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

DEC 6 1985

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Request for Tolerances and Registration for the Use of Poast® on Sunflowers and Peanuts

EPA No. 5F-3234/5H-5464/7969-58 Project No. 118/119/120
Record No. 149010/149012/149957 Caswell No. 72A
40 CFR § 180.412

TO: Robert J. Taylor, PM Team #25
Registration Division (TS-767c)

FROM: John E. Whalan, Toxicologist
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769c)

THRU. Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769c)

Background:

BASF Wyandotte Corporation is requesting the issuance of full tolerances and the registration of the herbicide Poast® (sethoxydim; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one) and its metabolites for use on sunflowers and peanuts.

These requests were previously received in PP 3F-2950 along with tolerances and registration for sugarbeets. The petition was amended on April 17, 1984 to exclude sunflowers and peanuts because of RCB's concern about potentially hazardous plant and animal metabolites that might result from the use of Poast on these crops. In the intervening time, further studies of the metabolites have been submitted in conjunction with PP 3F-2904 (tolerances and registration for the use of Poast on alfalfa and soybean forage and hay).

The proposed tolerances requested are as follows:

Raw Agricultural Commodities

Peanuts	25.0 ppm
Peanut hulls	5.0 ppm
Sunflower seeds	7.0 ppm

Animal Feed Items

Peanut soapstock	75.0 ppm
Sunflower meal	20.0 ppm

Poast herbicide will be applied with either ground or aerial equipment to young sunflower and peanut crops to control postemergence grass weeds. It will be applied as a single application on annual grasses at a rate of 1 to 2 pints/acre (0.2-0.4 lbs ai/A) depending on the hardiness of the grasses. Perennial grasses may require two applications at a maximum rate of 1.5 pints/acre (0.3 lbs ai/A) for the first application (15-30 days after planting), followed by an optional second application of 1 pint/acre (14-21 days after the first application). The preharvest interval for sunflowers and peanuts is 70 days, and no more than 2.5 pints/acre (0.5 lbs ai/A) may be applied. Sunflower forage and peanut forage and hay must not be fed to livestock.

The ADI (see page 3) is based on the 2-year chronic feeding/oncogenicity study in rats (NOEL = 360 ppm or 18 mg/kg/day) with a safety factor of 100. Granting these tolerances will commit 3.48% of the ADI for a TMRC of 0.3755 mg/day.

The Registrant failed to submit a complete label. Rather, a "Supplemental Labeling" was provided. The last complete label received (5-21-85) was for the use of Poast on soybeans, cotton, ornamental, nursery and other non-food crops. The label is acceptable provided it includes the "Danger" signal word.

Toxicology Branch has no objection to granting the proposed tolerances on sunflowers and peanuts.

An Eight Point Free Standing Summary commences on page 4.

File last updated 5/8/85

ACCEPTABLE DAILY INTAKE DATA DRAFT

RAT,Older NOEL mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day(60kg)
18.000	360.00	100	0.1800	10.8000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Meat,inc poultry(89)	0.200	13.55	0.04154
Milk&Dairy Products(93)	0.050	28.62	0.02146
Eggs(54)	0.500	2.77	0.02073
Cottonseed (oil)(41)	5.000	0.15	0.01125
Soybeans (oil)(148)	10.000	0.92	0.13772
Sugar,cane&beet(154)	0.100	3.64	0.00546

MPI	TMRC	% ADI
10.8000 mg/day(60kg)	0.2382 mg/day(1.5kg)	2.21

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Current Action 5F3234

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Peanuts(115)	25.000	0.36	0.13413
Sunflower(156)	7.000	0.03	0.00315

MPI	TMRC	% ADI
10.8000 mg/day(60kg)	0.3755 mg/day(1.5kg)	3.48

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Summary of Toxicity Data
and
Eight Point Free Standing Summary

1. Summary of selected toxicology data considered for these actions:

STUDY	RESULTS	TOX CATEGORY	CLASSIFICATION
Data on Technical NP-55 (sethoxydim):			
Acute Oral LD_{50}, Rat	3125 mg/kg (males) 2676 mg/kg (females)	III	Guideline
Acute Dermal LD_{50}, Rat	>5000 mg/kg (males and females)	III	Guideline
Acute Inhalation LC_{50}, Rat (4 hours)	6.03 mg/l (males) 6.28 mg/l (females)	III	Guideline
Primary Eye irritation, Rabbit	No irritation	IV	Guideline
Primary Dermal Irritation, Rabbit	No irritation	IV	Guideline
Dermal Sensitization, Guinea Pig	Negative	-	Minimum
14-Week Mouse Feeding Study	NOEL = 300 ppm	-	Minimum
14-Week Rat Feeding Study	NOEL = 300 ppm	-	Guideline
6-Month Dog Feeding Study	NOEL = 20 mg/kg/day (males and females) LEL = 177 mg/kg/day (males) 223 mg/kg/day (females) (values based on analysis of diet and food) Non-specific anemia, liver effects, and possible kidney effects.	-	Guideline

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STUDY	RESULTS	TOX CATEGORY	CLASSIFICATION
2-Year Mouse Chronic Feeding/ Oncogenicity Study 0, 40, 120, 360, 1060 ppm	NOEL = 120 ppm (18 mg/kg/day) LEL = 360 ppm (non-neoplastic liver lesions) Not oncogenic in BDF_1 mice.	- -	Guideline [Chronic feeding] Guideline [Oncogenicity]
2-Year Rat Chronic Feeding/ Oncogenicity Study 0, 40, 120, 360 ppm	NOEL $\geq$360 ppm (18 mg/kg/day - highest dose tested)	- -	Guideline [Chronic feeding] Guideline [Oncocenicity]
Teratology Study, Rats 0, 40, 100, 250 mg/kg/day	Teratogenicity NOEL = 250 mg/kg/day (highest dose tested) Maternal NOEL = 40 mg/kg/day Maternal LEL = 100 mg/kg/day (significantly decreased adrenal weight)	-	Guideline
Teratology Study, Rabbits 0, 40, 160, 480 mg/kg/day	No terata at <160 mg/kg/day. Effects observed at 480 mg/kg/day (increased number of a variety of random effects including skeletal and visceral abnormalities, reduced fetal weight, and changes in male/female ratios) considered due to extreme toxicity in dams, Maternal NOEL = 160 mg/kg/day. Maternal LEL = 480 mg/kg/day (severe weight loss, 5/16 deaths, 6/16 abortions, and reduction in the number of litters and viable fetuses).	-	Minimum
Two-Generation Reproductive Study, Rats 0, 2, 6, 18, and 54 mg/kg/day	No reproductive effects. NOEL = 360 ppm 18 mg/kg/day	-	Guideline

STUDY	RESULTS	TOX CATEGORY	CLASSIFICATION
Mutagenicity Studies:			
A. Rec-Assays and Forward Mutations, B. subtilis, E. coli, S. typhimurium	Negative at concentrations of chemical to 100%	-	Minimum
B. Mouse Host-Mediated Assay, S. typhimurium	Negative at up to 2500 mg/kg bw/day of chemical.	-	Minimum
Metabolism Study, Rats	Tissue accumulation of chemical negligible and excretion extremely rapid, assuming DMSO vehicle does not affect storage or excretion of the chemical.	-	Guideline
Data on Formulated Product - BAS 9052 OH (EPA #7969 - LI):			
Acute Oral LD_{50}, Rat	4918.7 mg/kg	III	Guideline
Acute Dermal LD_{50}, Rat	>4000 mg/kg	III	Guideline
Acute Inhalation LC_{50}, Rat	>7.6 mg/l	III	Guideline
Primary Eye Irritation, Rabbit Study No. 1	P.I. = 32 (24 hours); 35 (48 hours); 29 (72 hours) Scarring in 5/6 animals at 8 days, corneal opacity in one animal at 8 days.	I	Minimum
Primary Eye Irritation, Rabbit Study No. 2	P.I. indices: Washed eyes - 6.0, 6.0, 1.3, 0.7, and 0 at 24, 48, and 72 hours, and 4 and 7 days, respectively. Unwashed eyes - 32.0, 31.0, 28.0, 17.6, and 7.7 at 24, 48, and 72 hours, and 4 and 7 days, respectively.	I*	Minimum

STUDY	RESULTS	TOX CATEGORY	CLASSIFICATION
Primary Dermal Irritation, Rabbit	P.I. = 4.0 (numerical score indicates moderate irritation but one animal had necrosis and 5/6 had severe scaling at 8 days, thus upgrading classification to Category I).	I	Minimum
Data on Hydroxymetabolite 5-OH-MSO2 (MU-1):			
90-Day Feeding Study, Rat	NOEL >1080 ppm (70.2 mg/kg/day for males; 74.0 mg/kg/day for females) [HDT].	-	Minimum
Teratology, Rat	Teratogenic NOEL >250 mg/kg/day [HDT] Fetotoxic NOEL >250 mg/kg/day. Maternal NOEL >250 mg/kg/day.	-	Minimum
Mutagenicity Studies:			
A. CHO-HGPRT Forward Mutation Assay in Chinese Hamster Ovary Cells	Not mutagenic with or without S-9 activation at doses of 2.0-10.0 mg/ml.	-	Acceptable
B. Chinese Hamster Bone Marrow Cytogenetic Assay	Not mutagenic at oral doses as high as 10,000 mg/kg.	-	Acceptable
Data on Hydroxymetabolite MeMSO (Nor-MSO):			
Acute Oral LD_{50}, Rat	>5000 mg/kg in males.	IV	Minimum
Mutagenicity - Ames Assay	Negative in nonactivated and activated systems.	-	Acceptable
Metabolism Study, Rat	Radiolabelled MeMSO represented 2.1% of the radioactivity in urine at an unspecified time.	-	Minimum

2. Summary of Data Considered Desirable but Lacking for This Action:

A protocol to evaluate unscheduled DNA synthesis in rat liver primary cell cultures was reviewed by the Toxicology Branch (ref. M. Sochard memorandum, 7-9-84); the final report has not yet been received.

3. Action Being taken to Obtain the Lacking Information or Other Additionally Needed Information:

John Whalan (TB) asked Vickie Walters (RD) the status of the mutagenicity study. The registrant believes that the study was performed, and will ask the performing laboratory in Germany to expedite completion of the final report.

4. A Summary of Other Permanent Tolerances Granted for This Herbicide:

Meat (including poultry) - 0.2 ppm; Milk and dairy products - 0.05 ppm; Eggs - 0.5 ppm; Cottonseed (oil) - 5.0 ppm; Soybeans (oil) - 10.0 ppm; Sugar (cane and beet) - 0.1 ppm

5. Granting the proposed tolerances for sunflowers and peanuts will commit 3.48% of the ADI for a TMRC of 0.3755 mg/day (see page 3).

6. The 2-Year rat chronic feeding/oncogenicity study with a NOEL of 360 ppm (18.0 mg/kg/day) was used to set the ADI. The safety factor employed was 100. The ADI is 0.18 mg/kg/day. The MPI is 10.8 mg/day (for a 60 kg person).

7. There are at this writing no pending regulatory actions against the registration of this pesticide.

8. Other Relevant Considerations in Setting These Tolerances:

None.