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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Revised Exposure Assessment for Application of Frontline Spray Treatment and Frontline Spot Treatment on Dogs and Cats for Flea and Tick Control.

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THRU: Mark I. Dow, PhD, Section Head
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Health Effects Division (7509C)

DP Barcode: D219825 and D222391

Pesticide Chemical Code: 129121

EPA Reg. No. 6533-1; 65331-EUP-E

PHED: Version 1.1

I. INTRODUCTION

In April and May of 1996, RCAB requested that OREB provide exposure assessments for the application of two fipronil-containing products for use as a pet spray and a pet spot treatment for flea and tick control.

An initial exposure estimate was included in a memorandum dated April 23, 1996 from



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OREB to RCAB, for one-time use of fipronil by a consumer/pet owner for flea and tick control on dogs and cats. A second exposure estimate was developed and included in a memo finalized on May 20, 1996, from OREB to RCAB; this latter estimate assumed application by veterinarians or pet groomers. No data were available to quantify actual exposure to either the spray or spot treatment, hence the estimates made of exposure were extremely conservative, that is, overestimates or "catastrophic worst case scenarios" of the possible exposure in an effort to be protective of the user of the products.

Typically, in situations in which appropriate data are not provided or are not available, OREB conducts a very conservative or "catastrophic" estimate of exposure. If the resulting MOEs are acceptable, OREB assumes there is actually little, if any, risk. If MOEs are unacceptable under these conservative assumptions, OREB requests data or pursues information with which it might refine its estimates.

In the scenarios used in these "worst case scenarios" for Frontline products' exposure assessments, it was assumed that an applicator would be exposed to the amount of product required to treat a large dog (>25#), and that the applicator (a veterinarian or pet groomer) might treat 20 such dogs in the course of one day. In these earlier assessments, MOEs were determined to be acceptable.

Regrettably, in the course of developing the aforementioned exposure estimates during late April and May of 1996, a mathematical error was made in the calculations related to the estimate of exposure to the active ingredient, fipronil. Review of these calculations, and the recent clarification from the Science Advisory Branch recommending against use of a dermal absorption factor in this assessment, alters significantly what would have been a highly theoretical margin of exposure for the Frontline products. Use of the original catastrophic scenario to estimate exposure yields unacceptable MOEs for the spray and spot Frontline products. Hence, as is customary, OREB considered available information with which it might refine its estimates of exposure.

For point of reference, OREB reviewed other scenarios in which pesticides are applied as a spray from a hand-held container, such as an aerosol spray can application. This is a scenario of potentially high exposure for the applicator, and, though not identical to application from a pump spray bottle, is somewhat similar to that mode of application. Estimates of possible exposure from application by aerosol spray can, and related MOEs are attached as Appendix A. While there is a likelihood that exposure from an aerosol spray can application may exceed that using a spray pump bottle with nozzle directed at the pet, we have no data which we can use to support this at this time. On the other hand, application of a liquid spray to an animal with label directions to ruffle the coat during application may cause additional exposure to the individual applying the spray product.

With regard to application of the Frontline spot treatment product, given the acceptable MOEs obtained for the scenario using PHED surrogate data for an aerosol spray can (a high exposure scenario), OREB believes that application of the Frontline spot treatment is highly likely to be much less than that using the spray product. This is predicated on the applicator following directions on the label, wearing gloves as required by the label, and, on the unit

dose packaging of the product (maximum net contents <3 ml) and the narrow neck of the packaging for dispensing product to the animal, limiting efflux of large amounts of liquid product from the dispenser, as might happen with a wide necked bottle, for example.

Of note is the fact that OREB has no product-specific data on which to base actual exposure and risk assessments. Therefore, the above assessments are, at this time, based on surrogate data for similar, but not identical, scenarios for exposure, and the risk assessments are based on numerous assumptions and OREB's judgement.

APPENDIX A

Use of Frontline Spray Treatment based on surrogate PHED data for application of a liquid pesticide via an aerosol spray can. (Source: PHED "Best Available" Surrogate Exposure Table, dated July 25, 1996.)

**Scenario 1**

Use of aerosol spray can, application of quantity of product adequate for treatment of 20 large dogs (>25 pounds), applicator in single layer work clothes [long-sleeved shirt, long pants, and wearing gloves (use of latex gloves is recommended on label)].

Amount of product applied: approximately 100 ml per treatment X 20 large dogs = approx. 66 ounces = approx. 1/2 gallon = approx. 4 pounds of product (1 gallon = 8 pounds).

Amount ai per 20 treatments = 4 pounds X 0.29% = 0.0116 pound ai/d

Exposure estimate

0.0116 #ai/d X 81.43 mg/ #ai (PHED, see above) = 0.945 mg/d (dermal exposure) + inhalation exposure of 0.0147 mg/d (1,271 ug/ #ai X 0.0116 #ai/d = 14.71 ug/d divided by 1000 [1000 ug/mg]) = 0.959 mg/d divided by 70 kg body weight of applicator = 0.014 mg/kg/d

$$\text{MOE} = \text{NOEL divided by exposure} = \frac{5 \text{ mg/kg/d}}{0.014 \text{ mg/kg/d}} = 357$$

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**Scenario 2**

Amount of product applied: approximately 100 ml per treatment X 1 large dog = approx. 3.3 ounces = 0.2 pounds (1 pound = 16 ounces)

Amount ai per 1 treatments = 0.2 pounds X 0.29% = 0.00058 pound ai/d

Exposure estimate

0.00058 #ai/d X 81.43 mg/ #ai (PHED, see above) = 0.047 mg/d (dermal exposure) + inhalation exposure of 0.0007 mg/d (1,271 ug/ #ai X 0.00058 #ai/d = 0.737 ug/d divided by 1000 [1000 ug/mg]) = 0.0477 mg/d divided by 70 kg body weight of applicator = 0.0007 mg/kg/d

$$\text{MOE} = \text{NOEL divided by exposure} = \frac{5 \text{ mg/kg/d}}{0.0007 \text{ mg/kg/d}} = 7{,}143$$

cc: CLang, OREB; MJohnson, RD; Chemical File (129121); Correspondence File