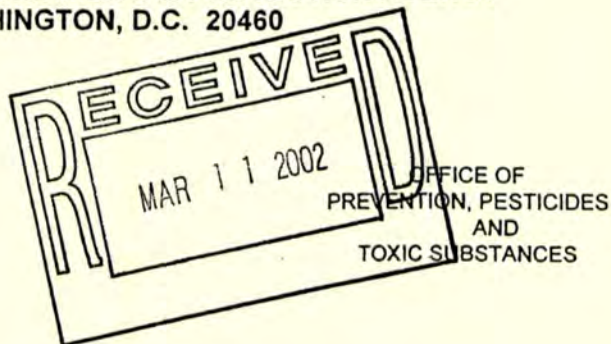


US EPA ARCHIVE DOCUMENT



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



February 25, 2002

MEMORANDUM

Product Name: FRONTLINE TOP SPOT FOR DOGS
EPA Reg. No.: 65331-3
DP Barcode: D278799
Case No: 060305
Submission: S605213
Chemical: 129121 Fipronil

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

*Byron T. Backus
2/25/2002*

To: Ann Sibold/Arnold Layne, PM 03
Insecticide Branch
Registration Division (7505C)

Company: MERIAL LIMITED

ACTION REQUESTED: "Please review the attached analysis of incident data (no guideline, no MRID) and determine if

1. incidents are excessive
2. label changes would be appropriate and
3. the registrant should be requested to continue annual analysis of incident data...

BACKGROUND: According to the report received from the registrant, there were 267 incident reports in which 277 dogs or puppies were involved. Overall, there were 285 incident reports involving 300 affected animals; apparently there were 18 incidents involving 23 affected animals of other species (where reported, cats and rabbits).

COMMENTS AND RECOMMENDATIONS:

1. The reported incidents for which details are provided are mostly those in which deaths occurred. There were two reported incidents involving rabbits. In one case, approximately half a large size vial of Top Spot was divided among five rabbits, which afterwards showed poor appetite and lethargy, with three eventually dying. In the other case involving a rabbit, there was mild anorexia and moderate depression, with the rabbit surviving. "The DVM said the rabbit had a condition that was unrelated to Frontline." There was a single reported case in which a cat died; the animal had been dosed with the contents from a "large dog size pipette" and exhibited seizures 3 days later.
2. For dogs, there was one incident (#1) in which a nursing bitch was treated with Frontline Top Spot and two 7-week-old puppies developed adverse reactions, with one subsequently dying. The labeling states "Do not use on puppies under 10 weeks of age." and "This product may be harmful to debilitated, aged, pregnant or nursing animals." This was a single reported incident involving a nursing bitch
3. In six cases (reported incidents #5, #9, #11, #15, #18 and #20) dogs were treated with another pesticide or drug. In incident #5 a 9-week-old puppy was vaccinated with distemper/parvo combination and treated with Top Spot and Panacur (for roundworms) and was found dead the next day. The labeling states not to use on puppies under 10 weeks of age and also states that certain medications can interact with pesticides. In incident #9 a 2-year-old German shepherd; the dog went into "status epilepticus" 18 hours after Top Spot administration, and following a thunderstorm that went through the area. Aspiration pneumonia was found on gross examination. In incident #11 the dog developed acute renal failure 9 days after exposure to TopSpot and an unspecified period after exposure to Durammune C4/CCV. "Leptospirosis [was diagnosed?] on differential. Owner feels Top Spot caused the problem. DVM does not." In incident #15 a 12-year-old German Shepherd dog was treated with Top Spot and Panacur granules, experienced severe dyspnea about 12 hours after exposure, and died. In incident #18 a 12-year-old Golden retriever was also administered Heartgard Chewables; the dog apparently died of an intestinal obstruction caused by an intact Heartgard Chewable. In incident #20 the owner applied Hartz 2 in 1 powder to a 7-year-old Brittany spaniel on Nov. 29 2000, then applied Top Spot on Nov. 30. The following day the dog was in shock, with severe pulmonary edema and hypothermia. The dog died on Dec. 5; Top Spot had been previously used on this animal with no adverse reactions. The label for this product includes the following: "Certain medications can interact with pesticides. Consult a veterinarian before using on medicated animals. Consult a veterinarian before using this product with other pesticides."
4. In incident #4 the dog showed symptoms six hours after exposure to Top Spot, but three hours after ingestion of a spoiled turkey breast that had been in the garbage. The dog was euthanized the following day.

5. In incident #16 the DVM felt the dog died as a result of anemia and the death was related to a transfusion reaction.
6. There were a number of reported incidents in which Top Spot was administered to elderly dogs (≥ 10 years), including #3, #7, #12, #15, #17, and #19.
7. There appears to be only a single case in which exposure to Top Spot alone was associated with mortality of a dog between 10 weeks and 10 years old. This was #6 (8 months old; second time dog was treated with Top Spot, found dead about 24 hours later).
8. There is one case (#19) where it is stated that a 12-year-old golden retriever that had been treated with Top Spot on four occasions developed seizures following each treatment. In another reported incident (#17) a 12-year old Bichon Frise died following treatment and it is noted that the dog had previously appeared lethargic for 24-48 hours following a previous treatment. There is nothing on the current label stating that if a dog has previously had an adverse reaction to treatment then it should not be treated again.
9. Overall, it is stated that there were a total of 267 reported incidents involving dogs, with a total of 277 dogs affected, out of a total of 27,537,963 doses sold. This is less than 1 incident per 100,000 dose levels sold, which is not an excessive incidence. Nevertheless, TRB notes that there is nothing on the current label stating that if a dog has previously had an adverse reaction to treatment then it should not be treated with the product (or another Fipronil-containing product) again. TRB recommends that such a statement be added to the label for this product.
10. The registrant should continue annual reporting and analysis of incident data.