

US EPA ARCHIVE DOCUMENT



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

APR 16 1997

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Fipronil - Review of Incident Reports for Three Products

DP Barcode: D233461
PC Code: 129121
Case: 014261
Submission: S517858

FROM: Virginia A. Dobozy, V.M.D., M.P.H., Veterinary Medical
Officer *Virginia A. Dobozy 4/1/97*
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

TO: Richard Griffin
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

and

Rick Keigwin/Ann Sibold/PM 10
Registration Division (7505C)

THRU: Jess Rowland, M.S., Acting Section Head *Jess Rowland 4/8/97*
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

and

Yiannakis M. Ioannou, Ph.D., Acting Branch Chief
Toxicology Branch II
Health Effects Division (7509C) *Ki Clark printed for 4/14/97*

Action Requested: Review incident reports for three fipronil products used for flea and tick control, Frontline® Spray Treatment (65331-1), Top Spot™ for Cats (65331-2) and Dogs (65331-3).

Recommendations: The number and type of adverse reactions reported for these Frontline® products are not excessive or unexpected. Misuse in cats, especially instillation of the spray formulation into the ears, should be monitored and the label revised to warn against this practice if it continues. See pages 3 and 4 for a more detailed discussion (Conclusions and Recommendations).



Recycled/Recyclable
Printed with Soy/Canola Ink on paper that
contains at least 50% recycled fiber

Review of Incidents

1. Frontline® Spray Treatment (65331-1)

Rhone Merieux, Inc. (RMI), the registrant submitted a summary of 21 incidents with Frontline® Spray Treatment. A breakdown by species and type of reaction appears below.

	<u>Cats</u>	<u>Dogs</u>
Number of Incidents	9	12
Dermal Irritation	1	9
Systemic Reaction	8	4

An additional incident of a fish kill was reported when a dog treated with Frontline® jumped into a pond of gold fish. Three of the incidents in cats resulted after misuse; in two of these, the product was instilled into the ears. One incident of overdosing was reported in dogs. Some of the clinical signs seen with the systemic reactions included lethargy, recumbency, salivation, dilated pupils and ataxia. Several of the reports in cats postulated that the reactions were due to ingestion or inhalation of the alcohol in the product formulation.

An additional two incidents were included in OPP's Incident Data System for this product, as of March 17, 1997. In one, a Springer spaniel puppy playing with a treated puppy developed muzzle swelling and a dermal reaction. In the second incident, a cat went berserk and developed ataxia and possibly Horner's syndrome after the product was instilled into the ear.

2. Frontline® Top Spot™ for Cats (65331-2)

RMI summarized 21 incidents in cats; 13 were dermal irritation and 8 involved a systemic reaction. Signs reported for the systemic reactions were similar to those for Frontline® Spray.

As of March 17, 1997, there were an additional 13 incidents in IDS for this product; 8 were dermal irritation and 5 involved systemic reactions. One report of a death in a cat was received by the Registration Division directly from EPA Region 5. Allegedly, the cat died immediately after application of the product. A necropsy was conducted at Ohio State University, but the results have not been forwarded to OPP.

3. Frontline® Top Spot™ for Dogs (65331-3)

RMI summarized 17 incidents in dogs; 16 were dermal irritation and 1 was a systemic reaction (facial edema and lethargy).

As of March 17, 1997, there were an additional 15 reactions in IDS; 14 were dermal irritation and 1 was a systemic reaction. The latter

reaction was reported from Region 5. An older dog went into convulsions after application of the product. On follow-up, it was reported that the dog had prior health problems. Of the total 32 adverse reactions, 4 (12.5%) occurred in Bichon Frise's, a relatively uncommon breed of dogs.

4. Comparison of Number of Incidents to Total Sales

RMI compared the number of adverse reactions [6(a)(2) reports] to the estimated number of treatments sold (based on data collected through December 31, 1996). The ratios for the three products are as follows:

Product	Estimated No. of Treatments Sold*	No. of 6(a)(2) Reports Submitted to EPA	% of 6(a)(2) Reports vs. No. of Treatments Sold
Frontline® Spray Treatment	5,433,744	21	0.0004
Frontline® Top Spot™ for Cats	1,387,410	15	0.0011
Frontline® Top Spot™ for Dogs	3,960,810	13	0.0003
Total Frontline® Products	10,781,964	49	0.0005

* Treatments sold estimated using the average weight of a cat = 8 lbs. and the average weight of a dog = 30 lbs.

Conclusions and Recommendations

1. The use of number of treatments sold based on the average weight of a cat and dog may underestimated the above ratios. The number of treatments per bottle of product overestimates use because many containers are only used for one animal, whereas multiple treatments per container are feasible. However, the percentages calculated are very low and comparable to those reported during the 13-month pharmacovigilance study in France with Frontline® Spray (see April 3, 1996 memo from Virginia Dobozy for DP Barcodes D221800 and D222392).

2. Dermal irritation was seen in some of the safety studies done with the Top Spot™ final formulation prior to registration. The labels for both Top Spot™ for Dogs and Cats state under HAZARDS TO DOMESTIC ANIMALS, "Pets may experience some temporary irritation at the site of product application." Therefore, incident reports of this nature are not unexpected.

3. There were three reports of systemic reactions when Frontline® Spray was misused and instilled into cats' ears. If reports of this misuse continue, label revisions should be considered to warn against this practice.

4. Results of the necropsy examination on the cat which died should be forwarded to Toxicology Branch II for evaluation when they are received by the Registration Division.