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

JUN - 1 1990

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Hartz 2 in 1 Plus Long Lasting Collar for Dogs
Cholinergic Effects of Collar in Puppies

TO: Mr. George LaRocca, Product Manager 15
Registration Division (H7505C)

FROM: Byron T. Backus, Ph.D., Toxicologist Byron T. Backus 5/31/90
Herbicide/Fungicide/Antimicrobial Support Branch
HED (H7509C)

THROUGH: K. Clark Swentzel K. Clark Swentzel 5/31/90
Section Head, Review Section II
Herbicide/Fungicide/Antimicrobial Support Branch
HED (H7509C)

and

Marcia van Gemert 5/31/90

Marcia van Gemert, Ph.D., Branch Chief
Herbicide/Fungicide/Antimicrobial Toxicology Branch
HED (H7509C)

EPA Record No. 251968

Project No. 9-2180

EPA Reg. No. 2596-62

Tox. Chem. 217A

Action Requested:

Review comments from the registrant regarding a previous review of a cholinesterase study involving beagle bitches and their offspring and in-use exposure to 1-2 Tetrachlorvinphos collars.

Background:

The previous recommendation from Toxicology (memorandum dated November 4, 1988) was: "...if labeling does not exclude pregnant bitches, newborn and nursing puppies from exposure to this collar then there should be a statement on this collar that it contains a cholinesterase inhibitor. Both competitor's labels include this information. Also, the previously reviewed study reported significantly lower plasma cholinesterase in 1 and 2-collar puppies relative to their controls at days 30 and 42."

Comments and Recommendations:

1. The registrant's letter of September 13, 1989 includes the statement: "At issue are some small mean plasma cholinesterase depressions at two data points (30 and 42 days) within the puppy group." Additional comments include the fact that the puppy cholinesterase measurements involved a single baseline reading, and consideration of ≤30% inhibition as being "background."

   There has been considerable debate both within the Agency and between the Agency and other groups regarding the significance of plasma ChE inhibition, particularly at the levels (up to means of about 25%) observed in the puppies in this study. These findings do suggest that exposure to (and absorption of) a cholinesterase inhibitor took place in these animals, particularly as the greatest degree of apparent inhibition occurred at 42 days (12 days after the collars were applied). As far as ≤30% being "background," the current methods used to measure ChE activity (in this study, a Boehringer-Mannheim reagent kit was used) appear to be considerably more consistent than previously used methods (such as the delta pH procedure of Michel) in which wide (such as 30%) variations were normally observed.

2. Toxicology Branch 2 will accept the precautionary statement as proposed by the registrant: "It is not advisable to use this collar on puppies less than six weeks of age." in lieu of the previously recommended statements.