US EPA ARCHIVE DOCUMENT

Toxicology Branch/HED Review

JAN 3 1984

Caswell No.: 447AB: Oftanol (Isofenphos, SR 1289, AMAZE)

To: William Miller (PM 16)

Registration No(s).: 3125-324 (AMAZE 20% G); -322 (AMAZE 6 EC); -323 (AMAZE 15 % G).

Pesticide Petition No(s).: 4F2989/4H5417; AMAZE/Potatoes

Chemical(s): 1-Methylethyl 2-[[ethoxy[(1methylethyl)amino] phosphinothiol]oxy] benzoate and its ChE inhibiting metabolites.

Requested Action(s): A proposed tolerance of 1.5 ppm in/on rac. potatoes, and a proposed food additive tolerance in potato granules (5.0 ppm), potato chips (5.0 ppm) and dried potatoes (5.0 ppm).

Recommendation: At the present time, the above requested tolerances in/on potatoes cannot be supported until the issue of delayed neurotoxicity associated with Oftanol is adequately addressed by the registrant. See the attached copies of our 12/7/83 and 12/28/83 memos.

Inert(s) cleared 180.1001: YES (See RCB review of PP#8F2025).

% ADI occupied; Existing: 11.32% (see comments below) Resulting: N/A

Resulting % increase in TMRC: N/A; However the existing TMRC from the 1983 published tolerance is 0.0340 mg/day/1.5 diet.

Data considered in setting the ADI: A 2-year rat study with a NOEL of 1.0 ppm and a safety factor of 10x (based on ChE inhibition) was used for the ADI calculations.

Attached (?): ADI printout: YES/NO; Tox "one-liner": YES/NO; DER: YES/NO

Existing regulatory actions against registrations: NONE

RPAR status: NONE

New Data: NONE (however see our 12/28/83 review of the neurotoxicity studies in hens).

Data gaps: (1) An acute delayed neurotoxicity study in chickens; (2) a subchronic delayed neurotoxicity study in chicken; (3) mutagenicity studies.

Comments: Tolerances for Oftanol havebeen already established in/on corn, eggs, meat and poultry, see Section 180.387 in CFR #40, 1983. However-TOX approved tolerances represented 16.3% of the ADI and the associated TMRC is 0.0489 mg/day/1.5 diet.

NOTE : According to new studies by Barry Wilson of the University of California (see our memo of 12/7/83 and 12/28/83) Oftanol is found to cause delayed neuropathy in chicken. The registrant's data did not reflect this effect. Hence, the above data gaps #1 and #2 should be filled before any consideration of a new tolerance.

Reviewer: Amal Mahfouz 12/30/83 Date: 12.30.83

Section Head: for LDE Branch Chief: [illegible]

File last updated 5/3/83

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day (60kg)
0.050	1.00	10	0.0050	0.3000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Corn, all types (38)	0.100	2.[illegible]1	0.00377
Meat, inc poultry (89)	0.100	13.85	0.02077
Milk&Dairy Products (93)	0.020	28.62	0.00858
Eggs (54)	0.020	2.77	0.00083

MPI	TMRC	% ADI
0.3000 mg/day (60kg)	0.0340 mg/day (1.5kg)	11.32

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Unpublished, Tox Approved 1F2451

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Onion (dry bulb) (106)	1.000	0.72	0.01073

MPI	TMRC	% ADI
0.3000 mg/day (60kg)	0.0447 mg/day (1.5kg)	14.89

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last A.M. 12/30/83

~~Current~~ Action 3F2917

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Broccoli (19)	0.300	0.10	0.00046
Brussel Sprouts (20)	0.300	0.03	0.00014
Cabbage, sauerkraut (22)	0.300	0.74	0.00331
Cauliflower (27)	0.300	0.07	0.00032

MPI	TMRC	% ADI
0.3000 mg/day (60kg)	0.0489 mg/day (1.5kg)	16.30

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.0489
.0447
.0042

$.00047\sqrt{.0042} = 8.970$ increase TMRC

Note:
Current Action on potatoes was not approved because the proposed tolerance cannot be supported at the present time.

DRAFT (Generated for the previous action on Ethanol, See C. Frick memo of 7/28/83)

Amal Mahfouz
12/30/83