Carroll-Loye Biological Research

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

3 January 2007

HSRB Submission
Carroll-Loye Protocol SCI-001– Test of a Topical Insect Repellent

IRB CORRESPONDENCE REGARDING PROTOCOL REVIEW PART II:
29 December 2006-3 January 2007

IRB:
Independent Investigational Review Board, Inc.
6738 West Sunrise Blvd. Suite #102
Plantation, FL 33313

From: "Robert Roogow" <rroogow@iirb.com>
To: "'Scott P Carroll'" <spcarroll@ucdavis.edu>
Subject: SCI-001
Date: Wed, 3 Jan 2007 13:56:30 -0500
Thread-Index: AccvaN/Uij64UoiCRWaGOPp2jDwKVQ==
X-Scanned-By: MIMEDefang 2.57 on 128.120.32.35
Status:

Scott,

I have attached the documents for the revised SCI-001 protocol. I am also attaching the Board's revised Membership List and revised Policies & Procedures. I will send the approved Minutes from yesterday's meeting as soon as they are available. Lastly I am attaching a word version of the approved ICF in case future revisions are required.

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

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To: "Robert Roogow" <rroogow@iirb.com>
From: Scott P Carroll <spcarroll@ucdavis.edu>
Subject: RE: Revised protocol and ICF SCI-001
Date: 2 January 2007
X-Attachments: :André Rublev:477395:SCI-001_ICF_Changes.doc:

Dear Robert,

Thanks for your request. I have used the Word function 'Compare Documents' to highlight the differences between the original version and this revision. They are shown in the attached file 'SCI-001_Changes.doc'. This file shows in blue italics the words added to create the submitted revised version, which has the suffix 'v3' (we had draft second version, 'v2', that you did not see).

Please let me know if you find you need additional records from me.

Thanks for your suggestion regarding how we should proceed with any additional revisions. We look forward to the Board's response.

Best,
Scott

From: "Robert Roogow" <rroogow@iirb.com>
To: "'Scott P Carroll'" <spcarroll@ucdavis.edu>
Subject: RE: Revised protocol and ICF SCI-001
Date: Tue, 2 Jan 2007 10:52:04 -0500
Thread-Index: AccrlOFl0hXf77cuRYWFuvkp2+5xXwC7gfJQ
X-Scanned-By: MIMEDefang 2.57 on 128.120.32.9
Status:

Dear Scott,

The ICF you sent did not track the changes you wanted to make. I just want to be sure that the only change to the ICF you are requesting are on page 3 to the "Study Design" and page 5 the last paragraph in "Visit 2". For future changes please use the currently approved ICF which I will send to you. Click "Accept all changes", and then make sure that you "Track Changes". I am attaching the current ICF. If there are additional changes needed other than the changes listed above, please make sure they are made to the ICF attached. If there are no other changes needed please let me know. I will make the changes listed in the email and await further instruction. Please call if you have any questions.

Regards,
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From: Scott P Carroll [mailto:spcarroll@ucdavis.edu]
Sent: Friday, December 29, 2006 5:00 PM
To: Robert Roogow
Cc: Carley.John@epamail.epa.gov; Tim Dickens
Subject: Revised protocol and ICF SCI-001

Dear Robert,

Our family has had a great holiday season, thanks.

First let me note that we very much appreciate IIRB review of these documents. In the current regulatory circumstance, where former procedural stasis been punctuated by rapid evolutionary change, we frequently have only a few hours to respond adaptively once sponsors or the EPA have determined what the next wave of "selective pressures" shall be. Your assistance in assuring the quality and viability of the fresh documents that result remains critical to moving the process forward. I hope that together we are all gradually moving again toward a more stable period in which the general practice standards are improved and the burden to IRBs, sponsors, and regulators remains reasonable.

I have attached revised Protocol SCI-001 and its associated ICF. The former is in pdf form, that latter in MS Word (for greater editing flexibility on your part).

We have made a number of changes in response to review commentary from US/EPA. I will describe the changes to the documents with a some general statements, and then give more detail on those most pertinent to what subjects will actually experience.

A. General Changes

1. The protocol and ICF contained some references to delivery systems other than lotion, including the notion of an untreated control for dosimetry, which does not apply to lotion testing. These references have all been eliminated/modified for accuracy.

2. The positive control has been included in the dosimetry phase.

3. Training material is now included in the appendices.

4. the number of subjects testing the positive control has been augmented to 10, and now matches the *N* for each test material.

5.We have further clarified that subjects will receive only one treatment at a time.

6. We have added clarifying language explaining that subjects may be asked to participate in more than one field trial of the test materials, but need not do so.

7. An sponsor reference has been corrected.

B. Recruitment and consent of Untreated ("control") subjects

The qualifications required for subjects that serve as untreated controls need to be more stringent because they probably have a greater change of receiving mosquito bites unless they are capable of comporting themselves in a more rigorous fashion than average treated subjects. In addition, a few basic details regarding how they should comport themselves differ.

As I noted in the foregoing email, the ICF has been changed to reflect those differences. The first change, repeated here, is as follows:

On page 3, the section **STUDY PROCEDURES, Study Design** formerly began:

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 of them 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. Experienced personnel will also be present to record the activity of mosquitoes by exposing their own arms or legs without repellent applied. However, you will not be asked to expose untreated skin and should avoid doing so.

It has been revised by beginning a new paragraph after the fifth sentence, and adding text to that second paragraph, to read:

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 of them 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.

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.

Complementing that change, on page 5, we have added the short paragraph at the end of the section 'Visit 2' as follows:

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.

To support this differentiation among untreated versus treated subjects, we have added the following inclusion material to the protocol as a new section 9.1.2:

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.

Once we have arrive at changes that can be approved, I will insert the ICF at the indicated place in the protocol and re-paginate that last part of the document to reflect its inclusion.

Thanks very much again.

Sincerely,
Scott

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Hello Scott,

My Holidays have been very nice so far and I hope yours have been as well. I do not foresee any problems with your approach as far as the IRB is concerned. If you feel it will meet the EPA expectations, it will meet ours.

Best regards,

Robert Roogow, MS, RAC

Director of Operations

Independent Investigational Review Board, Inc.

Ph: 954-327-0778

Fax: 954-327-5778

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From: Scott P Carroll [mailto:spcarroll@ucdavis.edu]
Sent: Friday, December 29, 2006 1:10 PM
To: rroogow@iirb.com
Subject: ICF question for SCI-001

Hi Robert,

I hope that you holidays have been pleasant. Thank you for your continuing help in dealing with the ongoing EPA oversight of our protocols.

I plan to submit revised documents for SCI-001 in the next couple of hours, so I wanted to touch base, and also address a question about a fundamental point to you, as follows.

The EPA has asked that we consider a separate consent form for the two subjects in each field trial who will be not be treated with insect repellent in order to monitor what is called the intensity of mosquito activity during the trial. That is because they will be predesignated and will have a different experience. I discussed that with Ms. Lerner yesterday, and she thinks a separate form would be acceptable, though not necessarily mandatory.

In working on such a change, however, I have only needed to make a single substantive alteration (below), which leads me to think that it might work to keep it all in a single ICF. Based on your experience, I would like to know what you think before submitting a version for review.

On Page 3 formerly began, under **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 of them 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. Experienced personnel will also be present to record the activity of mosquitoes by exposing their own arms or legs without repellent applied. However, you will not be asked to expose untreated skin and should avoid doing so.

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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.

Please let me know if you see any inherent problems with this approach. The qualifications for being called "experienced" will be inserted into the protocol. I realize the Board will need to decide, but I wanted you to have a chance to see it. There are also a few other minor clarifications to the ICF and protocol that I will describe to you as part of the submission, but they are likely less important than this one.

Thanks again and best regards,

Scott

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