COVER PAGE

EFFICACY TEST PROTOCOL WPC-001

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TEST OF AN OIL OF LEMON EUCALYPTUS-BASED PERSONAL INSECT REPELLENT

SYNOPSIS

The study pursuant to this insect repellent efficacy protocol is intended to provide data under the requirements of United States Environmental Protection Agency Guideline OPPTS 810.3700. This protocol, dated 16 January 2007, was reviewed and approved by a private IRB, the Independent Investigational Review Board (IIRB), located in Plantation Florida, on 23 January 2007. The document in hand is that which IIRB reviewed, with the addition, on 29 January 2007, of the following elements for review by the United States Environmental Protection Agency, including its Human Studies Review Board. 1) This synopsis page; 2) the approved, signed Informed Consent Form, which has been substituted for the submitted Informed Consent Form; 3) the IRB study set-up form and Site Questionnaire, which were also reviewed by IIRB, as separate documents, during protocol review; 4) record of PI–IRB correspondence; 5) approved minutes of IRB protocol review meeting; 6) IRB membership roster. The Table of Contents on the next page reflects those changes and additions.

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EFFICACY TEST PROTOCOL WPC-001

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1 TITLE: TEST OF PERSONAL INSECT REPELLENTS

2 PROTOCOL NUMBER:

WPC–001

3 SPONSOR:

WPC Brands, Inc

3.1 Address:

P.O. Box 4406
Bridgeton, MO 63044

4 PROTOCOL OBJECTIVE:

4.1 Type of Protocol:

This protocol will indicate the specific methods to be used, and direct the conduct of, Study WPC–001. The study will be conducted in the laboratory at the letterhead address and at locales in nature with mosquitoes.

5 STUDY OBJECTIVE, RATIONALE AND STANDARDS:

5.1 Objective of Research:

The objective of this study is to test the mosquito repellent efficacy characteristics of the test material. It is formulated with a reduced concentration of the active ingredient compared to products previously registered by the sponsor, in order to lower its cost to the consumer. The active ingredient, Oil of Lemon Eucalyptus, is of known high efficacy, but has not been studied at very many concentrations in the United States. Based on the scientific literature, it is very likely that subjects will be well protected for several hours by the new formulation, so that subjects will not be at added risk from participating in a test of a reduced concentration product.

Note that efficacy will be measured as Complete Protection Time. Complete Protection Time, or CPT, is defined herein as the time between application of test material and the First Confirmed 'Lite with Intent to Bite.' A 'Lite with Intent to Bite', or 'LIBe', occurs when a mosquito alights on the treated test skin of a subject and extends its proboscis to the skin surface while ceasing locomotion. A 'First Confirmed LIBe' is that which is followed by another within 30 minutes. The work conducted pursuant to this protocol will be initiated by determining the amount of each of the repellents that subjects typically apply. Dosimetry will consist of a behavioral assay.

5.2 Rationale and Main Endpoint:

This study will test the efficacy of a new formulation of Oil of Lemon Eucalyptus (OLE) that is intended to improve its value and increase user acceptance. US/EPA requires new repellent formulations to be registered, and some registrants must present new efficacy data as part of the registration review. The rationale for this study is to provide those efficacy data, which have not been previously collected. OLE has been used worldwide for decades, but is comparatively recent in the United States market. The US Centers for Disease Control has acknowledged the existence of substantial consumer interest in new and effective insect repellent products, and that OLE-based

repellents are among the very few of sufficiently high efficacy to offer reliable personal protection against vectors of West Nile Virus (in April 2005). However, few OLE products are currently marketed in the US. Thus there is substantial merit in the development and registration of a new OLE-based repellent.

Stability of the end-product will be tested in a different study.

The main endpoint of this study will be the conclusion of a mosquito repellent efficacy field test of a novel OLE-based topical repellent formulation, with the data set suitable for submission to US/EPA for insect repellent registration purposes. The efficacy study will consist of two field trials. In each trial, the OLE-formulation, will be tested by 10 subjects, with two untreated control subjects. Initial dosage determination ('dosimetry') will be also be conducted with a total of 10 subjects per formulation, some of whom may then go on to participate in efficacy testing. Dosimetry will be conducted at the letterhead address. When 10 subjects have completed dosimetry for each formulation, including the comparison article, those data will be used to determine dosing for the efficacy testing.

5.3 Rationale for use of Human Subjects:

Human subjects are required because they represent the target system for the test material, and sufficiently reliable models for repellency testing have not been developed. In addition, subjects will self-administer the test articles during dose determination. Ten subjects are required in order to reduce variation around the population means we will describe.

5.4 Balance of Risks and Benefits:

The study-associated risks are of three types: exposure to the test material itself, exposure to biting arthropods, and possible exposure to vectors of arthropod-borne diseases. As described below, subject health and safety are unlikely to be impacted by any study-associated risks during or after the study.

The repellent active ingredient has a low acute and chronic risk profile, established both through experimentation and through a

history of consumer use. The concentration of the active ingredient in the product being tested is lower than that of other products currently EPA-registered and marketed in the US. Subjects with known allergic reactions to insect repellents and common cosmetics are excluded from participating. 'Repeat' exposures during dosimetry are all of brief duration before the repellent is washed off, and likely total a much shorter duration of exposure than would a typical single consumer application. Risks associated with inhalation and ingestion would only ensue from serious mishandling by subjects, a scenario that the study methods do not promote.

The risk of a skin reaction to a mosquito bite is reduced by excluding candidate subjects who are aware of having a history of such reaction. In addition, subjects will be trained to quickly remove any mosquitoes that attempt to bite them, before penetration or injection of saliva if possible. Moreover, a stopping rule instructs subjects to cover any treated skin immediately if more than one mosquito attempts to bite during any exposure period. Subjects will be exposing small areas of treated skin for only 4 minutes per hour. Other parts of the body will be protected with provided fabric. Subjects will be teamed with a partner for joint observation and experienced technical personnel will be present at all times to assist.

The US Centers for Disease Control estimates that about 1-in-5 people who become infected with West Nile virus will develop West Nile fever. Subjects are instructed to be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever, or a rash on the trunk of the body) for up to two weeks after the test. About 1-in-150 infected people will develop more serious symptoms, which will be described to the subjects. Most people (about 4 out of 5) who are infected with West Nile virus will not develop any type of illness.

In addition, the techniques employed to minimize exposure to mosquitoes and mosquito bites render the possibility of contracting a disease carried by mosquitoes very low. Field tests are being conducted in an area where such viruses have not been detected by county and state health or vector/mosquito control agencies for at least a month, so the risk is probably low that any individual

mosquito present carries a disease. In each trial, only two experienced, qualified subjects (qualification criteria described in §9.1) will expose untreated limbs to monitor biting pressure, at the same infrequent, brief intervals as treated subjects, and with multiple assistants to remove any mosquitoes that lite with intent to bite.

In summary, the combination of technical precautions and natural factors means that the chances that any subject will contract West Nile fever or another disease from a mosquito bite are probably extremely small. There is probably no more risk to subjects than they would experience when engaged in normal outdoor activities in a similar rural area at the same time of year. If at anytime during the study a subject suffers a skin reaction or feels ill, he or she is instructed to inform the Study Director (i.e., the 'Principal Investigator'), or anyone else who is also working to direct the study. Such subjects will be immediately withdrawn from testing and medical management will be implemented (§9.5). Subjects may also request access to standard first aid materials (such as bandages, antiseptics, and mild topical and oral antihistamines) and request qualified first aid assistance at any time. Epi-Pens will also be on-site in case of Type 1 (anaphylactic) allergic reaction. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject. Subjects are clearly and repeatedly informed that they may remove themselves for any reason from the study at anytime, without penalty to their compensation.

Against the slight risks are balanced substantial and reasonably likely benefits. Insect-borne disease is of growing significance in the United States and around the world where U.S. citizens are active. Moreover, discomfort associated with nuisance biting restricts many work and pleasure activities. Because EPA registration requires efficacy data, a test such as that proposed here is the only path toward further product development and greater availability of new OLE mosquito repellent to consumers in the United States.

5.5 Standards Applied:

U. S. EPA Good Laboratory Practice Regulations (40 CFR 160); 40 CFR 26 subparts K and L; FIFRA § 12(a)(2)(P); California State EPA Department of Pesticide Regulation study monitoring (California Code of Regulations Title 3, Section 6710).

6 INVESTIGATIONAL AND TEST MATERIAL CONTROL:

6.1 Test Substance:

6.1.1 Description of the Test Material

Details of the test formulation are appended.

6.1.2 Trade Name:

Repel Insect Repellent 30LE
EPA Reg. No. 305-62

6.1.3 Dosage Form:

Pump spray applied to the skin.

6.1.4 Dose:

Determining dosage is a main objective of this study. Dosage for repellency testing will be the mean of the subject means determined for each product in the dosimetry portion of this study. Dosage will be measured in weight and reported by weight and volume.

6.1.5 Manufacturing Site:

Laboratory-prepared by WPC Brands, Inc.

6.1.6 Test Material Storage During Study:

Prior to application, the test material will be stored indoors, at room temperature and away from direct sunlight or direct sources of moisture. Storage will be at Carroll-Loye Biological Research.

6.1.7 Test Material Safety:

EPA regulates use of inert ingredients (also termed "other" ingredients) by toxicology profiles in animal tests and by their inclusion in EPA lists of "approved" other ingredients. Ingredients on lists 4a or 4b are considered relatively safe for all uses. The ingredients in the proposed insect repellent formulation are mainly on lists 4a or 4b with a few ingredients on list 3 because of ocular irritation potential. EPA normally regulates the presence of materials on list 3 by labeling to avoid contact with eyes and to prohibit application by children. The other ingredients in the test formulation are commonly used in marketed products for application to human skin as components of cosmetic and drug formulations.

The insect repellent product proposed for testing has been tested in animals for potential oral and dermal toxicity. The OLE active ingredient has an extensive toxicity data file, has been previously registered by EPA, and has a positive safety record in consumer use.

MSDS documentation is appended.

6.1.8 Test Material Composition and Stability:

The test material formulation is typical of topical cosmetics and insect repellent products marketed to consumers. It is produced under Good Laboratory Practices (GLPs) with records available to EPA. It will be couriered to Carroll-Loye Biological Research, with Chain-of-Custody

documented. After that time it will be stored at the Carroll-Loye Offices in a closed cabinet at room temperature (19-24°C). The composition and content of active ingredient in the product used for the proposed efficacy studies will be confirmed by analytical methods prior to and following human subject efficacy testing. The sponsor believes that the formulation will be stable for the duration of the study, based on storage stability studies previously conducted. The EPA has extensive experience with enforcing requirements for such tests based upon their history with similar products applied to humans and WPC Brands, Inc. intends to provide any requested information as appropriate to safety and efficacy issues.

6.2. Negative Control:

6.2.1 Description of the Negative Control

The negative control is untreated for both dosimetry and repellency assays.

6.2.2 Rationale for Employing a Negative Control

Repellent efficacy can only be measured in the presence of biting mosquitoes. In addition, the duration of repellency recorded is likely a function of the number of host-seeking mosquitoes active during the study. The US/EPA uses a standard minimum rate of mosquito attack on untreated subjects to insure that the repellents under study are sufficiently challenged to provide meaningful data. Traditionally, the measure rate is termed the 'ambient biting pressure'. We adopt that value, but use LIBes ('Lites with Intent to Bite') rather than bites. A mean study LIBe rate of ≥ 1 LIBe per untreated (negative control) lower leg or lower arm per 1 minute is required.

We take several precautions to minimize the probability that untreated control subjects receive any bites (see §§ 5.4, 8.2, 8.3.1, 8.4.1, 10.3.6). Recognizing that individual subjects differ in their inherent attractiveness to mosquitoes, US/EPA

science reviewers have recommended that we use two untreated control subjects for this study in order to improve the likelihood of sampling ambient biting pressure in a representative fashion, while still exposing a very small number of untreated subjects to risks from foraging mosquitoes. Having separate untreated subjects also avoids the problem of interaction between treated and untreated limbs that may arise when subjects serve as their own simultaneous controls. In reviewing a similar protocol in May 2006, the California Department of Pesticide Regulation initially requested use of a single negative control, but compromised at two such subjects based on the position of the US/EPA. The prospect of receiving approval to use more than two untreated control subjects is probably small in this case.

There is no control in which the formulation matrix without the repellent active is tested. There is no a priori basis for anticipating significant repellent activity in the matrices, and the study objective is to examine efficacy of the end products. The question of whether there is interaction between matrix and active is external to that objective. Accordingly, the added risk of including additional subjects testing matrix-only formulations cannot be justified.

6.3 Comparison Article:

None.

6.4 Test Arthropod Species:

Testing will be conducted with all or some of wild *Aedes vexans*, *Aedes melanimon, Aedes taeniorhynchus, Culex tarsalis* and *Culex pipiens* mosquitoes, and possibly other mosquito species that occur in the same habitats. Mosquito specimens will be collected from untreated control subjects, and from the protective clothing of all subjects, during testing and identified in the laboratory using taxonomic keys and stereomicroscopy.

7 STUDY SCHEDULE:

7.1 Proposed Date of Initiation:

TBD, within one year of IRB approval.

7.2 Schedule of Events:

Test day	Date	Activities
-30 to -2	TBD	Begin subject recruitment. Introduce subjects to test plan and procedures; explain compensation; review subject rights and consent forms; option to sign consent forms in order to participate; measure limb surface areas; determine individual dosing behavior and rates, mean dosing rates, and individual dosage values
1	TBD	Prepare individual dosages for application. Meet with subjects to review day plan and safety procedures. Administer repellent, or do so after travel to field site. Travel to field site. Review safety and data collection procedures. Commence repellency data collection. Monitor subject safety, comfort, comportment, and compliance with data collection protocol.

7.3 Proposed Date of Completion:

Experimental Completion Date (Test Day 1): TBD.
Final Report Completion Date: TBD.

8 STUDY DESIGN:

8.1 Treatment Groups:

For efficacy testing, there are two experimental groups, namely 1) a 'treated' group of subjects treated with the single test product, and 2) an untreated ('negative') control group. The dosimetry study is an examination of dosing behavior, with each subject treated, and also serving as their own untreated control for the dosimeters.

8.2 Experimental Design:

The experiment will be partially randomized by subject. Because the treated condition will be evident to experimenters and subjects, and a single test material is under study, neither group will be effectively blinded. The clear criteria on which failure is determined (definition of LIBe) will help to eliminate any influence of experimenter or subject bias. Also note that for subject safety, control subjects will be chosen only from among individuals that are experienced in entomological testing or biological science (see §8.3.1, below). Whether arms, legs or both are tested at a given site will depend on the species of mosquitoes present and their behavior. That decision will be made by the Study Director based on visits to the field sites prior to data collection.

8.3 Randomization Procedures for Repellent Efficacy Testing:

8.3.1 Allocation of subjects to treatment groups:

All subjects that are not untreated controls will be assigned to the treatment group. Treatments will be balanced between arms and legs if both limbs are used. Negative control subjects will be selected exclusively from among experienced personnel. To be regarded as experienced personnel, a candidate subject must have an undergraduate (or higher) degree in life sciences, or be a vector control professional, or have participated in at least five Carroll-Loye repellent efficacy studies. In addition, that person must meet all of the other participation criteria listed in §§9.1.1.1 and 9.1.1.2.

8.3.2 Treatment allocation table:

Materials will be distributed among subjects as tabulated below. Two additional personnel who will monitor ambient biting pressure with untreated limbs during the test are also shown.

Subject	30% OLE	Untreated
1	Left limb	
2	Right limb	
3	Left limb	
4	Right limb	
5	Left limb	
6	Right limb	
7	Left limb	
8	Right limb	
9	Left limb	
10	Right limb	
11		Left limb
12		Right limb

8.4. Conditional Boundaries or Limits of Study

8.4.1. Ambient 'Lite with intent to bite' Pressure:

A mean study LIBe ('Lite with Intent to Bite') rate of ≥ 1 LIBe per untreated (negative control) lower leg or lower arm per 1 minute is required. No more than 10% '0' values for individual exposure periods are permitted. Ambient LIBe pressure is measured from continuous exposure during 1-minute exposure periods commencing once every 15 minutes, beginning at the onset of data collection. Negative control subjects are attended by two assistants who use mechanical aspirators to remove all mosquitoes that LIBe before biting commences.

8.5. Monitoring of Environmental Conditions During the Study

Records will be made of environmental conditions (temperature, relative humidity, wind speed, light intensity and precipitation (presence/absence and general rate/quality) at approximately one-hour intervals throughout the course of the field trial.

9 STUDY PROCEDURES:

9.1 Test Subjects:

9.1.1 Inclusion criteria, all subjects:

9.1.1.1 Age: 18-55 years
9.1.1.2 Sex: Male/female
9.1.1.3 Race: Any race
9.1.1.4 Written consent: (see 9.4, below)
9.1.1.5 Language: Speak and read English

9.1.2. Inclusion criteria specific to the two untreated subjects

9.1.2.1 To qualify for candidacy as a subject who exposes untreated skin, an individual must be regarded as competent to do so by the Principal Investigator, must have participated in at least five prior Carroll-Loye repellent efficacy trials, or have participated in at least three such trials and have at least two years of experience as a college life sciences major, or be professionally employed in vector control services.

9.1.3 Exclusion criteria, all subjects:

9.1.3.1 Known to be hypersensitive to mosquito bites or exhibiting hypersensitivity during test
9.1.3.2 Known to be sensitive or showing sensitivity to any of the test product ingredients, after application.
9.1.3.3 Poor physical condition.
9.1.3.4 Unwilling to submit to brief query about personal condition.
9.1.3.5 Use of insect repellent within one day preceding the study.
9.1.3.6 Unwilling to refrain from use of perfumed products, alcoholic beverages or smoking after

9 PM the evening preceding the test and throughout the test.

9.1.3.7 Known to be pregnant or lactating. Pregnancy will be self-checked by each female volunteer on the morning of the repellent test using an OTC test kit provided by the Study Director. Results of each such test will be immediately verified by direct inspection by a female technician trained to make that assessment. Only volunteers scored as nonpregnant will be allowed to participate.

9.1.3.8 Unable to deliver the test materials to own left and right limbs.

9.1.3.9 Unable to see mosquitoes on skin or otherwise effectively monitor and remove mosquitoes that alight on skin.

9.1.3.10 Student or employee of the Study Director.

9.1.3.11 Does not regularly spend time in outdoor settings.

9.1.4 Number of Subjects and Rationale for Sample Sizes:

In efficacy testing, we will use 10 subjects per treatment and 2 untreated control subjects per field trial. In the dosimetry portion of the study, 10 subjects will be engaged to apply each repellent, including the comparison article. Each subject is a replicate.

The number of subjects is chosen as a compromise between several conflicting factors. In the absence of clear means of estimating the distribution of outcome values, it is difficult to predict an ideal sample size. From a strictly scientific standpoint an appropriate response under such circumstances is to increase size, but ethical and economic considerations demand the opposite in the present study, particularly during the efficacy testing phase.

The US/EPA has historically required a minimum of six subjects. Given that test repellents are nearly certain to exhibit greater than zero efficacy, and that testing is

conducted under adequate ambient biting pressure, it is nearly certain that no untreated subjects will register fewer or later LIBes than any treated subjects. As a result, from the standpoint of statistical power, six treated and one untreated subject are sufficient to demonstrate a significant treatment effect at $P<0.05$. In the same vein, six is often regarded as a statistically sufficient sample for an observation subset because the increment in the confidence of means estimate begins to drop off sharply at that point. Notably, under the historical guidelines, there seem to have been few problems with EPA registering repellents that commonly fail to meet their labeled performance specification.

The main scientific risk of using a very small sample is that the probability of over-representing subjects inherently unattractive to mosquitoes is rather large. Note, however, that for US/EPA registration purposes, the test for mosquito repellency is conducted twice, once in each of two ecologically different habitats. In our experience, some or all of the subjects in one test normally do not participate in the other (due to geographic distances between sites). In addition, two negative controls are used for a more robust baseline comparison. Those facts decrease the probability of such sampling error substantially.

However, further considerations indicate that a somewhat larger sample would be superior. Note that the draft EPA guidelines state that the response variable, 'Time to First Confirmed Bite' (or LIBe in this study) is calculated as the average duration for all treated subjects. There is no consideration of variation. In any given study, increasing the number of treated subjects to 10 will improve the probability of estimating the population mean accurately.

The 95% confidence interval computation is useful for assessing the certainty of a means estimate, and for normal probability density function that interval is ±1.96 standard error of the mean. The normal density function is part of the exponential family of density functions, and in this study we anticipate that the distribution of Times to First Confirmed LIBe will be truncated toward the origin. However,

available mean and variance data on efficacy (e.g., Carroll, S., 2006, In Debboun et al. (eds.), *Insect Repellents*, CRC Press) indicate that no individual values will be near zero. Using the rule of thumb that a distribution in which the mean is greater than three standard deviations above zero may be regarded as effectively normal, it is sensible to compute and report the normal 95% confidence interval in this study.

To consider an example, in a study of repellency employing eight subjects, Cilek et al. (J. Amer. Mosq. Control Assoc. 20: 299-304, 2004) recorded a mean protection time of approximately 180 minutes, with a standard error of about 15 minutes. Had the *N* been six, we can roughly predict that the 95% CI would be 148-212. At N=10, the estimate would be 155-205. At N= 20, the interval would be roughly 162-198. Evidently, adding the additional 10 subjects to reach an N of 20 shrinks the interval, in absolute terms, no more than did the addition of four subjects to increase the sample size from 6 to 10.

To summarize, adding subjects beyond six increases the precision of the means estimate only slowly. However, the individual and public health importance of avoiding inaccuracy in this study, coupled with the fact that data collection is only 'replicated' once (in a different habitat at that), argues for a prudent approach. To reduce the risk of over-representing atypically attractive subjects, as well the weight of the value obtained from any one subject, we regard 10 (rather than six) treated subjects as a better sample size for the repellency portion of the study.

9.1.5.1 Initial Recruitment Process in California:

Participants are recruited by verbal networking through our academic and personal communities of friends, neighbors and scientists in Davis, California. Individuals are recruited from the community specifically for each study. Studies are not conducted with individuals from particular employers or agencies. Initial contact is through word-of-mouth and telephone contact with subjects who have participated in

previous Carroll-Loye repellent efficacy tests and have agreed to be in our Volunteer Database. At the time of such contact, interested individuals often ask if one or more of their lab mates or acquaintances may participate as well.

Our subjects are mainly University of California–Davis graduate and undergraduate students in life science programs with which the Principal Investigator is associated. Students in his laboratory who depend on him directly for employment or scholastically are not eligible to participate. Other subjects are science, education and health care professionals. Those who will serve as untreated control subjects are limited to experienced technical personnel, who are screened with the same exclusion criteria as are other subjects, and have additional inclusion requirement.

9.1.5.2 Initial Recruitment Process in Florida:
For over a decade we have worked with the Florida Keys Mosquito Control District in a variety of scientific programs. Our principal season for testing repellents in the Florida Keys is winter. At that time, the District is normally less busy with activities than at other times of year, but still employs a large number of full time mosquito and vector control professionals. We contact the administration of the District to inform them of our need for subjects. The administration gives District employees the option of participating in our field studies.

9.1.5.3 Screening of candidate subjects

All such potential participants are screened or re-screened for suitability for each test in a private, one-on-one conversation with the Study Director. The Exclusion Criteria (section 9.1.2) are exercised by asking each candidate to address them in the interview with the Study Director. It is explained that to female candidates that pregnancy will be assessed directly on the test day. The Study Director encourages candidates to ask questions and ask for clarification at any time during the interview and in all

activities that follow. To candidates that pass screening the Study Director describes the test purpose in plain language (in English), and the procedures and comportment to be followed are described in detail. Candidates are then asked if they would like to retire from consideration at that point. If they wish to remain in consideration, it is explained and emphasized that they may withdraw from the test at any time during the test without penalty to their compensation. This freedom is especially re-emphasized in cases in which considerable effort or expense has been required to include a subject (e.g., air travel to a distant site), to discourage the conception that that effort or expense creates any added obligation in the subject.

Candidates in California are given copies of the State of California Department of Pesticide Regulation 'Experimental Subjects' Bill of Rights' (Appendix 4) to read as the Study Director reads it aloud. They are also given a copy of the IRB-approved consent form to read as the Study Director reads it aloud. The amount and form of compensation is described. They are again encouraged to ask any questions they have about the test, which may include understanding its purpose more fully, understanding risks and discomforts more fully, and understanding treatment and compensation for injury more fully. While the majority of our subjects have worked with us on an occasional basis for a number of years, we encourage them to personally evaluate their interests and concerns about participation seriously each time. We ask them not to sign on immediately but to give the situation due consideration (normally at least one day, sometimes less for those who have participated in multiple prior studies). Because most of the volunteers are researchers and/or have advanced degrees in life sciences, or are mosquito control professionals that work directly with mosquitoes in infested habitats, we regard their motivations and decisions to participate as being unusually well considered and well informed. Accordingly, we normally accept their decisions to participate if they so choose following due consideration. Nonetheless, the Study Director retains the final right to refuse participation to any candidate.

9.1.6 Identification method and records retention:

Subjects will initially be identified by first and last name, and assigned a unique number for purposes of this study. Individual data will be entered into the computer for retention and analysis with reference to individual number, not name. Records relating individual names to individual numbers will be retained separately. The Study Director will retain records indefinitely. Subjects may obtain their own records from the Study Director.

9.1.7 Enrollment of alternate subjects and its relation to individual privacy:

We will enroll three more subjects than are required to meet our sample size. All subjects will be informed during the Consent process that on the day of testing, a small number of subjects may be designated as alternates and sent away after being compensated for coming to the test site. Alternate subjects may return later to replace subjects that initiate testing but withdraw before useful data are generated. They also serve as insurance against any enrolled subjects who fail to appear.

The possibility that any subject may be designated as an alternate will assist in protecting the privacy of any subject that must withdraw in or near the presence of other subjects at the start of the test day (i.e., before treatment and testing begins), for reasons such as a positive pregnancy test result, or for any other personal circumstance to which possibly inappropriate attention might otherwise more readily be drawn. In the case of privacy concerns related to pregnancy detection, we regard this "indirect" approach as potentially as discrete and less likely to result in errors that would be the case if we were to employ, e.g., separate male and female Informed Consent Forms, with pregnancy only mentioned on the female form. The latter approach does not address loss of privacy among females, nor does it control the possibility of indiscrete revelation of pregnancy testing by females to males during the test or later, and it also creates the risk of a female subject using the wrong form. Separate forms would also assume that we may fairly

treat individual subjects unequally on the basis of postulated gender-based differences in the information they merit receiving in order to arrive at their informed consent decision. The soundness of making such an assumption enters ethically complex grounds requiring an intricacy of analysis and breadth of treatment beyond the scope appropriate to the privacy concerns of the present study.

9.2 Blinding of Study:

None

9.3. Study Material Administration:

Study Materials will be administered to each subject by Carroll-Loye technicians. Test products will be applied volumetrically to the skin surface from a tuberculin (1 ml) syringe, and spread on the site as evenly as possible with two fingertips in a surgical glove, using a light rubbing motion. Skin surfaces to be treated are first cleansed with water and a fragrance-free detergent soap, rinsed with a 50% ethanol in water solution, and then towel-dried.

9.4 Subject Consent:

Written subject consent is an inclusion criterion.

9.5 Stop Rule and Medical Management:

Specific adverse reactions in subjects to the test materials are not anticipated based on low acute and chronic toxicity, as well as the research design to minimize exposures, and the training of subjects to aspirate landing mosquitoes before they probe or bite. Because the products are topical, technical personnel will monitor, and subjects will self-monitor, for allergic and irritant skin reactions, particularly redness, edema, itching or pain, and report any such reactions to the Study Director. Any subject showing adverse skin reactions will immediately stop further participation. The treated skin will be gently washed with clean water and mild soap to

remove the test product, and the area will be gently dried with a clean towel. The subject will be removed from further exposure to mosquitoes.

On the day of testing, a physician who has read the protocol and discussed the research with the Study Director will be on call. In unlikely event of a Type 1 allergic reaction (anaphylaxis), we will contact 9-1-1 by cellular or satellite telephone and cooperate as instructed with emergency personnel. We will be prepared to instruct emergency personnel on how to reach our site via multiple routes. In addition, we will personally transport affected persons to the nearest hospital if so advised by emergency personnel. There is sufficient redundancy in personnel that in such a case subjects remaining at the study site will still receive appropriate technical, scientific and safety guidance.

All subjects are asked to contact the Study Director and a physician of their own choice at any time should they develop a rash (a delayed hypersensitivity reaction) within 48 hours of the conclusion of the test day.

The risk of mosquito-associated health risks is likewise regarded as very low due to the complementary precautions outlined herein. However, the Study Director will assess skin condition of affected subjects should any bites inadvertently occur during efficacy testing. In addition, subjects will be asked to make contact with Study Director at any time should they have health concerns relating to their participation in the efficacy testing.

As part of Medical Management, the Study Director will record all benign and adverse health observations.

9.6 Subject training for research with mosquitoes

Approximately one week to one day before repellent efficacy testing, subjects will be trained by technical personnel in handling mechanical aspirators and observing mosquitoes in the laboratory. Subjects will be shown how to turn on and manipulate the aspirator to capture mosquitoes by a technician who first demonstrates the following procedure, which subjects then emulate: Two laboratory-

reared, disease-free female mosquitoes are released in a cage. A small area (less than one-half) of the forearm is uncovered and exposed in the cage, with no insect repellent applied. Subjects will learn how to watch approach and land on the arm, how to detect a mosquito's intention to bite, and how to quickly remove LIBing mosquitoes with the aspirator. A technician will be present to instruct and guide throughout; mosquitoes will not be exposed to more than one subject before being destroyed. This training will be documented. This 'hands-on' experience will assist subjects in collecting data accurately and handling mosquitoes safely during the repellent efficacy trial.

10 TEST VARIABLES AND THEIR MEASUREMENT:

10.1 Variables to be Measured:

Subject forearm and lower leg surface area.
Subject self-dosing behaviors.
Weight of test materials delivered to the surrogate skin (gauze) dosimeters.
Number of mosquito lites with intent to bite (LIBes) on the treated surface.

10.2 General Considerations

Dosimetry data collection may be conducted on subject arms, legs, or both. Which limbs are used depends on whether efficacy testing, which will follow dosimetry, is to be conducted with repellents sprayed on arms, legs or both. That determination will be made in advance of the dosimetry study, based on the behavior of the mosquitoes present at the chosen field study sites.

10.3 When Variable will be Assessed:

Dosage will be calculated on the basis of surface area of the limb skin that is treated. Measurements to calculate that surface area will be made on each subject in advance of application of the test materials.

Self-dosing behavior will be measured prior to Test Day 1.

In efficacy testing, subjects will record any 'lites with intent to bite' (LIBes) as they occur. Data are recorded in one-minute exposures at 15 minute intervals. The time at which the application of a treatment is completed is recorded as t_0 ('time zero'). The time between application of test materials and the initiation of exposure will be measured. Subjects will practice removing mosquitoes exhibiting LIBes before the field test.

10.4 Procedures for Assessing Variable:

10.4.1 Limb dimensions and surface area:

The term 'limb' refers to the forearm and the lower leg. The surface area of each limb is computed as the average of four evenly spaced circumferences (two peripheral, two central) of the forearm (elbow to wrist) or lower leg (back of knee to ankle) multiplied by the length of treatment area.

10.4.2 Familiarization with, and subject use, of the spray apparatus:

Variable assessment will involve a two-step process, namely subject familiarization with the spray apparatus, followed by dosage measurement.

Subjects will practice application of test material to their own limbs under the procedure in the Training Materials appendix, which will be reviewed for the subjects by a researcher before practice commences. That material explains that goals of this behavioral part of the study, describes that partnership between the subject and the technician in dosimetry data collection, and details the procedures to be conducted in simple language that is intentionally scripted as somewhat redundant in order to emphasize the structure of the work.

10.4.3 Spray Sampling

Spray Sampling is the procedure by which the spray is subsampled with patch dosimeters. Dosimeters of known surface area will be placed on subject lower arms. These dosimeters will intercept a portion of the spray applied to the arm. Be weighing dosimetry patches before and after treatment, the mass of the intercepted material can be calculated. The spray delivery systems will also be weighed before and after each application.

Spray sampling will be conducted according to the procedure appended under Training Materials.

10.4.4 Equipment Used to Assess the Dosimetry Variable:

Passive dosimeters are 2.5 cm wide strips of 3M Brand Nexcare™ Co-Flex™ self-adhesive roll gauze.

There will be eight bracelets per replicate. Each arm and/or leg will be treated three times. Each subject will therefore use a total of twenty-four or forty-eight bracelets.

Bracelets will be weighed before and after treatment on a traceably calibrated Sartorius H51 balance (measurement increment 0.0001 g, 30 g capacity). Test material containers will be weighed before and after dispensing on a traceably calibrated Sartorius GC 2502 (measurement increment 0.001 g, 500 g capacity).

10.4.5 Repellency and LIBes:

Repellency is assessed in the field. Preparatory training of the subjects to recognize and remove mosquitoes that lite with intent to bite contributes to subject safety. Subject safety is also enhanced by brief periods of exposure at intervals, as well as by careful dosing and application.

Subjects will have approximately one hour of training and practicing observing foraging mosquitoes and catching them from their own arms in a laboratory cage, using an aspirator. A researcher will first demonstrate the procedure using his or her own arms, and will be present to instruct and guide each subject throughout the exercise. Subjects will be shown how to place both arms in a screen cage and to turn on the aspirator using the switch on the handle. One mosquito will be released in the cage. A small area (less than one-half of the forearm) will be uncovered, with no insect repellent applied. Subjects will be instructed to carefully watch the mosquito as it flies in the cage, to observe the mosquito as it lands on the skin, and to watch to see if its needle-like mouthparts are placed against the skin. Once a mosquito lands on the skin, places it mouth against the skin and stops walking, subjects will immediately attempt to catch the mosquito in the plastic nozzle of the aspirator. They may practice as many times as they wish with additional mosquitoes, and the researcher will be certain that the use of the aspirator is correct. After several captures of single mosquitoes, a maximum of two mosquitoes will be placed in the cage. Two LIBing mosquitoes may be readily captured after little practice. Two represents the maximum number of mosquitoes that may LIBe on limb before the exposure stopping rule is reached (below), and so the exercise in the cage with two mosquitoes is highly appropriate.

The mosquitoes used for this training are *Aedes aegypti* reared in the laboratory and free from diseases. The source colony of *Aedes aegypti* was established from eggs collected in Northern Thailand in 2004. F_1 adults were tested by Vero cell (African green monkey kidney, *Cercopithecus aethiops*) plaque assay for possible transovarial infection of viruses. Typically, 20 females from subsequent generations are tested routinely, and no infection has been detected in the 2 years since this colony was established. Individual mosquitoes will not be used for more than one subject.

At the field site, the subjects and researchers will gather in an area without biting mosquitoes. Subjects are instructed not leave this area until guided by a researcher.

The technicians and other researchers who will assist subjects during the test will be introduced or reintroduced to the subjects. Subjects are instructed to call on them whenever they have questions. Each subject is given and must wear a head net, Tyvek coveralls, latex, nitrile or vinyl gloves in their size, and is given a mechanical aspirator to remove any mosquitoes that land on treated skin and attempt to bite (LIBe) once formal exposures begin. A researcher will remind subjects about how to identify LIBes and when and how to operate the aspirator. Subjects will be further instructed about protecting themselves from mosquito bites during the test, and about reporting when a mosquito that lands on skin treated with repellent.

Before the repellent is applied, subjects will be guided to wash the lower arms and/or legs with mild, fragrance-free soap, rinsing them with a spray of ethyl alcohol (mixed with an equal part of water), and then drying the limbs with a clean towel. A technician will then apply the test material to a forearm or lower leg of each subject, giving even, complete coverage of the skin. The amount of repellent to be applied to any limb will be calculated in advance for each subject. The dosing rate will be the product of the subject's limb surface area multiplied by the grand mean (mean of subject means) rate calculated in the dosimetry data analysis for the test material. Each subject will therefore be dosed at the same rate, even if their voluntary individual application rates might otherwise differ from the grand mean.

Treated subjects will be partnered into groups of two. A researcher will then guide subjects into the area of the field site in which mosquitoes are active. For a one-minute period, members of a partner pair will watch their own exposed limbs and those of their partner for mosquitoes that land. A technician will advise subjects when the one-minute period begins and ends. During exposure subjects will immediately remove any LIBing mosquitoes from the exposed skin with the aspirator. They may also use the plastic nozzle of the aspirator or a finger to interrupt any

mosquito even more quickly. Partners will assist one another in removing mosquitoes as needed.

At the end of the one-minute exposure period, subjects move away from the area with mosquito activity. Partners will assist one another in covering the treated skin with the sleeve of the protective garments. Each subject will report the number of mosquitoes that attempted to bite their own treated skin during that one-minute period when asked by a technician who will record it on a data sheet. For perspective, note that in a typical test of a reasonably effective repellent, dozens of '0' LIBe values will be recorded for each '1' or '2'. In other words, during most exposure periods, potentially for the first several hours, subjects do not experience close contact with mosquitoes. The probability of eventual direct contact, if any occurs before the cessation of exposure due to darkness or subject withdrawal, increases at a slow rate.

Stopping Rule: Subjects are instructed to immediately cover exposed skin with the protective clothing provided if more than one LIBe occurs in a one-minute exposure period. Similarly, if subjects receive a LIBe and recall receiving another in either of the two previous exposure periods, they are to ask their data recording technician to verify that recollection from the data record. If verified, the subject is instructed to immediately cover the limb as above.

Ambient LIBe pressure will be measured by experienced, untreated personnel from continuous exposure of a single limb during 1-minute periods commencing once every 15 minutes, beginning at the onset of data collection, concurrent with treated subjects. Such negative control subjects are attended by two assistants who use mechanical aspirators, switched on throughout the exposure period, to remove all mosquitoes that LIBe before biting commences. If mosquitoes are too abundant to permit ready aspiration, the controls may protect the exposed limb as soon as a LIBe occurs.

10.4.6 Forms for Retention of Source Data:

Dosimety data will be recorded on two data forms. 'Lite with intent to bite' (LIBe) data will be recorded on a field repellency data form. Data forms are appended.

10.5 Study Facility:

Dosimetry data collection will take place in the main laboratory building and on the terrace of Carroll-Loye Biological Research.

11 DATA ANALYSIS:

11.1 Experimental Unit:

The individual subject will be the experimental unit.

11.2 Replicates per Treatment:

For dosimetry, there will be 10 treated subjects. For efficacy testing, there will be 10 subjects treated with the test material and two serving as untreated controls, at each of two sites.

11.3 Statistical Methodology:

Statistics will be computed with the software 'SAS JMP' Version 5.0.1.2 (SAS Institute, Cary, NC).

11.3.1 Dosimetry:

Dosage will be calculated per square centimeter of skin. The amount of test material delivered to each dosimeter set in each trial will be calculated as:

weight after application – weight before application

The **total captured** by all treated dosimeters per trial will be calculated by adding the mass changes in all four dosimeters together, and then subtracting or adding, respectively, any total gain or loss of weight in the paired control dosimeters.

The **proportion covered** of the total limb surface area by the dosimeters is:

$$\frac{\text{Surface area of a set of 4 dosimeters}}{\text{Surface area of the limb}}$$

The estimated **dosage per trial** is:

Total captured x 1/proportion covered

Subject means and standard deviations will be calculated for all measures of dosimeter weight changes as well as application behaviors (distance from nozzle to skin, number of pump actuations). We will use subject dose means for the test material to calculate the dosing grand mean (± SD). That mean, expressed as repellent weight per unit skin surface area, will be converted to volume and used to determine individual subject doses in the field repellency test. To accomplish that, the specific gravity of the test material will be used to convert the dosage weight data to volumes, prepared for each subject on the basis of their skin surface area.

Subject effects on dosing behavior will be examined with nonparametric tests for *n*- sample independent cases (Kruskal-Wallis tests). In multiple regression analysis, the average amount of test material intercepted by each subject's dosimeters, as well as dosing per unit skin surface area, will be examined in relation to the distance from nozzle to skin, the number of times the pump was actuated, and limb size. The relationship between dosing behavior and dosage will also be examined with Spearman-rank correlation tests.

11.3.2. Repellency:

Field tests are conducted with large populations of arthropods. This permits the analysis of the replicates (data by subject) as independent values. The hypothesis that the test material will significantly reduce the number of mosquitoes LIBing on treated versus untreated skin is not the focus of this study. The focus is to compute, for each test material, a reasonable estimate of mean and standard deviation for the duration between application and repellency breakdown sufficient such that two mosquitoes LIBe on a subject within a half hour period. That pattern is here assessed at a resolution of 15 minutes. The untreated limbs serve to monitor whether the ambient biting pressure remains at or above the EPA standard.

Complete protection time (CPT) is measured as the length of time from initial application to the first confirmed LIBe. A confirmed LIBe is a LIBe followed by another LIBe within 30 minutes. For example, a LIBe at 90 minutes followed by another at 135 minutes is not confirmed, but a third LIBe at 150 minutes would confirm that at 135 minutes, giving a CPT of 135 minutes.

CPT measured in this way will yield a single time value for each subject. Mean CPT will be calculated across all 10 subjects, and will be presented with standard deviation and 95% confidence interval information as well. Ambient LIBing pressure as measured by untreated subjects will be presented tabulated by individual and exposure period. Mean LIBing pressure will be calculated as the number of LIBes received per untreated control subject and per period and span of exposure.

12 STUDY LOCATION(S):

Field sites are in or adjacent to the Central Valley of California, southern California, and the Florida Keys (depending on season). Test site information will be furnished to EPA once it is clear when testing will be permitted, since season influences the availability of test arthropods on both regional and local scales.

13 QUALITY ASSURANCE:

A separate, professional Quality Assurance Unit (QAU) will inspect the study. The QAU will report to the Study Director. Protocol Review and Comments must take place before data collection commences. In-Life Inspection must include observing the measurement and recording of key variables by subjects and researchers. In addition, the Final Report will be audited for completeness and accuracy. A QAU Statement will address compliance and noncompliance or any omissions in auditing. Findings from the In-Life Inspection and the Final Report, as well as the QAU Statement will be transmitted to both the Study Director and to the Sponsor Monitor.

14 PERSONNEL:

14.1 Investigator (Study Director):

14.1.1 Address:

Dr. Scott Carroll
Carroll—Loye Biological Research
711 Oak Avenue
Davis, CA 95616

14.1.2 Telephone:

530-297-6080
530-297-6081 (Facsimile)

14.1.3 Training and experience of investigator:

CV on file with sponsor

14.2 Study Monitor:

Charles Duckworth or Kathleen Cearnal

14.2.1 Address:

Spectrum Brands, Inc.
13260 Corporate Exchange Dr.
Bridgeton, MO 63044

14.2.2 Telephone:

Phone: 314-683-2733; Fax: 314-254-5907

14.3 Quality Assurance Unit:

Dr. Jenella Loye

14.3.1 Address:

Carroll—Loye Biological Research
711 Oak Avenue
Davis, CA 95616

14.3.2 Telephone:

530-297-6080
530-297-6081 (Facsimile)

14.1.3 Training and experience of QAU:

CV on file with sponsor

15 AMENDMENTS AND DEVIATIONS TO THE PROTOCOL:

Protocol amendments or deviations will be reviewed by the Study Monitor and the Study Director. Any changes that may affect the health or safety of study participants must be approved the Study Director, the State of California Department of Pesticide Regulation, and the approving IRB. The amendments, deviations as well as any adverse events will be documented in the Study Director's final report. Documentation will include a description of the change, the reason for the change and the effect of the change on the conduct and outcome of the study.

16 PROTOCOL APPROVAL SIGNATURES:

16 January 2007

Scott P. Carroll, Ph.D.
Study Director

Date

18 January 2007

Kathleen Cearnal
Sponsor Monitor

Date

INDEPENDENT
INVESTIGATIONAL
REVIEW BOARD INC.
Your Advocate for Clinical Research Participants

DATE: January 23, 2007

TO: Scott P. Carroll, PhD
Principal Investigator

FROM: Kim Lerner, Chairman or
Anita McSharry, Vice-Chairman
Independent Investigational Review Board, Inc.

SUBJECT: Approval Clinical Research Protocol dated: 1/16/2007
- Informed Consent Form (Ver. 1/23/2007)
- Site Questionnaire
- The Experimental Subject's Bill of Rights

PROTOCOL: (WPC-001) Test of Personal Insect Repellents

The Independent Investigational Review Board, Inc. is an institutional review Committee structured in compliance with the regulations of the Food and Drug Administration contained in the Code of Federal Regulations (2ICFR 50 and 56) and is in compliance with the International Conference of Harmonization (ICH) Good Clinical Practice (GCP) guidelines for IRB/IECs.

At the meeting held on January 23, 2007, the Committee reviewed and unanimously approved the Research Protocol, the Investigator, The Experimental Subject's Bill of Rights and Informed Consent Form for the above noted research study. The Site Questionnaire was reviewed and unanimously accepted.

The Informed Consent Form is unanimously approved as revised. The Committee recommended that changes be made to the Informed Consent Form. The approved Informed Consent Form is identified as Version 1/23/2007 and stamped, "Approved 1/23/2007". The Informed Consent Form contains all regulatory required consent elements.

The California Experimental Subject's Bill of Rights is stamped "Approved 1/23/2007".

The study has been approved for a 12 month period. At the end of this time, you are required to provide the Independent Investigational Review Board with a written progress report for this research and obtain approval for continuing the research. Changes to the protocol or use of non-approved recruitment materials cannot be initiated without IIRB review and approval.

In the event of any serious adverse reactions, significant deviations from the protocol or problems in the research, written notice to the Independent Investigational Review

phone 954-327-0778 • fax 954-327-5778 • 6738 West Sunrise Blvd., Suite 102 • Plantation, FL 33313 • info@iirb.com (email) • www.iirb.com

Board is required. Please provide this reporting to the above-noted address so that appropriate follow-up will be initiated.

Thank you for your cooperation.

KL/AMS/yc:kk

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: (WPC-001) Test of Personal Insect Repellents

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 297-6080

Site of Investigation: _____
_____
_____

Sponsor: WPC Brands, Inc.

Participant's Name: _____

You are being asked to participate in a research study. Your participation is voluntary. The information in this Informed Consent Form explains the study. You will receive a copy of this form, and you may take it home and think about it before making your decision. If you have any questions, or do not understand anything in this form, please ask the Principal Investigator to explain any words or information you do not clearly understand.

NATURE AND PURPOSE

Carroll-Loye Biological Research is conducting this research study in order to develop effective mosquito repellents. Many people are interested in having new and better insect repellents available to them. The insect repellents that we will study were developed with the botanical insect repellent called 'Oil of Lemon Eucalyptus', formulated at a lower concentration to be less expensive to the consumer. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this new pump spray insect repellent product works outdoors against mosquitoes. This product is similar to some already being sold at higher concentrations. The information gained from the study will assist in the development of these repellents for commercial marketing. During the study we will first measure how much insect repellent subjects put on their own arms and legs in a visit to the study laboratory. On a later date, we will go to a field site to test the insect repellents against mosquitoes in nature. You may be asked to participate in one or in both parts of the study.

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Independent IRB
Signature 1/23/07 Date

Initials: _____
Date: _____

The sponsor, WPC Brands, Inc. has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator in charge of the study.

SUBJECT SELECTION

You have been offered an opportunity to participate in this research study because you read and speak English, consider yourself to be in good physical condition and are 18-55 years of age. If you are a female of child bearing potential you cannot be pregnant or breastfeeding.

Up to about 20 volunteers will be enrolled in this field research study. A few more subjects will be enrolled than are needed in order to make up for anyone who is unexpectedly unable to participate once testing begins. If more subjects are present than are needed for any part of the test, you may be asked not to participate, but will instead be an 'alternate subject' who may be contacted to participate later if needed. If you are designated as an alternate subject, you will be compensated for your participation up to that point and for your inconvenience.

STUDY INTRODUCTION AND DURATION

Schedule of visits and time required to participate in the study

Activity	Visit 1 (1-7 days before the field test)	Visit 2
1. Orientation and Dosage visit	X	
2. Field study visit		X
Total time	2-3 hours	8-14 hours

You will be given a training manual and will have a chance to review it and to read along with the instructions.

Visit 1 for Orientation and determining Dosage

Within 7 days before the field study visit you will meet with a researcher to perform orientation introductory activities for the repellent study. The researcher will also tell you more about what you will experience while participating and what is expected of you. At the time you may also work with a researcher to determine how much insect repellent you apply. If not done at this time, it may be done up to 30 days prior to the field study visit. Completing those measurements will take 1.5-2.0 hours.

You will also be shown how to use a handheld mosquito catching device called an aspirator. These devices resemble flashlights except that they have a small electric fan and suction tube rather than a light bulb. You will carry one of these devices with you during the field study. During this visit you will also practice

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removing mosquitoes from a small area of your arm with the aspirator. This training and practice will take about ½ to 1 hour.

The total time for Visit 1 activities will be about 2-3 hours.

Visit 2 for the Field Test against Mosquitoes
The study will also require one visit to the site of the field study. The field site visit will most likely require approximately 10 hours of your time. However, it may require as few as 8 hours (including travel time) and as many as about 14 hours, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. There is a small chance that weather conditions will require that the test be canceled or rescheduled. The Principal Investigator will inform you in a timely manner if that happens.

The Principal Investigator may also ask if you would like to participate in a second field test of these products, using the same procedures as in the first test, on a later date. You may refuse to participate in additional testing without penalty to your compensation.

STUDY PROCEDURES

Study Design

This study will test one insect repellent in a pump spray. You will have an amount typical of what people commonly use applied to your forearms and lower legs.

Two experienced subjects will also participate to record the activity of mosquitoes by exposing their own arms or legs without repellent applied. Experienced subjects are pre-qualified by the Principal Investigator, and designated before the field test begins. Unless you have been qualified in advance as an experienced subject and agreed to expose untreated skin, you will not be asked to expose untreated skin and should avoid doing so.

If you are a female, you will perform a pregnancy test using an Over the Counter (OTC) pregnancy kit in the morning prior to the start of each of your study visits. The results of your test will be verified by a female technician that is qualified to make that determination. If you are pregnant, you will not be allowed to participate in the study. Information regarding your pregnancy test results will be kept in confidence.

Procedures

Visit 1
At the laboratory, a researcher will measure the length and circumference of your forearm and/or lower leg. If you are participating in this part of the study, you will then practice using the product to decide how you best like to apply it and how

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much you would apply to your forearm or lower leg in order to have thorough and even coverage. The researcher will answer any questions you have about the application. Once you have a method you are satisfied with, you will wash your arms and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of the repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

You will also spend 15-30 minutes practicing catching mosquitoes in a laboratory cage, using an aspirator. You will be shown how to place both arms in a screen cage and turn on the aspirator using the switch on the handle. Two mosquitoes will be released in the cage. A small area (less than ½ of your forearm) will be uncovered, with no insect repellent applied. You will carefully watch the mosquitoes as they fly in the cage. Once they land on your skin, you will watch carefully to see if their needle-like mouths are placed against your skin. A researcher will be present to instruct and guide you. You may carefully move your arms to get better views and access to the mosquitoes. Once you observe a mosquito mouth touching your skin, you will immediately attempt to catch the mosquito in the plastic nozzle of the mosquito catcher. The researcher will first demonstrate the procedure to you using his or her own arms. You may practice as many times as you wish, and the researcher will be certain that your use of the mosquito catcher is correct. The mosquitoes used for this training are reared in the laboratory and free from diseases.

Visit 2

At the field site, the subjects and researchers will gather in an area without biting mosquitoes. You should not leave this area until instructed by a researcher.

You will be given an aspirator to suck any mosquitoes that land on your treated skin and attempt to bite you once the test begins. A researcher will show you again how to operate it. You will also be introduced to the technicians and other researchers who will assist you during the test. You will be instructed to call on them whenever you have questions about using the aspirator, protecting yourself from a mosquito, or reporting on a mosquito that lands on skin treated with repellent.

Before the repellent is applied, a technician will guide you in washing the lower arms and legs with mild, low fragrance soap, rinsing them with a spray of ethyl alcohol (mixed with an equal part of water), and then drying them with a clean towel. A technician will then apply insect repellent to your forearm or lower leg to give even, complete coverage of the skin. The amount of repellent applied on any one arm or leg will be no more than about ¼ teaspoon. You will also be

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given protective material to prevent bites on other parts of your arms and legs, plus a head net.

The Principal Investigator or one of his technicians will guide you into the area of the field site in which mosquitoes are active approximately 15 minutes after you have had the test repellent applied. You and a partner will watch your own exposed arms or legs and those of your partner for mosquitoes that land during a one-minute peroid. A technician will let you know when the one-minute period begins and ends. If any mosquitoes land and attempt to bite the skin with repellent, you will remove them immediately with the mosquito catcher. If at any time you have difficulties using the mosquito catcher you should push the mosquito from your skin with the plastic nozzle of the catcher. You may also use your finger to brush any mosquito aside. If you brush a mosquito aside watch carefully because it may quickly return to your skin., You will report the number of mosquitoes that attempted to bite your own treated skin during the one-minute period when asked by a technician who will record it on a data sheet. At the end of the one-minute period you should immediately cover the skin with the protective mesh or clothing provided. Every 15 minutes a project leader will announce the beginning of the next one-minute period for testing the treated skin and watching for mosquitoes that might attempt to bite it. If more than one mosquito attempts to bite you on your treated skin in one of the one-minute periods, or if one mosquito attempts to bite in two of three consecutive exposure periods (that is, 15 or 30 minutes apart), you should cover the skin and not expose it again.

If you are one of the two untreated ("experienced") subjects, two technicians with aspirators will assist you in watching for and removing mosquitoes during each one-minute exposure, and in each exposure you should cover your limb with the protective fabric as soon as the first mosquito lands and attempts to bite, and keep it covered until the next exposure period, 15 minutes later.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator
- You must not be hypersensitive (allergic) to mosquito bites
- You must not be sensitive to any of the test product ingredients
- You must regularly spend time in outdoor settings
- You must not have used repellents within a day prior to the start of the study
- You must not use perfumed products after 9 PM the night before and throughout the tests
- You must refrain from smoking or alcoholic beverages after 9 PM the night before and throughout the tests
- You must wear specified protective clothing during mosquito testing

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RISK/DISCOMFORTS

If at anytime you feel ill, inform the Principal Investigator (or anyone else who is also assisting to direct the study) immediately, and you will be taken to receive medical attention at the nearest hospital. You may also request access to standard first aid materials (such as bandages, antiseptics, and mild antihistamines) and request first aid assistance at any time. You may remove yourself for any reason from the study at anytime. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

The repellent will irritate the eyes on contact, and it is harmful if swallowed. You may obtain more information about the safety of the repellents by asking the Principal Investigator, and he will provide you with the official "Material Safety Data Sheets" which give safety details similar to those found on commercial product labels.

In addition, even if you have not had a serious skin reaction to a mosquito bite previously, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the site of the bite are all symptoms of an allergic reaction to a mosquito bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. There will be a first aid kit at the field site with treatments to reduce allergic symptoms from bites. Inform the Principal investigator if you are allergic to any nonprescription medicines. At least one technician with current first aid training will be present during the field test.

In addition, there is a slight possibility that you will contract a disease carried by mosquitoes if you are bitten, such as West Nile virus or equine encephalitis. This test is being conducted in an area in which such viruses have not been detected by state health or mosquito control agencies for at least a month, so the risk is probably low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing repellent and other protective measures, and are carefully watching for mosquitoes that land and try to bite, you are probably at no more risk than you would experience when engaged in normal outdoor activities in a similar rural area at the same time of year.

The US Centers for Disease Control estimates that about 1-in-5 people who become infected with West Nile Virus will develop West Nile fever. For up to two weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever, or a rash on the trunk of the body). About 1-in-150 infected people will develop more serious symptoms including neck stiffness, stupor, disorientation and possibly coma and paralysis.

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Most people (about 4 out of 5) who are infected with West Nile virus will not develop any type of illness. Since you will work to quickly remove mosquitoes before they have an opportunity to bite, and few of the mosquitoes present are likely to carry the virus, your chances of getting West Nile fever or another disease from a mosquito bite are probably extremely small.

If you experience any of the symptoms described above in the month following the field test you should contact a medical practitioner and inform the Principal Investigator.

PREGNANCY RISKS

The risks to the unborn are unknown and if you are a woman of childbearing potential, it is important that you do not participate in this study if you are, or if you think you may be pregnant, or are lactating.

Pregnancy will be self-checked by each female volunteer on the morning of the repellent test using an OTC test kit provided by the Study Director. Results of each such test will be immediately verified by direct inspection by a female technician trained to make that assessment.

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks and discomforts listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this product, including allergic reaction or interaction with a medication. You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue participation in this study.

RESEARCH RELATED INJURIES

If you are injured as a result of being in this study, a consulting physician who is aware of the study will be contacted immediately by telephone. Medical treatment will be available from a health care facility. Carroll-Loye Biological Research will cover the costs of such medical treatment that are not covered by your own insurance or by a third party. If necessary, Carroll-Loye Biological Research will transport you to receive medical attention and pay costs associated with the reasonable and appropriate treatment for any injuries incurred as a result of participation in the study. For further information about this, the research test subject should call the office of Carroll-Loye Biological Research (530) 297-6080.

You <u>DO NOT</u> waive your legal rights by signing this form.

TREATMENT ALTERNATIVE

Since this study is not intended to provide any therapeutic or other health-related benefit, your alternative is to not participate in this study.

APPROVED BY
Independent IRB
Signature 1/23/07 Date

Initials: _____
Date: _____

BENEFITS
There are no immediate benefits to you from your participation. However, by serving as a participant you may assist in making new insect repellent products available to consumers.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY
If you have any questions or problems during this study, or if you think that you may have experienced a research-related injury, you should contact Scott Carroll of Carroll-Loye Biological Research at (530) 297-6080 or (530) 902-8267.

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chairman of the Independent Investigational Review Board, Inc. at toll free (877) 888-IIRB (4472) during regular working hours. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study.

COSTS AND REIMBURSEMENT
There will be no costs to you from participating in this study.

For participation in the study, each research study participant will receive a cash payment of $20 per hour. Payment will be made at the end of each visit or whenever you withdraw from the study. If you are designated as an 'alternate subject', you will be paid for the hours you spent being trained, plus you will receive a payment of $50 dollars to compensate for being inconvenienced by the administration of the study.

CONFIDENTIALITY
Carroll-Loye Biological Research will retain records of this study indefinitely. You may access you own records by contacting the Study Director. Representatives from the Sponsor, WPC Brands, Inc., the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation, and the Independent Investigational Review Board, Inc. Review Board (an independent committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants) may have access to all non-personal information collected in this study. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. Any information or reports published as a result of this study will not identify you by name, or any other personal identification.

STATEMENTS OF UNDERSTANDING
Right to withdraw or removal from study
I understand that I am free to withdraw from this study at any time, and I agree to inform the Principal Investigator immediately if I intend to withdraw. It is understood that my decision to participate in this study or to withdraw from this

APPROVED BY
Independent IRB
Signature 1/23/07 Date

Initials: _____
Date: _____

study will not influence the availability of my future medical care and will involve no penalty or loss of compensation to which I am otherwise entitled. I may withdraw from this study at any time.

I agree that the Principal Investigator in charge of the study can remove me from this study without my consent for any reason, including, but not limited to:

a. His/her judgment that any condition or circumstance may jeopardize my welfare or the integrity of the study.
b. My failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator participating in the study prior to completion.

Consent and signatures

I have read, in a language that I understand well, and understand the information which has been stated above. I have received satisfactory answers to all of the questions, which I have asked. I hereby voluntarily consent to take part in this study and to be a research study participant in this study. I do **not** waive my legal rights by signing this Informed Consent Form. I shall receive a copy of the signed Informed Consent Authorization.

_____	_____	_____
Date/Time	**Print** Subject Name	**Sign** Subject Name
_____	_____	_____
Date/Time	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Independent Investigational Review Board, Inc.
Approval: 1/23/07

APPROVED BY
Independent IRB
Signature 1/23/07 Date

Initials: _____
Date: _____

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:

1. Be informed of the nature and purpose of the study.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

8. Be instructed that consent to participate in the study may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of a signed and dated written consent form when one is required.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

_____ _____
Signature of Subject Date

_____ _____
Signature of Witness Date

APPROVED BY
Independent IRB

Signature 1/23/07
Date

Study WPC-001 **Dosimetry Data Form** **Date:**

Subject name: **Data recorder name:**

Subject number: **Data recorder signature:**

I. Practice Application				
Trial no.	Distance from skin (cm)	No.pumps for full coverage	Container before (g)	Container after (g)
A. Pump spray, left arm				
1				
B. Pump spray, right arm				
1				
A. Pump spray, left arm				
1				
D. Pump spray, right leg				
1				

II. Pump Sampling						
Trial no.	Distance from skin (cm)	No.pumps for full coverage	Container before (g)	Container after (g)	Dosimeter before (g)	Dosimeter after (g)
A. Pump spray, left arm						
1						
2						
3						
B. Pump spray, right arm						
1						
2						
3						
C. Pump spray, left leg						
1						
2						
3						
D. Pump spray, right leg						
1						
2						
3						

Limb Measurement Form

Subject number: _____ **Date:** _____

Subject name: _____

		Circumference					
Limb	**Length**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference**	**Surface area**
Left forearm							
Right forearm							
Left lower leg							
Right lower leg							

Data collector name: _____

Data collector signature: _____

Subject no.	Surname	Name	Sex	Limb	Length	Lower A	Lower mid B	Upper mid C	Upper D	Surface area (cm^2)	Dose rate gm per cm^2	Dose rate ml per cm^2	Total dose by limb ml
				L arm									
				R arm									
				L leg									
				R leg									

Surface area = [(A+B+C+D)/4] x Length
Dose rate in g is from dosimety analysis
Dose rate in ml = dose rate in g/specific gravity
Total dose by limb ml = Dose rate ml;/cm2 x Surface area

Study: WPC-001

Date:

Site:

Application Time:

Time of first exposure: **LIBe recording code:** **0=none** **1=1** **2=2**

Incidence of LIBes at 15-minute intervals

Subject code	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30

Data collected by:

Data collector's signature:

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Test Reference: WPC-001

CLBR Training Manual

§1.c. Practicing and performing dosimetry with a Pump Spray delivery system

A. Goals of exercise

1. Determine your preferred practices for applying ('self-dosing') a pump spray repellent to your arms and/or legs.
2. Assist technicians in measuring the amount of repellent that you apply when using your practices

B. General information

1. A technician will measure the surface area of your forearms and/or lower legs. He or she will introduce you to the repellent and its dispenser
2. You will work in open air, practicing applying the repellent. A technician will help you keep track of your preferred technique.
3. Using small gauze "bracelets" around your limbs to collect samples of repellent you spray on, you will apply repellent with your preferred practices several times. The bracelets will be quickly removed and weighed. You will thoroughly wash your limbs with a gently skin cleaner between each application of repellent.

C. Materials and equipment needed

1. Test materials
2. Latex or vinyl gloves (various sizes)
3. Bracelet dosimeters with nonabsorbent backing
4. Temperature, humidity and wind speed measuring devices
5. Written copy of the procedures for subjects to read
6. Flexible metric rule

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D. Practicing the methods and performing the measurements

Measuring arms and legs[1]:
Limb is use to refer to your forearm and your lower leg. A technician will measure the distance around your limbs at four evenly spaced places on the forearm (elbow to wrist) and lower leg (back of knee to ankle), and also length of those limbs.

Working with the pump spray and determining your preferred method of applying the repellents:

Your trainer/technician will help to introduced you to how the spray bottle works and how you will determine your preferred methods of applying them. You will read the written procedures that follow here together.

"Read along on your copy of the procedure as the Researcher reads them to you. Ask questions of the Researcher as they occur to you or at any time thereafter. Be sure to get answers to any questions you feel should be answered before proceeding at any step of this work.

This is a study of your behavior in applying spray insect repellents. You may have had experience with applying pump spray products of some kind to your skin before. If you are uncertain about how to use a spray dispenser, be sure to ask the Researcher or one of the technicians. You will each have the opportunity to practice these procedures with the aid of a technician.

Insect repellents function to repel insects from biting the skin. Their effectiveness is influenced by the completeness of their application to the skin surface. Our goal is to determine your preferred method for achieving **full coverage**. At minimum, **full coverage** is defined as a continuous and complete layer of test material. Orienting the limb to light may aid in determining whether full coverage has been achieved. Spray as much as necessary to achieve full coverage.

---

[1] **Limb dimensions and surface area (technical details):**
The term 'limb' refers to the forearm and [1]the lower leg. The surface area of each limb is computed as the average of four evenly spaced circumferences (two peripheral, two central) of the forearm (elbow to wrist) or lower leg (back of knee to ankle) multiplied by the length of treatment area. The locale along the limb at which each circumference is taken will be recorded (for later use to place dosimeters) as the distance in centimeters from the distal margin of the site of the most distal circumference site (i.e., at wrist or ankle).

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In these instructions, the act of spraying a repellent on your limb will be termed 'spraying', 'application', or 'dispensing.'

You may work with the spray on your arms, legs, or both. The technician will inform you. Wash your limbs to be tested thoroughly with the provided cleanser and dry with a clean towel. Place new latex or vinyl gloves on each hand, choosing the size that fits you most snugly without being uncomfortably restricting or likely to tear when you put them on.

You will work with a technician who will assist you in measuring and recording your use of a repellent product in a pump spray delivery system.

First, familiarize yourself with the spray mechanism. Any actuation (pushing down on the pump plunger) of the spray must take place out-of-doors. Work at a distance of no less than 6 feet (1.9 meters) from other subjects. Do not dispense the spray at or near your face or anyone else's. Minimize inhalation of airborne spray while working.

Testing will take place out-of-doors during daylight hours at an air temperature (shade) above 10 °C (50 °F) and wind speed below 12 kph (7 mph), with no precipitation. The researcher or a technician will inform you when these conditions are not met and spraying of the repellents will cease until those conditions resume.

Dispense the spray on one limb designated by the technician. By successively moving the spray nozzle closer to and farther from the limb, identify a distance between nozzle and skin that seems most appropriate for effective application to the skin. The technician will measure and record that distance to the nearest centimeter on the provided datasheet.

Have the technician wash and dry the treated limb so that none of the repellent you have applied is visible on close inspection.

Now, using the spray nozzle at or near the distance from the skin that you have just chosen to be effective for application, determine the minimum number of actuations (pumps of the pump spray). Depress the plunger fully each time, and count them aloud beginning with "1, 2, 3 ...." etc. If you partially depress the plunger (rather than fully depress it) in order, e.g., to apply to a small skin area not covered be initial application, report that to the technician as a "half pump." Each partial depression should be so reported as it occurs. If on any given actuation material fails to be delivered, do not count that actuation. If a partial amount is delivered, estimate its volume as 'whole', 'half' or 'none' and report it as such. For 'none', simply resume counting at the next actuation that delivers material to the skin.

Report the count to the technician who will record it on the data sheet. The technician will also assist you in keeping track of whole versus half pumps. Discard your latex gloves, and wash both test limbs (arms or legs) with cleanser and dry them thoroughly with a towel.

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Next, repeat the application procedure and collect the same data for the other limb. In doing so, try to be consistent with your use of the spray apparatus. If you are clear and confident about the distance from the limb that works best, pay enough attention to keep the nozzle in that general range while maintaining a natural delivery as you would use the product under normal personal use. Keep the nozzle aimed at the skin surface, and avoid orienting the containers in any ways that you determine, as you proceed with the trial, to interfere with delivery of the repellent to the skin surface.

Now move on to the **Spray Sampling** exercise described in the next section."

Spray Sampling[2]

Spray Sampling is the procedure by which the spray is "subsampled" with "patch dosimeters". Dosimeters of known surface area will be placed on subject lower limbs. These dosimeters will intercept a portion of the spray applied to the limbs. Be weighing dosimetry patches before and after treatment, the mass of the intercepted material can be calculated. The spray delivery systems will also be weighed before and after each application.

Spray sampling will be conducted according to the following procedure.

"Please read along with the Study Director as he reads aloud the following description of the procedures you will employ in spray sampling. Please be sure to ask questions at any point.

This procedure is very similar to what you have just performed. The main difference is that for spray sampling, a technician will place four narrow rings of plastic-backed gauze around each of your test limbs. The rings are about one inch (2.5 cm) wide. Each of these "gauze bracelets" will be centered on each of the four positions on the limb at which we initially

---

[2] **Equipment Used to Assess the Dosimetry Variable (technical detail):**

Passive dosimeters are 2.5 cm wide strips of 3M Brand Nexcare™ Holdfast™ self-adhesive roll gauze.

a) Subject number
b) L (for left placement) or R (for right arm placement)
c) Position letter: a (wrist), b (next proximal), c (next proximal), d (elbow)
c) T (for treatment) or C (for control)
d) Replicate number (1, 2 or 3)

There will be eight bracelets per replicate. Each arm and/or leg will be treated three times. Each subject will therefore have a total of twenty-four or forty-eight custom bracelets made and labeled in advance.

Bracelets will be weighed before and after treatment on a traceably calibrated Sartorius H51 balance (measurement increment 0.0001 g, 30 g capacity). Test material containers (pump spray and aerosol) will be weighed before and after dispensing on a traceably calibrated Sartorius GC 2502 (measurement increment 0.001 g, 500 g capacity).

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measured the circumference. These positions may be marked on the skin with small but visible dot using a temporary marker.

The function of the "gauze bracelets" is to capture some of the spray that would otherwise reach your limb as you apply the test products. It is important that you do not alter the way in which you apply the materials in any intentional or substantial way from what you have already determined is your best procedure. The technician will review your results from your previous applications with you to assist you in repeating your general procedure (distance of nozzle to skin, number of spray pumps or aerosol sweeps) as you apply the materials to one of your limbs with the bracelets in place.

The gauze bracelets are narrow in order to minimize the extent to which your sensation of receiving the spray on the limb is changed. Do your best to proceed as if the sensation is not changed. In other words, attempt to avoid spraying additional material onto areas under the bracelets where the sensation of test material on the skin will be different or absent. Do not attempt to spray additional material directly onto a bracelet unless it is within an area that needs additional treatment. Again, attempt to repeat the procedure that you have already developed, and apply the materials "as if the bracelets were not there."

Put a new latex glove on each hand. Spray material onto one limb only. The technician will tell you to which limb to apply spray. You and the technician will collect the same data as previously.

After you have completed spraying, keep both limbs from making contact with any surface. All bracelets will be removed by a technician and taken for weighing.

Discard your gloves, and wash both limbs with cleanser and dry them thoroughly with a towel.

Repeat these procedures until you have made at total of three spray samples for the first limb, and three more for the second limb. If you have completed sampling on, e.g., both arms, the technician may then ask you to repeat the same measurement on both legs. Be sure to discard your gloves, and wash all limbs with cleanser and dry them thoroughly with a towel, including after the last application."

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Test Reference: WPC-001

CLBR Training Manual

§1.a. Observing mosquito landings and learning mechanical aspiration

A. Goals of exercise

1. Learn to determine when a mosquito on your arm is about to bite.
2. Learn to use a "mechanical aspirator" to remove such a mosquito before it bites. Catch at least 10 mosquitoes.

B. General information

1. A technician will show you how to watch mosquitoes that land on you to see if they are about to bite. He or she will then show you how to remove mosquitoes. quickly with a handheld mosquito catching device called a mechanical aspirator
2. You will work with you arms in a screen cage about 1 foot square, with up to two mosquitoes in the cage at one time.
3. You may be bitten by a mosquito while learning to use the aspirator. The mosquitoes were reared in the laboratory and are free from disease.

C. Materials and equipment needed

1. Mosquito cage with entrance stocking
2. Latex or vinyl gloves (various sizes)
3. "Ace" bandage
4. Approximately 12 mature unfed adult female *Aedes aegypti* mosquitoes
5. Mechanical aspirator with charged batteries and collection tube

D. Learning the methods

Spend at least 15-30 minutes practicing observing and catching mosquitoes, working with one or two at a time. Aspirators resemble flashlights except that they have a small electric fan and suction tube rather than a light bulb. You will carry one with you during the field test of the repellent. Your trainer will first demonstrate the method of use and capture. The trainer will then cover your upper forearm with the bandage to protect that area from biting.

Put on gloves. Practice using the switch on the aspirator handle to turn it on, and insert the sucking tube into the cage through the elastic cloth. Then place your arm with the bandage into the cage. About half or your forearm will be uncovered, with no insect repellent. Carefully watch the mosquito as it flies in the cage. Once it lands on your skin, watch carefully to see if it stops walking and places its needle-like mouth against your skin. You may move your arms to get better views and access to the mosquito. Once you observe a mosquito mouth touching your skin, you will immediately attempt to catch the mosquito in the plastic nozzle of the mosquito catcher. You may practice as many times as you wish, with one and then two mosquitoes, and the researcher will be certain that your use of the mosquito catcher is correct.

REPEL

Insect Repellent 30 LE

KEEP OUT OF REACH OF CHILDREN

WARNING: See back panel for precautions and first aid statements

Active Ingredients:
Oil of Lemon Eucalyptus*.....30.0%
Other Ingredients:.....70.0%
TOTAL.....100.0%
*Approx. 65% p-menthane-3,8-diol

NET 4 fl oz (116 mL)

OPTIONAL MARKETING LANGUAGE
[Repel Insect Repellent 30 LE is designed to repel mosquitoes for up to six hours. This unique formula is guaranteed to repel mosquitoes and ticks . You can use Repel Insect Repellent 30 LE with confidence knowing that it will not harm your fishing line, camping gear, watch crystals or tackle box. Apply Repel Insect Repellent 30 LE and get your adventure started.]

You can use Repel Insect Repellent 30 LE with confidence knowing that it will not harm your fishing line, camping gear, watch crystals or tackle box. Apply Repel Insect Repellent 30 LE and get your adventure started.

The active ingredient in Repel Insect Repellent 30 LE is derived from the leaves of the Lemon Eucalyptus tree.

STOP. READ ENTIRE LABEL BEFORE EACH USE.

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals

WARNING. Causes substantial but temporary eye injury. Harmful if swallowed. Do not get in eyes. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. After returning from outdoors, wash product from all exposed skin. Do not allow children to apply this product to themselves. Do not apply to the hands of children. Do not use on children under the age of three years. May cause skin reactions for some people. Discontinue if irritation or rash appears. Do not apply over cuts, wounds or irritated skin.

First Aid

If in Eyes Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a poison control center or doctor for treatment advice.
If swallowed Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to by a poison control center or doctor. Do not give anything by mouth to an unconscious person.
Have the product container or label with you when calling a Poison Control Center or doctor, or going for treatment. In case of emergency call 1-800-332-5553.

Physical or Chemical Hazards

COMBUSTIBLE. Do not use or store near heat or open flame.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. **Read and follow all directions and precautions on this product label.**

To repel insects, apply to exposed skin and clothing. For best results, spread evenly with hand to moisten all exposed skin. Do not spray directly on face. To apply to face, dispense on palm of hand and spread on face and neck. Reapply once as needed. Do not apply more than twice per day.

STORAGE AND DISPOSAL: Store the product in a cool, dry place, out of reach of children. **If empty:** Do not reuse this container. Place in trash or offer for recycling if available. **If partly filled:** Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

NOTICE: Buyer assumes all responsibility for safety and use not in accordance with directions.

Questions or Comments? Call 1-800-332-5553

Made in the USA for WPC Brands, Inc.
PO Box 4406
Bridgeton, MO 63044

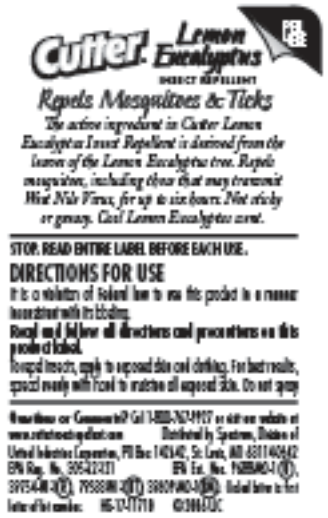
EPA Reg. No. 305-62

Est. No. 9688-MO-1

© 2005

OPTIONAL MARKETING CLAIMS

1. Contains Lemon Eucalyptus Oil
2. Active Ingredient extract of Lemon Eucalyptus
3. Active Ingredient Derived from Plant Extracts
4. Gives Mosquitoes and Ticks the Brush-Off
5. Active Ingredient derived from plant extracts
6. Active Ingredient Derived from Lemon Eucalyptus
7. Contains plant extracts [of Lemon Eucalyptus]
8. Repels [annoying] mosquitoes (and ticks)
9. Delivers up to 6 hours of repellency of Mosquitoes
10. Repels up to 6 hours against mosquitoes
11. Repels mosquitoes for up to 6 hours
12. Won't harm your gear
13. Will not [melt][damage][weaken] your fishing line
14. Will not harm watch crystals, tackle boxes, backpacks, fishing line, tents or bedding.
15. Goes on easy
16. Lemon Eucalyptus scent
17. Cool, refreshing [lemon eucalyptus] scent
18. Fisherman's Formula
19. Botanically-based active ingredient
20. Plant-based active ingredient
21. Effective, Dependable mosquito repellency for up to six hours
22. Unique formula
23. Unique plant-based active ingredient
24. New formula! [to be removed 6 months after first shipment]
25. [Contains][made with] Oil of Lemon Eucalyptus
26. Powered by Citriodiol® Nature's Repellent (logo)
27. Naturally-based active ingredient
28. Active ingredient derived from [the leaves of] the Lemon Eucalyptus tree
29. [By][From][Brought to you by] the makers of Repel®
30. Not Sticky or greasy
31. Repels mosquitoes including those that may transmit West Nile Virus for up to six hours
32. Repels annoying mosquitoes[and ticks]
33. Cool Lemon Eucalyptus scent



directly on face. To apply to face, dispense on palm of hand and spread on face and neck. Reapply once as needed. Do not apply more than twice per day.

STORAGE AND DISPOSAL

Store the product in a cool, dry place, out of reach of children. If empty: Do not reuse this container. Place in trash or offer for recycling if available. If partly filled: Call your local solid waste agency or 1-800-CLEANUP for disposal instructions. Never place unused product down any indoor or outdoor drain.

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals

WARNING: Causes substantial but temporary eye injury. Harmful if swallowed. Do not get in eyes. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. After returning from outdoors, wash product from all exposed skin. Do not allow children to apply this product to themselves. Do not apply to the hands of children. Do not use on children under the age of three years. May cause skin reactions for some people. Discontinue if irritation or rash appears. Do not apply over cuts, wounds or irritated skin.

First Aid

If in eyes • Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a Poison Control Center or doctor for treatment advice.

If swallowed • Call a Poison Control Center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a Poison Control Center or doctor. Do not give anything by mouth to an unconscious person.

Have the product container or label with you when calling a Poison Control Center or doctor, or going for treatment. In case of emergency call 1-800-767-8927.

Physical or Chemical Hazards

COMBUSTIBLE. Do not use or store near heat or open flame.

NOTICE: Buyer assumes all responsibility for safety and use not in accordance with directions.

Questions or Comments? Call 1-800-767-8927 or visit our website at www.cutterproductfacts.com

Distributed by Spectrum, Division of United Industries Corporation
PO Box 142642, St. Louis, MO 63114-0642
EPA Reg. No. 30543-121 EPA Est. No. 9688-MO-1, 39754-MN-1, 79558-MN-1, 39609-MO-1
Circled letter to first letter of lot number. 116-14-8227 © 2006 UIC

Spectrum
Div. of United Industries Corp.
P. O. Box 142642
St. Louis, MO 63144-0642

Material Safety Data Sheet

Complies with OSHA's Hazard Communication Standard, 29 CFR 1910.1200

Hazardous Material Identification System – (HMIS)	
HEALTH – 2	REACTIVITY – 0
FLAMMABILITY – 3	PERSONAL –

I Trade Name: Cutter Lemon Eucalyptus Insect Repellent

Product Type: Insect Repellent Pump

Product Item Number: HG-95606 **Formula Code Number:** 21-0922

EPA Registration Number	Manufacturer	Emergency Telephone Numbers
305-62-121	Chemsico Division of United Industries Corporation 8494 Chapin Industrial Drive St. Louis, MO 63114	**For Chemical Emergency:** 1-800-633-2873 **For Information:** 1-800-767-9927 **Prepared by:** Charlie Duckworth **Date Prepared:** July 11, 2006

II Hazards Ingredient/Identity Information

Chemical	%	OSHA PEL	ACGIH TLV
Oil of Lemon Eucalyptus CAS #129828-24-6	30.00	NE	NE
Ethanol CAS #64-17-5	45.00	1000	1000

III Physical and Chemical Characteristics

Appearance & Odor: Wet narrow fan spray with clear wet film and a citrus odor.
Boiling Point: NA
Melting Point: NA
Vapor Pressure: <1
Specific Gravity: 0.901 (H_2O = 1)
Vapor Density: Greater than 1 (Air = 1)

Solubility in Water: Greater than 40%
Evaporation Rate: Less than 1 (Butyl Acetate = 1)

IV Fire and Explosive Hazards Data

Flash Point: 77° F (TCC) (liquid portion)
Flame Extension: NA
Flammable Limits: NA
Autoignition Temperature: NA
Fire Extinguishing Media: Water fog, Carbon dioxide, Dry chemical
Decomposition Temperature: NA
Special Fire-Fighting Procedures: Keep cans cool. Use equipment or shielding to protect personnel against bursting, rupturing or venting cans.
Unusual Fire & Explosion Hazards: At elevated temperatures (over 54° C/130° F), cans may vent, rupture or burst. Also see Section V.

V Reactivity Data

Stability: Stable
Polymerization: Will not occur
Conditions to Avoid: Temperatures over 130° F
Incompatible Materials: NA
Hazardous Decomposition or Byproducts: Carbon dioxide, carbon monoxide

VI Health Hazard Data

Eye Contact: Causes substantial but temporary eye irritation. ***First Aid***: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes then continue rinsing eye. Call a Poison Control Center or doctor for treatment advice.
Ingestion: Harmful if swallowed. **First Aid**: Call a Poison Control Center or doctor Immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a Poison Control Center or doctor. Do not give anything by mouth to an unconscious person.
Special Notes: Have the product container with you when calling a Poison Control Center or doctor, or going for treatment.
Health conditions Aggravated by Exposure: None known
Ingredients listed by NTP, OSHA, or IARC as Carcinogens or Potential Carcinogens: None

VII Precautions for Safe Handling and Use

Steps to be Taken in Case Material is Released or Spilled:
Avoid breathing vapors. Avoid contact with liquid. Remove ignition sources. Soak up spills with absorbent material.

Waste Disposal:
If empty: Do not reuse this container. Place in trash or offer for recycling if available. If partly filled: Call local solid waste agency or 1-800-CLEANUP for disposal instructions.

Handling & Storage Precautions:
Store in a cool dry place out of reach of children

VIII Control Measures

Read and follow label directions. They are your best guide to using this product effectively, and give necessary safety precautions to protect your health.

IX Transportation Data

DOT: Not Regulated by DOT (limited quantity exception)
IMDG: Not Regulated by IMDG (limited quantity exception)
IATA: Not Regulated by IATA (limited quantity exception)

The information and statements herein are believed to be reliable but are not to be construed as warranty or representation for which we assume legal responsibility. Users should undertake sufficient verification and testing to determine the suitability for their own particular purpose of any information or products referred to herein. NO WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE IS MADE.

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

Study Specific Instructions

Protocol Title: (WPC-001) TEST OF AN OIL OF LEMON EUCALYPTUS-BASED PERSONAL INSECT REPELLENT

Sponsor: WPC Brands, Inc.
Contact Info:

Contact/Title	Phone/Fax	email
Scott P. Carroll, Ph.D/Study Director	(530) 297-6080/6080	spcarroll@ucdavis.edu
Kathleen Cearnal or Charlie Duckworth/ Sponsor Monitor	314-683-2753/ 314-254-590	kathy.cearnal@spectrumbrands.com charlie.duckworth@spectrumbrands.com

CRO:
Contact Info:

Contact/Title	Phone/Fax	email

PROGRESS REPORT NOTIFICATION PROCEDURES: (To whom do we send the notice, etc.) Study Director

SPANISH LANGUAGE REQUIRMENTS: (If it is determined that a Spanish language ICF is necessary).

___ Use translations Services though IIRB (Americo Gomez)

___ We will provide our own Spanish Translations

Mailing Instructions: address for Sites do NOT need to be listed – just identify as "sites" (so that we have on file who get copies and who gets originals!)

Originals to: Scott P. Carroll — Sent by: FedEX **X** UPS - USPS
Address: Carroll-Loye Biological Research — Account #: 177-484-318
711 Oak Avenue, Davis, CA 95616
Copies to: — Sent by: FedEX – UPS - USPS
Address: — Account #:

Notes: (include if routine correspondence get copies sent to CRO/Sponsor, sent US Mail, etc.)

Progress Report Information:
To Study Director
Scott P. Carroll, Carroll-Loye Biological Research, 711 Oak Avenue, Davis, CA 95616

Billing Instructions:
To Study Director: Scott P. Carroll

Billing Address: Scott P. Carroll, Carroll-Loye Biological Research, 711 Oak Avenue, Davis, CA 95616

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

SITE QUESTIONNAIRE

Non-Local Review

Protocol # & Complete Study Title: **(WPC-001) Test of Personal Insect Repellents**

Principal Investigator: Scott P. Carroll, Ph.D

Sub Investigator(s): None

Please indicate the location where study activities will be performed (where patients will be seen excluding Diagnostics) If more than on location is being used you may attach additional pages.

Site Address: Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 951616 USA

PI's Mailing Address: _____
(If different)

If the study is being conducted at more than one location and information requested differs for each location, please provide separate information for each location.

Regulatory/Study Coordinator: Scott Carroll Phone: 530-297-6080 Fax Number: 530-297-6080

Office Phone: 530-297-6080 24 Hour Phone: 530-297-6080

Please complete the following: You may attach copies of relevant procedures.

1. Is this study federally funded requiring review under HSS standards? X No ☐ Yes

2. How will Study Participants be recruited?
   - ☐ Principal Investigator's Clinical Practice
   - ☐ Referrals from other clinical Practices
   - X Data base of potential Volunteers
   - ☐ Advertising in the community* *(*advertisements Must be approved by the IIRB)*
   - X Other *(please specify)*: Word of mouth via Volunteers in data base

3. Will you recruit volunteers from vulnerable study populations? X No ☐ Yes *(please specify below)*
   - ☐ Persons kept in detention
   - ☐ Members of the Armed Forces
   - ☐ Nursing Home Resident/Elderly
   - ☐ Patients with incurable disease
   - ☐ Patients in emergency situations
   - ☐ Unemployed/on Public Assistance
   - ☐ Persons of limited capacity
   - ☐ Homeless
   - ☐ Minors
   - ☐ Employees (Site or Sponsor, etc)
   - ☐ Pregnant women
   - ☐ Disabled
   - ☐ Illiterate
   - ☐ Other: _____

   If yes, describe procedures to be followed (if applicable): Our subjects are mainly University of California–Davis graduate and undergraduate students in life science programs with which the Principal Investigator is associated. Students in his laboratory who depend on him directly for employment or scholastically are not eligible to participate.

4. Do the subjects that you intend to enroll in this study come from any type of ethnic background or cultural environment that might have an impact on their ability to understand that participation in the study is voluntary and refusal to participate or discontinuing their participation will not have any adverse impact on the care that they will receive? No

5. Indicate the approximate demographics of your site's anticipated subject population:
___5__% African American __65__% Caucasian __15_% Hispanics __15__% Asian __<1__% Other

6. Will you be enrolling only subjects who speak English in this study? X Yes No
If No, Is a "local dialect" or translation needed? Translation needed: Spanish Other _____

7. Who will discuss the research study with the volunteer and obtain informed consent (signed informed consent)? *(Check all that apply)*

X Principal Investigator Sub Investigator Study Coordinator
Explain consenting procedures: We contact subjects who participated in previous Carroll-Loye repellent efficacy tests by selecting them from our Volunteer Database. At that time interested individuals often ask if one or more of their lab mates or acquaintances can participate as well. All such potential participants are screened or re-screened for suitability for each test in a private, one-on-one conversation held at the office of the Principal Investigator (PI). The Exclusion Criteria (section 9.1.3) are exercised by asking each candidate to address them in the interview with the PI. The PI encourages candidates to ask questions and ask for clarification at any time during the interview and in all activities that follow. To candidates that pass screening the PI describes the test purpose in plain language (in English), and the procedures and comportment to be followed are described in detail. Candidates are then asked if they would like to retire from consideration at that point. If they wish to remain in consideration, it is explained and emphasized that they may withdraw from the test at any time during the test without penalty to their compensation. They are also given a copy of the IRB-approved consent form to read as the PI reads it aloud. The amount and form of compensation is described. They are again encouraged to ask any questions they have about the test, which may include understanding its purpose more fully, understanding risks and discomforts more fully, and understanding treatment and compensation for injury more fully. While the majority of our subjects have worked with us on an occasional basis for a number of years, we encourage them to personally evaluate their interests and concerns about participation seriously each time. We ask them not to sign on immediately but to give the situation due consideration (normally at least one day, sometimes less for those who have participated in multiple prior studies). Because most of the volunteers are researchers and/or have advanced degrees in life sciences, we regard their motivations and decisions to participate as being unusually well considered and well informed. Accordingly, we normally accept their decisions to participate if they so choose following due consideration. Nonetheless, the PI retains the final right to refuse participation to any candidate.

8. Describe the setting(s) where the study will be conducted (ie, private office, clinic, hospital environment) and if the Investigator is required to seek any type of administrative or Corporate approval in order to implement the study:
Private Laboratory owned by Principal Investigator and Field Sites accessed by the PI that are mosquito habitats

*If being done in a Hospital or Outpatient Surgery Center, please provide a copy of that facility's License/accreditation and/or Hospital IRB Waiver Form.

9. Distance between the nearest hospital and research site: 1.8 miles from Laboratory, within 25 miles of field sites.

10. Describe the on-site emergency equipment available for the subjects: First aid kit that includes antihistamines and Epi-pens, skin washing soap and mild dermal detergent, eye wash.

11. How long has the PI been conducting clinical research? ___17_____years ____3_____months

12. Within the past 3 years has the FDA/OHRP audited your site/Principal Investigator? X No ☐ Yes*
**If yes, please provide a copy* of all 483's *and any applicable correspondence.*

13. Has the FDA/OHRP or any State Medical Board ever sanctioned the Principal Investigator? X No ☐ Yes*
**If yes, please provide a summary of the action and applicable correspondence.*

14. Are subject files adequately stored and protected to ensure subject confidentiality, i.e. HIPAA, HIV, etc.? ☐ No* X Yes
**If no, please explain:* _____

15. Does the Principal Investigator, Sub Investigator(s) or any immediate family member have a conflict of interest with the study sponsor, sponsor representatives or other study related entities? X No ☐ Yes*
**If yes, please provide explanation:*
_____
_____

Subject Compensation:

Will subject be paid for participation in this study? ☐ No X Yes*
**If yes, please specify the total amount, the amount for each visit and the timing of payment (i.e. at each visit, at the last visit, within 2 weeks of the last visit) in the draft Informed Consent Form.*

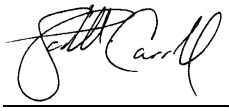
Site Specific Informed Consent Form Information

Is there any additional wording needed in the Informed Consent Form? X No Yes*
**If yes, please specify the section and additional wording below.*
Already present in attached draft form.
_____
_____

Investigator Acknowledgment

On behalf of all of the investigators listed on page1, I agree that the responses provided on the Site Questionnaire are true and accurate and I agree to notify the Independent Investigational Review Board, Inc. of any changes in the research activities and to report any unanticipated problems involving risk to the research subjects. In addition, I agree not to make any changes in the research without IRB approval. I confirm that study personnel are familiar with the study and that either an Investigator or a study coordinator acting as my designee will orally explain the Informed Consent Form to all prospective subjects before obtaining their signed informed consent. Furthermore, by signing this form I confirm that I agree to conduct the study in accordance with the requirements of the protocol, for which I am seeking approval.

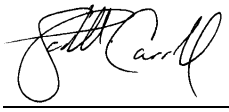
Scott P. Carroll
Print name of individual completing Site Questionnaire



Signature of individual completing Site Questionnaire

18 January 2007
Date

Scott P. Carroll
Print Name of Principal Investigator



Signature Principal Investigator

18 January 2007
Date

Please contact the Independent IRB, if you have any questions regarding this questionnaire 954.327.0778

Date: Thu, 18 Jan 2007 11:23:11 -0800
To: "Robert Roogow" <rroogow@iirb.com>
From: Scott P Carroll <spcarroll@ucdavis.edu>
Subject: New Protocol Submission: WPC-001
Cc:
Bcc: spc, Kathy.cearnal-spectrumbrand.com, Charlie_Duckworth
X-Attachments: :André Rublev:622060:Site_Questionnaire WPC-001.doc: :André Rublev:622060:WPC-001.study_setup.doc: :André Rublev:630649:Carroll_WPC-001.pdf: :André Rublev:613684:WPC-001 ICF.doc:

Dear Robert,

We submit a new study of insect repellent efficacy for your review. The study is (WPC-001) TEST OF AN OIL OF LEMON EUCALYPTUS-BASED PERSONAL INSECT REPELLENT, sponsored by WPC Brands, Inc.

After satisfying IIRB requirements for the conduct of the study, our plan is to forward it on to the US/EPA Office of Pesticide Programs for HSRB review. It is our desire to submit a protocol and ICF approved by IIRB to EPA by 1 February 2007. We submit it to you today in order that we will have time to address any points your Board may raise, and that you will perhaps have time to submit approved minutes of your pertinent Board meeting, to John Carley (Carley.John@epamail.epa.gov) at US/EPA by that date.

The following documents for WPC-001 are attached:

1. Completed IIRB Study Set-up Form (MS Word doc)
2. Completed IIRB Site Questionnaire (MS Word doc)
3. Signed protocol with appendices, including the proposed ICF (pdf)
4. Proposed ICF as a separate document (MS Word doc)

I hope that you find these materials satisfactory for your needs. Please let me know if you need anything else.

Thank you.

Sincerely,
Scott
—

Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616

Tel (530) 297-6080
Fax (530) 297-6080
email spcarroll@ucdavis.edu

http://www.carroll-loye.com/

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****

From: "Robert Roogow" <rroogow@iirb.com>
To: "'Scott P Carroll'" <spcarroll@ucdavis.edu>
Subject: WPC-001
Date: Mon, 22 Jan 2007 16:47:42 -0500
Thread-Index: Acc+bvD8C9jySYL7Tcif6V5z5cS5SA==
X-Scanned-By: MIMEDefang 2.57 on 128.120.32.37
Status: RO

Scott,

Here are potential changes that the committee will review. The changes are only on page 2 under Study Introduction and Study design on page 3.

Let me know your comments and/or concerns.

Regards,
Robert Roogow, MS, RAC
Director of Operations
Independent Investigational Review Board, Inc.
Ph: 954-327-0778
Fax: 954-327-5778
rroogow@iirb.com

****

Date: Mon, 22 Jan 2007 16:33:32 -0800
To: "Robert Roogow" <rroogow@iirb.com>
From: Scott P Carroll <spcarroll@ucdavis.edu>
Subject: Re: WPC-001
Cc:
Bcc:
X-Attachments: :André Rublev:613684:WPC-001.icf.v2.doc: :André Rublev:615130:§8.1 Changes tracked .doc: :André Rublev:615130:§9.1.5 rvsd Changes tracked: :André Rublev:630649:Carroll_WPC-001v.2.pdf:

Hi Robert,

Thanks for the chance to review this in a timely manner.

Proposed Change 1
The proposed change on page 2 of the ICF reduces the number of days in advance of efficacy testing in which preparatory activities may be performed from 21 to 7. I presume that the rationale is that practicing the handling of mosquitoes should be fresh for the participants, and that suggestion is fine. However, this section also addresses dosimetry, and that work could reasonably be expected to take place more than 7 days in advance of some of the efficacy testing (e.g., in a scenario in which orientation and all dosimetry took place in week 1 in California, immediately followed by an efficacy trial there; three weeks later, the second field trial takes place in Florida, with no more dosimetry required, just orientation for Florida subjects within one week of their field trial.

Accordingly, I have altered the language (see attached, changes tracked) in that section to leave the timing of dosimetry ambiguous in relation to the efficacy work.

Proposed Change 2

The proposed wording change on page 3 of the ICF uses text resembling that of previous ICFs for similar studies, but in which there is more than one test material. In study WPC-001,

there is only one test material. The reviewer is responding to section 8.1 of the protocol, which implies otherwise. That section is now reworded to better reflect the study plan as presented in the other sections of this protocol (see, e.g., §§8.2 and 8.3 immediately thereafter).

The changed wording is shown in the attached Word file '8.1 Changes tracked.doc'.

With that clarification, I think it will be understandable that I wish to retain the original wording of the paragraph. The Revised ICF 'WPC-001.icf.v2.doc' is attached.

A third change, Proposed by the PI
Subject recruitment outside of California is not extensively described in the protocol, as recently noted by US/EPA staff. Because testing in the cooler months is more likely to take place in Florida, improving that description is especially pertinent to the present test and we need to get the wording right.

Accordingly, we propose the modifications to the test subject recruitment section of the protocol, 9.1.5. Those changes are shown in the attached Word document '9.1.5 rvsd Changes tracked'.

The last attachment is the revised protocol 'Carroll_WPC-001v.2.pdf', which reflects all of these changes.

Please let me know what you think of these responses and suggestions. I will be traveling to DC tomorrow, and will be available on my cellular telephone until about 0940 EST and after about 1445 EST at 530-902-8267.

Thank you very much.
Scott

****

From: "Robert Roogow" <rroogow@iirb.com>
To: <Carley.John@epamail.epa.gov>
Cc: "'Scott P Carroll'" <spcarroll@ucdavis.edu>
Subject: Protocol WPC-001

Dear Gentlemen,

We had an extra meeting this week and were able to approve Tuesday 1/23/07 minutes earlier than expected. Please find attached the portion of the meeting minutes that refer to the WPC-001 protocol. There have not been any changes to our policies since the last submission. Please let me know if you require any additional documentation.

Regards,
Robert Roogow, MS, RAC
Director of Operations
Independent Investigational Review Board, Inc.
Ph: 954-327-0778
Fax: 954-327-5778
rroogow@iirb.com

Tuesday, January 23, 2007
MINUTES

ATTENDANCE:

PRESENT	GUEST
David Wells, MD	Katy Kysela
Anita McSharry, RN	
Shari Somerstein, RPh	ALSO PRESENT
Edward Wiederhorn	Marcos Rejtman, DO
Robert Lettman, Esq	
Rabbi Akiva Mann	NOT PRESENT
Kim Lerner	George Garbarino

I. CALL TO ORDER

The meeting was called to order at 10:05 AM, by Chairman, Kim Lerner. The meeting was held at 6738 West Sunrise Blvd., Suite 102, Plantation, FL 33313.

II. APPROVAL OF THE 1/16/2007 MINUTES

The minutes of the meeting held 1/16/2007 were reviewed and unanimously approved as reviewed.

III. REVIEW PROTOCOLS

E (Protocol WPC-001) Test of Personal Insect Repellents
Principal Investigator: Scott P. Carroll, PhD

- Approval Clinical Research Protocol dated: 1/16/2007
- Informed Consent Form (Ver. 1/23/2007)
- Site Questionnaire
- The Experimental Subject's Bill of Rights

Motion was made, seconded and the Committee unanimously approved the Research Protocol, the Investigator(s), Informed Consent Form, The California Experimental Subject's Bill of Rights for the above noted research study. The Site Questionnaire was reviewed and unanimously accepted.

The Informed Consent Form is unanimously approved as revised. The Committee recommended that minor changes be made to the Informed Consent Form. The approved Informed Consent Form is identified as Version 1/23/2007 and stamped, "Approved 1/23/2007". The Informed Consent Form contains all regulatory required consent elements. The California Experimental Subject's Bill of Rights is stamped "Approved 1/23/2007".

The Committee evaluated that the risks to the subjects were minimized and that a reasonable risk/benefit ratio is established. Based on the duration of the study and the risks to the subjects, the approval is granted for a 12 month period, with a progress report required prior to continued approval. See Approval Letter for Investigator's responsibilities and file for supporting documents.

Chairman, Kim Lerner, B.S.

Ms. Lerner is co-founder of the Independent Investigational Review Board and has acted as Chairman for the past 16 years. She has transformed her experience as Director of the IRB at a large teaching hospital into directing a large and diverse independent IRB. Her experience serving as the Director of a Hospital Quality Assurance Program provides the foundation for implementation of the Independent IRB's continuous quality improvement and regulatory compliance programs

Vice Chairman, Anita Mc Sharry, RN (scientific)

Ms Mc Sharry is co-founder of the Independent Investigational Review Board and has acted as President for the past 16 years. She has extensive knowledge of principles of medical research, regulatory compliance and clinical safety. Previous experience included development of Research Study budgets, liaison between the Pharmaceutical Sponsor and the Principal Investigator at the University of Miami, Department of Clinical Pharmacology.

David D. Wells, MD (physician/scientific)

Dr. Wells graduated from the University of Havana, is English-Spanish bilingual and brings this international experience to the IRB. He has served as the Emergency Medicine Department Chairman at a local hospital, has health care Clinic experience working with financially disadvantaged patients and is presently volunteering as a Family Practice Physician serving migrant farm workers. This hands-on experience enables him to clearly assess overall research risks and benefits and understand vulnerable population issues.

Rabbi Akiva D. Mann, M.A. (non-scientific)

Rabbi Mann is presently the Spiritual Leader of the Hallandale Jewish Center and is the Director of the Institute of Jewish Knowledge and Learning. He has served on Mayorial Commissions addressing the issues of Medical Ethics and Geriatric Care, as well as having served on Hospital Ethics Committees.

Edward Wiederhorn (non-scientific)

Mr. Wiederhorn is the community representative to the IIRB and is a member of the American Association of Retired Persons (AARP). Mr. Wiederhorn has longstanding experience as a Civic Activist and has been a member of Fraternal and Charitable Organizations, at present he is actively involved in support of the City of Hope.

Shari Somerstein, B.S., R. Ph. (scientific)

Ms. Somerstein has served as a member of the Independent IRB for more than 6 years and has extensive experience in the interpretation and assessment of clinical research findings and study design. She brings extensive clinical pharmacy experience in a Hospital setting and in the community. She has broad administrative experience in IRB activities including, protocol review, assessment of adverse drug experiences and informed consent form development.

George J. Garbarino (non-scientific)

Mr. Garbarino has been an advocate for Labor Union members and brings a wide range of experience in the area of worker's rights and contract negotiations. He is the Business Manager of the Tile, Marble and Stone Workers Local 121 and is associated with the School Board of Broward County.

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

Membership Roster

Glenn K. Moran, DO, FACOFP (Alternate for: physican/scientific)
Dr. Moran is Board Certified in Family Practice and is presently in private practice. He maintains privileges at local hospitals and is active in the areas of Medical Quality Assurance and Peer Review and other community organizations. He is an Assistant Clinical Professor at Nova Southeastern College of Osteopathic Medicine and is familiar with current medical research requirements.

Marcos Rejtman, DO, (Alternate for: physican/scientific)
Dr. Rejtman is Board Certified in Family Practice, Geriatric Medicine and Hospice &Palliative Medicine and is presently the Medical and Team Director for VITAS Innovative Health Care (Hospice) and provides in hospital patient management for a multi-specialty group. He also has recent experience in Emergency Department Medicine. He maintains privileges at local hospitals and is active in the areas of Medical Quality Assurance and Peer Review and other community organizations. He is English-Spanish bilingual.

Maria L. Rodriguez, MS, CCRC,RHIT (Alternate for: non-scientific)
Ms Rodriguez brings to the Board extensive experience in the clinical research field and knowledge of regulatory requirements, policy and procedure development, and the implementation of the quality assurance function. Her educational background focuses on education and training in the clinical research field. She is English-Spanish bilingual.

Robert Lettman, Esq. (Alternate for: non-scientific)
Mr. Lettman is a practicing Attorney in South Florida with extensive experience in civil litigation and serves as a resource in the consideration of the legal aspects of the informed consent process. Having been in the community for 30 years he brings insights and knowledge of the needs of the community.

MEMBERSHIP CHANGES FROM PREVIOUS ROSTER (Dated: 01/03/06)
Resignation
Elsie P. Remy, MSN, ARNP-c (Alternate for: scientific)