



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

JAN. 1/10/95

JAN 10 1995

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Fipronil (0.25% w/v) (Tradename: Frontline)
Review of Risk Assessment

P.C. Code: 129121
DP Barcode: D209378
Case: 040837
Submission: S476978

FROM: Virginia A. Dobozy, V.M.D., M.P.H., Veterinary
Medical Officer *Virginia A Dobozy 1/5/95*
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

TO: Marion Johnson/Daphne Waldo/PM 10
Registration Division (7505C)

THRU: Yiannakis M. Ioannou, Ph.D., Section Head *Y.M. Ioannou 1/5/95*
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

and *management 1/6/95*

Marcia van Gemert, Ph.D., Branch Chief
Toxicology Branch II
Health Effects Division (7509C)

Registrant: Rhone-Merieux, Inc.

Action Requested: Review An Assessment of Risk to the Applicator
Under Conditions of the Frontline® Spray
Treatment EUP

Recommendation: Toxicology Branch II has reviewed the risk
assessment and recommends that an EUP be
granted for testing in adult dogs.



BACKGROUND

In an April 19, 1994 memo from Virginia Dobozy to Robert Brennis/Daphne Waldo/PM 10, Toxicology Branch II recommended that an EUP be granted for this 0.25% formulation for use in testing on adult dogs only. The basis for the limitation to adult dogs was the finding of some adverse signs (decreased food consumption and increased incidence of vomiting and soft/liquid feces) in treated cats in a French study. Subsequent to that, review of the rat combined chronic toxicity/carcinogenicity study submitted for the agricultural product showed that treated animals had an increased incidence of thyroid tumors. (The chemical will be presented to the Cancer Peer Review Committee in February 1995.) Therefore, the registrant for the domestic animal product was asked to supply a risk assessment analysis for the applicator of the product.

REVIEW

An Assessment of Risk to the Applicator Under Conditions of the Frontline® Spray Treatment EUP

Summary of Proposed Treatment Schedule for EUP

The product will be tested at six veterinary practices. Applications of the product will be performed by one or two individuals at each center. Ten households, each with up to five pets, is the maximum number each veterinarian is allowed to accept into the testing program. Treatment of the pets in the households will be staggered.

Applicator Exposure

Using a worst case scenario, an average 10 kg cat or dog treated at a dosage of 6 ml/kg would have a total of 60 ml of product (150 mg of active ingredient) applied at each application. An applicator's exposure would be 2.5 mg/kg/day (150 mg ÷ 60 kg). Assuming that the applicator is exposed to 1.0% of the total application and that 10% of this exposure penetrates the protective clothing (plastic aprons extending from the neck to the knees, tyvek splash resistant sleeves and gloves), the applicator would be exposed to 0.0025 mg/kg/day. An estimate of relative bioavailability was < 1% from studies conducted with the fipronil topical spray formula. Therefore, the veterinarian's exposure risk is 0.000025 mg/kg/day.

Margin of Safety to Applicator

The lowest NOEL in the toxicology studies was 0.025 mg/kg/day in the rat chronic toxicity/carcinogenicity study. The estimated applicator exposure of 0.000025 is 1000 times less than this NOEL.

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Conclusions

The use of a 10 kg dog or cat does not really represent the worse case scenario, in that 22 lbs. is a rather small dog. However, the margin of safety would be adequate even if an 100 dog was used for a worse case scenario. Toxicology Branch II recommends that an EUP be granted for adult dogs.