Background Information for the FIFRA Science Advisory Panel Addressing the Draft Guidelines Titles OPPTS 810.3700 Insect Repellents for Human Skin and Outdoor Premises.

Introduction

The decision to draft product performance testing guidelines and protocols was made when DEET was being reevaluated for reregistration. The DEET Reregistration Eligibility Decision (RED), published September, 1998, required updated product performance data for insect repellents containing N, N,-diethyl-meta-toluamide (DEET) as the active ingredient. At that time, the Agency realized a standardized approach to labeling and testing all insect repellents was needed. Experts were consulted during development of the draft guidance in 1998 and 1999. The first comments were received at the National Entomological Society of America (ESA) meeting held in Las Vegas, NV in November 1998. As other stakeholders became aware that these guidelines were being developed, they voluntarily submitted comments and suggestions to the Agency. The Agency published an official draft of the guidelines for comment and made them available to the public via the Federal Register (FR) December 15, 1999. That comment period ended February 14, 2000. All comments were reviewed and incorporated into the protocols or are still under consideration pending the outcome of this FIFRA Scientific Advisory Panel (SAP).

Inconsistencies have developed in product performance testing and labeling of insect repellents. In order to minimize this variance, EPA developed these draft product performance testing guidelines and appropriate label language. The guidelines and label language proposed by the Agency are intended to standardize and improve the information provided to the consumer. These guidelines are also intended to create an "even playing field" among companies registering insect repellents. By creating a standardized guideline, the Agency expects product performance tests for insect repellents to be equally acceptable. In addition, the product performance testing guidelines are intended to supercede EPA, Pesticide Assessment Guidelines, Subdivision G: 95-9 and OPPTS 810.3300, "Treatments to control pests of humans and pets;" and Subdivision G: 95-10 and OPPTS 810.3400, "Mosquito, black fly, and biting midge (sand fly) treatments." These new guidelines provide direction on insect repellent testing protocols, data citation, and labeling.

Topical Treatments

Failure of the product to repel mosquitoes adequately may result in the contraction of an arthropod-borne disease or less serious effects from bites such as discomfort, scarring, infection, or allergic reactions. EPA's policy includes minimum guideline efficacy standards for repellents generally, and additional standards for repellents intended for situations where there is a threat of arthropod-borne disease. The minimum standards are EPA's interpretation of the minimum product performance necessary for a repellent to pass FIFRA/FQPA risk/benefit balance assuming minimal toxicological risk. EPA believes these minimal guideline standards are necessary in order to offset the risks presented by ineffective repellents.

A product performance standard represents the minimum level of repellency which would normally be acceptable for protecting the public health, when required, or for economic control of a pest or pest combinations at a specific site. For mosquito repellents, the current Subdivision G Guideline 95-9 specifies that these products "[s]hould generally provide a minimum of 2-3 hours protection time based upon first confirmed bite field tests, depending upon the biting pressure evidenced in the testing." As emphasized in the generic provisions in the guidelines, the performance standards are guidance not rules. The performance standards in this PR Notice are expressed as percentages of repellency over time. Public health related label claims should meet the specific performance standards in this notice. If these standards are not met, the registrant may only use a label claim such as "aids in repelling" or "may reduce bites."

EPA's proposed minimum guideline standard for all repellents is that they provide either an average of 1 hour of protection or reduce biting pressure on average for 1 hour by 95 percent under moderate biting pressure. EPA has chosen 1 hour as the minimum period because it is unreasonable to expect the consumer to reapply a repellent more frequently than once per hour. EPA has used average protection time and 95 percent reduction because occasional bites do not raise significant concerns regarding the non-disease risks from nuisance bites. EPA chose moderate biting pressure because it is reasonable to expect that repellents will frequently be used in situations where mosquito pressure rises to a moderate level (e.g., 5 bites/5 minutes).

Since these guidelines involve testing with human subjects, EPA's policy on human studies of this type will be strongly influenced by the recommendations of the joint SAB/SAP Subcommittee on Data from Testing with Human Subjects. For the present, to make the guideline less likely to require change when the policy emerges, the guideline cites two authorities unlikely to change--FIFRA section 12(a)(2)(P), and the list of elements of informed consent contained in EPA's version of the Common Rule. The eventual EPA policy will be constructed to apply to these and all other test guidelines involving research with human subjects.

Laboratory tests can use captive populations of pest insects, bred to be disease-free. Although this reduces the potential risk to study subjects, some of the public comments received regarding these guidelines questioned the validity of results obtained from laboratory tests--at least with mosquitos and other biting flies (public comments can be found in Appendix V). Field tests involve wild populations of pest insects which may not be disease-free, and thus may pose a potential risk to test subjects of contracting a disease as a consequence of their participation in the test. Ideal testing methods would assess repellent efficacy without putting human subjects at risk; unfortunately the current state of the science does not provide any alternative to human testing.

The focus of this SAB/SAP is to evaluate the product performance guidelines to address certain inconsistencies in the current guidelines. It is not EPA's intention for this Subpanel to address human testing issues. The use of human test subjects is being addressed by the Agency in a different forum. A SAB/SAP was convened in a previous meeting to address concerns regarding the use of human test subjects.

Area Repellents

Repellents that repel insects or ticks from a unit area of open space (e.g., candles, coils, or vaporizing mats) do not pose risks similar to personal repellent products because area repellents are not applied directly to human skin. Given their typical marginal performance, a reasonable consumer would not be expected to use such a product to protect against the spread of mosquito-borne disease. Nonetheless, area repellents can be useful to consumers and such products that result in a 50% reduction in bites would meet EPA's efficacy standard for this type of product.

In the proposed product performance guidelines for repellents, EPA has made several changes designed to produce more reproducible results and more accurate information for inclusion on labels. Two important changes involve use of the "first confirmed bite" test and the level of arthropod pressure in studies. The Agency is proposing to no longer rely upon the first confirmed bite (FCB) test. The FCB test discounts bites that are not confirmed by a second bite within a specific time interval. The proposed revision includes that all bites should be counted and considered. The Agency does not believe that 100% protection is typical and realizes there is variability in the efficacy of insect repellents among consumers. EPA, therefore, is changing it's guidance on repellent product performance testing to specify that repellency be measured either by determining the mean time to the first bite (FB) or comparing bites of treated subjects to untreated subjects to document the percent reduction in bites.

The Agency is changing the current guidance to propose a minimum biting pressure for these product performance studies. Minimum biting pressures were established by reviewing standards recognized by the research and testing community as levels needed to generate data that can be evaluated for its statistical significance. A minimum biting pressure of five bites or probes per five minutes is proposed for most mosquitoes and biting flies and one bite or probe per five minutes for stable flies in the field. For laboratory studies, the following biting pressures are specified: For mosquitoes, the standard is a minimum of ten lands or probes within a 30 second exposure period; for stable flies, a minimum of five lands or probes within a 60 second exposure period; for fleas, a minimum of ten lands or probes within a 30 second exposure period; for ticks and chiggers, five ticks or chigger mites should be exposed to a negative control for five minutes.

The draft guidelines titled OPPTS 810.3700; Insect repellents for human skin and outdoor premises and associated questions are attached below. The Agency would like advice from this Subpanel regarding these guidelines and protocols. The questions presented below are intended to point out specific areas the Agency would appreciate comments.