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Product Performance Review
By
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Date: June 27, 2007

PM: Richard Gebken, PM 10

EPA Reg. No.: 806-30
Product Name: Avon Skin So Soft SSS Bug Guard Plus Picaridin Insect Repellent Towelettes

Dec: 372919 S: 803292 DP: 339021

Active ingredient: 10% Picaridin

Formulation: RTU Towelette

EPA Reg. No.: 806-31
Product Name: Avon Skin So Soft SSS Bug Guard Plus Picaridin Insect Repellent Towelettes

Dec: 372922 S: 803290 DP 339020

Active ingredient: 10% picaridin

Formulation: RTU Spray

Use pattern/sites: Human skin

Pests: Repels mosquitoes, biting midges (no-see-ums), sand flies, and gnats.

Request: add deer ticks to the label

OPPTS Guideline: 810.3300 and draft 810.3700 to the extent that they apply

The following GLP studies were submitted to support the subject product registration. These are the same studies with different MRIDs. Only one study should have been submitted and assigned an MRID.

MRID 47010301 Repellency of Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent Spray EPA Reg. No. 806-31 Against Deer Ticks by Scott Carroll

MRID 47010201 Repellency of Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent Towelette EPA Reg. No. 806-30 Against Deer Ticks by Scott Carroll

Science Review of the Submitted Study

Avon should have submitted one MRID for 806-31 and cited in the data matrix for 806-30. I reviewed the MRID corresponding to 806-31. These studies were also the subject of an ethics review by John Carley.

MRID 47010301 Repellency of Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent Spray EPA Reg. No. 806-31 Against Deer Ticks by Scott Carroll

The subject product formulation was identified as 1004024-010 in this study.

Purpose: To evaluate the repellency of the subject repellent product, EPA Reg. No. 806-31, against the deer tick, *Ixodes scapularis,* (also known by the name "blacklegged tick").

Methods: This was an in-vitro study with human subjects.
Ten humans served as treated test subjects. A positive or negative control was not tested.

A dosimetry study was not performed. The repellent formulation application was made by a syringe to an exposed forearm at a treatment rate of 1.67 mg/cm^2. This resulted in product application volumes ranging from 0.7 ml to 1.3 ml per subject with a mean volume of 1.0 ml per subject. The treated subjects were exposed to a tick for 3 minutes every 15 minutes until the "First Confirmed Crossing" (first crossing 2 cm or greater into the treated zone followed by a second crossing within one half hour.). Each tick was used only once. Untreated limbs on each subject were used to test the questing behavior of the ticks to be used in the test. The test lasted for 15 hours but not all subjects participated until the end of the study.

Results:
GLP and related experimental deviations were reported. Raw data sheets were attached. The repellent lasted for at least 12 hours on subjects 2, 4, 5, 6, 7, 9, and10. The repellent was effective for 10 hours on Subject #1 and for 10.5 hours on Subject #8. Subjects 1 and 8 were the only subjects where the repellent failed according to the First Confirmed Crossing (FCC). On the other hand, Subject #3 withdrew after 10.5 hours but was included in the calculation of CPT.

Therefore, by 12 hours post-treatment, the repellent had failed on two subjects and one withdrew, leaving 7 successful replicates in the study at 12 hours. After 12 hours, subjects continued to withdraw with the last subject leaving at 15.25 hours.

Unconfirmed crossings (Time to First Crossing) occurred as follows: Subject#7 at 1 hr. 15 mins.; Subject #4 at 2 hrs. 45 mins; Subject #2 at 3 hours and at 3 hours and 45 mins.; Subject #5 at 8 hrs. 45 mins.; Subject #6 at 8 and 10 hours; and Subject #10 at 10 hours. There were no crossings on Subject #9. These crossings were not considered significant and not included in the analysis. Only FCC data were analyzed in accordance with EPA guidance resulting in a standard deviation associated with the Mean CPT that was within a very narrow range (± 1 hour). **NOTE**: EPA Insect Repellent Guidelines are undergoing revision. These data may need to be analyzed by other statistical test methods such as survivorship or other appropriate statistical analysis that takes into account all tick crossings in a repellent test when determining the CPT in the future.

Conclusion: The data supports a claim of "Repels deer ticks for up to 12 hours".

Entomologist's Recommendations:

The subject studies are acceptable and support the following repellency duration label claims: "Repels deer/blacklegged ticks for up to 12 hours for the labels of EPA Reg. Nos. 806-30 and 806-31.

Avon response to an August 2006 letter from EPA in which EPA requested that Avon Products:

1. EPA request: "Please explain how the extended duration and time-release technology is supported."

Avon Response: In their letter dated December 16, 2006 toXcel, consultant to Avon Products, responded as summarized below:

Four bullets were presented to summarize their response:

- Sustainable controlled release of picaridin, resulting in less of a need for reapplication and prolonged efficacy times;
- Enhanced spreading characteristics, allowing for even coverage of exposed areas;
- Reduction of product rub-off and loss due to perspiration, decreasing the risk of unprotected areas due to normal activity; and
- Providing an aesthetically acceptable feel

Two of the four bullets (the first and the third) support their position while two can be considered as supplemental reasons for "extended duration and time-release technology" In addition, the registrant included a discussion of inert ingredients added to the formulation to control the release and vapor pressure in conjunction with a patented process. They cited the patent pertaining to the technology in question. Avon also provided examples of claims previously accepted on other EPA registered products.

EPA Response to the December 16, 2006 request: The requested claim is acceptable based on the evidence presented by Avon in their letter dated December 16, 2006.

2. EPA request: "Please remove all references to an invisible, hidden, or unseen barrier for protection."

Avon Response: In their letter dated December 16, 2006 toXcel, consultant to Avon Products, insists this is a factual statement.

There is no doubt that the repellent is not visible after it is applied to skin due to the clear colorless nature of the subject formulations. But these claims are meaningless and are not pertinent to repellent application or results. This claim leads may lead a user to believe that they are protected by some type of invisible barrier, an implied safety claim.

EPA Response to the December 16, 2006 request. The argument presented in the December 16, 2006 letter as justification for adding such a marketing claim is not acceptable.

3. EPA Request: "The claim for repelling WNV vectors is not supported by the submitted data." Please cite or submit additional data with WNV vectors or remove this claim. The mosquitoes tested in these studies are not WNV vectors. Species from the genera *Culex* should be tested. Testing should also be conducted against *Aedes albopictus.*"

Avon Response: In their letter of December 16, 2006 toXcel, consultant to Avon Products, provided information that I discuss below.

The registrant included a list of species present in the previously submitted and reviewed efficacy studies. These are mosquitoes in which WNV has been isolated as described on the CDC web site (A total of 62 species have been found with WNV isolates). However, most of these 62 mosquito species are not vectors of WNV. Isolation of virus in a mosquito does not serve as evidence that a species is a vector of a disease. Evidence must also exist to show that once infected, a mosquito can transmit the virus in a competent manner.

The following is quoted from the published CDC National Guidance and their interpretation of such data as it relates to WNV. The last report was published in 2003, but related publications and citations on the CDC web site since that time are consistent with the 2003 recommendations except that *Culex tarsalis* has also been shown to be a competent vector of West Nile virus.

"During 1999-2002, WNV was detected in 36 mosquito species in the U.S. (see www.cdc.gov/ncidod/dvbid/westnile/mosquitoSpecies.htm). The vast majority of isolates came from *Cx. pipiens*, *Cx. quinquefasciatus* and *Cx. restuans*. Numerous isolates have also come from several potential accessory vectors (i.e., *Cx. tarsalis, Cx. salinarius, Oc. Ae. albopictus, Oc.*

triseriatus, Ae. vexans, Cx. nigripalpus). While detection of WNV in these species demonstrates intensified virus transmission (i.e., virus in primarily mammal-feeding or opportunistic mosquitoes), the contribution of these species to human risk is poorly understood." **From CDC publication: "Epidemic/Epizootic West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control. 2003."**

EPA Response to the December 16, 2006 request. Therefore, the claim is not acceptable based on the submitted data and cited references. The registrant should cite or submit additional data with WNV vectors or remove this claim. The mosquitoes tested in these studies are not WNV vectors. Species from the genera *Culex* should be tested. Testing should also be conducted against *Aedes albopictus.* Examples of acceptable *Culex* spp. include Cx. *tarsalis*, *Cx. quinquefasciatus,* and *Cx. pipiens.* Laboratory data with uninfected mosquitoes should be used to support this claim. A protocol should be submitted before conducting the test with human subjects. Note that *Cx. restuans*, although a vector of WNV, will not colonize in the laboratory. *Culex quinquefasciatus and Aedes albopictus* will be the easiest species to obtain for laboratory repellent testing.

Label claims for the subject products

Avon requested the addition of new claims in the subject amendments. The label claims on the proposed labeling for both products are acceptable except as listed below.

Remove:

1. "Creates an invisible, unseen, hidden, barrier of protection to repel insects mosquitoes, deer ticks, mosquitoes and deer ticks, gnats, non-see-ums, sand flies and biting midges."

2. "Repels mosquitoes that may carry transmit West Nile virus up to 8 hours."

3. "Repels mosquitoes that may carry transmit West Nile virus for 8 hours."

4. "Repels mosquitoes that may carry transmit West Nile virus."

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R160530

Chemical Name: Picaridin

PC Code: 070705
HED File Code: 512500 RD Efficacy Reviews Skin applied Insect Repellents
Memo Date: 6/27/2007
File ID: DPD339020
Accession #: 000-00-0125

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