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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

February 25, 2002

MEMORANDUM

Product Name: FRONTLINE TOP SPOT FOR CATS
EPA Reg. No.: 65331-2
DP Barcode: D278798
Case No: 046906
Submission: S605212
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 127 incident reports in which 132 cats or kittens were involved. Overall, there were 138 incident reports involving 144 affected animals; apparently there were 11 incidents involving 12 affected rabbits.

COMMENTS AND RECOMMENDATIONS:

1. The reported incidents for which details are provided are apparently mostly those in which deaths occurred. Of the 30 reported incidents, mortality occurred in 29. Twelve of the reported incidents involved cats, with a total of 14 animals (2 of the three cats in one incident did not show any reaction, so that only 12 cats showed showed adverse reactions) involved; 18 incidents involved rabbits, with a total of 22 rabbits involved (in 2 cases only one of two treated rabbits were adversely affected, so 20 rabbits were adversely affected). Since these incidents: "Revised labels for the entire Frontline brand, bearing the statement "Do not use on rabbits" have since been submitted to and accepted by the EPA."

2. In three cases (reported incidents #1, #15, and #20) cats were treated with another pesticide or pharmacologically active substance. In incident #1 the cat had been admitted for dental prophylaxis and was given Telosol as a sedative. The cat recovered and was given amoxicillin and Frontline was applied, collapsing about 10 hours [after treatment with Frontline] and subsequently died. In incident #15 the cat was treated with a Permethrin dip two days after treatment with Frontline; symptoms (including muscle fasciculations, drooling and ataxia) appeared after the Permethrin dip treatment, and are consistent with exposure (and/or sensitivity) to Permethrin. In incident #20 it is stated there was also exposure to Hartz 2 in 1 dip Eliminator, but the time frame for this exposure is not indicated, only that: "The cat showed signs of aggression, mydriasis, and anorexia on 09-02-00. This was followed by anorexia, salivation, and vomiting. Death occurred on 10-06-00..." The label for this product includes the statements: "Certain medications can interact with pesticides... Consult a veterinarian before using this product with other pesticides..."

3. In some other cases (#2, #8, #11, #14) cats were elderly ($\geq$13 years old) and had pre-existing conditions (such as renal or heart problems) that may have played a role in their deaths. Labeling for this product includes the statement: "This product may be harmful to debilitated, aged, pregnant, or nursing animals..."

4. There appear to be only 3 reported incidents in which there was no evident pre-existing health problem and in which exposure to Frontline may have resulted in death to a cat. These are #3 (10-week old kitten that went into a seizure, then coma, with subsequent euthanasia); #4 (11-year old Himalayan cat with ataxia and depression 16 hours after exposure, coma 4 hours later, subsequent death); #12 (3-year-old cat, with seizures, hypothermia appearing 8 hours after exposure, subsequent death).

5. Overall, it is stated that there were a total of 127 reported incidents involving Frontline Top Spot for Cats, in which 132 cats were affected, out of a total of 7,659,606 doses sold. These are not excessive numbers, and, given the circumstances of the reported incidents, additional label changes do not appear necessary.

6. The registrant should continue annual reporting and analysis of incident data.