



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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

October 14, 2008

MEMORANDUM

Subject: Name of Pesticide Product: SVP9
EPA Reg. No. /File Symbol: 83399-10
DP Barcode: D355053
Decision No.: 397287
Action Code: R340
PC Codes: 044312 (Dinotefuran)
129032 (Pyriproxyfen)

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

Byron T. Backus
10-14-2008
U. Hashu
10-15-08

To: Rita Kumar/Venus Eagle, RM 1
Insecticide-Rodenticide Branch
Registration Division (7505P)

Registrant: SUMMIT VETPHARM, LLC

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
044312 Dinotefuran	22.00%
129032 Pyriproxyfen	3.00%
<u>Inert Ingredient(s):</u>	<u>75.00%</u>
TOTAL	100.00%

ACTION REQUESTED: The Risk Manager requests:

“...Please review and comment on registrant’s rebuttal to your review. Also comment on revised labelling to change age restriction for puppies from 6 months to 7 weeks...”

BACKGROUND:

The material received for review primarily consists of a document (MRID 47466701) titled: "Companion Animal Safety Study – Rebuttal EPA May 6, 2008 Review." This document essentially contains material (about coccidiosis and its treatment in puppies) that was presented by SVP in a meeting on August 5, 2008.

COMMENTS AND RECOMMENDATIONS:

TRB's recommendations remain unchanged from the previous review (dated August 18, 2008) which included material discussed at the August 5, 2008 meeting, at which the questions of coccidiosis and its treatment in puppies were discussed. The companion animal (puppy) safety study in MRID 47246601 remains classified as unacceptable, so that the use of this product on puppies less than 6 months of age is not supported. The following comments and recommendations (originally made August 18, 2008) remain in effect:

1. From the information in the letter dated August 11, 2008, the puppies were treated in identical sets on two consecutive days (Set 1 completed at 3:37 pm on June 5, and Set 2 completed at 3:26 pm, June 6, 2007). They were all subsequently dosed on June 7, 2007 (between 1:37 pm and 3:55 pm; approximately 48 hours after dosing for Set 1 animals and approximately 24 hours after dosing for Set 2 animals) with UAA [Universal Animal Antidote]. They were then treated a second time with UAA ("On June 8, 2007, the treatment times for UAA were between the hours of 8:45 am to 11:15 am, approximately 65 and 41 hours post-dosing for Set 1 and Set 2 respectively.").

2. Our previous understanding (see the TRB review for 83399-RN dated May 6, 2008) was that each of these puppies was treated once with UAA on either Study Day 0 or 1. There was no indication that they were subsequently treated with UAA again approximately 17 hours later.

Since additional information on medical treatment was provided in the August 11th letter that was not included in the original study report or in the August 5th meeting, RD is requesting the registrant to send copies of the raw data (from the study notebooks) to TRB specifying the dates and times of treatment with UAA. This would be submitted formally so that a MRID number will be assigned for future reference.

3. The Agency's concern is that the UAA may have masked or altered symptoms of toxicity in the puppies. These signs of toxicity may not have been from the Dinotefuran alone, but also from the inerts or solvents in the formulation. In addition, the August 11, 2008 letter included a short discussion of the pharmacokinetics of Dinotefuran in the rat. However, any test material is expected to pass through a rat's gastrointestinal tract more quickly than that of a dog.

4. As discussed at the meeting on August 5, 2008 (and as stated in the letter of August 11, 2008) SVP is agreeable to submitting a study conducted on 8 puppies with dosage at 5X (there could be a control group of 3 or 4 animals, which would not be treated). TRB would have no problems with the treatment of the puppies with a coccidiostat three days before dosage with the Dinotefuran-Pyriproxyfen spot-on; the puppies could also be treated with a coccidiostat and UAA no sooner than 3 days after exposure to the spot-on.