermal	Tech	472 mg/kg	sedation, tremors and salvation	II
Rabbit Acute Dermal	Formulation	241 mg/kg	erythema, 2nd degree burns, escharosis and fissuring at 14 days	~~I~~ II
Rabbit Acute Dermal	Use dilution 1:8 and 1:40	1830 mg/kg		
Rat Acute Inhalation	Tech	2624 micro-grams/liter	dyspnea, tremors, exophtalmos	III

(formulation LC_{50} is greater than 2450 mg/meter^3) = I

> 2.45 mg/L

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Rat Eye Irritation	Formulation	Draize eye score is 39/100 and was therefore considered to be a severe eye irritant.	I
Rabbit Primary Skin Irritation	Technical	Draize score of 0.9/8 or minimally irritating to the skin.	
	Formulation	Draize score of 7.4/8.0 was considered to be a severe dermal irritant.	I
Guinea Pigs Dermal Sensitivity		negative	

SUBACUTE TOXICITY:

1. 90-Day Rat Feeding Study (Hazelton #1519).

   A clear cut NEL for RBC or Brain CHE inhibition was not demonstrated at the lowest dose offered, 3 ppm. All other parameters studied were not remarkable for effect; hence the principle toxic manifestation is RBC CHE inhibition. This study is validated as "Core Minimum Guideline" even though only two levels of Curacron were offered; however there was no NEL demonstrated.

2. 90-Day Dog Feeding Study (IBT #611-05122-B).

   Dogs receiving diets containing 0, 2, 20 or 200 ppm Curacron showed no gross or histopathological changes indicative of systemic toxicity at any level. RBC CHE inhibition was noted as low as 2 ppm; however, the controls also showed CHE inhibition. Thus, no sound conclusion as to NEL for CHE inhibition can be made. This study is validated as "Core Guideline".

CHRONIC FEEDING STUDIES:

1. 2-Year Rat Feeding Study - 12 month interim report (IBT #622-06895); 8/26/76. Summary to date: 60 males and 60 females per group were offered diets containing 0, 0.2, 1, 20 or 200 ppm Curacron. Results indicate no adverse effects at any level on clinical parameters (blood and urine) performed on 20 rats per sex per group for the high dose and control levels. CHE effects: In 20 rats per sex per group of all groups/there was significant depression at 20 ppm but not at the lower levels.

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NEUROTOXICITY STUDY

1. Chicken Delayed Neurotoxicity Study (IBT #8580-10426).

   A standard 42 day, two-challenge test was performed with Curacron formulation containing 38% AI. A TOCP positive control group was included. Birds surviving the challenge period at doses up to 44.5 mg/kg AI failed to show gross or overt signs of neurotoxicity; Specially stained microscopic preparations of nerve tissue revealed no signs of degeneration of demyelination. This study is validated as "Core Guideline".

   All studied reported here have been properly validated by Ciba-Geigy personnel. See the report of R. Engler, 8/5/77, PP#7G1888.

   For consideration of any permanent registration tolerances we will need completed studied as noted below.

   1. Complete multi-generation rat reproduction study
   2. Complete oncogenic evaluation (18-month mouse)
   3. Complete teratology study
   4. Mutagenicity study

There are no RPAR triggers in the data before the Agency at this point.

DLR 11/2/78

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