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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: January 18, 2006

MEMORANDUM

Subject: EPA File Symbol: 2724-LNU RF2004 (CCSO)
DP Barcode: D325415
Decision No.: 355865
PC Codes: 128965, Etofenprox (40%); 105402, S-Methoprene (3.6%)

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

Byron T. Backus 1-18-2006 Signature Redacted 1.18 2006

To: George LaRocca RM 13
Insecticide Branch
Registration Division (7505C)

Registrant: Wellmark International

FORMULATION DECLARATION FROM LABEL:

Active Ingredient(s):	% by wt
Etofenprox (CAS 80844-07-1)	40.0%
(S)-Methoprene (CAS 65733-16-6)	3.6%
Inert Ingredients:	56.4%
Total:	100.00%

ACTION REQUESTED:

The Risk Manager requests:

"This submission (MRID 46725801) is in response to our 12/14/05 conference call with Wellmark and to your 8/24/05 review of their companion animal safety study showing that the isolated sores in the 3 and 5x groups are not at the actual

application sites."

BACKGROUND: This report provides additional clarifications regarding possible effects (salivation and dermal lesions) seen in the companion animal safety study (MRID 46513409) for this product, as well as information regarding the application ("The animals received 1, 3 or 5 mL of the control material (and presumably the test material) as a single application. The test material was applied to the neck at the base of the skull.").

COMMENTS AND RECOMMENDATIONS:

1. The response includes the following: "...A clinical observation of excessive salivation was noted for one male and one female from Group 1 a few minutes after dosing and for one male at approximately 20 minutes after dosing. One Group 1 female was observed with salivation at the 1-hour observation and one Group 4 female at the 2-hour observation. The salivation lasted no more than approximately 10 minutes for the animals. The salivation was considered related to treatment with the control or test material. The two groups that were noted with salivation received the largest amount of the control or test material, 5-mL. The salivation was probably due to oral contact with the control or test material."

   Since the test material was applied (at 1, 3 or 5 mL) as a single application, there may have been sufficient runoff that these particular cats were able to ingest some of it. Labeling should specify that if there is more than one cat in a household then they should not be allowed to groom each other immediately after treatment, and should not be allowed to contact one another until the spot-on has dried.

2. In the memorandum of August 24, 2005 with the DER for the previously reviewed companion animal safety study (MRID 46513409) for this proposed product, it was noted that: "A small (5 mm or less) sore or scabbing was noted at the application site on Day 7 or later for one Group 4 (5X) male and one Group 4 (5X) female, and in one Group 3 (3X) female. In each case the lesion scabbed over and by Day 14 was barely detectable. It is stated (p. 17 of MRID 46513409) that the cause of these sores is unknown. These sores and scabbing are consistent with scratching at the application site. Etofenprox is structurally similar to pyrethroids which are known to cause sensations (such as tingling, burning, itching or numbness) at dermal exposure sites. Fully-grown cats would be capable of more vigorous scratching than 12-week old kittens, and (if $\geq$ 5 lbs) would be receiving a 2 mL dose."

   The performing laboratory has now responded (report amendment dated December 15, 2005; in MRID 46725801) that: "A small sore/scabbing (5 mm or smaller) area on the mid-dorsal back (between shoulders, site 6M) adjacent to the application site (site 5M)(see Appendix E for animal map) was noted on Day 7 or later for one Group 4 male, one Group 3 female, and one Group 4 female. The area scabbed over and, by Day 14 of the study, it was barely detectable. The cause of the sores is unknown."

From the diagram on p. 14 the sores/scabbing were on the dorsal back of the kittens, somewhat behind the application site (on the dorsal head region).

These lesions could have resulted from attempts by the kittens to scratch the application site; they may have simply been unable to reach it. However, as this effect was seen in only one 3X and two 5X kittens, and was non-life-threatening, it does not preclude the acceptance of this study. Another possibility is that because dosage (at both 3 and 5 mL) was as a single application, then this resulted in increased absorption of the etofenprox than would have occurred if several 1X applications had been made, with drying between applications.