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REPORT OF THE HIARC

Time Limited Tolerance: DICHLORMID (PC Code 900497) For Use As A Safener in/on Corn

August 5, 1999

REPORT OF THE HIARC - EXPEDITED ACTIONS

CHEMICAL NAME: Dichlormid
PC CODE: 900497
ACTION / REQUEST: Time Limited Tolerance
REQUEST *ID#*: Not Provided
REQUESTOR: William Dykstra, RAB1
DATE: August 5, 1999

SUMMARY OF PROPOSED USE: Time-limited tolerance for use as a safener with Acetochlor in/on corn.

I. Toxicology Endpoint Selection for this Time Limited Tolerance

The Hazard Identification Assessment Review Committee (HIARC) met on August 5, 1999 and selected doses and endpoints for dietary and non-dietary exposure risk assessments. **Please note the decisions made at this meeting are only for this TIME LIMITED TOLERANCE.**

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT / STUDY	RATIONALE
Acute Dietary (General Population including Females 13+, Infants & Children)	10	Maternal LOAEL = 40 mg/kg/day based on decreased body weight gain and food consumption (most significant on days 7-10 of dosing) in the developmental study in rats	The endpoint is appropriate because the effects were observed after the first day of dosing (GD 7). This maternal NOAEL is lower than the developmental NOAEL of 30 mg/kg/day in the developmental rabbit study (wherein qualitative increased susceptibility was observed at 180 mg/kg/day) and will be protective of Females 13+ as well as the general population including infants and children.
	UF = 100	**Acute RfD = 0.10 mg/kg/day**	

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EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT / STUDY	RATIONALE
Chronic Dietary	6.5	LOAEL = 32.8 mg/kg/day (♂) based liver clinical pathology / histopathology and increased liver weight in the 2-year study in rats	The duration of this study is appropriate for this risk assessment. The results of the 90-day study in rats supports this endpoint. Extra 3x UF due to data gap for the chronic study in dogs.
	UF = 300	**Chronic RfD = 0.22 mg/kg/day**	
Dermal Absorption	100% default; neither a dermal absorption study nor a dermal toxicity study (for extrapolation) is available in the database.		
Short-Term (Dermal)	Oral NOAEL 10.0 MOE = 100	Maternal LOAEL = 40 mg/kg/day based on decreased body weight gain and food consumption (most significant on days 7-10 of dosing) in the developmental study in rats.	This dose/endpoint/study was used for deriving the acute RfD. Dermal toxicity study is not available. Since an oral NOAEL was selected 100% dermal absorption factor should be used for this risk assessment.
Intermediate- and Long-Term (Dermal)	Oral NOAEL 6.5 MOE = 100	LOAEL = 32.8 mg/kg/day (♂) based liver clinical pathology / histopathology and increased liver weight in the 2-year study in rats	This dose/endpoint/study was used for deriving the chronic RfD. Since an oral NOAEL was selected 100% dermal absorption factor should be used for this risk assessment.
Inhalation (All Durations)	2 µg/L	LOAEL = 19.9 µg/L based on clinical signs, increased liver and kidney weights, gross pathology and liver histopathology.	The route of exposure in this study is appropriate for this risk assessment.

II. FQPA Assessment for this Time Limited Tolerance

The HIARC concluded that there is qualitative evidence of increased susceptibility demonstrated following *in utero* exposure in the prenatal developmental toxicity study in rabbits. Additionally there is a data gap for the two generation reproduction study in rats and the requirement for a developmental neurotoxicity study in rats is reserved.

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Summary of the Developmental & Reproduction Studies

Developmental Toxicity -Rat			
Maternal Toxicity (mg/kg/day)		Developmental Toxicity (mg/kg/day)	
NOAEL =10	LOAEL =40	NOAEL = 40	LOAEL = 160
Basis for LOAEL: decreased body weight gain and food consumption		Basis for LOAEL: marginal increases in skeletal variations	

Developmental Toxicity -Rabbit			
Maternal Toxicity (mg/kg/day)		Developmental Toxicity (mg/kg/day)	
NOAEL = 30	LOAEL = 180	NOAEL = 30	LOAEL = 180
Basis for LOAEL: increased alopecia; decreased body weight gain and food consumption		Basis for LOAEL: increased resorptions, decreased live fetuses per litter, and decreased fetal body weight	

The HIARC concluded that there is qualitative evidence of increased susceptibility demonstrated following *in utero* exposure in the prenatal developmental toxicity study in rabbits since the fetal effects observed are considered to be more severe than those observed in maternal animals.

Two-Generation Reproduction Toxicity -Rat	
Parental Toxicity (mg/kg/day)	Offspring Toxicity (mg/kg/day)
DATA GAP	

Based solely on the hazard assessment (with no consideration of the exposure assessments), the HIARC recommended that the FQPA safety factor be retained at 10x since: 1) there is qualitative evidence of increased susceptibility in the developmental study in rabbits; 2) the toxicity data base is incomplete: there is a data gap for the 2-generation reproduction study in rats; 3) the recommendation for a developmental toxicity study in rats is placed in reserve pending receipt and review of the findings of the acute and subchronic neurotoxicity studies.

Report Preparation: _____ Date: August 5, 1999

Brenda Tarplee
Executive Secretary

Report Concurrence: _____

Jess Rowland, Co-Chair
HIARC