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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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SUBJECT: Science review of DEET study reports of completed efficacy studies for mosquitoes.

FROM: Kevin J. Sweeney, Senior Entomologist
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TO: Marion Johnson, Chief
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RE: Carroll, S. (2007). Test of Dermaegis LipoDEET 302 Personal Insect Repellent, EPA Reg. No. 82810-1 (MRID 47322501).

Carroll, S. (2007). Test of Coulston's Duranon Personal Insect Repellent, EPA Reg. No. 50404-8 (MRID 47322401).

ACTION REQUESTED

Conduct a science review of two completed studies. Evaluate and assess efficacy of the subject repellent formulations. Determine the adequacy of the methods employed and the scientific validity of the reported data.

CONCLUSIONS

Studies MRID 47322401 and MRID 47322501 were conducted in accordance with Good Laboratory Practices that provided scientific data that are acceptable. Based on the experimental results, LipoDEET 302 (EPA Reg. No. 82810-1) and Duranon (EPA Reg. No. 50404-8) repelled mosquitoes for about 11 hours. The Human Studies Review Board will be asked to comment on these data sets and related science issues.

SCIENCE REVIEW

Study Objectives:

To determine the Complete Protection Time (CPT) for two repellent formulations, Dermaegis LipoDEET 302 Personal Insect Repellent (EPA Reg. No. 82810-1) and Duranon Personal Insect Repellent (EPA Reg. No. 50404-8).

Materials & Methods:

Study locations: Two State of California locations were used in this study. Test Site 1 "The forest" was located in Glenn County and will be referred to as "Site 1-Glenn County" in the rest of this review and data tables. Test Site 2 "lakeside grassland", was located in Butte County and will be referred to as "Site 2-Butte County" in the remainder of this review.

Date(s) of each study: The dosimetry phase was conducted on November 7-9 2007. Repellent testing was conducted on November 10, 2007 in Glenn County and November 11, 2007 in Butte County.

Repellents Tested: The repellents tested were DEET based formulations. The tested products were DermAegis LipoDEET 302 Personal Insect Repellent (30% DEET) (EPA Reg. No. 82810-1) and Duranon Personal Insect Repellent (20% DEET) (EPA Reg. No. 50404-8). Both products were lotions with specific gravity approximately equal to 1 g/ml.

Tested positive control/comparison repellent: None

Untreated Control: Two untreated subjects served as "untreated controls" on each test date to monitor ambient mosquito landing pressure.

Protocol: Protocol SCI-001 was used as amended. Amendments are included in Appendix 7 of the study.

Experimental design: The study was conducted at two sites on November 10-11, 2007. The test sites represented different ecological habitats, which had similar mosquito fauna and population size present (Table 2 of this review). Ten subjects each were randomly assigned to one of two repellent treatments per site for a total of 10 subjects per treatment at each site. Subjects did not know the identity of a repellent treatment at the time of testing. Repellent doses were prepared for each subject based on the surface area of the forearm. The dosing rate was based on the results of a dosimetry analysis performed for each product in early November with a sample of ten subjects participating in the study. Untreated control subjects and subjects treated with repellent were exposed to mosquitoes for one minute every 15 minutes until the repellent failed. Mosquitoes landing with intent to bite were recorded and aspirated

into containers. Collected mosquitoes were identified and pooled for viral detection assays employing the Polymerase Chain Reaction (PCR) methodology. No viruses were isolated from any of the collected mosquitoes.

Data analyses: Subjects remained in the test until the repellent failed as determined by the first confirmed landing with intent to bite. The time at which the repellent failed equaled the Complete Protection Time (CPT), and a CPT was recorded for each subject. The CPT for treated subjects where product failure did not occur equaled the test period length. The mean CPT for each repellent was calculated. The CPT results for each repellent were reported as mean CPT$\pm$ SD based on a 95% confidence interval. Collected data were not analyzed by Kaplan-Meier survival analysis or by an Analysis of Variance (ANOVA). The two products were not subjected to any type of comparative statistical analysis to determine if the treatment means were the same or different.

Protocol Deviations: Three protocol deviations were reported in Appendix 7d of each study. Of these, the most significant is the pre-treatment of subjects with repellent 150 minutes (Site 2) and 180 minutes (Site 1) before field exposure.

Results:

Table 1
Dosimetry Results (See Table 2 in each study)

Report volume	MRID 47322501	MRID 47322401
Repellent tested	LipoDEET 302 (30% DEET)	Duranon (20% DEET)
Mean product dose per subject	1.16 g	0.97 g
Mean dose rate	1.314 g/600 cm^2	1.110 g/600 cm^2
Mean dose rate	0.00219 g/cm^2	0.00185 g/cm^2
Mean dose DEET	0.00066 g/cm^2	0.00037 g/cm^2
Number of Subjects	10	10

Table 2
Repellent Field Trial Results (See Table 5 and Appendix 4 in each study)

Report volume	MRID 47322501	MRID 47322401
Repellent tested	LipoDEET 302 (30% DEET)	Duranon (20% DEET)
Site 1 Glenn County Mean CPT	11.25 h ± 0.0 h	11.25 h ± 0.0 h
Site 2 Butte County Mean CPT	11.28 h ± 0.79 h	10.78 h ± 1.3 h
Sites 1 & 2 Pooled Mean CPT	11.27 h ± 0.4 h	11.27 h ± 0.4 h

Table 3
Mosquito species and relative population abundance
(See Table 3 and Appendix 6 in each study)

Species	Site 1: Glenn County		Site 2: Butte County		Disease Vector?	Pathogen Detected?
	No. Mosquitoes	% Abundance	No. Mosquitoes	% Abundance		
Ae. melanimon	119	87.50	108	72.00	WEE	No
Ae. vexans	3	2.21	32	21.33	No	No
Ae. stichticus	0	0	6	4.00	No	No
Ae. increpitus	3	2.21	1	0.67	No	No
Ae. sierrensis	1	0.74	0	0	No	No
Ae. nigromaculis	1	0.74	0	0	No	No
Culiseta inornata	5	3.68	0	0	No	No
Cx. tarsalis	4	2.94	0	0	WNV SLE	No
C. pipiens	0	0	3	2.00	WNV SLE	No
Total	136	100%	150	100%	—	No

Discussion, Conclusions, and Recommendation:

The methods employed in these studies were adequate to produce scientifically reliable data. They were based on the study protocol (SCI-001) that was amended before testing began. Protocol deviations were reported.

The sample size was 10 subjects for dosimetry and 10 for each treatment at each field site. There were two treatments per day at each test site. Repellent was applied before traveling to the field. Field exposure began 150 to 180 minutes after application, and lasted for 8.25 h. (Site 1) or 8.75 hours or less (Site 2) if the repellent application failed on a subject. Repellent treatments were made to different limbs of subjects who participated on both days of field testing to avoid any residual effect from a repellent treatment the day before. The studies were conducted at the same time of day at each site to minimize temporal effects.

Dosimetry results are summarized in both studies. The mean repellent product dose applied per unit area of skin surface for each product was somewhat higher than the industry standard of 1g/600 cm^2. The mean DEET dose was significantly higher for the 30% LipoDEET 302 product as compared to the 20% Duranon product, but this difference was not reflected in repellency results.

Statistical analyses were conducted on the dosimetry data employing MS Excel and SAS JMP Version 5.0.1.2 (SAS Institute, Cary NC). The experimental results were statistically analyzed with MS Excel and were reported as mean CPT values with their standard deviations. Evaluation of the results with the Kaplan-Meier analysis was not useful because of the low number of failures. No explanation was provided for not conducting an Analysis of Variance, but it is likely that this analysis would not provide much useful information because the sources of variation were minimized.

The subject sets treated with each repellent at each site did not overlap--i.e., nobody was treated with both repellents on the same day. Twelve subjects were treated with one repellent on November 10 and with the other on November 11; five were treated with the same repellent on both days of field testing; and six participated in only one day of field testing, and thus were treated only once.

The mosquito species composition and population size were similar between sites; and the raw Mean CPT values with their associated standard deviations were nearly the same. Neither repellent failed at Site 1. However, a t-test may have been useful in comparing the two repellent treatment means on each day Results were reported in table form and the degradation of the repellent at Site-2 Butte County was plotted for illustrative purposes. Site-specific data for each repellent were not pooled.

The variance in the experiment is better understood by examining the mean CPT values, each one with a small standard deviation around the calculated mean. The Duranon product results were more variable at Site-2 Butte. Neither product failed after 11.25 hours at Site 1-Glenn County. When the mean CPT values for the tested repellents are compared, the confidence intervals overlap greatly and there is not much difference between the means.

In conclusion, the data collected from this experiment shows that LipoDEET 302 (30% DEET) (EPA Reg. No. 82810-1) performed only slightly better than Duranon (20% DEET) (EPA Reg. No. 50404-8) despite the higher content of DEET in the formulation and the use of liposomal technology (by encapsulating DEET in liposomes) to aid in controlling the rate of DEET vaporization from the skin. Both of the repellent products performed successfully for about 11 hours. A positive control treatment and a comparative analysis of treatment means, though not required by the EPA, would have improved the experimental design and our ability to compare these results to other tests.

Recommendation: The studies are scientifically sound and acceptable.