



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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Via Certified Mail

SEP 30 2011

Mr. Doug Spilker
Bayer HealthCare LLC
Animal Health Division
PO Box 390
Shawnee Mission, KS 66201-0390

Re: Implementation of Label Changes to Pet Spot-On Products

Dear Mr. Spilker:

You are receiving this letter as a registrant of pesticide products applied topically to a localized area on cats and dogs for the control of fleas and ticks (pet spot-on products). With this letter, EPA is providing information to you necessary to implement the Agency's proposed mitigation measures developed to reduce adverse events occurring from the use of these products.

I. Background

In the spring of 2009, EPA observed a significant increase in incident reports associated with pet spot-on products. EPA investigated this increase, received additional information on those incidents from the pet spot-on pesticide registrants, and conducted an intensive evaluation of the incidents and the pet spot-on products themselves. EPA prepared Data Evaluation Records (DERs) on the currently-registered products that, at that time, represented the largest market share of the pet spot-on products. The DERs formed the basis of the analysis conducted in 2009 and released in March 2010. These DERs, the Agency's analysis, and a mitigation plan developed from that analysis are all available in the docket (docket number EPA-HQ-OPP-2010-0229).

As the first step in implementing the necessary product-specific changes, EPA contacted all registrants and met in person with those registrants that own products for which DERs were prepared. This letter is being sent to all registrants of pet spot-on products, including new products registered after mitigation measures were initially proposed, to provide instructions on how to make necessary label changes to reduce adverse events associated with your pet spot-on product(s). All of these changes are intended to address the concerns the Agency identified in the analysis provided to registrants and the public in March 2010.

II. Products addressed in this letter

The following pet spot-on products are addressed in this letter:

- 11556-116, 117, 118, 119, 120, 121, 122, 125, 127, 128, 130, 132, 133, 134, 135, 141, 142, 143, 144, 150, 151, 152

If you are aware of any registered spot-on product not listed above please notify EPA immediately and the list(s) will be amended accordingly.

III. What you need to do

For your registered pet spot-on products and any pending spot-on registrations EPA expects registrants to submit revised labels addressing all changes described below no later than six months from the receipt of this letter, as discussed individually with product registrants. If EPA does not receive amendments for these changes within that time frame, the Agency will consider whether further regulatory action is necessary to ensure your products continue to meet the standard for registration set forth in the Federal Insecticide, Fungicide and Rodenticide Act (“FIFRA”). These changes are provided separately for dog products and cat products. If you have a registration bearing uses on both dogs and cats, please split the registration into two products by first submitting an application for a new, “me-too” registration for one of the species. After that registration is granted, a voluntary FIFRA section 6(f) request should then be submitted to delete use on the duplicate species from the old product.

A. Label changes – Dog Products

1. Front Panel

- a. Include the word “dog” in your product’s brand name and increase the size of the word “dog” to at least 75% the height of the largest letter in the primary brand name.
- b. Include the word “only” when referring to dog size and age and place this restriction in a box prominently on the front panel. Examples: “Only for use on dogs larger than 55 lbs.”; “Use only on dogs weighing 35 – 45 lbs.”; and “Only for use on puppies 8 weeks and older.”
- c. Place a large, clear picture of a dog in the weight range for the product as packaged on the front panel of the label.
- d. Place a [1.5 cm x 1.5 cm] cat prohibition icon in a box located at the lower right hand corner of the front panel in yellow with black images. If the box itself is yellow, or a yellow and black icon may blend into the box, propose an alternate color scheme.

2. Back Panel

- a. Place a [1.5 cm x 1.5 cm] cat prohibition icon and warning text in a box located at the lower right hand corner of the back panel in yellow with black images and text. If the box itself is yellow, or a yellow and black

icon may blend into the box, propose an alternate color scheme. Please note that this language can, but is not required to, replace other cat warning language present on any product label. The text must read as follows:

- i. Products containing permethrin, cyphenothrin, or phenothrin - “DO NOT USE ON CATS – MAY BE FATAL. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian immediately.” or
 - ii. All other dog spot-on products - “DO NOT USE ON CATS. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.”
- b. Place a box on the back panel labeled “Side Effects” immediately above the cat warning box. Either include the language below or propose your own side effects language based on incident reports, companion animal safety data, and/or clinical trials, if available. *“Monitor your dog after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects occur, consult your veterinarian or [Registrant at 1-800-number].”* Please note that the Agency prefers product-specific warnings, where available, but understand that some registrants were requesting more specific guidance. In the event that you want to provide alternate or varying language please discuss your reasons for the change.

3. Directions for Use

- a. Repeat the word “dog” throughout the directions for use.
- b. Include the word “only” when referring to dog size and age restrictions.
- c. To avoid overdose for dogs larger than 55 lbs, please provide specific language which instructs consumers to not double-dose animals larger than the upper weight limit on the package for the largest size dogs.
- d. On the smallest package size, please include a lower weight limit which corresponds to the lower limit of the dose ranges based on animals tested in your supporting companion animal study. Include the language “Do not apply to dogs weighing less than [insert weight] lbs” where [insert weight] is replaced with the lowest weight in pounds of the animals tested in your supporting companion animal study.
- e. Include the language, “Do not allow your dog to ingest this product.”

4. Applicator Vial

- a. Place weight and age restrictions on the immediate container for the vial and/or the vial itself.
- b. Place a cat prohibition icon on the immediate container for the vial and/or the vial itself.

B. Label change – Cat Products

1. Front Panel

- a. Include the word “cat” in your product’s brand name and increase the size of the word “cat” to 75% the height of the largest letter in the primary brand name.
- b. Include the word “only” when referring to cat size and age and place this restriction in a box prominently on the front panel. Examples: “Only for use on cats larger than 9 lbs.”; “Use only on cats weighing between 1 and 7 lbs.”; and “Only for use on kittens older than 8 weeks.”
- c. Place a large, clear picture of a cat in the weight range for the product as packaged on the front panel of the label.

2. Back Panel - Place a box on the back panel labeled “Side Effects” at the lower right hand corner of the back panel. Either include the language below or propose your own side effects language based on incident reports, companion animal safety data, and/or clinical trials, if available. *“Monitor your cat after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects occur, consult your veterinarian or [Registrant at 1-800-number].”* Please note that the Agency prefers product-specific warnings, where available, but understand that some registrants were requesting more specific guidance. In the event that you want to provide alternate or varying language please discuss your reasons for the change.

3. Directions for Use

- a. Repeat the word “cat” throughout the directions for use.
- b. Include the word “only” when referring to cat size and age restrictions.
- c. To avoid overdose for cats larger than 20 lbs, please provide specific language which instructs consumers to not double-dose animals larger than the upper weight limit on the package for the largest size cats.
- d. On the smallest package size, please include lower weight limit which corresponds to the lower limit of the dose ranges based on animals tested in your supporting companion animal study. Include the language “Do not apply to cats weighing less than [insert weight] lbs” where [insert weight] is replaced with the lowest weight in pounds of the animals tested in your supporting companion animal study.
- e. Include the language, “Do not allow your cat to ingest this product.”

4. Applicator Vial - Place weight and age restrictions on the immediate container for the vial and/or the vial itself.

C. Documentation

When you submit your amendment for a registered product, provide the following items in addition to items routinely submitted in amendment applications. When you submit your revised labeling for pending products, please also provide the following information along with your revised labeling and 8570-1 form. While not routinely reviewed in approving pesticide products, EPA is asking for this additional documentation when reviewing pet spot-on products due to the nature of the changes we've requested.

- Master labels as they will appear when printed on product boxes for all product dose ranges.
- Copies of any package inserts that may be provided in product packaging (including such things as monthly reminder stickers and additional directions for use).
- Images of vial packaging and labeling (actual empty vial can be provided instead, but it is not required).

D. Addresses

Registrants must send revised labels to one of the following addresses:

U.S. Postal Service Deliveries

The following official mailing address should be used for notifications and amendments sent to the Office of Pesticide Programs by U.S. mail:

Document Processing Desk (AMEND – Pet Spot-On)
Office of Pesticide Programs (7505P)
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

Personal/Courier Service Deliveries (e.g., FedEx)

The following address should be used for amendments that are hand-carried or sent by courier service Monday through Friday, from 8:00 AM to 4:30 PM, excluding Federal holidays:

Document Processing Desk (AMEND – Pet Spot-On)
Office of Pesticide Programs (7505P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

IV. Additional Information

Several registrants have had questions about the following topics since the mitigation proposal was released last March. We are documenting those questions and answers here.

1. Alternate formulations

Some registrants have requested clarification concerning alternate formulations for pet spot-on products. EPA acknowledges that our regulations, in general, allow for alternate formulations. See 40 CFR 152.43. As allowed by the regulations, EPA can also determine that separate registrations are needed in some cases. In light of the large numbers of adverse incidents and, the fact that inert ingredients could be a contributor, EPA has determined that it needs to review each change in inert ingredients as an amendment. However, please note that alternate confidential statements of formulation (CSFs) simply reflecting an alternate source of a specific ingredient would still be acceptable as an alternate formulation. Further, alternate fragrances, where applicable, are also acceptable as alternate formulations. Alternate formulations to add a new inert, such as a bittering agent, would require a new registration or a formal amendment to a basic CSF. The purpose of this change is so that the Agency can identify if any specific inerts might be associated with adverse events.

2. Dermal sensitizers

The Agency is looking closely at products that test positive in the dermal sensitization study required to support registration (OPPTS Guideline Number 870.2600, Skin Sensitization). A positive result indicates the potential for allergic contact dermatitis and generally triggers a requirement for precautionary label language, as follows: "Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals" (source: EPA label review manual, Chapter 7, Precautionary Statements). Because these products are designed to be applied directly to a pet's skin, the Agency is concerned that a positive result may indicate the potential for serious adverse effects in the target species. Currently, we are recommending against registration of pet spot-on products that test as dermal sensitizers unless it can be shown that sensitization in the animal species receiving direct application of the finished product is unlikely.

3. Individual mitigation proposals

Some registrants have requested that the Agency provide individual mitigation proposals. Although EPA is stating that general statements/restrictions would alleviate the concern for spot-on products, the Agency will be reviewing each product on a case-by-case basis to determine if specific changes are necessary from the instructions in this letter. Therefore, EPA is willing to discuss specific label changes for any individual product, if requested. If Agency consideration of a registrant proposal is desired, please submit such a proposal within 4 months of receipt of this letter and request a meeting to discuss your proposal with EPA.

4. Package inserts

Please note that any package insert or other materials provided with packaged product is considered labeling. (See FIFRA section 2(p).) Further, bulletins, leaflets, circulars, brochures, data sheets, flyers or other written, printed or graphic matter which are referred to on the label or which are to accompany the product are known in Agency practice as "collateral labeling." Such labeling is subject to applicable requirements of FIFRA and the Agency's regulations. In addition, collateral labeling may not bear claims or representations that substantially differ from those accepted in connection with registration of the product. (See FIFRA 12(a)(1)(B).) Collateral labeling must be submitted along with the application for registration and must be accepted by EPA before it can be distributed. (Source: Label Review Manual, Chapter 3, General Labeling Requirements.)

5. Placement of label statements

If additional space is required for label statements on product packaging, the Agency is amenable to moving statements such as the environmental hazards statement to the side panels of boxes to allow room for the statements described above. Please identify clearly where label statements will be placed on product final printed labels so that EPA can consider these placement proposals in its approval of product labels.

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Please note that the response to comments regarding the EPA's incident analysis and mitigation plan is being posted to the Agency's pet web page to inform the public of the Agency's intentions. If you wish to meet with us to discuss the information contained in this letter, please contact Wade Britton at 703-308-0139 or britton.wade@epa.gov, or Kimberly Nesci at 703-308-8059 or neski.kimberly@epa.gov.

Sincerely,



Lois Rossi, Director
Registration Division
Office of Pesticide Programs

cc: Linda Arrington, PM 11, RD
Driss Benmhend, Acting PM 01, RD
Wade Britton, Acting Coordinator of Pet Spot-On Product Mitigation, RD
Richard Gebken, PM 10, RD
John Hebert, PM 07, RD
Linda Hollis, Chief, Biochemical Pesticides Branch, BPPD

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