SUBJECT: Carbaryl Flea Collar RF-76 for cats  
DATE: July 29, 1975

FROM: TB

TO: Mr. Frank Sanders

Registration #: 2724-ETE

Formulation:

**ACTIVE INGREDIENTS**

<table>
<thead>
<tr>
<th>Carbaryl (from 97.5% Technical, 1-naphthyl N-methylcarbamate)</th>
<th>% by weight</th>
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<td>9.73*</td>
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**INERT INGREDIENTS:**

INERT INGREDIENT INFORMATION IS NOT INCLUDED

* Includes overage to compensate for manufacturing loss.
Recommendations:

1) The acute oral study was performed on a single animal and therefore is not a valid study.

2) The method used to measure cholinesterase inhibition has been demonstrated to be unacceptable for use in detecting inhibition by carbamates due to the ready reversibility of the enzyme-inhibitor complex. The inclusion of a DDVP-collar positive control group and an increase in size of the test population is recommended.

3) TB recommends against the registration of this collar until the above deficiencies are corrected.

Background data:

Carbaryl (Technical) Acute Oral LD50 (rat)-500-700 mg/kg

Acute Dermal LD50 (rat)->4000 mg/kg

Chronic NEL (rat, dog)-200 ppm.

The following studies were performed with the 8.5% carbaryl flea collar.

I. Dermal Irritation

Evaluation of dermal irritation was conducted on 20 cats wearing single collars. These cats were examined for signs of dermal irritation around the neck and other body areas once per week for 18 weeks. Two other groups were fitted with multiple collars. One group consisted of 2 kittens (approx. 8 weeks old) each wearing 3 collars. The other group consisted of 9 mature cats each fitted with 2 collars. In addition, 10 cooperators tested the carbaryl collar under home-use conditions and were asked to answer questionnaires regarding toxic or allergic reactions to the collar.
In no case was any sign of dermal irritation reported.

(TB considered only the laboratory observations in this evaluation since testimonials are not considered admissible sources of data).

II. Acute Oral Toxicity

Approximately 3/4 of 1 complete carbaryl collar (7.23g) was cut into small pieces, inserted into gelatin capsules and fed to one 3-kg adult cat. The cat was observed every 30 minutes for 6 1/2 hours for signs of toxicity. No toxic signs were observed.

TB objections to the Study

1) No mention was made regarding the age of the collar (i.e., the actual amount of carbaryl present)

2) The study was performed on a single animal, therefore the data is not considered valid or representative.

III. Cholinesterase Inhibition (Woodard Research-Carter Johnston, Ph.D.)

# of animals: 5 experimentals each wearing one carbaryl collar - 3 controls

assay schedule: 7, -5, -3, 0 days before fitting the animals with a collar and + 2, 5, 7, 14 and 28 days afterward.

Type of AChE determination: plasma and RBC

Method: Electrometric (A pH/hr)
method as modified by Frawley et al (J. Pharmac. Exp. Therap. 105, 156; 1952)

Results: Cholinesterase fluctuations similar to those of controls.
TB objections to study:

Williams and Casterline (Fd. Cosmet. Toxicol. 7 149-151; 1969) demonstrated that the electrometric (A pH) method of Michel and its modification by Frawley failed to detect cholinesterase inhibition in animals displaying classical signs of anticholinesterase intoxication (tremors, salivation, etc.). An alternative (titrimetric) method (Casterline and Williams, J. Lab. Clin. Med. 69, 325; 1967) was able to detect a 50-80% inhibition of cholinesterase in these same animals (rat, RBC). Presumably the prolonged manipulation of blood samples necessary in the Frawley method results in a reversal of inhibition by carbamates. For this reason the data obtained in the above study is not meaningful. The inclusion in this study of a DDVP-collar positive control group which exhibited cholinesterase inhibition would have lent credence to this data. In addition, a larger test population is recommended.

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Toxicology Branch
Registration Division

cc: Branch Reading File
DMReisa: gac 7/29/75

Initial: O.E. Paynter
OEP 8/11/75