HED

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

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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Date: July 12, 1999

SUBJECT: **Chlorothalanil**: Determination of toxicologic concern under FQPA for the 3-Carbamyl-2,4,5-trichlorbenzoic acid (SDS-46851) soil metabolite.

DP Barcode: D257652
Chemical: Chlorothalanil
Caswell no.: 215B
PC Code: 081901
Registrant: Fermenta ASC Corporation

FROM: Roger Hawks, Ph.D.
Health Effects Division (7509C) Roger Hawks 7/12/99

THROUGH: Jess Rowland, Branch Chief
RCAB (7509C) Jess Rowland 7/12/99

TO: Dan Helfgott
Special Review and Reregistration Division
(7508C)

cc. : Ed Zager
Chair FQPA Safety Factor Committee
HED

Action Requested: The toxicology data base for the Chlorothalanil soil metabolite 3-Carbamyl-2,4,5-Trichlorobenzoic acid (also known as SDS-46851) has previously been reviewed (Memo dated 2/21/92, From Elizabeth Doyle, TXR 009322). Based on the low toxicity seen, HED exempted SDS-46851 from the need for a tolerance (40 CFR §180.1110).
The Food Quality Protection Act (FQPA) was passed in 1996. FQPA mandates that any potential effects of a compound on sensitive subpopulations - such as infants and children - be examined. A rereview of the toxicology database for SDS-46851 was deemed necessary in order to determine if a tolerance exemption was still appropriate under FQPA. This memo describes the results of this rereview of the SDS-46851 toxicology database.

Response: The toxicology database for SDS-46851 has been rereviewed. In regards specifically to FQPA, developmental toxicity studies in both the rat and rabbit and a one-generation reproduction study in the rat have been rereviewed by the agency. These studies indicate:

- the toxicology database is adequate (as shown in Table 1);
- no developmental toxicity was seen at 2000 mg/kg/day (double the limit dose of 1000 mg/kg/day) in the rat developmental toxicity study;
- no developmental toxicity was seen at the limit dose (1000 mg/kg/day) in the rabbit developmental toxicity study;
- the effects in the offspring in the one-generation reproduction study were seen at a higher dose than the dose which caused parental toxicity;
- based on these data there is no increased susceptibility of rat or rabbit fetuses, or rat and rabbit offspring, following *in utero* or pre/post natal exposure;
- the toxicology database supports the exemption of a tolerance in rotated crops for SDS-46851.

The toxicology database for SDS-46851 has been rereviewed with an emphasis on the criteria imposed by FQPA. The available data indicates no increased susceptibility to rat or rabbit fetuses following *in utero* exposure, or to offspring following pre/post natal exposure to SDS-46851. Therefore, RCAB reiterates the previous conclusion (Elizabeth Doyle memo of 2/21/92) that, based on toxicologic concerns, there are no objections to the exemption of a tolerance in rotated crops for SDS-46851.

A table displaying the toxicology database for SDS-46851 follows. Diagrams of the structures of the parent compound and the SDS-46851 metabolite are also attached.

Table 1: The Toxicology database for the Chlorothalanil soil metabolite SDS-46851.

Study Type	MRID #	Doses	Results	Classification
28-Day Feeding-Mouse (CD-1)	42090102	0, 50, 102, 203, 993, 2070 mg/kg./day	LOAEL not found in either sex NOAEL= >2070 mg/kg/day	Acceptable-Non-Guideline
90-Day Feeding-Mouse (CD-1)	42090103	0, 44, 134, 412, 1401 mg/kg/day	LOAEL not found in either sex NOAEL= >1401 mg/kg/day	Acceptable-Non-Guideline
Acute Oral Toxicity- Rat (Sprague-Dawley)	41564801	200, 1000, 5000 mg/kg/day	LD_{50} in both sexes was found to be >5000 mg/kg/day. Toxicity Category IV	Acceptable-Non-Guideline

Study Type	MRID #	Doses	Results	Classification
14-Day Feeding Study- Rat (Sprague Dawley)	41564801	0, 125, 250, 500, 1000, 2000 mg/kg/day	LOAEL= 2000 mg/kg/day in females based on increased liver weights relative to body weight. A male LOAEL was not found. NOAEL= >2000 mg/kg/day in males; 1000 mg/kg/day in females.	Acceptable-Non-Guideline
30-Day Feeding Study- Rat (Sprague Dawley)	41564803	0, 500, 2000 mg/kg/day	LOAEL= 500 mg/kg/day in both sexes based on ↑ liver weights NOAEL= < 500 mg/kg/day	Acceptable-Non-Guideline
90-Day Feeding study- Rat (Sprague Dawley)	41564806	0, 250, 750, 2000 mg/kg/day	LOAEL= 750 mg/kg/day in males based on ↑ relative liver and kidney weights. NOAEL= 250 mg/kg/day	Acceptable-Guideline
30-Day Feeding study- Dog (Beagle)	41564804	0, 100, 500, 1000 mg/kg/day	LOAEL= 100 mg/kg/day based on histopathology and hematology alterations. NOAEL= None found	Unacceptable
90-Day Feeding Study- Dog (Beagle)	41564805	0, 5, 15, 50, 100 mg/kg/day	LOAEL= 50 mg/kg/day based on ↑ liver weights, ↓ urinary pH and ↑ blood glucose concentrations in both sexes.	Acceptable-Guideline
Developmental toxicity, Range-finding - Rat (Sprague-Dawley)	41564808	0, 250, 500, 100, 2000 mg/kg/day	<u>Maternal LOAEL/NOAEL</u> LOAEL not found NOAEL was highest dose tested - 2000 mg/kg/day <u>Developmental LOAEL/NOAEL</u> LOAEL not found NOAEL was highest dose tested - 2000 mg/kg/day	Acceptable-Non-Guideline
Developmental toxicity- Rat (Sprague-Dawley)	41564808	0, 500, 1000, 2000 mg/kg/day	<u>Maternal LOAEL/NOAEL</u> LOAEL not found NOAEL was highest dose tested - 2000 mg/kg/day <u>Developmental LOAEL/NOAEL</u> LOAEL not found NOAEL was highest dose tested - 2000 mg/kg/day	Acceptable-Guideline

Study Type	MRID #	Doses	Results	Classification
Developmental toxicity, Range-Finding - Rabbit (New Zealand White)	41564809	0, 250, 500, 1000 mg/kg/day	Maternal LOAEL/NOAEL LOAEL=500 mg/kg/day based on reduced body weight gain and food consumption NOAEL=250 mg/kg/day Developmental LOAEL/NOAEL LOAEL= Not found NOAEL= was highest dose tested - 1000 mg/kg/day	Acceptable-Non-Guideline
Developmental toxicity - Rabbit (New Zealand White)	41564810	0, 250, 500, 1000 mg/kg/day	Maternal LOAEL/NOAEL LOAEL=500 mg/kg/day based on reduced body weight gain and food consumption NOAEL=250 mg/kg/day Developmental LOAEL/NOAEL LOAEL= Not found NOAEL= was highest dose tested - 1000 mg/kg/day	Acceptable-Guideline
One-generation reproduction study- Rat (Sprague-Dawley)	41564806	0, 250, 750, 2000 mg/kg/day	Maternal LOAEL/NOAEL LOAEL=750 mg/kg/day based on increased relative liver and kidney weights NOAEL=250 mg/kg/day Developmental LOAEL/NOAEL LOAEL= 2000 mg/kg/day based on decreased day 21 pup weights NOAEL= 750 mg/kg/day	Acceptable-Guideline
Mutagenicity-Ames Assay (TA 1535, 1537, 1538, 98 and 100)	41564812	39 to 3900 µg/plate	No evidence of mutagenicity reported at any dose with or without activation.	Acceptable-Guideline
Mutagenicity- In vitro gene mutation assay (L5178Y Mouse Lymphoma Cells)	41564813	500 to 4000 µg/ml	No mutagenic effects at any dose without activation. Mutagenic effects with activation were seen at all doses tested.	Unacceptable

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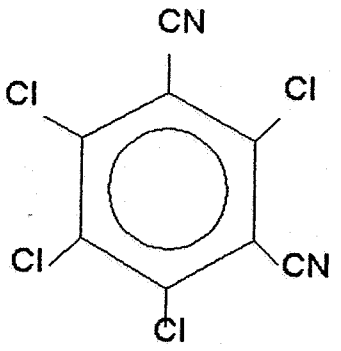
Study Type	MRID #	Doses	Results	Classification
Mutagenicity- *In vitro* gene mutation assay (L5178Y Mouse Lymphoma Cells)	41564814	75 to 1000 µg/ml	No evidence of mutagenicity reported at any dose with or without activation.	Acceptable-Guideline
Mutagenicity- UDS Assay (Primary Rat Hepatocytes)	41564815	24 to 240 µg/ml	No evidence of mutagenicity reported at any dose with or without activation.	Acceptable-Guideline
Mutagenicity- *In vivo* SCE Assay (Swiss Mice)	41564816	200 to 2000 µg/ml	No evidence of mutagenicity reported at any dose with or without activation.	Unacceptable
Metabolism- Rat (Sprague-Dawley)	41564818	10 and 1000 mg/kg/day	The test material was quickly excreted through both the urine and feces with the half life for elimination being 2.5 and 6.2 hours in the low and doses respectively.	Acceptable-Guideline

Figure 1: Structures of Chlorothalanil and SDS-46851

Chlorothalanil



SDS-46851