US EPA ARCHIVE DOCUMENT

Registration Human Safety Review PM: Gardner (#15) TOX Reviewer: W. Greear

EPA #	Date	Product Name	Use Classification	Toxici Catego
2596-AG	6/23/76	Hartz 2 in 1 Tick and Flea Collar for Cats		

RECOMMENDATION: I B objects to the registration of the "collar" on the basis that the data submitted is insufficient to support toxicity data requirements under the section 3 regulations. Further data required can be grouped into 2 categories

1) HUMAN SAFETY DATA
A) acute oral
B) acute dermal
C) eye and skin irritation
} ~~formulation~~ & technical
d. skin irritation on Formulation (data submitted are inconclusive)

		TECH	TECH	FORMULATION	USE DILUTION	DATA ACCEPT ABLE
Acute Oral (Rat)	LD50					

Toxic signs:

Comments:

2) Domestic Animal Safety DATA
A) subacute cholinesterase inhibition study - designed to determine the maximum degree of cholinesterase inhibition occuring under actual use conditions.
① to be done with the collar on the most sensitive specie (cat or dog)

Acute Dermal (Rabbit)	LD50					

Toxic signs:

Comments:

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Acute Inhalation ( )	LC50					

Toxic signs:

Comments:

Primary Eye Irritation (Rabbit)					

Comments:
*not: cholinesterase study in progress!
7/19/76

E CroEP 6/24/76

Primary Skin Irritation (Rabbit)					

Comments:

Other Studies: 1590 stirifos
1) long-term repetitive exposure study in dogs
a statistical analysis of the blood biochemistry, hematology, body wt., and kidney and liver function tests indicated no significant effects due to the test collar. Blood samples were taken on days 0, 83 and 180. Collars were replaced every 30 days.

2) drug interaction study - cats exposed to 15% stirifos collars for 60 days were shortly thereafter given either an anthelmintic or a phenothiazine tranquilizer - no drug interactions (as indicated by systemic toxicity) occured. unknown dosage - study is unacceptable

3) subacute eye and irritation studies on the actual use of the flea collar on cats cats wore a stirifos collar for 60 days (collar replaced at 30 days). No ~~[illegible]~~ difference in irritation occured between the use of the test and placebo collars. Results were not quantitated!

10% stirifos

1) eye and skin irritancy studies in dogs [redacted] placebo, chain and test collars were worn for 11-37 days. The study states that no irritation was observed in the animals which could be attributed to stirifos. The test was poorly designed so that the results are questionable.

2) forced feeding study in dogs - 21g collar was the dose used, 2 dogs used. Experimental methods were limited to observation and body wt determination. No effects were observed.

3) effect of moisture on skin irritancy in dogs - no effect. dogs wore 2 collars for 63 days and were submerged in water on a weekly basis.

4) long term repeated exposure in dogs - duration 180 days, collars were replaced every 30 days. Biochemical, hematologic and irritant effects were assessed. - no significant effects were observed

5) drug interaction study - commonly used veterinary drugs (Ronnel, Quadravac dh-L vaccine, corticosteroids, anthelmintics and Thionium-Lindane) produced no deleterious effect when administered concurrently with the 10% stirifos collar.

6) Liver function test on animals in #4 (immediately above) - no effects observed

7) Kidney function test on animals in #4 - no effect observed

8) effects of repeated exposure of cats to stirifos collars in cats - no skin irritancy was observed (length of observation 60 days)

9) drug interaction study - an ultra-short acting barbituate was administered concurrently with the collar - those animals wearing the test collar recovered more slowly than did animals wearing the placebo collar.

10) Reproduction study in cats wearing stirifos collars - no effect out of the ordinary were observed.

THEST INTERDICTIONS INFORMATION IS NOT INCLUDED