



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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

forward 5/27/08

May 15, 2008

MEMORANDUM

Subject: Name of Pesticide Product: FREEDOM 50 PLUS IGR SPOT ON FOR DOGS
EPA Reg. No. /File Symbol: 75844-I
DP Barcode: D350262
Decision No.: 389796
Action Code: R301
PC Codes: 109701 (Permethrin: 50.0%)
129032 (Pyriproxyfen: 1.2%)

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

Byron T. Backus
5-15-2008
W. Backus

To: Linda DeLuise/George LaRocca, RM 13
Insecticide Branch
Registration Division (7505P)

Registrant: ANDREW M MARTIN CO. NV. INC.

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
109701 Permethrin	50.0%
129032 Pyriproxyfen	1.2%
<u>Other Ingredient(s):</u>	<u>48.8%</u>
	100.0%

ACTION REQUESTED: The Risk Manager requests:

"PL, they request a waiver of acutes and companion animal study."

BACKGROUND: The material available for review includes a proposed label (product name: Freedom 50 Plus IGR Spot On For Dogs) with the following dosages: for dogs weighing 33 lbs or less: 1.5 cc applied to the skin of the dog's back between the shoulder blades; for dogs weighing 33-66 lbs: 1.5 cc applied to the skin of the dog's back between the shoulder blades and 1.5 cc to the skin directly in front of the base of the dog's tail; for dogs weighing more than 66 lbs: 3.0 cc applied to the skin of the dog's back between the shoulder blades and 3.0 cc to the skin directly in front of the base of the dog's tail. The label includes the statement: "DO NOT USE ON CATS." The material received also includes a Memorandum of Intent between the registrant and Ecto Development Corporation (ECTO), which states that ECTO agrees to provide all its data for [presumably used to support the registration of] its Nylar/Permethrin Spot-On dog product (EPA Reg. No. 67505-3). In the Application for Pesticide ["Other" checked], Section I, the registrant states this product is similar or identical in composition and labelling to EPA Reg. No. 67505-3. The Method of Data Support indicates the registrant is using the selective method of support (or cite-all option under the selective method); however, on page 3 of the Data Matrix all of the six acute toxicity studies and the companion animal safety study are listed as waiver requests.

COMMENTS AND RECOMMENDATIONS:

1. The registrant is proposing, at least for some weight classes of dogs, greater dosages (by volume) than those given for the existing registered product, EPA Reg. No. 67505-3. The last (January 13, 2004) accepted label for EPA Reg. No. 67505-3 specifies the following dosages: for dogs weighing 15 lbs or less: 1.0 mL applied as a spot or stripe between the shoulder blades; for dogs weighing 15-33 lbs: 1.5 mL as a spot or stripe between the shoulder blades; 33-66 lbs: 1.5 mL as a spot or stripe between the shoulder blades and 1.5 mL as a spot or stripe on the dog's back directly in front of the base of the tail; and for greater than 66 lbs: an application of 4.5 mL on the dog's back between the shoulder blades and running to the base of the tail. Additionally, the proposed product has a greater label percentage declaration for Permethrin (50% vs. 45% for EPA Reg. No. 67505-3), and, from a comparison of the specific gravities of the two products and using the stated label percentages for Permethrin, 75844-I would contain 0.555 g permethrin/mL, while 67505-3 contains 0.387 g permethrin/mL. Application of 6 mL of 75844-I to a dog weighing 66 or more pounds would represent a dosage of 3.33 g permethrin, while application of 4.5 mL of 67505-3 to the same dog involves a dosage of 2.322 g permethrin. The companion animal safety study (in MRID 43612601) used to support the registration of 67505-3 used dosage rates of 1X (1.5 mL/dog < 33 lbs; 3.0 mL/dog > 33 lbs) and 5X (7.5 mL/dog < 33 lbs; 15 mL/dog > 33 lbs), consistent with the dosage rates for that product. Since the proposed permethrin application rate for 75844-I is higher than the 1X dose level in MRID 43612601, that study cannot be used to support the registration of 75844-I.

2. TRB recommends against the waiver request for the companion animal safety study or studies. Studies should be submitted that demonstrate a 5X margin of safety associated with the proposed use application rate. If the proposed product is intended for use only on adult dogs, then only a study on dogs > 6 months would be required, and labelling would have to specify that the product is not to be used on dogs of less than 6 months. If the product is also proposed for use on puppies above a certain age (such as 12 weeks), then a second companion animal safety study demonstrating a 5X margin of safety on 12-week old dogs would also be required. These studies would have to be conducted according to the 870.7200 OPPTS Guidelines.

3. The 6 acute toxicity studies used to support the registration of 67505-3 are in MRIDs 43396402 through 43396407. These studies have been reviewed and classified as acceptable (memorandum dated October 10, 1995, from S.E. Oonnithan of PRS to Rick Keigwin, PM 10). The product formulation was in EPA Toxicity Category III for acute oral toxicity, acute dermal toxicity, primary eye irritation, and in Toxicity Category IV for inhalation toxicity and primary dermal irritation. It was not a skin sensitizer in guinea pigs. However, after an examination of the CSFs for 75844-I and 67503-3, TRB concludes that the acute toxicity data requirements to support the registration of 75844-I cannot be waived (with the exception of the acute inhalation toxicity study), and, because of solvent and/or inert differences between 75844-I and 67505-3, as well as the higher percentage of permethrin in the proposed product, the acute toxicity studies used to support the registration of 67505-3 do not satisfy the acute toxicity data requirements for the registration of 75844-I. The acute inhalation toxicity study data requirement can be waived, based on the proposed product use (application to dogs as a spot-on; the inhalation study requirement has been waived for similar-use products). The remaining 5 acute toxicity studies (oral toxicity, dermal toxicity, primary eye irritation, primary dermal irritation and dermal sensitization) should be conducted on the formulation for 75844-I.

4. In addition to packaging individual dosages (1.5 cc, 3 cc, 6 cc) the registrant is proposing to market this product in a 240 cc bottle for use with a dosing gun "for use only in kennels, shelters and humane societies." This is a new use, with the potential for a higher applicator exposure to permethrin than that associated with the use of the currently registered product(s) consisting of individual dosing units. According to the April 2006 Reregistration Eligibility Decision (RED) for Permethrin, the Agency has classified permethrin as "Likely to be carcinogenic to humans by the oral route." TRB recommends that this proposed new use be referred to HED for review and comment.

5. The CSF (copies dated 01/19/2008 and 02/06/2008) for the proposed product should also be reviewed and accepted by the TRB Chemistry Team.