Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530)297-6080 http://www.carroll-loye.com/

5 March 2008

John M. Carley
Program Analyst
U.S. Environmental Protection Agency
Office of Pesticide Programs

Dear John,

In your email of 26 February 2008, you requested additional documentation for your review of MRIDs 47322401 and 47322501. I am glad to supply the missing information. I have copied the text of your four items, and my response to each, in turn, is embedded (with a broader left-hand margin).

1. A letter from the IIRB dated 10/30/07 approving amendments 1(a) and 1(b) and the protocol deviations reported to EPA earlier is present (p. 137 in each volume), but I found no correspondence transmitting these amendments to the IIRB.

> Correspondence:
> 10/24/07 18:24
> To: Robert Roogow
> From: Scott P Carroll <spcarroll@ucdavis.edu>
> Deviation reports, SCI-001/Amendment review request
>
> Dear Robert,
> Attached are two deviation reports concerning amendments I made to Protocol SCI-001 without understanding that all such amendments require IRB review. The two amendments in question are also attached. The attached amendments a) support the deviation reports that reference them and b) are hereby submitted for retrospective review by the IIRB.
> Regards,
> Scott
> --
> Scott P. Carroll, Ph.D.
> Carroll–Loye Biological Research

> The completed IIRB deviations submission forms are included at the end of this file.

2. A letter from the IIRB dated 11/6/07 (p. 135 in each volume) approves the progress report and extends IIRB approval of the protocol, but I found no progress report or request for extension.

11/02/07 12:43
To: Robert Roogow
From: Scott P Carroll <spcarroll@ucdavis.edu>
Subject: SCI-001 renewal
Cc: "Yesenia Crespo" <ycrespo@iirb.com>

Dear Robert,
Attached is our progress report for study SCI-001 (insect repellents). A relevant completed consent form is also attached (with the subject's name and initials censored by masking on each page). Please let me know if you have any additional questions. Thank you very much.

Sincerely,
Scott
--
Scott P. Carroll, Ph.D.
Carroll–Loye Biological Research

The request for the extension (which is in the form of a progress report), is included herein. Accompanying it is the required 'most recently completed consent form', with the enrollee's personally identifying information censored.

3. The email exchange provided (pp. 141-143) between Carroll-Loye Biological Research and IIRB leaves several matters up in the air, including what should be said in a revised consent form. Is this really all there is?

A principal matter was the IRB's concern about the disqualification of the pertinent data sets. The Director contacted me be telephone to get more information about decision-making at EPA, with reference to the HSRB process, and to the context in which any comments would be received.

In addition, the ICF material I submitted, and asked about in the submission letter, went before the IRB at the subsequent meeting, with their letters of 11/06/08 comprising their response.

4. Most important, the letter from the IIRB dated 11/6/07 approving amendment 1(c) (p. 136 in each volume) also indicates approval of a revised consent form, which I do not find elsewhere in the volume.

> That revised consent form, which was used for the testing, was inadvertently omitted during the compilation of each report's pdfs. It is included herein.

Please let me know if you have any further questions. A list of further contents (below) points you to supporting documents. Thanks again for you help.

Sincerely,

Scott P. Carroll
Director

On the following pages, please find:

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

Progress Report X
Close Out Report ☐

Principal Investigator: Scott Carroll **Protocol #** SCI-001

Protocol Title: **TEST OF PERSONAL INSECT REPELLENTS**

IIRB approval/re-approval date(s): 7 November 2006

PLEASE COMPLETE THE FOLLOWING AND RETURN TO THE IIRB

#Subjects Screened (signed a Consent Form)				40
#Subjects Enrolled (randomized subjects only do not include Screen Failures) this # should equal 1+ 2+3				40
1. #Subjects Presently Active				0
2. #Subjects Completed Study				40*
3. #Subjects Dropped from Study	0	➲➲➲➲ explain	**# due to AE's**	
#Serious Adverse Events ___0_____			**# for non-compliance**	
All SAE's reported? Yes_____ *No_____ NA			**# lost to follow up**	
**If no, please submit at this time*			**# withdrew consent**	
			# other reasons (explain)	

Explanations (if needed): The study is being continued to collect additional data due to US EPA HSRB concerns about study conduct raised at the October 2007 HSRB meeting. Those concerns have been addressed with amendment submitted or being submitted to IIRB. *Some subjects listed as having completed the study may therefore participate again.

❶ Is your site currently recruiting subjects for this study? Yes_____ No__X___

❷ Has all information been submitted for review, i.e, Amendments, Advertisements, Significant Deviations, Changes to the Form FDA 1572 etc.? Yes_____ No__X__ *(please submit)*

❸ Any FDA audit during the current approval period? Yes _____ *(please submit)* No_X___

❹ Any significant problems or relevant new information? Yes __X_ *(please submit)* No_____

❺ Please provide a copy of the Principal Investigator's current medical license. NA

❻ Please provide a copy of the last consent form completed by a subject for this study (include copies of translated consent forms if applicable).

Anticipated Date of completion: __October 2008_____ or Date of Closure_____
(For Progress Report) (For Close Out Report Date of last subjects last visit)

Principal Investigator Signature:  Date: _____31 October 2007_____

Signature on this Progress Report by the Principal Investigator is required.

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

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

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

Site of Investigation: CLBR BUTTE GLENN

Telephone #: (530) 297-6080

Sponsor: Scientific Coordination, Inc.

Participant's Name: Subject #1 Name censored

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 popular insect repellent called 'DEET' formulated to be more pleasant and convenient to use. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well new lotion insect repellent products work outdoors against mosquitoes. These four products, which are similar to some already being sold, have been formulated to be more cosmetically acceptable to users. The information gained from the study will assist in the development of these repellents for future 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 both parts of the study.

APPROVED BY
Independent IRB
Corrected 1/22/07
Signature 1/2/07 Date

Initials:
Date: 1/12/07

The sponsor, Scientific Coordination, 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 40 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 (1-21 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 21 days before the field study visit you will meet with a researcher to perform 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. You will work with a researcher to determine how much insect repellent you apply. 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 removing mosquitoes from a small area of your arm with the aspirator This training and practice will take about ½ to 1 hour.

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials:
Date: 1/12/07

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
The study will test four different insect repellent lotions. You will be randomly (by chance) assigned to receive one product, so your chance of receiving any one product is one-in-four. You will not have a choice as to which repellent product you receive. If you participate on more than one day, you will receive a different product on different days. For each product assigned to you, you will have an amount typical of what people commonly use applied to your forearms or 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 the two 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

APPROVED BY
Independent IRB
Corrected 1/22/07
Signature 1/2/07 Date

Initials:
Date: 1/12/07

forearm and lower leg. If you are participating in this part of the study, you will then practice using the products to decide how you best like to apply them and how 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 lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of the lotion repellent product to your skin that you think gives complete and even coverage. We will use the amounts you 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 repellents to your forearms or lower legs to give even, complete coverage of the skin. The amount of repellent applied on

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials:
Date: 7/24/07

any one arm or leg will be no more than about ¼ teaspoon. You will also be given protective material to prevent bites on other parts of your arms and legs, plus a head net.

During the field test you and the Investigator will not know which repellent you are using. The study is done this way because knowing which repellent you are using can change the results of the study. If you start having any side effects from the repellent, the investigators can find out what you are taking in order to help you. Please ask the investigator if you have any questions at all about this kind of study.

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 repellents applied. You and a partner will watch your own exposed arms or legs and those of your partner for mosquitoes that land for one minute. 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

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials:
Date: 1/24/07

- You must be able to apply spray and lotion repellents to your left and right arms
- 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

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.

There is a small possibility that the repellents may cause skin, lung and eye irritation. Excessive inhalation can cause lung irritation, headache and dizziness. Swallowing the products may cause temporary stomach distress. 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

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials:
Date: 7/12/07

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.

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

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials:
Date: 2/12/07

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 DO NOT 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.

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 $15 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, Scientific Coordination, 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

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials: _____
Date: 7/12/07

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 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.

07/12/07	Subject #1 Name Censored	Subject #1 Signature Censored
Date/Time	**Print** Subject Name	**Sign** Subject Name
12 July 2007 2200	Scott P. Carroll	
Date/Time	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Independent Investigational Review Board, Inc.
Approval: 11/7/06, Revised: 1/02/07

Version : 1/2/07
Protocol: SCI-001

APPROVED BY
Independent IRB
Corrected 1/22/07

Signature 1/2/07 Date

Initials:
Date: 07/12/07

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

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

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

Site of Investigation: _____
_____
_____

Telephone #: (530) 297-6080

Sponsor: Scientific Coordination, 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 popular insect repellent called 'DEET' formulated to be more pleasant and convenient to use. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well new lotion insect repellent products work outdoors against mosquitoes. These two products, which are similar to some already being sold, have been formulated to be more cosmetically acceptable to users. The information gained from the study will assist in the development of these repellents for future 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 both parts of the study.

APPROVED BY
Independent IRB

Signature

11/6/07
Date

Initials: _____
Date: _____

The sponsor, Scientific Coordination, 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. Data for this study were originally collected in July 2007. More data are needed to complete this study due to an administrative error that took place then. At that time, the sponsor added a new test repellent to the study, for which the Principal Investigator did not obtain proper approval. While regulatory authorities at the US Environmental Protection Agency have not suggested that participants were at risk due to that error, the data collected at that time are likely not acceptable for ethical reasons. Accordingly, your participation would serve to replace some of those data. The repellent formulation added in July is not being tested now.

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 40 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 (1-21 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 21 days before the field study visit you will meet with a researcher to perform 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. You will work with a researcher to determine how much insect repellent you apply. Completing those measurements will take 1.5-2.0 hours.

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

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 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

The study will test two different insect repellent lotions. You will be randomly (by chance) assigned to receive one product, so your chance of receiving any one product is one-in-two. You will not have a choice as to which repellent product you receive. If you participate on more than one day, you will receive a different product on different days. For each product assigned to you, you will have an amount typical of what people commonly use applied to your forearms or 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 the two 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

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

to participate in the study. Information regarding your pregnancy test results will be kept in confidence, but it is nevertheless possible that obtaining pregnancy results in the research setting would cause you social discomfort.

Procedures

Visit 1

At the laboratory, a researcher will measure the length and circumference of your forearm and lower leg. If you are participating in this part of the study, you will then practice using the products to decide how you best like to apply them and how 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 lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of the lotion repellent product to your skin that you think gives complete and even coverage. We will use the amounts you 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

APPROVED BY
Independent IRB
Signature 11/6/07 Date

Initials: _____
Date: _____

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

During the field test you and the Investigator will not know which repellent you are using. The study is done this way because knowing which repellent you are using can change the results of the study. If you start having any side effects from the repellent, the investigators can find out what you are taking in order to help you. Please ask the investigator if you have any questions at all about this kind of study.

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 repellents applied. You and a partner will watch your own exposed arms or legs and those of your partner for mosquitoes that land for one minute. 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

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

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 be able to apply spray and lotion repellents to your left and right arms
- 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

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.

There is a small possibility that the repellents may cause skin, lung and eye irritation. Excessive inhalation can cause lung irritation, headache and dizziness. Swallowing the products may cause temporary stomach distress. 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.

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

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.

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.

APPROVED BY
Independent IRB

Signature

11/6/07
Date

Initials: _____
Date: _____

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 DO NOT 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.

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 $20.00 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.

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

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, Scientific Coordination, 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 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.

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

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: 11/7/06, Revised: 1/02/07, 11/6/07

APPROVED BY
Independent IRB

Signature 11/6/07 Date

Initials: _____
Date: _____

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

PROTOCOL DEVIATIONS/VIOLATIONS REPORTING FORM

-Use this form to report protocol deviations or violations that occur at your site-
Significant Deviations should be reported at the time that they are identified
Non-Significant Deviations should be reported at the time of Progress Reporting

Principal Investigator Name: Scott P. Carroll, PhD

Sponsor: Scientific Coordination, Inc. Sponsor Protocol No.: SCI-001

Subject ID: 1, 7, 8, 13, 14, 15, 18, 24, 27, 28, 32, 37, 39, 40, 43, 46, 52, 53, 56, 57, 60, 61, 63, 64, 70.

Study Drug/Device LipoDeet (34.34%) Insect Repellent

Date of Occurrence: July 3-5, 7, 8, 12-15, 2007

Describe the deviation/violation:

Study amended without IRB review. The Study Director ('PI') did not understand that any and all amendments to an approved protocol must also be reviewed by the approving IRB before being adopted, regardless of perceived inconsequentiality of such amendments for subjects' safety and rights.

The specific amendment is attached (see Word file 'SCI-001 add 34% Lipodeet.doc'). It specifies the removal of a test material that the sponsor no longer wanted to develop (Insect Guard II) and its replacement with a test material better suited to a principal objective of the study (LipoDeet at 34.34% deet, exactly matching the deet concentration of the comparison article Ultrathon).

No other changes were made to the study design in terms of subject exposure to repellents or mosquitoes. Lipodeet at 34.34% deet was nearly identical to another product already approved for testing (Lipodeet at 30% deet), so that there was no consequential change to the risk profile. The deet concentration in these formulations is much lower than that in many products already registered, which, in addition, lack properties that reduce skin absorption of the deet.

As the Study Director, my decision to respond as I did to the Sponsor's request to substitute a test material was based on feedback that I have had, from multiple parties, including California EPA and certain IRBs, that only proposed changes likely to increase risk to participants require review. Fundamentally, that misunderstanding may come from a lack of clarity on my part about whether deviations or amendments are under discussion. Personally I have found the apparent latitude in making the decision about whether review is required somewhat disconcerting or at least confusing, and I am pleased, upon further discussions with expert parties IIRB, to have this basic matter fully clarified.

☐ Prior Sponsor Approval Obtained (no follow up action required)
☐ *Deviation Not Significant (no follow up action required)

X *Deviation Significant (follow up action required)

Describe the follow up actions taken to prevent future occurrences:

Study Director is now fully aware of the requirement that all amendments be reviewed. No protocols will be amended without IRB-approval henceforth**.** Study Director will complete the CITI Ethics for Researchers refresher course.

Definitions of Significant Deviation available on web site.

Scott P. Carroll _____ _____
Printed Name of Person Completing this form Investigator Signature

(530 297-6080 (530) 297-6080 _____ 23 October 2007
Phone Number Fax Number Date

Return this form to: Independent Investigational Review Board, Inc.
6738 West Sunrise Boulevard Suite 102
Plantation, FL 33313

INDEPENDENT INVESTIGATIONAL REVIEW BOARD INC.

PROTOCOL DEVIATIONS/VIOLATIONS REPORTING FORM

-Use this form to report protocol deviations or violations that occur at your site-
Significant Deviations should be reported at the time that they are identified
Non-Significant Deviations should be reported at the time of Progress Reporting

Principal Investigator Name: Scott P. Carroll, PhD

Sponsor: Scientific Coordination, Inc. Sponsor Protocol No.: SCI-001

Subject ID: 1, 3, 5, 6, 8, 10, 13, 14, 15, 18, 20, 21, 22, 24, 25, 28, 32, 37, 39, 40, 43, 46, 52, 53, 60, 61, 62, 63, 64, 67, 68, 69, 70, 71, 72

Study Drug/Device Deet-based Insect Repellents

Date of Occurrence: July 3-5, 7, 8, 12-15, 2007

Describe the deviation/violation:

Study amended without IRB review. The Study Director ('PI') did not understand that any and all amendments to an approved protocol must also be reviewed by the approving IRB before being adopted, regardless of perceived inconsequentiality or benefit of such amendments for subjects' safety and rights.

The specific amendment is attached (see Word file 'SCI-001 Virus PCR.doc'). It specifies conducting viral screening of mosquitoes captured during the conduct of study SCI-001 to the protocol. Such screening was recommended by the US/EPA Human Studies Review Board for insect repellent registration efficacy studies.

As the Study Director, my decision to respond as I did to the HSRB recommendation, without seeking IRB review, was based on feedback that I have had, from multiple parties, including California EPA and certain IRBs, that only proposed changes that are likely to increase risk to participants require review. I now understand that any proposed amendment to an approved protocol requires IRB review, even if the wording has already been so approved for other, similar protocols.

☐ Prior Sponsor Approval Obtained (no follow up action required)
☐ *Deviation Not Significant (no follow up action required)
X *Deviation Significant (follow up action required)

Describe the follow up actions taken to prevent future occurrences:

Study Director is now fully aware of the requirement that all amendments be reviewed. No protocols will be amended without IRB-approval henceforth**.** Study Director will complete the CITI Ethics for Researchers refresher course.

Definitions of Significant Deviation available on web site.

Scott P. Carroll
Printed Name of Person Completing this form

Investigator Signature

(530 297-6080 (530) 297-6080
Phone Number Fax Number

23 October 2007
Date

Return this form to:

Independent Investigational Review Board, Inc.
6738 West Sunrise Boulevard Suite 102
Plantation, FL 33313