

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 have been 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 ulakfour

Section Head: for the LDC

Date: 12.30.83

Branch Chief: W. B. B...

file not updated 5/3/83

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL	S.F.	ADI	MPI
mg/kg	ppm	mg/kg/day	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	2.1	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	THRC	% ADI
0.3000 mg/day (60kg)	0.0340 mg/day (1.5kg)	11.32

Unpublished, Tox Approved 1F2451

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

MPI	THRC	% ADI
0.3000 mg/day (60kg)	0.0447 mg/day (1.5kg)	14.59

last A.M. 12/30/82

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

0.0489

0.0447

0.0042

$$0.00047 \sqrt{0.0042} = 8.970 \text{ increase THRC}$$

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 draft)
See C. Fitch memo of 7/28/83
Shirley Mahoney
12/30/83