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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

6 May 2008

MEMORANDUM

Subject:	Name of Pesticide Product:	SVP9
	EPA Reg. No. /File Symbol:	83399-RN
	DP Barcode:	D351224
	Decision No.:	375169
	Action Code:	R31
	PC Codes:	044312 (Dinotefuran: 22.00%)
		129032 (Pyriproxyfen: 3.00%)

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

Byron T. Backus May-6-2008
R. Whatley 5/7/2008

To: Rita Kumar/Venus Eagle, RM Team 01
Insecticide-Rodenticide Branch
Registration Division (7505P)

Registrant: SUMMIT VETPHARM, LLC

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt.
044312 Dinotefuran		22.00%
129032 Pyriproxyfen		3.00%
Other Ingredient(s):		75.00%
	Total:	100.00%

ACTION REQUESTED: The Risk Manager requests:

"...Please review registrant's response to your review dated 2/28/2008. A copy of the revised label recently submitted by registrant is enclosed..."

BACKGROUND:

The material received (in MRID 47385501) addresses a previous TRB review (memorandum dated March 3, 2008) of a companion animal (puppy) study in MRID 47246601. In the memorandum of March 3, 2008 it was stated that this companion animal safety study with

puppies is currently classified as unacceptable, although it may be reclassified to marginally acceptable provided data adequately addressing the deficiencies indicated below are provided:

- The exact nature of the control material should be provided or stated.
- Individual animal data should be provided regarding the time of observation for each abnormal sign, its severity, and its subsequent course.
- A tabular summary of clinical signs data should be provided including a description of the observations and the time of onset. Clinical signs such as ocular discharge, abnormal feces, or abnormal urine should be further characterized.
- The study report should include mention of which particular puppy or puppies had "cherry eye" and required treatment with topical ophthalmic ointment over the entire study duration. All medications given to the puppies, even during acclimation, should be included in the study report.
- Any discrepancies or inaccuracies in the reporting of the clinical signs should be resolved. For example, the text (p. 26 of MRID 47246601) mentions one "situation" that occurred on day 13 and included tremors of the ears, followed by diaphragmatic spasms, and then vomiting, which in turn was followed by depression/lethargy, and disappearance of the tremors while the animal slept. However, according to Table 94 (p. 119) the only incident involving depression/lethargy occurred on day 4 in a 5X female; while tremors only occurred in a 5X female on day 13. In addition, one 5X female is reported (p. 129) to have vomited on day 4, and a 5X female (whether this was the same animal that vomited on day 4 is unknown) is reported to have vomited on day 5, while a control male vomited on day 8. There is no mention of a 5X female which vomited on day 13.

COMMENTS AND RECOMMENDATIONS:

1. The listing above includes the requirement that: "All medications given to the puppies, even during acclimation, should be included in the study report." In the registrant's response (MRID 47385501) it is reported (in the Summary of Veterinary Reports and Medical Records on pages 8-9) that all 48 puppies showed "Bloody feces or spots of blood under pen" on Study Day 0 or 1, and all were treated with UAA [Universal Animal Antidote] Gel.

2. According to the text of the original report (pages 23-24) in MRID 47246601: "...Bloody feces also showed up in some puppies during acclimation that was attributed to *Isospora* spp. and/or giardia (based on fecal examinations)... Three puppies did not respond to treatment for the upper respiratory infection (nasal discharge) and/or the intestinal infestation and were removed during acclimation due to health reasons." The inference made in the first Agency review of this study was that at least some of the puppies had been diagnosed and treated for bloody feces prior to treatment, but the registrant's response has now indicated that diagnosis and treatment of all puppies occurred on Study Days 0 and 1.

3. The OPPTS 870.7200 Guidelines specify that animals should be free of infectious diseases which could complicate the interpretation of the study results. As all puppies showed "Bloody feces or spots of blood under the pen" and were treated with UAA Gel on Study Days 0 or 1, and this may have masked any signs of toxicity from incidental ingestion of (or exposure to) the test material that was administered on Day 0, the study is reclassified as Invalid. It cannot be used to support the proposed use of this formulation on puppies from 8 weeks to 6 months of age.