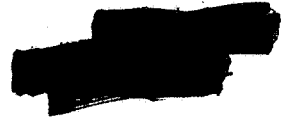




UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

#938B



OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

JUL - 7 1994

SUBJECT: Fipronil (0.25%) - Preliminary Domestic Animal Safety Study in Kittens to Support Experimental Use of Product in Cats and Kittens

PC Code: 129121
DP Barcode: D204709
Case: 040837
Submission: S468476

FROM: Virginia A. Dobozy, V.M.D., M.P.H., Veterinary Medical Officer *Virginia A Dobozy 7/6/94*
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

TO: Robert Brennis/Daphne Waldo/PM 10
Registration Division (7505C)

THRU: Yiannakis M. Ioannou, Ph.D., Section Head *Y. Ioannou 7/6/94*
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

and

Marcia van Gemert, Ph.D., Branch Chief
Toxicology Branch II
Health Effects Division (7509C) *M. van Gemert 7/6/94*

Registrants: Rhone Merieux Inc.

Action Requested: Review preliminary domestic animal safety study in kittens to support EUP in cats and kittens.

Recommendation: Toxicology Branch II will not review the study until missing or confusing information is included or corrected in the study. (See list on the following page.) There is concern that a 5X dose was not achieved using a single application method. Until this study is reviewed, the EUP testing should not include cats and kittens.



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BACKGROUND

The data from the study *Domestic Animal Safety Study of RM1601C 0.25% Topical Spray in Juvenile Cats* were submitted in response to Toxicology Branch II's review of the EUP request for field testing the product in client-owned dogs/puppies and cats/kittens. (See April 19, 1994 memo from Virginia Dobozy to Robert Brennis/Daphne Waldo/PM 10). The study report has not been finalized, however the results were submitted to allay concerns about the findings in the French domestic animal safety study in cats (MRID # 431211-12). In that study, food consumption in the high dose group (2.5X the recommended dose) was decreased and the incidences of vomiting and soft/liquid feces were increased. After a cursory review of the present study, the registrant was contacted concerning missing or confusing information. A response was conveyed in a June 30, 1994 telefax which is attached to this memo. Although some of the questions have been answered, there are other issues that should be addressed before the study is finalized.

- 1) There should be some assurance that the treated animals received a 5X dose. The original study protocol indicated that the product would be applied in increments with drying between reapplications to achieve the 5X dose. (See September 3, 1993 memo from Virginia Dobozy to Joseph Tavano/Richard Mountfort/PM 10.) However, the preliminary study report and the telefax information state that the 5X dose was applied as a single application and that the tails were used to wipe up any runoff if it occurred. At the beginning of the study, some of the kittens weighed less than 1 kg (2.2 lbs.). It is difficult to imagine that the 30 ml dose (5X) would not runoff considering this small body surface area. The final report should indicate why this deviation from the original protocol occurred.
 - 2) The study report is unclear as to what type of control was used. The telefax information states that the control group was treated with the product vehicle. The final report should identify the vehicle used.
 - 3) The preliminary report states that the kittens were ≤ 8 weeks, however the age of each individual kitten is not reported. This information should be included in the final report.
 - 4) Parameter evaluations (clinical observations, physical examinations, gross pathology examinations) should be included even if they were within normal limits. The preliminary report states that no compound related lesions were detected on gross pathology. The findings, whether or not considered treatment-related, should be included with the final report.
 - 5) Reference values for the hematology and clinical chemistry parameters should be included in the final report.
 - 6) Summary tables of the mean values of the study parameters are helpful for review of the study.
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