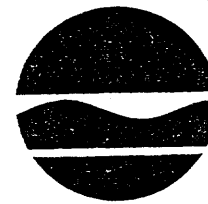


**New York State Department of Environmental Conservation**

Division of Solid & Hazardous Materials  
50 Wolf Road, Albany, New York 12233-7250  
Phone 518-457-6934 FAX 518-457-0629

*Product file*



John P. Cahill  
Commissioner

**JUN 08 1999**

**CERTIFIED MAIL**  
**RETURN RECEIPT REQUESTED**

Mr. Timothy Gilman  
Avon Products, Inc.  
1251 Avenue of the Americas  
New York, NY 10020-1196

Dear Mr. Gilman:

**Re: Registration of Avon Authentic SSS Skin-So-Soft Bug Guard Plus IR3535<sup>®</sup>  
Insect Repellent SPF30 Moisturizing Sunblock Lotion (EPA Reg. No. 806-12)  
Containing the New Active Ingredient Ethyl Butylacetylaminopropionate/  
Butylacetylaminopropionic Acid**

The Department has completed the review of your application, together with all the supplemental supporting information supplied to date by Covington & Burling, EM Industries, Inc., Avon Products, Inc. and Katz Associates, regarding registration of the referenced pesticide product in New York State. Avon Authentic SSS Skin-So-Soft Bug Guard Plus IR3535<sup>®</sup> Insect Repellent SPF30 Moisturizing Sunblock Lotion (EPA Reg. No. 806-12) contains the new active ingredient Butylacetylaminopropionate/Butylacetylaminopropionic Acid (IR3535<sup>®</sup>).

Avon Authentic SSS Skin-So-Soft Bug Guard Plus IR3535<sup>®</sup> Insect Repellent SPF30 Moisturizing Sunblock Lotion (7.5% Ethyl Butylacetylaminopropionate/Butylacetylaminopropionic Acid) is a formulated end-use insect repellent product labeled for application to exposed skin to repel mosquitoes, deer ticks, black flies, sand flies, gnats, no-see-ums and biting midges. Product label also bears non-pesticidal claims as a moisturizer and sun block.

The Department's review of the technical grade active ingredient (IR3535<sup>®</sup>) and the formulated product (Avon Bug Guard Plus) addressed the potential for adverse human health impacts.

The registration package contained limited toxicological information and few United States Environmental Protection Agency (USEPA) Data Evaluation Record reports. Most of the available information on the toxicity of IR3535<sup>®</sup> and the products formulated with it comes from summaries of studies in the USEPA Registration Eligibility Document or from the USEPA correspondence. No data on IR3535<sup>®</sup> were found in a search of the open literature.

Based on the information in the registration package, IR3535<sup>®</sup> was not very toxic following acute oral, dermal or inhalation exposure. It was moderately irritating to the eyes of rabbits, but was not a skin irritant or sensitizer. Avon Bug Guard Plus was not very toxic following acute oral or dermal exposures. The acute inhalation exposure study requirement was waived. Studies conducted with Avon Bug Guard Plus indicate that it

is not very irritating to rabbit eyes nor a sensitizer to the skin of humans. A dermal irritation study in humans involved the simultaneous application of ten different materials to the skin of 52 test subjects. The application sites were covered for 48 hours and evaluated at the 48- and 72-hour points following application. This study reports that application of "fresh" product produced mild erythema in three, and questionable erythema in two, of the 52 test subjects, 48 hours after application. Six subjects had mild erythema and four had questionable erythema in at the 72-hour evaluation. The "aged" sample (product stored at 120° F. for one month and room temperature for 20 months) produced definite erythema in 21, and questionable erythema in three, of the 52 test subjects, 48 hours after application. Twenty-nine subjects had definite erythema and three had questionable erythema at the 72-hour evaluation. No edema or blistering occurred in any test subjects from the use of either the fresh or the aged product. The registrant indicated that the test subject's irritation score to the aged product was similar to the score from an insect repellent product containing a low concentration of the active ingredient N,N-diethyl-m-toluamide (DEET) and the score from a common skin moisturizer product. This study used only one application during the course of the test and did not evaluate skin irritation from multiple applications each day as are allowed by the product label (up to nine per day).

The registration package contained a study in which 29 children age three to ten had Avon Bug Guard Plus applied to their bodies. After an exposure period of five hours, an evaluation of the children's skin was conducted by a dermatologist and a pediatrician. Overall, the product did not appear to cause any skin irritation in the study, but some facial and eye discomfort was reported. It was determined that these effects resulted from either product migration, contact with chlorinated pool water at the test site or perspiration.

Information in the registration package indicates that IR3535® has been used in Europe for over 20 years. The manufacturer of IR3535® requested that its European customers provide any information they had on known incidents of adverse reactions related to use of IR3535® - containing products. The manufacturer has not received from its customers any reports of adverse effects related to use of IR3535®.

Several subchronic toxicity studies have been conducted on IR3535®. In a 90-day dermal exposure study in rats, no systemic effects were noted at dose levels up to 3,000 milligrams per kilogram body weight per day (mg/kg/day). Some skin irritation was reported in this study, but these effects were believed due to shaving and bandaging of the application site. In a 28-day feeding study in rats, no effects were reported at doses up to 2,600 mg/kg/day, the highest dose tested. In dogs given IR3535® by gavage for 28 days, no toxicological effects other than vomiting and slightly increased salivation were reported at doses up to 1,800 mg/kg/day. Rabbits given IR3535® by gavage for a 28-day period had some clinical effects (deeper breathing, restlessness, decreased food consumption and body weight gain) at 1,500 mg/kg/day; no effects were noted at the 500 mg/kg/day dose level.

No chronic studies or oncogenicity data were provide in the package nor found in the open literature. IR3535® was negative in several genotoxicity studies.

Several developmental toxicity studies have been conducted with IR3535<sup>®</sup>. While only one of these studies was acceptable to the USEPA on an individual basis, the Agency considered them to collectively fulfill the registration requirement for developmental toxicity evaluation. In the acceptable study, pregnant rabbits were given doses of either 0, 100, 300, or 600 mg/kg/day during gestation. Marginal maternal toxicity (decreases in defecation, body weight and body weight gain) was reported, but these effects were considered so slight that the no-observed-effect level was reported to be greater than or equal to the highest dose tested, 600 mg/kg/day. There were no developmental effects reported at any dose level in this study, nor in any of the other developmental toxicity studies conducted. In a multi-generation reproduction study in rats, no effects on reproductive parameters were reported. However, the study reported increased liver, kidney, adrenal and spleen weights at a dose level of 300 mg/kg/day. The USEPA questioned these results because no other effects were reported even at dose levels up to 1,000 mg/kg/day. Details of the study were not available to the USEPA for evaluating the study results further nor were they contained in the registration package. It was also not clear if the offspring of animals in the study received the compound postnatally, either directly or through lactation.

A number of studies were conducted on the efficacy of Avon Bug Guard Plus against mosquitoes, black flies, sand flies and deer ticks. None of the efficacy studies were conducted in New York State and the studies on deer ticks were done in a laboratory setting, not in the field. Overall, these studies report that Avon Bug Guard Plus provides complete protection from the above arthropods for a period of 1.6 to over four hours duration.

The label of Avon Bug Guard Plus states to reapply about every two hours, or sooner if effectiveness diminishes, for continued insect protection. The label further states not to exceed nine applications per day. The basis for the nine application per day restriction appears to come from a USEPA estimate of the maximum number of applications that can be made to a child while still providing a 100-fold margin of exposure over the no-observed-effect level from a rabbit developmental toxicity study (600 mg/kg/day).

The information available on the toxicity of IR3535<sup>®</sup> and Avon Bug Guard Plus is limited and does not allow a thorough evaluation of these materials. Nevertheless, the data that are available indicate that neither IR3535<sup>®</sup> nor Avon Bug Guard Plus are very irritating or toxic on an acute basis and IR3535<sup>®</sup> was not very toxic following subchronic exposures nor did it cause reproductive, developmental or genotoxic effects. Given this apparent low toxicity, IR3535<sup>®</sup>'s reported favorable use history in Europe and the label restriction on the maximum number of applications per day, as well as the statement to discontinue use if irritation or rashes appear, Avon Bug Guard Plus should not cause unreasonable adverse effects when used as labeled.

The human skin irritation data indicate that "aged" product (e.g., that stored and used over several seasons) is more irritating to skin than is the fresh product. It is not uncommon for people to use and store such products over the course of several years and concerns for future potential irritation problems in the general public cannot be

Mr. Timothy Gilman

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discounted. Also, because Avon Bug Guard Plus is labeled as a sun screen and a moisturizer in addition to an insect repellent, it is likely that some people will use it for these other purposes even when it is not needed as a repellent. Such use results in unnecessary exposure to pesticides. Given this potential for irritation and misuse, Avon Products, Inc. is reminded of the Department's regulation regarding the reporting of unreasonable adverse effects. Pursuant to 6 NYCRR Part 326.14(f), a registrant is required to submit all information, which is required to be submitted under Federal Insecticide, Fungicide and Rodenticide Act 6(a)(2) and implementing regulation 40 CFR Part 159, regarding adverse effects of a pesticide product or any of its ingredients to the Department within thirty (30) days after the reportable information is first possessed or known.

The Department hereby accepts Avon Authentic SSS Skin-So-Soft Bug Guard Plus IR3535<sup>®</sup> Insect Repellent SPF30 Moisturizing Sunblock Lotion (EPA Reg. No. 806-12) for registration in New York State. Enclosed for your files are the Certificate of Pesticide Registration and New York State stamped-"ACCEPTED" labeling.

If you have any questions, please contact Maureen P. Serafini, Chief of our Pesticide Product Registration Section, at (518) 457-7446.

Sincerely,



Stephen Hammond, P.E.  
Director  
Division of Solid & Hazardous Materials

Enclosures

cc: w/enc. - H. Estreicher, Covington & Burling  
N. Kim/D. Luttinger/J. Leach, NYS Dept. of Health  
E. Biel/R. Mungari, NYS Dept. of Ag. & Markets  
G. Good/W. Smith, Cornell PMEP