Questions for the Science Advisory Panel (SAP) regarding OPPTS 810.3700. Insect repellents for human skin and outdoor premises.

FIRST BITE vs. FIRST CONFIRMED BITE vs. 95% REDUCTION IN BITES

1. First Bite (FB) vs. First Confirmed Bite (FCB): Historically, the Agency has used the First Confirmed Bite (FCB) test to assess the effectiveness of human insect repellents. However, the Agency is concerned that the FCB method will result in the loss of valuable information. The FCB method does not appear to have been developed using a statistically valid approach. For this reason and because some insect bites may disregarded when all bites should be counted, the Agency does not currently approve of the FCB method. The Agency recommends use of the First Bite (FB) method or a 95% reduction in bites, because all bites are counted and the method provides a more "real-world" assessment of insect repellent efficacy.

   Is the Panel aware of any scientifically valid justification for using the FCB method, or, conversely with using the FB or 95% reduction in bites methods. Should we use 95% and a first bite test or choose just one of these as the standard - why or why not?

GENERAL CONSIDERATIONS FOR ALL TESTING

2. If a product effectively repels a particular pest based upon the time to first bite, the Agency is considering allowing a claim of protection against potential disease vectors. For example: "May repel deer ticks which carry lyme disease."

   What degree of protection is necessary to warrant allowing claims of protection from specific diseases? What rationale can the Agency use to demonstrate a high enough level of efficacy to claim protection against potential disease vectors? What suggestions if any does the Panel have for changes to these protocols that would allow a claim for protection against potential disease vectors? Can you suggest a way to account for differences in level of repellency for different products?

3. The Agency is recommending five treated test subjects for a label claim of less than five hours of repellency and ten treated test subjects for a label claim of five or more hours of repellency. The Agency considered the publications by Rutledge and Gupta (1999) as a resource in the development of recommendations for the numbers of replications to be used in field tests of insect repellents (Appendix I). Although the Agency believes that the data are scientifically sound, a direct and literal use of these data may not be practical (either economically or logistically) for all registrants. However, after review of Rutledge and Gupta (1999), the Agency realized that more test subjects may be necessary to test repellents with longer durations of repellency.

   What number of test subjects would provide statistically-valid results? If more test

subjects then currently recommended by EPA are appropriate, would it then be feasible for Registrants to conduct the test? If the number of test subjects should be different for repellents with shorter claims of duration of repellency, how many test subjects should repellents with longer claims include?

4. How should exposure testing be designed to take into account that some test organisms (e.g., mosquitoes) only bite during specific times in a day which may exceed the duration of repellency. For example, would it be acceptable to apply repellent to test subjects at varying number of hours before exposure (e.g., 1,2,4,8, and 12 hours) and then expose all subjects at once? Why, or why not? For this method, how many times should each test subject be exposed? Can you recommend an alternative way to address this problem that might be better?

5. Are the application rates proposed in "OPPTS 810.3700; Insect repellents for human skin and outdoor premises" acceptable for a scientifically sound study? If not, how should application rates be derived? Should an application rate be recommended in these protocols or left to the discretion of the registrant? If a repellent is applied as a thick layer, how will it affect the results of the efficacy test?

MOSQUITO AND STABLE FLY LABORATORY TESTS

7.How valuable are cage studies in assessing the efficacy of a repellent? If the Agency decides to require submission of the cage studies, are there better ways to perform the studies than the Agency-recommended protocols? If so, what are they? Are there advantages to the Klun and Debboun (2000) study that might justify including it as an alternative method (Appendix 2)? If so, what are they?

MOSQUITO, BLACKFLY CERATOPOGONID, SANDFLY, TABANID, AND STABLE FLY FIELD TESTS

8. What biting pressures are appropriate, e.g., five bites in ten minutes for Ceratopogonids and one bite in five minutes for Tabanids? How should biting pressure be determined, e.g., should lands be considered as well as probes and/or bites? If landing rate data collection can be justified for laboratory and/or filed studies, what rates would be acceptable?

CANDLES, COILS, AND VAPORIZING MATS

9. The agency has proposed a 50% reduction in bites for a label claim that the repellent may aid in reducing bites and a 95% reduction in bites for a label claim that the product repels, e.g., mosquitoes. What level of reduction in bites is acceptable to show efficacy for candles, coils, and vaporizing mats?

FLEAS

10. What laboratory tests will provide adequate data to determine flea repellency? Of those, including the USDA test found in Appendix III, are any better than the Agency-proposed tests? How many lands should be required within three or five minutes to verify biting pressure (e.g., the Agency proposed ten)?

TICKS AND CHIGGER MITES

11. Due to the high incidence of Lyme disease in the U.S., EPA did not recommend deer tick field tests using human subjects. How adequate are the proposed laboratory tests in determining deer tick repellency? Evaluate the tick and chigger tests found in Appendix III (Smith 1955) and IV. Should these protocols be considered in lieu of or addition to the Agency proposal?

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