

Toxicology Branch/HED Review

FEB 8 1984

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

To: Donald Stubbs (PM 41)

Registration No(s): 3125-324 (AMAZE 20% G)

Pesticide Petition No(s): Section 18, No. 84-OR-02;

Oftanol/dry bulb onions in Oregon.

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

Requested Actions: The Oregon Department of Agricultural requested approval  
of a specific exemption under Section 18 for use of Amaze 20% Granular  
Insecticide (isofenphos) for control of thrips and maggots in onions in  
approximately 7,000 acres in Malheur County, Oregon. The expected level of  
residues is 1 ppm Amaze in onions.

Recommendation: At the present time, the above requested tolerances in/on  
onions (dry bulb) cannot be supported until the issue of delayed neurotoxicity  
associated with Oftanol is adequately addressed by the registrant. See the  
12/7/83 and 12/28/83 memos to William Miller (PM# 21) and the note at the end  
of the next page.

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 (however, see note below)

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, and (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: °A tolerance of 1 ppm of Amaze in/on onion was previously approved (PP#1F2451, 1981), see attached printout. However, due to the recent finding on the neurotoxicity of Oftanol (see below), PM#21 was asked in December 1983 to not process this approval until further information will be available on this neurotoxicity issue.

°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 <sup>acute</sup> 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: Shuaif Mahfouz 1/20/84

Section Head: James D. Little 1/23/84

Date: \_\_\_\_\_

Branch Chief: W. J. C. J. S. 8/6/84