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

OCT 2 1986 OCT 2 1986

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Concurrence with the Proposed Amendments to 40 CFR §180.412 and 21 CFR §561.430 for Poast® (Sethoxydim)

Tox. Chem. No. 72A

TO: Robert J. Taylor, PM #43
Registration Division (TS-767c)

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

John E Whalan 10-1-86

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

ERBudd 10.1.86

The Toxicology Branch has reviewed the summaries and proposed amendments to 40 CFR §180.412 and 21 CFR §561.430 and found the summaries and supporting data to be in agreement. There have been recent developments regarding the ADI (RFD), however, which impact on these submissions.

The existing ADI of 0.18 mg/kg/day (based on a 2-Year Rat Chronic Feeding/ Oncogenicity study NOEL of 18 mg/kg/day, and an uncertainty factor of 100) has come under scrutiny. The Toxicology Branch recommended that the ADI be changed to a PADI of 0.002 mg/kg/day (based on a 6-Month Dog Feeding study NOEL of 2.0 mg/kg/day and an uncertainty factor of 1000). The reason for this was the discovery of nephrotoxicity in dogs. It was recommended that a one-year dog study be performed to clarify the nephrotoxicity issue. This decision was peer reviewed twice, by the Toxicology Branch RFD Committee and the Agency RFD Committee. Thus, a PADI of 0.002 was established effective September 2, 1986. The ADI was based on Toxicology Branch study reviews.

Prompted by the need to concur/nonconcur with the proposed CFR amendments, the Toxicology Branch requested copies of the two dog studies in question. This was done in hopes of better understanding the nature of nephrotoxicity in dogs. One of the dog studies was unacceptable, while the other was well performed and documented. After reviewing these studies, I recommended further ADI modifications based on a better understanding of the nephrotoxicity issue.

Thus, the Toxicology Branch will recommend to the Agency RFD Committee that the uncertainty factor be changed from 1000 to 100. This will establish an ADI (RFD) of 0.02 mg/kg/day. The requirement for a 1-year dog study is waived since one of the studies was sufficient to resolve most of the nephrotoxicity questions. It is uncertain whether the Agency RFD Committee will comply with the Toxicology Branch recommendations.

The Toxicology Branch concurs with the submitted CFR amendments. The summaries will have to be changed, however, to reflect the revised ADI value.

Attachments

TOXICOLOGY BRANCH ADI PRINTOUT Date: 09/10/86

Poast (Sethoxydim) 6mo feeding- dog PADI = 0.002000 mg/kg/day
Caswell #072A NOEL = 2.0000 mg/kg Safety Factor = 1000
CFR No. 180.412 LEL = 20.0000 mg/kg
Status: TOX complete 7/18/86. ORD verified 9/02/86.

RESIDUE CONTRIBUTION OF PUBLISHED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
41	Cottonseed (oil)	5.000		0.15	0.011250
54	Eggs	0.500		2.77	0.020775
89	Meat, including poultry	0.200		13.85	0.041550
93	Milk and dairy products	0.050		28.62	0.021465
148	Soybeans (oil)	10.000		0.92	0.138000
154	Sugar, cane and beet	0.100		3.64	0.005460

TMRC %PADI
0.003975 mg/kg/day (60kg BW, 1.5kg diet) 198.750000

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
60	Fruiting vegetables	4.000	5F3284	2.99	0.179400000
115	Peanuts	25.000	5F3234	0.36	0.135000000
135	Raspberries	10.000	6F3383	0.03	0.004500000
152	Strawberries	10.000	6F3383	0.18	0.027000000
156	Sunflower	7.000	5F3234	0.03	0.003150000
182	Flax seed	5.000	6E3411	0.03	0.002250000

TMRC %PADI
0.009830 mg/kg/day (60kg BW, 1.5kg diet) 491.500000

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