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HEALTH EFFECTS DIVISION
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MEMORANDUM

SUBJECT: Fipronil - Review of Registrant's Incident Analysis for Three Products

DP Barcodes: D262511, D262513, D262514
PC Code: 129121
Cases: 014261, 046906, 060305
Submissions: S568879, S568881, S568882

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THRU: Whang Phang, Ph.D., Branch Senior Scientist
Health Effects Division (7509C) Whang Phang 02/29/00

Action Requested: Review incident analysis.

Recommendations: 1. The data submitted by the registrant are inadequate. RRB1 is interested in the types and rates of suspected adverse events for the year 1998, not from the inception of product sales. The total number of incidents for that year should be used in calculating the rates, which should be expressed consistently, either as a function of amount of product sold in 1998 or per 100,000 units. In addition, the suspected adverse events in dogs, cats and other species should be categorized by breed, age and sex, as was done in the 1998 analysis. Detailed information on the deaths should be submitted, including product and amount applied, animal species, breed, sex, age, clinical signs, time between Frontline® treatment and initiation of clinical

1999.

Background

Reviews of fipronil incident data have been reported in two previous memoranda dated April 16, 1997 and April 29, 1998. The 1998 memo included an analysis of incident data in a paper by Merial Limited titled "Frontline® Products Reports of Suspected Adverse Events Analysis of Breed, Age and Sex Distribution of Dogs and Cats." In this report, the total number of incidents (from product sales inception to December 23, 1997) were analyzed according to breed, sex and age for each of the three products, Frontline® Spray for Cats and Dogs (Reg. No. 65331-1), Frontline® Top Spot™ for Cats (Reg. No. 65331-2) and Frontline® Top Spot™ for Dogs (Reg. No. 65331-3). In the 1998 memo, it was recommended that the registrant submit similar data for the year 1998 to monitor the trend in suspected adverse events.

Review of Letters dated December 16, 1998 and March 1, 1999

In a December 16, 1998 letter, the registrant submitted updated information on the rate of incidents per dose sold for each Frontline® product. The data provided include units sold (expressed as bottles or cards), total AERs (adverse events reactions), overall AER rate, AERs resulting in death rate, death AER rate, other AERs and other AER rate. The rates were expressed as event per 100,000 units sold. In the 1998 analysis, the rate was expressed as a function of the total number of doses sold. The information is based on data from the inception of US sales through September 30, 1998. In a March 1, 1999 letter, information was submitted on the amount of product sold October through December, 1998. No rates were calculated based on this updated data. No information was submitted on the number of incidents during the October-December, 1998, period.

RRB1 Conclusions/Recommendations

1. The data submitted by the registrant are inadequate. RRB1 is interested in the types and rates of suspected adverse events for the year 1998, not from the inception of product sales. The total number of incidents for that year should be used in calculating the rates, which should be expressed consistently, either as a function of amount of product sold in 1998 or per 100,000 units. In addition, the suspected adverse events in dogs, cats and other species should be categorized by breed, age and sex, as was done in the 1998 analysis. Detailed information on the deaths should be submitted, including product and amount applied, animal species, breed, sex, age, clinical signs, time between Frontline® treatment and initiation of clinical signs, treatment received and where (veterinarian, owner,etc.) and time between treatment and death.

2. A similar analysis, as described under item number 1, should be submitted for calendar year 1999.

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