Science Assessment: Mark 3 - Maximum Strength Pump Spray Deep Woods OFF!

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Mark - 3 Study

- Conducted on July 29, 2015 in Wisconsin and September 10, 2015 in Florida
- Tested a 98.25% Deet pump spray
- EPA Reg. No. 4822-276
- 10 treated subjects and 2 untreated subjects
  - Wisconsin site tested 6 females and 4 males (deviation 1)

Methods: Application Rate

Site	Test Subject No.	Date	Limb Treated	Target Amount [1] (g)	Actual Amount (g)	% of Target
Wisconsin	26	7/29/15	Right Arm	0.50	0.51	**102%**
Wisconsin	27	7/29/15	Left Arm	0.40	0.41	**103%**
Wisconsin	28	7/29/15	Right Arm	0.38	0.37	**97%**
Wisconsin	29	7/29/15	Left Arm	0.45	0.45	**100%**
Wisconsin	32	7/29/15	Right Arm	0.45	0.45	**100%**
Wisconsin	37	7/29/15	Left Arm	0.45	0.45	**100%**
Wisconsin	38	7/29/15	Right Arm	0.54	0.56	**104%**
Wisconsin	41	7/29/15	Left Arm	0.39	0.39	**100%**
Wisconsin	43	7/29/15	Left Arm	0.49	0.49	**100%**
Wisconsin	45	7/29/15	Left Arm	0.54	0.55	**102%**
Florida	241	9/10/15	Left Arm	0.46	0.47	**102%**
Florida	242	9/10/15	Right Arm	0.48	0.50	**104%**
Florida	243	9/10/15	Left Arm	0.51	0.51	**100%**
Florida	244	9/10/15	Right Arm	0.48	0.49	**102%**
Florida	245	9/10/15	Left Arm	0.57	0.58	**102%**
Florida	253	9/10/15	Left Arm	0.39	0.40	**103%**
Florida	254	9/10/15	Right Arm	0.42	0.41	**98%**
Florida	255	9/10/15	Left Arm	0.34	0.35	**103%**
Florida	256	9/10/15	Right Arm	0.55	0.56	**102%**
Florida	257	9/10/15	Left Arm	0.40	0.40	**100%**
					Average	**101%**
					Min	**97%**
					Max	**104%**

[1]Target amount was based upon forearm surface area calculation.

Methods: Endpoints

- The study was ended after 20 exposure periods at the Wisconsin site because landings on the untreated control were not adequate (< 5 landings per 5 minutes)

- At the Florida site the study was ended at the discretion of the study director after 19 exposure periods

Data Analysis

- Kaplan-Meier Survival Analysis used to calculate median CPT

- For those subjects who did not experience FCL by the end of the study, their CPT values are conservatively assumed to be the post-treatment duration of the study in a given site.

- At the Florida site 4 subjects did not receive an FCL, and 2 subjects did not receive an FCL at the Wisconsin site

Results: Landings on Untreated Controls

- At the Florida site, five landings occurred on all untreated control subjects during all exposure periods.
- At the Wisconsin site, less than five landings occurred on one subject in exposure periods 19 and 20 and on the other subject in exposure periods 14 and 19.
- The time to five landings ranged from 17 seconds to just under 5 minutes during all exposure periods where 5 landings occurred.

Results: Mosquito Species Collected in Wisconsin

Table 1. Wisconsin Site Mosquito Species collected - July 29, 2015

Species	Number Collected	% of Total
Coquillettidia perturbans	1	**1.4%**
Psorophora ferox Anopheles crucians	3	**4.2%**
Aedes vexans	2	**3%**
Aedes trivittatus	63	**90%**
Aedes stimulans	1	**1.4%**
Total	**70**	**100%**

Results: Mosquito Species Collected in Florida

Table 2. Florida Site Mosquito Species collected - September 10, 2015

Species	Number Collected	% of Total
Anopheles atropos	9	**3%**
Anopheles crucians	4	**1.3%**
Aedes atlanticus	95	**31.4%**
Aedes infirmatus	137	**45.4%**
Aedes taeniorhynchus	7	**2%**
Coquillettidia perturbans	2	**0.7%**
Culex erraticus	4	**1.3%**
Mansonia dyari	4	**1.3%**
Mansonia titillans	4	**1.3%**
Psorophora ferox	30	**10%**
Wyeomyia mitchellae	6	**2%**
Total	**302**	**100%**

Results: Median Complete Protection Time

MARK-3 (98.25% DEET aerosol) Repellency Duration Results Summary, Hours, Sample size = 10 Wisconsin site, Sample size = 10 Florida Site.

Measure	Wisconsin Site	Florida Site
Median	12.0	12.0
95% LCL	6.0	8.5
95% UCL	12.0	12.0
Range	**4.5 - 12.0**	**8.5 - 12.0**

Median CPT for Graphic = 12 hours

Conclusion

The methods used in this study were adequate to produce scientifically reliable results. The methods were based on the protocol reviewed and accepted by the EPA and HSRB on April 23, 2015 as amended to incorporate EPA and HSRB recommendations before testing began. The data in the study are acceptable to support a median CPT of 12.0 hours against mosquitoes for the EPA Repellency Awareness Graphic on the label for Mark-3.

Ethics Assessment: Mark 3 - Maximum Strength Pump Spray Deep Woods OFF!

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Slides Applicable to All Mark Studies

- The EPA slides applicable to all Mark studies which are under review were discussed during the January 12, 2016 HSRB meeting. Those slides will not be repeated per study.

Study Specific Data for Mark-3

- 44 subjects were enrolled for the Mark-3 study
- 8 no-shows, 1 for training session & 1 on test day
- 24 subjects assigned to participate in tests with 12 alternates/extras
- 21 subjects completed the testing

Protocol Amendments & Deviations

- No amendments to protocol
- Appendix B to study documents 2 deviations
- SCJ adhered to IRB instructions and protocol in documenting the deviations
- Deviations did not negatively impact subjects' rights, health or safety

Reporting of Incidents

- No adverse events or incidents of concern were reported during or after test implementation

Substantive Acceptance Standards

- 40 CFR §26.1703
  - Prohibits reliance on data involving intentional exposure of pregnant or nursing women or of children
- 40 CFR §26.1705
  - Prohibits reliance on data unless EPA has adequate information to determine substantial compliance with subparts A through L for 40 CFR 26. Subparts K & L applicable to third-party research.
- FIFRA §12(a)(2)(P)
  - Makes it unlawful to use a pesticide in human tests without fully informed, fully voluntary consent

Findings

- Study in compliance with acceptance standards
- All subjects were at least 18; pregnant and nursing women were excluded
- No significant deficiencies in ethical conduct of the research
- Deviations did not compromise health and safety, consent or rights of subjects
- Subjects were fully informed and their consent was fully voluntary, without coercion or undue influence

Conclusion

- Available information indicates that the study was conducted in substantial compliance with subparts K and L of 40 CFR part 26

Charge Questions to HSRB

- Is the study sufficiently sound, from a scientific perspective, to be used to estimate the duration of complete protection against mosquitoes provided by the tested repellent?
- Does available information support a determination that the research was conducted in substantial compliance with 40 CFR Part 26, subparts K and L?