4-30-76

EEE BRANCH REVIEW

DATE: IN _____ OUT _____ IN _____ OUT _____ IN 3-31 OUT 4-30

FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO. 2596-AE

PETITION OR EXP. PERMIT NO. _____

DATE DIV. RECEIVED 2-20-76

DATE OF SUBMISSION _____

DATE SUBMISSION ACCEPTED _____

TYPE PRODUCT(S): (I) D, H, F, N, R, S

PRODUCT MGR. NO. 15

PRODUCT NAME(S) Hartz 2-in-1 Flea Collar for Dogs

COMPANY NAME Hartz Mountain

SUBMISSION PURPOSE New

CHEMICAL & FORMULATION Rabon 13.7%

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200.0 Introduction

This is a review of a new 14% Rabon Cat Collar. The previously registered rabon collars were only 10% active ingredient.

200.1 Uses - See Label

Flea and Tick Claims are for 4 months efficacy. This is an extension of 1 month for the flea claims and 2 months for tick claims. The claims for activity after wetting are similar.

201.0 Data Summary

See the submission for 2596-RE.

A. FLEA DATA SUMMARY - DOGS

STUDY	SITE	DOGS/REP	DAYS CONTROL	COMMENT
Gower	FL	12	??? 90 ???	Not averaged, Controls too erratic
TurTock	CA	6	155	Good population
Sharp	TX	12	105 -- 133	Low control pop.
Mounce	PA	12	126	Controls break
Ecl	VA	10	85 -- 92	Definite limit & break
TOTAL ANIMALS:		52	118 -- 127($\bar{x}$)	

B. BROWN DOG TICK DATA SUMMARY

STUDY	SITE	DOGS/REP	DAYS CONTROL	COMMENT
Gower	FL	12	50	High pop. = Zodiac
Turlock	CA	6	155	
Sharp	TX	12	70 -- 98	Pop. Break = Zodiac
Mounce	PA	12	119	
Ecl	VA	10	82 -- 105	= Zodiac
TOTAL ANIMALS:		52		
$\bar{x}$ DAYS OF CONTROL:			107 -- 119	

C. Other Data

Additional data was submitted on wetness claims and on the Rocky Mountain Wood Tick, Dermacentor andersoni. The wetness data indicate that this kind (10%) of rabon collar blooms equally well during and after immersion in water.

Data was submitted on a cat study which indicated highly effective control of fleas for 4 months, with good infestation pressure and control group stability.

The data on D. andersoni are insufficient to indicate control for any period of time but are adequate to show biological activity for a genus other then Rhipicephalus. The problem with the test is a lack of attachment and engorgement on the control animals.

The submitted data are adequate to indicate no particular need for an anatomical restriction, although some increase is noted for the legs toward the end of 90 days, for ticks.

In almost every test, the product was equal or superior to the standard which is registered for 5 months against fleas and 4 months against ticks. This comparison can be made in tests with a total of 46 dogs, increasing the reliability of the data.

Wetness data are bridged between the 10 and 13.7% collars via the rationale of similarity of composition and method of release.

202.0 Conculsions

The data would be sufficient to support tick and flea claims for four months. These are the effective intervals supported by the data. In some cases, control populations begin to decline after this period of time. In other situations, control seems to become erratic and decline. The reviewer has graphic representations and a more thorough summary of the submitted data.

(3)

In almost all tests, efficacy appears to be delayed for several days after collar attachment. This is primarily evident in the tick data:

Study	Delay in Efficacy
ECI	8 days
Sharpe	2-3 days
Turlock	not reported
Gower	7-14 days
Mounce	2-4 days
Average	5-7 days

202.2.3 Lesser Claims Supported

A. The data will support tick and flea claims for 4 months.

B. The reviewer met with Dr. William Perlberg of Hartz Mountain and PM 15 Tim Gardner on Tuesday, May 20, 1976. Dr. Perlberg requested that the label declaration for a delay in activity be expressed as "a few days". This is consistent with the labelling on other marketed collars and would be acceptable for this product.

C. The correct name for D. andersoni is the Rocky Mountain Wood Tick.

Phil Hutton, Entomologist
Efficacy Section, EEEB

WSW JHJ

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

EPA #	Date	Product Name	Use Classification	Toxicity Category
2596-AE	6/23/76	Hartz 2 in 1 Tick and Flea Collar for ~~Cats~~ Dogs		

RECOMMENDATION: TB 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 formulation (data submitted are inconclusive)

		TECH	TECH	FORMULATION	USE DILUTION	DATA ACCEPTABLE
Acute Oral (Rat)	LD50					

Toxic signs:

2) Domestic Animal Safety Data

A) subacute cholinesterase inhibition study – designed to determine the maximum degree of cholinesterase inhibition occurring under actual use conditions
① to be done with the collar on the most sensitive specie (cat or dog)

Comments:

Acute Dermal (Rabbit)	LD50					

Toxic signs:

Comments:

Acute Inhalation ( )	LC_{50}					

Toxic signs:

Comments:

B for OPP 6/24/76

Primary Eye Irritation (Rabbit)				//////////////	

Comments:

✓ note: cholinesterase study in progress!
7/19/76

Primary Skin Irritation (Rabbit)				//////////////	

Comments:

Other Studies: 1590 stirofos

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 not 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% stirofos 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 stirofos collar for 60 days (collar replaced at 30 days). No ~~[illegible]~~ difference in irritation occurred between the use of the test and placebo collars. Results were not quantitated!

10% stirofos

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 stirofos. The test was poorly designed so that the results are questionable.

2) forced feeding study in dogs - 21 g 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% stirofos 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) effect of repeated exposure of cats to stirofos collars in cats - no skin irritancy was observed (length of observation 60 days)

9) drug interaction study - an ultra-short acting barbiturate 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 stirofos collars - no effect ~~out of~~ the ordinary were observed.