



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

OFFICE OF PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

22 June 2007

**MEMORANDUM**

Subject: Name of Pesticide Product: SVP7  
EPA Reg. No. /File Symbol: 83399-A  
DP Barcode: D338144  
Decision No.: 373247  
PC Codes: 108701 [Permethrin: 36.08%]  
044312 [Dinotefuran: 4.95%]  
129032 [Pyriproxyfen: 0.44%]

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

*Byron T. Backus*  
*6-22-2007*  
*H. Hershman*

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

Registrant: SUMMIT VETPHARM, LLC

**FORMULATION FROM LABEL:**

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
044312 Dinotefuran	4.95%
129032 Pyriproxyfen	0.44%
108701 Permethrin	36.08%
<u>Other Ingredient(s):</u>	<u>58.53%</u>
Total:	100.00%

**ACTION REQUESTED:** The Risk Manager requests:

“...Please review the primary eye irritation study and data citations for acute toxicity and companion animal safety studies to support registration of this new dog spot-on product. Registrant claims that this product is substantially similar to SVP-1, 2, 3 and 4, with a single chamber delivery system (as opposed to dual chamber in the currently registered products...).”

**BACKGROUND:** The material received for review includes an eye irritation study (MRID 47027102) on material identified as TTE Single Tube (Sample 12928), a volume (MRID 47043701) from the registrant stating that the four acute toxicity studies in MRIDs 46552702 (acute oral LD50), 46552703 (acute dermal LD50), 46552705 (primary skin irritation) and 46552706 (dermal sensitization) are being used to support this registration, along with a waiver request for the inhalation study. The package also includes a 13 page data matrix, and a label and CSF for this proposed product.

**RECOMMENDATIONS:**

1. The eye irritation study in MRID 47027102 has been classified as acceptable. The test material is in EPA Toxicity Category II in terms of eye hazard potential.
2. A waiver for the acute inhalation study is appropriate, as no respirable particles would be generated based on the product's physical nature (viscous liquid), the method of application (directly to the dog's skin), and the relatively small amounts (mL quantities) involved. In addition, as noted by the registrant, TRB has previously recommended for acute inhalation toxicity study waivers for similar use pet-care products.
3. After comparing the CSFs of 83399-A and EPA Reg. No. 83399-1, TRB concludes that the remaining acute toxicity study requirements are satisfied by MRIDs 46552702, 46552703, 46552705 and 46552706. The resulting acute toxicity profile for 83399-A would be the following:

	Tox. Cat.	MRID	
Acute Oral LD50	III	46552702 <sup>1</sup>	Cited
Acute Dermal LD50	IV	46552703 <sup>1</sup>	Cited
Acute Inhalation LC50	IV	n/a	Waived
Primary Eye Irritation	II	47027102	Acceptable
Primary Dermal Irritation	IV	46552705 <sup>1</sup>	Cited
Dermal Sensitization	Negative	46552706 <sup>1</sup>	Cited

<sup>1</sup>Study conducted on a mixture containing approximately 32.1% Permethrin, 4.24% Dinotefuran and 0.42% Pyriproxyfen (obtained by mixing the two components of EPA Reg. No./ 83399-1). For the review of these studies, refer to a TRB memorandum dated December 14, 2005 from B. Backus to Rita Kumar for EPA File Symbol 2596-RLU.

4. Based on this acute toxicity profile, and from information on the proposed label and in the CSF, the following is the precautionary and first aid labeling for this product, as obtained from the Label Review System:

**PRODUCT ID #:** 083399-00006

**PRODUCT NAME:** SVP7

**PRECAUTIONARY STATEMENTS**

**SIGNAL WORD:** WARNING

**Hazards to Humans and Domestic Animals:**

Causes substantial but temporary eye injury. Harmful if swallowed. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse. Wear: Long-sleeved shirt and long pants, Socks, Shoes, and gloves.

**First Aid:**

If in eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

If swallowed:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to by a poison control center or doctor.
- Do not give anything to an unconscious person.

**NOTE TO PHYSICIAN:** Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

5. The companion animal safety study requirements for this product are satisfied by the studies in MRIDs 46552707 and 46552708. The dosage rates and frequency of applications cannot exceed those accepted for EPA Reg. No. 83399-1.

6. For the purposes of registration, the CSF (dated 12/19/2006) for the proposed product may also have to be reviewed and accepted by the TRB Chemistry Team.

Reviewer: Byron T. Backus, Ph.D.  
Risk Manager: 01

Date: June 21, 2007

**STUDY TYPE:** Primary Eye Irritation - Rabbit; OPPTS 870.2400; OECD 405

**TEST MATERIAL:** TTE Single Tube, Hartz Test Sample #12928. A clear yellow liquid, containing Permethrin (~36.08%), Dinotefuran (~4.95%) and Pyriproxyfen (~0.44%) in a solvent base.

**CITATION:** Lowe, C. (2006). Primary Eye Irritation of TTE Single Tube (Sample 12928). Eurofins | Product Safety Laboratories, Dayton, NJ. Report No. 20733. Study completion date: December 15, 2006. MRID 47027102. 17 p. Unpublished.

**SPONSOR AND SUBMITTER:** SUMMIT VETPHARM, LLC

**EXECUTIVE SUMMARY:** In a primary eye irritation study (MRID 47027102), 0.1 mL of TTE Single Tube, Hartz Test Sample #12928, a clear yellow liquid (containing the actives Permethrin [~36.08%], Dinotefuran [~4.95%] and Pyriproxyfen [~0.44%]) was instilled into the right eye of each of three female New Zealand white rabbits (age: young adult; body weights: not reported; source: Robinson Services, Inc., Clemmons, NC). Prior to instillation eyes were treated with ocular anesthetic. Rabbits were scored (Draize) for eye irritation at 1, 24, 48 and 72 hours, and at 4, 7, 10 and 14 days after instillation. Ophthalmic fluorescein sodium (2%) was used to evaluate the extent or verify the absence of corneal opacity at 24 hours and at subsequent intervals if the previous reading was positive.

All 3 eyes showed corneal opacity at all readings from 24 hours through day 7, with all 3 eyes scoring zero for corneal opacity on day 10. All eyes scored "1" for iritis at all readings from 1 hour through day 4, but all scored zero for iritis on day 7. 3/3 eyes were positive (score of 2 or greater) for conjunctival redness from 1 hour through 72 hours, and 2/3 eyes were positive (score of 2) for conjunctival redness on day 4. All eyes were positive (score of 2) for chemosis at 24 hours, and one eye was also positive for chemosis at 48 hours. All 3 eyes scored "1" (not considered positive for irritation) for conjunctival redness on days 7 and 10. All eyes had completely cleared (all scores zero) on day 14.

In this study, TTE Single Tube, Hartz Test Sample #12928, a clear yellow liquid (containing the actives Permethrin [~36.08%], Dinotefuran [~4.95%] and Pyriproxyfen [~0.44%]) caused positive irritation effects which were still present on day 7 in 3/3 rabbit eyes, but which had cleared by day 10. This formulation is in EPA Toxicity Category II in terms of eye irritation potential.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

**COMPLIANCE:** Signed and dated GLP Compliance (p. 3), Quality Assurance (p. 4), and [No] Data Confidentiality (p. 2) statements were provided.

## **RESULTS AND DISCUSSION:**

Observations	Hours				Days			
	1	24	48	72	4	7	10	14
Corneal Opacity	0/3	3/3	3/3	3/3	3/3	3/3	0/3	0/3
Iritis	3/3	3/3	3/3	3/3	3/3	0/3	0/3	0/3
Redness*	3/3	3/3	3/3	3/3	2/3	0/3	0/3	0/3
Chemosis*	0/3	3/3	1/3	0/3	0/3	0/3	0/3	0/3
Discharge*	3/3	3/3	2/3	2/3	2/3	0/3	0/3	0/3

\*Score of 2 or more required to be considered "positive."

**A. Observations** – All 3 eyes showed corneal opacity at all readings from 24 hours through day 7, with all 3 eyes scoring zero for corneal opacity on day 10. All eyes scored "1" for iritis at all readings from 1 hour through day 4, but all scored zero for iritis on day 7. 3/3 eyes were positive (score of 2 or greater) for conjunctival redness from 1 hour through 72 hours, and 2/3 eyes were positive (score of 2) for conjunctival redness on day 4. All eyes were positive (score of 2) for chemosis at 24 hours, and one eye was also positive for chemosis at 48 hours. All 3 eyes scored "1" (not considered positive for irritation) for conjunctival redness on days 7 and 10. All eyes had completely cleared (all scores zero) on day 14.

**B. Reviewer's Conclusions:** In this study, TTE Single Tube, Hartz Test Sample #12928, a clear yellow liquid (containing the actives Permethrin [~36.08%], Dinotefuran [~4.95%] and Pyriproxyfen [~0.44%]), caused positive irritation effects (including corneal opacity) persisting through day 7 in 3/3 rabbit eyes. This formulation is in EPA Toxicity Category II in terms of eye irritation potential.

# ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D338144
2. **PC CODES:** 108701, 044312, 129032
3. **CURRENT DATE:** 22 June 2007
4. **TEST MATERIAL:** TTE Single Tube, Hartz Test Sample #12928, a clear yellow liquid, containing Permethrin (~36.08%), Dinotefuran (~4.95%) and Pyriproxyfen (~0.44%) in a solvent base.

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Primary eye irritation / rabbit / Eurofins   Product Safety Laboratories / Lab Study No. 20733 / 15-DEC- 2006	47027102	3/3 eyes showed corneal opacity at all readings from 24 hrs through day 7, with all 3 eyes scoring zero for corneal opacity on day 10. All eyes scored "1" for iritis at all readings from 1 hr through day 4, with clearing by day 7. All eyes were positive for conjunctival redness from 1 through 72 hours, and 2/3 were positive on day 4. All eyes had completely cleared (all scores zero) by day 14.	II	A

**Core Grade Key:** A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived