NOT FOR USE IN CONSENTING SUBJECTS
DRAFT 1 IC TO CLIENT 02/13/18 AM

CONSENT INFORMATION FOR PARTICIPATION IN AN i2LResearch USA, Inc. MOSQUITO REPELLENT STUDY

Title:	Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings
Protocol No:	18/011
Study Director:	Timothy Foard, MS
Site of Investigation:	i2LResearch USA, Inc. 1430 Joh Ave., Suite ~~L~~ M Baltimore, Maryland 21227~~33703~~
Site Telephone #:	410-747-4500
24 Hour Telephone #:	202-905-1401
On-Call Nurse Telephone #:	410-598-7436

INTRODUCTION
Before you agree to participate in this study, you need to understand the proposed study described in this consent form. This consent document describes the purpose of the testing, the test materials, procedures, benefits, risks, discomforts and safety measures that the researchers will take during the study. It also describes your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

If you are not completely truthful with the study staff regarding your health history, you may harm yourself by participating in this study.

Timothy Foard, MS and the rest of the research teamwork for i2LResearch USA, Inc. ~~and~~ are paid to test repellents, but do not have a financial interest in the outcome of this study.

~~Advarra~~ Schulman Institutional Review Board (~~Advarra~~ Schulman IRB) has approved the information in this consent document and has given approval for the Study Director to run the study. An institutional review board (IRB) is an independent committee ~~that independently reviews research proposals to~~ established to help protect the rights of research subjects. This does not mean the IRB has approved your participation in the study. You must think about the information in this consent document for yourself. You must then decide if you want to be in the study.

PURPOSE OF THE STUDY
In this study, fabric is treated with a pesticide called permethrin. i2LResearch USA, Inc. (i2L) is conducting research to determine if fabrics treated with permethrin are effective for protection against bites by mosquitoes. Human volunteers will have their forearms wrapped in permethrin-treated fabric shaped in the form of a sleeve. The volunteers will then place their fabric-covered arms inside cages containing mosquitoes for 15 minutes at a time. The purpose of this study is to determine whether the treated fabric can prevent or lower the

number of bites from *Aedes aegypti* (yellow fever mosquitoes) and *Anopheles quadrimaculatus* (common malaria mosquitoes).

Test Material
Permethrin is a pesticide registered by the U.S. Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) to kill a variety of insect pests. Permethrin is an insecticide. It is approved for use on agricultural food crops and can also be used on surfaces or as a spray inside or around homes and other structures, as well as on gardens and lawns. Permethrin may be used in products to treat fleas, mites and other pests on house pets. Permethrin is also used to prevent mosquito bites by treating clothing with permethrin.

The fabrics being tested in this study contain the same or a lower percentage of the registered active ingredient, which is approximately 0.52% permethrin. The permethrin-treated fabrics that are being tested in this study have not yet been registered by the U.S. EPA under FIFRA. The data collected in this study will be used to support registration of the permethrin-treated fabrics being tested. Other permethrin-impregnated fabric products have been registered and are already being marketed to consumers.

Your Suitability for the Study
You are being asked to participate in this study because you are a healthy female or male, between 18 and 55 years old. You also do not have skin conditions that could become worse by wearing the treated fabric products.

A study employee asked you about any allergies or sensitivities to mosquito bites, surgical tape, latex, treated fabric products, insect repellents, skin care products, and about any skin conditions or open cuts and scrapes that you may have. If you have any of these allergies or sensitivities, skin conditions, or open cuts or scrapes, you cannot participate in the study and must tell a member of the study team. You must already use insect repellent products and/or other products used to repel biting mosquitoes.

In addition, female test subjects may not participate if they are pregnant or breastfeeding.

If you are a female, you must take a pregnancy test using an over-the-counter test (provided by i2L). You will be required to take the pregnancy test at the i2L facility at the start of each test day.

You will take the pregnancy test alone in a private bathroom. Once you know the test results, a female employee of i2L will ask you, in a private area, if you still want to take part in the study. If you say that you do, this employee will ask to see your test result to make sure it is negative. The result will be kept confidential. It will not be recorded or disclosed to anyone except the Study Director. You may choose not to disclose the results of the pregnancy test to anybody at i2L. In this case, you will not be allowed to participate in the study for health and safety reasons.

You must not be an employee of i2L or Pulcra or an immediate family member of any employee of i2L or Pulcra.

Before you test the permethrin-treated fabrics, your attractiveness to mosquitoes will be tested. This procedure is described in more detail later in this consent form.

If i2L decides that you should not take part in this test because of any answers to our screening questions, or if you are not sufficiently attractive to mosquitoes, you will be told this and allowed to leave. If this happens, it is no reflection upon you.

You will be asked to wear short sleeves on your scheduled test day. All other clothing choices will be yours.

Study Duration and Number of Volunteers
The length of this study will vary depending on how many fabrics the sponsor chooses to test. If selected to participate, you may choose to participate in multiple test days, but may not participate in more than one test day with the same fabric and same mosquito species. If you participate in multiple test days those test days must be spread out a minimum of 72 hours. You may be exposed to one or two types of fabric that have been treated with permethrin and washed 0, 50, 75, or 100 times. You will also test an untreated control fabric that is not treated with permethrin for each treated fabric tested (either one or two). Testing will involve one or two types of mosquitoes.

Testing on each test day could last up to eight hours. This includes up to one hour of preparation time prior to testing, the testing itself, and time in between testing for you to remove the test fabric, wash your forearms, take a short break of up to 10 minutes, and put the next test fabric on. It also includes time for technicians to remove all mosquitoes from the test cages and place a new batch of mosquitoes into test cages prior to the next 15-minute exposure.

Each day, there will be 5 test subjects (at least 2 males and 2 females). There will also be four alternate subjects (two males and two females) who will be asked to be available to replace any subjects who withdraw before or during testing. Therefore, a total of 9 subjects will be selected for each test day.

Test Subjects and Alternate Subjects
If you agree to participate in testing, and satisfy all the requirements noted in this consent form, you may be randomly chosen (by chance) to take part in the study as either a test subject or an alternate subject. The first two males and first two females, and another subject of either gender will be test subjects; another two male and two female volunteers will be alternates for each test day. Each subject will be assigned a code number in the study. Subjects will be identified by code number, rather than by name, in all study documentation.

The alternate subjects will replace any test subjects who withdraw from the test. Alternate subjects will also replace any test subject who is not attractive enough to mosquitoes to continue participating in the study. If you are chosen as an alternate, you will need to arrive at i2L's laboratory at the same time as the test subjects on any scheduled test days. If all the test subjects of your gender are present and are attractive enough to mosquitoes to continue participating in the study, you will be allowed to leave i2L and compensated for your time. You should know whether you will need to replace a test subject within approximately 2 hours

after arriving at the test site. If test subjects withdraw later in the test day, i2L will contact alternates to determine if they can return to the lab to participate in the study.

Training Session
i2L Research will host a training session to help you understand what will occur during the study. If you have not previously participated in the study will need to take part in a training session no more than 4 weeks before your first test day. If you choose to participate in up to two test days and the second test day is more than four weeks after your training session, you will be required to attend another training session. The training session will take about 2 hours. During this session the following will occur:

1. When you arrive, you will be asked to show a driver's license, passport, or other valid identification. You will be given time to read the Informed Consent Document (ICD).
2. The trainer will provide a brief outline of the study including its purpose, your potential role in the study, and the potential length of the study on any given test day. The trainer will also tell you what pesticide will be used and how it works, and the risks of participation and how they will be minimized. The trainer will also explain the criteria for being included in or excluded from the study.
3. You will be shown how the fabric will be applied to your arm for the testing, and how to position your arm for testing. The trainer will explain the procedures of each 15-minute exposure to mosquitoes and give a step-by-step demonstration.
4. The trainer will discuss and answer any questions or concerns about the study.
5. The trainer will tell you that the Study Director will be available after the training session if you need to speak to him or her in private about any aspect of the study.
6. The trainer will ask you a few questions to ensure that you are aware of the details of the study and your role in it before you sign the ICD.
7. If you meet the requirements for participation and agree to participate in the study, you will be asked to sign the ICD. You will receive a copy of the signed ICD and copy of the testing schedule.
8. The trainer will recommend that you bring your own form of entertainment (book, DVD player, computer, etc.) to minimize anxiety and potential boredom during testing procedures. The researcher will have drinks (e.g., bottled water, soft drinks, etc.) and snacks available for subjects during the study day. You can bring their own lunch to consume during a 30-minute lunch break which will overlap with one of the 10-minute breaks between test periods
9. The trainer will provide you with the Study Director and on-call nurse's contact information (name, email, and phone number) to field any follow up questions. This information is on the first page of this ICD.
10. Female participants will be notified that they will be required to undergo pregnancy testing at the beginning of each testing day.

Commented [AM1]: Per Section 2.25 #7

Study Design
On each test day, each subject will have up to two different permethrin-treated fabrics placed on each of their arms during each test period. Each fabric will have been washed 50 times, 75 times, 100 times, or not at all. In addition, you will do a test with a control fabric that does not contain permethrin. The study measures how each type of treated fabric protects against the bites of mosquitoes. The types of mosquitoes that will be used in the study are the *Aedes*

aegypti mosquito (also called yellow fever mosquitoes) and the *Anopheles quadrimaculatus* mosquitoes (also called common malaria mosquitoes). You may participate in testing with one or both types of mosquitoes.

Study Procedures

When you arrive at the lab on each test day, you will be asked to provide a valid form of identification.

i2L staff will verify that you have read and signed this consent form prior to any study procedure being done.

At the beginning of a test day, you will wash your arms using a gentle, unscented soap and dry them thoroughly with a paper towel before any fabric is wrapped around your arms.

Untreated control test

After you have washed and dried your arms, a technician will wrap an untreated piece of fabric around your forearm from wrist to elbow. The fabric will be secured with surgical tape. The fabric will need to be wrapped tightly enough that mosquitoes can bite through it; however, staff will make sure the fabric is not so tight that you are uncomfortable. You will also wear two pairs of nitrile gloves to protect your hands against mosquito bites. The technician will use tape that mosquitoes cannot bite through between the glove and the treated fabric to make sure no skin is directly exposed to mosquitoes.

Once the untreated fabric is on your arms, you will be taken to i2L's room where the mosquitoes are located. We call this room the test chamber. You will sit in a chair in front of two cages that will contain *Aedes aegypti* mosquitoes and/or *Anopheles quadrimaculatus* mosquitoes. First, a test will be done to make sure that you are attractive to mosquitoes. A staff member will assist you in inserting one of your arms into each cage.

There will be a bar inside each cage on which you can rest your hands. You will keep your arms inside the cages for 60 seconds. A staff member will count how many mosquitoes land on your arm during this time. The staff member will also tell you to shake your arm periodically to prevent mosquitoes from probing or biting. If at least 10 mosquitoes land within the 60 seconds you may proceed with the study. If not, you will not be eligible to continue in the study. You will be paid for your time and able to leave. Once your attractiveness to mosquitoes is confirmed, your arms will be placed into the cages containing the same mosquitoes used during the 60 second attractiveness test. You will keep your arms inside the cages for 15 minutes, allowing the mosquitoes to bite your forearm through the fabric.

After 15 minutes, a staff member will assist you in removing your arms from the cages.

After you have completed the steps described above, you will remove the untreated fabric from your arms, with assistance if needed. i2L USA staff will examine the mosquitoes and count how many bit you. The number of bites you receive through the untreated fabric will determine whether you can continue to participate in the study. You must receive at least 20 bites on each arm. If you do not receive enough bites you will not be able to continue participating in the study. You will be paid for your time and able to leave.

Treated fabric tests
If you receive enough bites to continue, you will be brought back to the lab. You will be asked to wash your arms with unscented soap and dry. Then up to two permethrin-treated fabrics will be placed on your arms, one fabric sleeve on each arm, in the same way as the untreated fabric.

Once the treated fabrics are on your arms, the gloves are on your hands, and tape covers any skin that might be exposed in the test cage, you will be taken to the test chamber. You will follow the same procedures for putting your arms into cages of *Aedes aegypti* and/or *Anopheles quadrimaculatus* mosquitoes for 15 minutes.

You will be asked to complete this process up to three times (in addition to the untreated control procedure). In between each test, you will be asked to wash your arms with unscented soap and dry.

Restrictions
You must avoid alcohol, moisturizers, nicotine, and fragrance products (e.g. soap, perfume, cologne, hair spray, lotion, antiperspirant/deodorant, etc.) for at least 24 hours before and during the test.

Discomfort and Hazard/Risks
Allergic reactions or irritated skin resulting from permethrin-treated fabric and exposure to biting mosquitoes are risks associated with participation.

The fabric placed on your arms will be treated with permethrin, a commercially-available pesticide that is commonly applied to skin and clothing as a spray to prevent mosquito bites. The maximum concentration of permethrin you will be exposed to is 1.25 g/m^2, or approximately 0.52%, which is similar to the amount found in many mosquito repellents you can buy at the store. You should avoid contact with eyes. It's possible that slight irritation to the skin of your forearms could occur. If you have a reaction to the treated fabric, you must inform i2L staff immediately. You will be removed from the study and/or given medical attention, if necessary.

You will receive many mosquito bites during the testing. You should receive the majority of the bites during the untreated control test. The permethrin-treated fabric should provide some protection from mosquito bites. Some people may develop small, itchy, light swelling, transient markings from mosquito bites. i2L will provide over-the-counter, non-prescription anti-itch gel or cream (e.g. hydrocortisone) after the completion of the study if you need it.

You may also notify the Study Director or other staff member at any time if you have become uncomfortable due to the mosquito bites and want to withdraw from the testing.

The mosquitoes used in this test have been raised in the laboratory. They are certified to be disease-free~~,~~ and have not been exposed to human blood sources. Since mosquitoes used during the preliminary attractiveness test are not allowed to probe or bite they will be reused for the

same test with an alternate. No other mosquitoes will be reused during the test. Completely new mosquitoes will be used every time you insert your arm into a cage for an exposure period. After each exposure period, mosquitoes that may have bitten you will be removed. Therefore, there is no potential for you to get a disease from the mosquito bites.

You may experience some irritation from the application and removal of the surgical tape. Staff will use the least amount of tape necessary to protect your skin from mosquito bites. If you want, staff can assist you with taking off the tape. If you do experience irritation from the tape, after completion of the study you can use a soothing or antibacterial ointment on the area until it heals.

There are non-physical risks associated with taking part in this study, such as the risk of accidental disclosure of your personally identifiable information. To help maintain confidentiality, only subjects' code numbers will be used on data sheets. Your name will not be included in the data sheets or study report.

Unknown Risks
In addition to the risks listed above, there may be unknown or infrequent risks and risks that cannot be predicted associated with the use of the permethrin-treated fabrics.

No Participation by Pregnant or Nursing Women
Federal regulations (40 CFR §26.1203) do not permit human research studies to be conducted on pregnant or nursing women. As described earlier in this consent form, if you are a female, you must take a pregnancy test using an over-the-counter test (provided by i2L) at the i2L facility. You will be required to take the pregnancy test at the start of each test day in which you participate.

Compensation for Participation
Training session: If you took part in a training session, you will be paid $30 for each training session, regardless of whether or not you are selected to participate in the study afterward. Potential test subjects that choose to withdraw or are asked to withdraw from the training session will still be paid $30.00 for attending all or part of each training session.

Test subjects: For each test day you participate in, you will be paid $104 (equal to $13 per hour) for any length of participation up to eight hours with some exceptions. In the unlikely event that a test day goes beyond eight hours, you will be paid an additional $19.50/hour (rounded up to the nearest hour) for the overtime hours.

Alternates: If you are an alternate, you will be paid $50 for each day of participation that you are not needed to replace a test subject. If you need to replace a test subject, you will be paid at the rate specified for test subjects above.

Payment schedule: Payment is provided by check on the 15th or on the last day of the month. Checks will be mailed or hand-delivered to subjects at the lab.

Exceptions:

If i2L asks you to withdraw from the test (e.g. if you do not receive the necessary number of bites during the first testing phase), and you have followed all of their directions, or if you need to withdraw early because of a health-related or emergency reason, you will receive the full payment for subjects ($104). This will not affect payment for any previous test days you have completed.

If i2L asks you to withdraw from the test because you have not followed their directions or if you choose to withdraw from testing early on a test day for a non-health related or non-emergency reason, full payment will not be made if you participate for less than eight hours. Instead, you will be paid for the number of hours you participated (rounded to the nearest hour) at a rate of $13.00 per hour. This will not affect payment for any previous test days you have completed.

Costs
There will be no charge to you for your participation in this study. Participating subjects will be given over-the-counter, non-prescription topical anti-itch cream or gel (e.g., hydrocortisone) at no cost once study procedures are complete.

Benefits
You will not personally benefit from this study. The benefit to society is the additional knowledge gained regarding how well the permethrin-treated fabrics work in preventing and/or reducing bites from mosquitoes.

Alternative To Participation
This study is for research purposes only. The only alternative is to not participate in this study.

Your Rights
You have been given an opportunity to discuss with i2L personnel any aspects of this document which are not clear to you. You have been informed that your consent must be freely given after you are certain that you understand the nature of the test, its purpose, and the procedure to be used together with the discomforts, risks or other adverse effects you may experience during or after the test. Participation in this study is voluntary. You may refuse to take part in this study or quit at any time without penalty or loss of benefits to which you may be otherwise entitled. You must contact the Study Director or any member of the study team if you wish to stop participating in this study. After you read, and sign to indicate your agreement to participate, you will receive a copy of the signed consent form.

The Study Director or the Study Sponsor can stop your participation at any time without your consent for the following reasons:

- If any condition or circumstance may jeopardize your welfare, such as your experiencing increased risks or adverse reactions.
- If you fail to follow directions for participating in the study.
- If it is discovered that you do not meet the study requirements.
- If the test day or study is cancelled.

New Information

In a timely manner, you will be informed both orally and in writing of any significant new findings discovered during the course of this study which may influence your continued participation.

In Case of Injury
If you are injured as a result of wearing the permethrin-treated fabric or from procedures done for the purpose of this study, Pulcra Chemicals will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third party coverage.

There are no plans to provide other compensation beyond that which is listed in this informed consent document. You will not lose any of your legal rights or release the Sponsor, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

Questions
If you have any questions about this study or suffer a research-related reaction, call i2L at 410-747-4500, or call 202-905-1401 after office hours. There will also be an on-call nurse for non-emergency related questions related to your participation in the study (410-598-7436).

If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, you should write to ~~Advarra~~ Schulman IRB, 4445 Lake Forest Drive – Suite 300, Cincinnati, Ohio 45242, or call toll-free 1-888-557-2472 during business hours Monday – Friday 8:00 a.m. to 6:00 p.m. EST.

If you have a serious reaction to the test material, the study director will tell you what ingredient(s) it contains in addition to the test substance, permethrin. The safety data sheet for the substance will also be provided, upon request.

You do not waive (give up) any of your legal rights by signing this consent form.

Confidentiality
The information obtained from your taking part in this test will be used by i2LResearch USA, Inc. and its sponsor and will become part of a study report. Only subjects' code numbers will be used on data sheets. Your name will not be included in the data sheets or study report. This report will be kept as confidential as possible under local, state and Federal law.

i2LResearch USA, Inc. cannot guarantee that your identity will be kept confidential. The Sponsor, Environmental Protection Agency (EPA), Schulman IRB has the right to review your records. The independent Research Monitor of the study will also have access to these records. If the results of this study are published or presented at meetings, you will not be identified.

Commented [AM2]: Per Section 9.1.3 Study Conduct and Oversight

NOT FOR USE IN CONSENTING SUBJECTS
DRAFT 1 IC TO CLIENT 02/13/18 AM

Closing Statement
You have read the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign this consent form. You will receive a copy of the signed informed consent form. You hereby consent to be a participant in this study.

Signatures
I have read the above information in a language that I understand well. The content and meaning of this information has been explained to me. I hereby voluntarily consent and offer to take part in this study.

_____	_____	_____
Date/Time	Print research participant name	Research participant signature
_____	_____	_____
Date/Time	Print name of person conducting the Informed Consent discussion	Signature of person conducting the Informed Consent discussion

Copy of consent form given to subject on (date) _____ by (initials) _____