EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BLACK FLIES UNDER FIELD CONDITIONS

Data Requirement: OPPTS 810.3700 US EPA

Author: Scott P. Carroll, Ph.D.

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Study Completion Date: 5 April 2010

Performing Laboratory: Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616

Laboratory Project ID: LNX-002

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

Statement of No Data Confidentiality Claims
No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA 10(d) (1) (A), (B), or (C).

Company: LANXESS Corporation

Company Agent: Heather F. Collins

Title: Senior Regulatory Affairs Specialist

Date: 4/5/10

Signature: Heather F Collins

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

Study Compliance for the final Carroll-Loye Biological Research Report for LANXESS Corporation entitled: EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BLACK FLIES UNDER FIELD CONDITIONS

This study meets the requirements of U.S. EPA Good Laboratory Practice Regulations; Pesticide Programs (40 CFR 160).

Scott P. Carroll, Ph.D. — 5 April 2010
Study Director — Date

Heather F Collins — 4/5/10
Sponsor and Study Submitter — Date
Heather F. Collins
Senior Regulatory Affairs Specialist
LANXESS Corporation

Carroll-Loye Biological Research Personnel for Study LNX-002:

Scott Carroll, Ph.D.
Study Director – Oversight of the study, data analysis and interpretation, report authoring.

William K. Johnson, M.S.
Laboratory Director – Managing the application and observation technicians, preparing Test Materials for application, application of test materials, data recording and entry.

Shawn B. King, M.S.
Director of Operations – Managing and assisting other staff, logistics, communicating with QAU, report editing and production.

Yoelia Perez, B.S.; Ralph Washington Jr., B.S.; Warren Jones
Application and Observation Technician – Application of test materials, guiding and observing subjects during field exposures, observing LIBe events and reporting to the Laboratory Director.

William Donahue, Ph.D.
Quality Assurance Unit.

TABLE OF CONTENTS

QUALITY ASSURANCE STATEMENT

Carroll-Loye Biological Research, GLP study for LANXESS Corporation, Protocol Number LNX-002 Entitled "Efficacy Test of KBR 3023 (Picaridin;Icaridin) – Based Personal Insect Repellents (20% Cream and 20% Spray) with Black Flies under Field Conditions" was inspected during various stages of the study. The data presented in the final report represent an accurate record of the raw data and the experimental findings. Records of results of facility inspections, study and final report audits are kept on file at Sierra Research Laboratories. The phases of the study inspected, dates and the findings were reported to the study director and management is as follows:

Phase Inspected	Date	Description
Protocol Review	19 March 2010	Protocol Review
In-Life Inspection and Audit	20 March 2010	Test Day O – Test Substance Application and Efficacy Evaluations in the Field – Data Collection
Letter to Management & Study Director (Verbal at test site)	20 March 2010	Discussion with C-LBR Management & Study Director
Raw Data Audit	19 Mar – 03 Apr, 2010	Audit of Raw Data
Final Report Audit	03 April, 2010	Final Report Audit and QAU Statement

William A. Donahue Jr. 03 April 2010

William A. Donahue, Jr., Ph.D. **Date**
Quality Assurance Unit

Information Summary for Final Report

This black fly repellent study was commissioned by LANXESS Corporation to provide efficacy data for purposes of US/EPA registration. The test materials, based on the active ingredient Picaridin, were KBR 3023 All-Family Insect Repellent Cream (20% Cream) and KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray).

KBR 3023 (Icaridin; Picaridin) is a synthetic repellent developed by the Bayer Corporation using molecular modeling techniques. From more than 800 substances, KBR 3023 showed the best repellent efficacy against a variety of arthropods (Boeckh, et al., 1996), along with desirable attributes regarding safety, low skin penetration, and compatibility with skin and plastic materials. It is now owned by Saltigo GmbH (LANXESS Group) and is managed in the USA by LANXESS Corporation (previously a Division of Bayer Corporation).

Nomenclature. Icaridin (US EPA Registration Name Picaridin, the current common name), was developed under the Code Name KBR 3023 and the registered trade name Saltidin™ (formerly Bayrepel™) and was sold under the Brand name Autan. The chemical name for Icaridin is 1-PIPERIDINECARBOXYLIC ACID, 2- (HYDROXY-ETHYL), 1- METHYLPROPYLESTER. However, the International Nomenclature of Cosmetic Ingredients (INCI) name was given as HYDROXY METHYL ISOBUTYL PIPERIDINE CARB. The product was submitted to US EPA under the common name Picaridin. However, the common name Picaridin was rejected by International Organization for Standards (ISO) as it was not considered a pesticide. The common name Picaridin was also rejected by World Health Organization/International Non-proprietary Name (WHO/INN), but the common name, Icaridin, was accepted by WHO/INN.

The study Protocol was reviewed and approved by Independent Investigational Review Board, Inc., and reviewed favorably by the US Environmental Protection Agency and its Human Studies Review Board, and by the California Environmental Protection Agency.

The KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray) dosage rate of 0.97 μl/cm^2 on arms was taken from the related study

LNX-001 (MRID 47506401). The KBR 3023 All-Family Insect Repellent Cream (20% Cream) dosage rate of 1.94 μl/cm^2 on arms was determined by pooling dosimetry data from studies LNX-001 and LNX-002. Estimated dosing, relative to acute dermal toxicity limit dose in Picaridin (>2000 mg/kg, see MSDS), resulted in Margin of Exposure (MOE) values of 690 for the repellent cream and 1429 for the repellent spray. Both MOE values were deemed sufficient to permit prolonged dermal exposure of the subjects to the test materials during efficacy testing.

Efficacy was measured in a field setting. For each of the two Test Materials, 5 female and 5 male treated subjects, each exposed one treated arm to wild populations of black flies (*Simulium vittatum*) for one minute every 15 minutes until the Test Material failed or until cessation of the test. In addition, two untreated subjects, 1 female and 1 male, exposed untreated arms in the same manner coincidentally with treated subjects as an assay for black fly biting pressure. Both controls experienced landings with intent to bite (LIBes) within one minute of exposure throughout the test, indicating black flies were actively foraging and suitably challenging for the efficacy trial.

Under field conditions, the repellent formulations provided substantial and prolonged protection against the black fly species (*Simulium vittatum*). Mean Complete Protection Time (CPT)(±sd) for KBR 3023 All-Family Insect Repellent Cream (20% Cream) was 9.9±2.0 hours (range 6.23 to 11.58 hours). Mean CPT for KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray) was 9.9±1.5 hours (range 6.88 to 11.43 hours).

In summary, the data indicate that LANXESS Corporation KBR 3023 All-Family Insect Repellents at 20% Picaridin concentration provided unusually long periods of Complete Protection against the black fly species *Simulium vittatum*.

1) Objective

The objective is to determine the duration and efficacy of the picaridin-based LANXESS Corporation insect repellent products KBR 3023 All-Family Insect Repellent Cream (20% Cream) and KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray) when applied at a typical consumer dose, in repelling wild populations of the black fly species (*Simulium vittatum*).

2) Protocol Reference

- Carroll-Loye protocol ID number and title: LNX-002, 'Efficacy test of KBR 3023 (Picaridin; Icaridin)-based Personal Insect Repellents (20% Cream and 20% Spray) with Black Flies under Field Conditions.'
- IRB: Independent Investigational Review Board Inc., Plantation, FL.
- IRB Approval date for protocol/Informed Consent Form: 18 Aug 2009.
- Human Studies Review Board review date for protocol: 25 Jun 2009.
- California Environmental Protection Agency approval: 14 Sep 2009.
- Amendment 1, 13 August 2010, provides for the collection and analysis of additional dosimetry data on the Cream 20% repellent product and includes changes to the Protocol and consent form language as needed regarding subject consenting, number of subjects recruited, and details of subject participation. It also includes changes to Protocol details as appropriate to focus the field efficacy test on black flies as a specific target insect for repellency challenge, including frequency and duration of subject exposures and the addition of an assay of subjects' attractiveness to the target insects. The Amendment is given in Appendix 8.
- Deviations from the Protocol and their consequences are given in Appendix 8. The deviation involved the inadvertent use of an older version of the data capture (recording) form for repellency data which was printed out and used at the field site instead of the intended version as provided in Amendment 1 of 13 August 2009.

3) Test Materials

Hereinafter, the Cream 20% picaridin repellent product is referred to as 'Cream' and the Spray 20% picaridin repellent product is referred to as 'Spray'. Table 1 summarizes information about the test material(s) relevant to this study.

Table 1: Test Materials as referred to in this Protocol:

	Cream 20%	Spray 20%
Test Material name (Picaridin conc.)	KBR 3023 All-Family Insect Repellent Cream (20%)	KBR 3023 All-Family Insect Repellent Spray (20%)
Manufacturer	LANXESS Corporation	LANXESS Corporation
Lot Number/Batch ID	XKOC 00712	XKOC 00331
Manufacturing Standards Applied	Good Manufacturing Practice standards, with records available to EPA.	Good Manufacturing Practice standards, with records available to EPA.
Transport	Commercial Courier, express, insulated container	Commercial Courier, express, insulated container
Chain of Custody	Documented	Documented
Specific gravity	0.98	0.96
Delivery system	Lotion	Pump Spray
Active ingredient(s) (%)	Picaridin 20%	Picaridin 20%
Inert ingredients	Proprietary, available to US EPA	Proprietary, available to US EPA
Stability	Stable	Stable
Storage conditions specified	Room temperature, max 30° C (86° F)	Room temperature, max 30° C (86° F)
Storage conditions applied	Locking, closed cabinet at room temperature (19-23°C) protected from light and moisture sources	Locking, closed cabinet at room temperature (19-23°C) protected from light and moisture sources
Cosmetic properties	White cream	Clear solution
NOAELs for Picaridin	NOAEL = 200 mg/kg (dermal); 308 mg/kg (oral)	NOAEL = 200 mg/kg (dermal); 308 mg/kg (oral)
Irritation and sensitization class	(Picaridin) No irritant or sensitizing potential	(Picaridin) No irritant or sensitizing potential
Hazard label requirements	Substantial but temporary eye injury. Do not get in eyes. Wash thoroughly with soap & water after handling, returning indoors, and before eating, drinking, chewing gum, or using tobacco. Discontinue use and consult a doctor if irritation or rash occurs; Flammable.	Moderate eye irritation, avoid contact with eyes or clothing, wash thoroughly with soap & water after handling, returning indoors, and before eating, drinking, chewing gum, or using tobacco. Flammable.
Reference materials	Sample labels, Safety Data Sheets, and Toxicology documents in Appendix 7, page 112-161	

4) Methods

a) Test Sites and Dates

We measured average subject application rates of the test materials (dosimetry) in order to determine the dose of the cream repellent to be applied in the repellency phase of the study. Dosimetry data were pooled with data reported in related study LNX-001 (MRID 47506401).

Dosimetry testing was conducted in the Arthropod Behavior Laboratory at Carroll-Loye Biological Research on 26–30 September 2009.

Field tests of repellent efficacy were conducted at one field site at Metropolitan Water District's Gene Facility in southeastern California. The site (Appendix 9) was chosen based on black fly and other biting insect reconnaissance by the Study Director two weeks before the anticipated test dates. Black flies were the only flying arthropod pest of humans present at the site during reconnaissance. The site was a relatively open landscape of Mojave desert shrub and herbaceous plants with several paved roads and small buildings as well as irrigated hedgerow plantings that moderated wind motion throughout the test day. Nearby domestic horses and wild burrow populations support the abundance of black flies on the site.

b) Environmental Conditions

Ambient temperature (°C), relative humidity, light intensity (lux), wind speed (mph, 10 minute average) were measured at approximately 1-hr intervals during the field efficacy test (Appendix 5). Skies were completely free of cloud cover for the duration of the test. Test Material storage temperature and humidity ranges were noted for both phases of the test, as were temperature and humidity ranges during handling for the efficacy phase of the test (Appendix 7).

c) Human Study Subjects

A total of 25 subjects (20 treated, 2 untreated, 3 alternates) participated in the efficacy phase of the study. 15 treated subjects participated in the dosimetry phase of the study. All subjects were selected randomly from a pool of 119 subjects. Their demographics are described in Table 2.

Table 2. Demography of test subjects

	Pool	Participated in Efficacy Testing (including Controls, excluding Alternates)	Participated in Efficacy Testing (including Controls and Alternates)	Participated in Dosimetry	All Subjects
Male	*52%*	50	52	47	51
Female	*48%*	50	48	53	49
Caucasian	*72%*	73	64	80	66
Asian	*11%*	9	8	7	8
Hispanic	*9%*	9	12	13	14
African-American	*3%*	0	8	0	6
Middle-Eastern	*5%*	9	8	0	6

In the efficacy phase, for each of the two Test Materials, 5 female and 5 male treated subjects, each exposed one treated arm to wild populations of black flies for one minute every 15 minutes until either Test Material failure or cessation of the test. In addition, two untreated subjects, 1 female and 1 male, exposed untreated arms in the same manner coincidentally with treated subjects as an assay for black fly biting pressure. A sample size of ten subjects was chosen to give a reasonably large statistical population size while avoiding exposing too many individuals to the minor but present risks associated with exposure to biting arthropods.

In the dosimetry phase, 8 female and 7 male subjects applied the Cream 20% repellent product three times each to arms and legs, washing the repellent off between applications and after the final application. Each subject was instructed to apply the repellent to achieve what they perceived to be thorough and even coverage on their own limbs.

All study subjects had the following attributes: they were 18-55 years old, reported themselves to be in good physical condition, were not students or employees of the Study Director, did not believe themselves to be hypersensitive to biting fly bites or phobic of biting flies, completed the consenting process including signing the IRB-approved Informed Consent Form, had not used repellents within 1 day prior to the repellency study, and refrained from using alcoholic beverages or perfumed products or smoking beginning at 9 PM the night before, and during, the test. Females were negative in pregnancy tests conducted immediately before they participated in efficacy testing, and stated that they were not lactating.

d) Black Flies

Black flies of the species *Simulium vittatum* were collected from subjects and from exposure areas during the test. Black flies of this species are not known or suspected to vector human pathogens in the US, though this species is a vector of the serious human disease, onchocerciasis, in Central and South America. Sample black flies were identified by the Study Director using keys and illustrations found in Adler et. al., 2004.

e) Dosage Determination and Margin of Exposure

The Spray dosage rate of 0.97 μl/cm^2 on arms is the mean from the dosimetry analysis reported in related study LNX-001 (MRID 47506401). The Cream dosage rate of 1.94 μl/cm^2 was determined by pooling data from study LNX-001 with additional dosimetry data collected in this study.

The individual subject means for the Cream dosimetry from 10 subjects in related study LNX-001 (MRID 47506401) were combined with the data from the 15 subjects in this study to yield a grand mean to be used as the dosage rate for Cream in efficacy testing. The 15 additional subjects were 8 female (nos. 4, 33, 37, 53, 83, 92, 99, 105) and 7 male (nos. 15, 52, 64, 104, 113, 114, 115) subjects. To determine dosage, we measured lower limb surface area for individual subjects based on the length and a set of four circumferences taken from each limb. The amount of Cream applied to limbs was quantified in a series of three applications (as in Pump Spray

sampling). The Test Material was contained in cream (lotion) dispensers, typical of consumer repellent products, for use by the subjects. The amount applied was the weight difference in the dispensing tube before and after application (measured on a Sartorius GC 2502 balance). These procedures are detailed in the Study Protocol Amendment 1 (Appendix 8).

Estimated dosing based on Spray and Cream grand means, relative to the acute dermal toxicity limit dose of Picaridin (>2000 mg/kg, MSDS), yielded Margin of Exposure (MOE) values that were deemed sufficient to permit prolonged dermal exposure of the subjects to the test materials during efficacy testing.

In efficacy testing, applications were made volumetrically, based on the limb surface areas of each subject and the specific gravity of the repellent (derived from density given in the Safety Data Sheets, Appendix 7). Despite the individual variation in dosing rate inevitable in actual consumer use, we used the same, average dosing rate in all subjects. The chief advantage of this approach is that it may guard against early failures in subjects who might otherwise "under-dose" for the test conditions. In consumer use, those who under-dose might be expected to re-apply repellent when protection fails, and to perhaps learn about adequate dosing from experience. That accommodation cannot take place in standard repellent efficacy trials. Consequently, the average values from dosimetry studies were chosen as a reasonable approximation of sensible dosing behavior. However, a consequence of employing values from dosimetry is that the dosing rate differed between the products.

f) Test Materials and their application (see also Appendix 3 and Appendix 7)

Test Materials were received at CLBR on 24 August 2009, with Chain-of-Custody documented. They were stored at the Carroll-Loye Offices in a closed cabinet at room temperature (19-23°C) within specifications provided by the sponsor. Temperature and relative humidity minimums and maximums experienced by the Test Materials during transport to the field site until time of application were recorded, as were Test Material storage temperature and humidity ranges. Test Material custody and storage

condition data, sample labels, Test Material container labels, Certificates of Analysis, Safety Data Sheets, and the toxicology profile for KBR 3023 are given in Appendix 7.

For blinding, the two Test Materials were coded 'A' and 'B' by the Laboratory Manager, who was then prohibited from judging LIBe events. Sealed physical and password-protected electronic keys to the Test Material identities were maintained for the duration of the repellency trial, to be opened by the Study Director only after the completion of the test or if needed for medical or legal reasons. This moderate level of blinding security is deemed appropriate for a test in which the performances of the test materials are not specifically being compared with each other.

Treatments were stratified by gender and allocated at random within each gender excepting minor adjustments needed to constrain the number of subjects treated with each Test Material to 10. Individual doses were prepared for each subject on the basis of the surface area of their forearm skin. Before repellent was applied, subjects washed their forearms carefully with a fragrance-free cleanser in tap water, rinsed them with tap water and then rinsed them again with 35% ethanol in water, and then dried them with clean cotton towels. Repellent was then applied by CLBR technicians and staff, using 1 ml syringes (0.01 ml measurement increment) and one fingertip in a surgical glove, to spread the material as evenly as possible. For subjects with arms large enough to require doses exceeding 1 ml, the total dose was measured into, and dispensed from, two syringes.

The treatment allocation and dosing are given in Appendix 3.

g) Exposure to Black Flies

During exposure in the field, all subjects wore head nets and surgical gloves in addition to Tyvek coveralls, and each carried a small artist's paintbrush to assist in the removal of biting flies. Treated subjects were partnered into groups of two, and each subject moved in a group of others from the shelter to the exposure area, where all were equally exposed to resident black flies. Each member of a partner pair was instructed to monitor the front of their own exposed limb and the back

of the exposed limb of their partner for biting fly landings with intent to bite (LIBes) during one-minute periods of exposure to black flies (a "buddy system"). Exposures were as follows:

- Attractiveness assay: all subjects (including Controls) exposed an untreated arm once for less than 1 minute before receiving a black fly LIBe to confirm each subject's attractiveness to the target insect
- Untreated Subjects (Controls): exposures to assay for biting fly foraging activity just prior to treated subject exposures for repellent challenge
- Exposure interval, all subjects: 15 min.
- Exposure duration per interval, all subjects: 1 min.
- Time between application and first exposure: varied by individual; approximately 2.5 hours
- 11 female subjects (10 treated, 1 untreated), numbers 20, 28, 35, 39, 40, 60, 81, 84, 85, 92, 105
- 11 male subjects (10 treated, 1 untreated), numbers 5, 12, 41, 52, 56, 61, 71, 86, 88, 102, 104

Hand-held timers and a clock were used to ensure adherence to specified protocols for exposure duration and frequency. Technical personnel monitored the results of each exposure in the subject group, and were equipped with mechanical aspirators to remove mosquitoes from subjects if mosquitoes were present. Other than black flies, no air-borne biting insects were observed at the field site during the test. All LIBes were reported to the Laboratory Manager who recorded the events by subject code and the clock time of exposure interval. At the end of most exposure periods, subjects moved into a protective screen house. Brushes that might have inadvertently contacted a Test Material in "shooing" or removing a LIBeing black fly from the treated area were removed from the test.

Ambient LIBe pressure was assessed by two experienced subjects on the same schedule as that for repellent exposure. Each of these negative control subjects was attended by two assistants who used artist's paintbrushes to quickly remove any LIBeing black flies. Each control exposed one limb then covered that limb as soon as a LIBe occurred.

A stopping rule for exposures was invoked when a subject experienced a LIBe following another in either of the two prior exposure periods. Subjects

were withdrawn from further exposure to biting insects when such an event occurred. All exposures were terminated at dusk when biting fly activity declined below the level needed to challenge the repellent.

h) Data recording

Typically, the Laboratory Manager recorded LIBe data for each subject on a data sheet after each one-minute exposure. When subjects spent more than one exposure interval away from the shelter, data were reported verbally to the Laboratory Manager by the observation technicians upon their return to the shelter.

i) Data Analysis

Dosimetry data were entered into an Excel 2004 (Macintosh) spreadsheet for calculations of surface area and dosing means. Those means were double-checked with a handheld calculator. All descriptive statistics were generated with the software 'SAS JMP' Version 5.0.1.2 (SAS Institute, Cary NC).

We calculated Complete Protection Time (CPT) as the interval between application and the First Confirmed Landing with Intent to Bite (FCLIBe). The FCLIBe was defined as the first LIBe that was followed by another within one-half hour, i.e., within either of the subsequent two exposure periods. This measure is analogous to that of First Confirmed Landing, which is commonly used in measures of repellency to blood-feeding flies including mosquitoes. CPT measured in this way gives a single time value for each subject. Mean CPTs were calculated across all 10 subjects for each Test Material, and are presented herein with standard deviations and 95% confidence interval information. Kaplan-Meier CPT survival plots were also generated. Kaplan-Meier median CPT values were calculated for both Test Materials. In addition, we estimated the time until 25% failure for each Test Material.

5) Results

a) Dosimetry (see also Appendix 3)

For All-Family Insect Repellent 20% Cream, the amount applied was measured as the mass of the material leaving the dispensing vessel (plastic squeeze bottle). The Cream dosing rate was based on a specific gravity of 0.98 (i.e., 0.98 kg/liter).

In this study we supplemented Cream dosimetry data from the related study LNX-001 (repellent efficacy against mosquitoes) with data from an additional 15 subjects. Data from both studies are given in Table 3. Raw data and data entry forms, using "lotion" to describe the Cream product, are given in Appendix 3.

The grand mean (±sd) of arm mean doses for Cream was 1.90±1.11 mg/cm^2. The grand mean (±sd) of leg mean doses was 1.74±1.17 mg/cm^2. For efficacy testing, arms were treated, based on the tendency of the black fly population to attack the upper body. Accordingly, dosing rates for arms were based on the grand means of arm dosimetry. Mean grams per subject for efficacy testing (i.e., on each subject's single treated arm) are given in Table 4.

For All-Family Insect Repellent 20% Spray, as indicated in the Methods sections, dosing was based on the dosimetry results of the related study LNX-001. The grand mean (±sd) of arm mean doses for Spray was 0.93±0.39 mg/cm^2. Mean grams applied for efficacy testing are given in Table 4.

Table 3. KBR 3023 All-Family Insect Repellent Cream (20%) dosimetry: mean mg applied per cm^2 by 15 subjects from study LNX-002 and 10 subjects from study LNX-001 (MRID 47506401). Each subject applied repellent to each limb three times. Means for each limb are calculated from those three values.

Subject code	Left arm	Right arm	Arm mean	Left leg	Right leg	Leg mean
Study LNX-002						
4	1.80	1.93	1.87	1.18	1.11	1.15
15	2.65	2.77	2.71	3.66	2.40	3.03
33	1.60	1.68	1.64	1.25	1.33	1.29
37	0.97	0.78	0.88	0.97	1.14	1.06
52	1.10	1.14	1.12	1.47	1.21	1.34
53	1.33	1.28	1.31	1.64	1.67	1.66
64	2.39	2.52	2.46	2.22	2.22	2.22
83	1.13	1.16	1.15	0.77	0.70	0.74
92	1.70	1.78	1.74	0.96	1.12	1.04
99	0.80	0.69	0.75	0.52	0.63	0.58
104	1.48	1.41	1.45	1.23	1.32	1.28
105	0.94	0.85	0.90	0.71	0.85	0.78
113	1.10	0.94	1.02	1.64	1.57	1.61
114	1.99	1.88	1.94	1.08	1.07	1.08
115	2.01	1.91	1.96	1.48	1.39	1.44
Study LNX-001						
6	1.30	1.59	1.45	1.86	1.80	1.83
13	2.07	2.00	2.04	1.60	1.60	1.60
20	2.39	2.79	2.59	2.21	2.03	2.12
24	2.01	2.22	2.12	2.22	1.97	2.10
47	5.62	6.27	5.95	6.72	5.82	6.27
60	4.24	3.69	3.97	3.74	3.20	3.47
63	2.40	2.53	2.47	2.24	1.90	2.07
67	1.56	1.44	1.50	1.73	1.82	1.78
77	1.07	1.22	1.15	0.69	0.67	0.68
82	1.33	1.48	1.41	1.22	1.41	1.32

Margins of Exposure (MOEs) relative to the acute dermal toxicity limit dose of Picaridin (>2000 mg/kg, see MSDS) were estimated for the chosen dosage rates (Table 4). The model target subject was a 70 kg adult. The resulting MOE values were deemed sufficient to permit risking prolonged dermal exposure of subjects to the test materials during efficacy testing.

Table 4. Margin of exposure estimation for the Test Materials: mean grams of test material and active ingredient to be applied based on efficacy test subject limb surface areas, and the resulting exposure values.

Test material	Test Material applied (g)	Picaridin applied (mg)	Rate in 70 kg human (mg/kg)	Margin of exposure
KBR 3023 All-Family Insect Repellent Cream (20%)	1.01	202	2.9	690
KBR 3023 All-Family Insect Repellent Spray (20%)	0.49	98	1.4	1429

b) Environmental Conditions

Efficacy data were collected under suitable environmental conditions. Environmental conditions during field exposures are summarized in Table 5. Environmental data are detailed in Appendix 5.

Table 5. Summary of temperature, relative humidity, light, and wind speed conditions at the field site on the test day.

Variable	Range
Temperature	17-25 °C
Relative humidity	22-33 %
Light intensity	7-12,450 lux
Wind speed(10min ave.)	0.5-2.2 mph

Test Materials were stored as specified, with measured minima and maxima of 19°C and 23°C temperature, and 30% and 50% relative humidity (RH). Conditions during transport to the field study area and preparation of dosages ranged from 21°C / 24%RH to 24°C / 65%RH. Additional details are given in Appendix 7.

c) Attractiveness Screening and LIBe Rate on Untreated Arms

All subjects experienced black fly LIBes on untreated arms during the initial 1-minute attractiveness screening. Likewise, both control subjects received at least one black fly LIBe within 1 minute of exposing their untreated arm throughout the duration of the test.

d) Efficacy: Influence of Test Material on Probability of Black Fly LIBes

To better understand the results presented in this section, note that no statistical comparisons between the two Test Materials are made or inferred in this report.

Subjects collected data until a Test Material failed against the black flies, or the test was formally concluded at 1900 hours due to the typical cessation of black fly activity at the onset of darkness.

In every case, black flies were strongly affected by the Test Materials, landing with intent to bite in only a minority of intervals (Tables 6-9, Figures 1 and 2; raw data are given in temporal sequence in Appendix 4). Despite the comparatively long duration of exposure after application in this study, only 5 of the 10 subjects testing Cream, and 6 of the 10 subjects testing Spray recorded failures. The Kaplan-Meier median values were calculated for both Test Materials (Tables 6 and 8).

Cream Efficacy

Cream protected subjects from black fly LIBes for at least 6.23 hours. The average total number of LIBes per subject was 1.4.

Cream performance statistics are given in Table 6, with individual subject results detailed in Table 7.

Table 6. KBR 3023 All-Family Insect Repellent Cream (20%) efficacy against black flies (*Simulium vittatum*): Mean CPT (hrs)(± sd), CPT 95% confidence interval, Kaplan-Meier (K-M) median CPT, time (*t*) to 25% failure, and mean number of LIBes per subject.

CPT mean (±sd)	95% CI	K-M median	*t* to 25% failure	Mean LIBes
9.9 ± 2.0	8.5–11.4	10.1	9.1	1.4

Table 7. KBR 3023 All-Family Insect Repellent Cream (20%) efficacy against *Simulium vittatum* (black fly): Complete Protection Times (CPTs) in hr (in descending order), whether a Confirmed LIBe (CLIBe) occurred, and number of LIBes per subject.

Subject number	CPT	CLIBe	Total LIBes
40	11.58	No	0
35	11.55	No	0
81	11.52	No	1
61	11.50	No	0
85	11.48	No	0
5	10.08	Yes	3
56	9.28	Yes	3
102	9.08	Yes	3
105	6.95	Yes	2
104	6.23	Yes	2

A Kaplan-Meier survival plot for the repellency of KBR 3023 All-Family Insect Repellent Cream (20%) against *Simulium vittatum* (black fly) is shown in Figure 1. Five subjects received Confirmed LIBes.

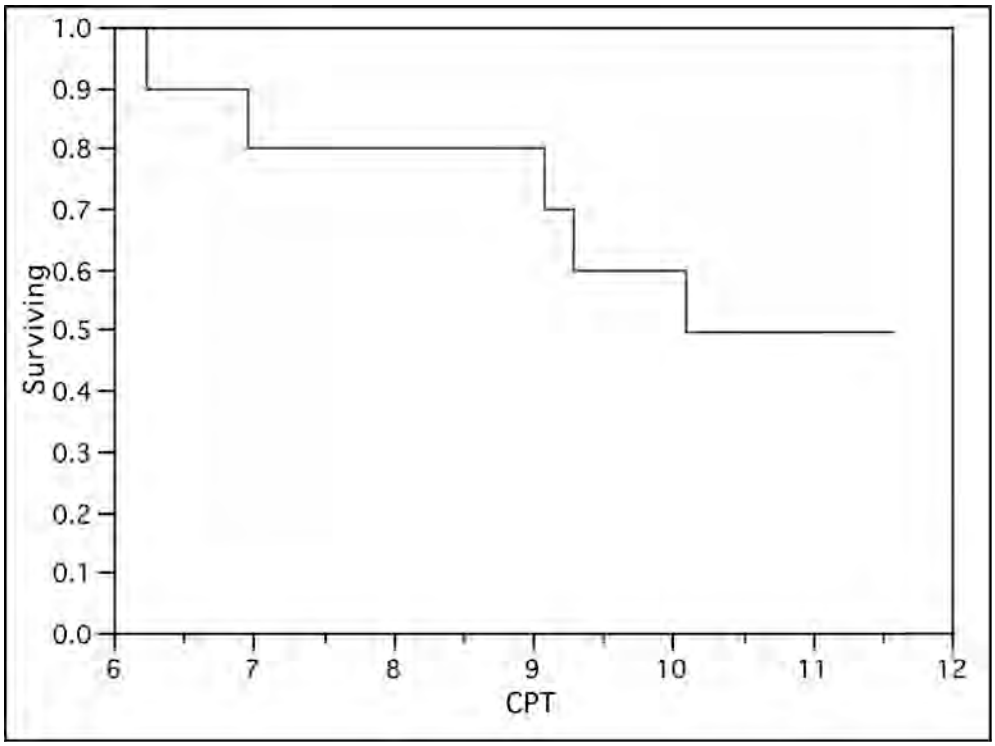


Figure 1. Survival plot of Complete Protection Time (CPT) for KBR 3023 All-Family Insect Repellent Cream (20%) against *Simulium vittatum* (black fly)

Cream protected absolutely from black fly landings with intent to bite for more than 6 hours.

Spray Efficacy

Spray protected subjects from black fly LIBes for more than 6.5 hours. The average total number of LIBes per subject was 1.9.

Spray performance statistics are given in Table 8, with individual subject results detailed in Table 9.

Table 8. KBR 3023 All-Family Insect Repellent Spray (20%) efficacy against *Simulium vittatum* (black fly): Mean CPT (hrs)(± sd), CPT 95% confidence interval, Kaplan-Meier (K-M) median CPT, time (*t*) to 25% failure, and mean number of LIBes per subject.

CPT mean (±sd)	95% CI	K-M median	*t* to 25% failure	Mean LIBes
9.9 ± 1.5	8.8–11.0	9.8	9.1	1.9

Table 9. KBR 3023 All-Family Insect Repellent Spray (20%) efficacy against *Simulium vittatum* (black fly): Complete Protection Times (CPTs) in hr (in descending order), whether a Confirmed LIBe occurred, and number of LIBes per subject.

Subject number	CPT	CLIBe	Total LIBes
41	11.43	No	2
28	11.42	No	0
60	11.42	No	0
92	11.38	No	1
12	9.75	Yes	3
71	9.63	Yes	3
20	9.58	Yes	2
86	9.10	Yes	3
39	8.38	Yes	2
88	6.88	Yes	3

A Kaplan-Meier survival plot for the repellency of KBR 3023 All-Family Insect Repellent Spray (20%) against *Simulium vittatum* (black fly) are shown in Figure 2. Six subjects received Confirmed LIBes.

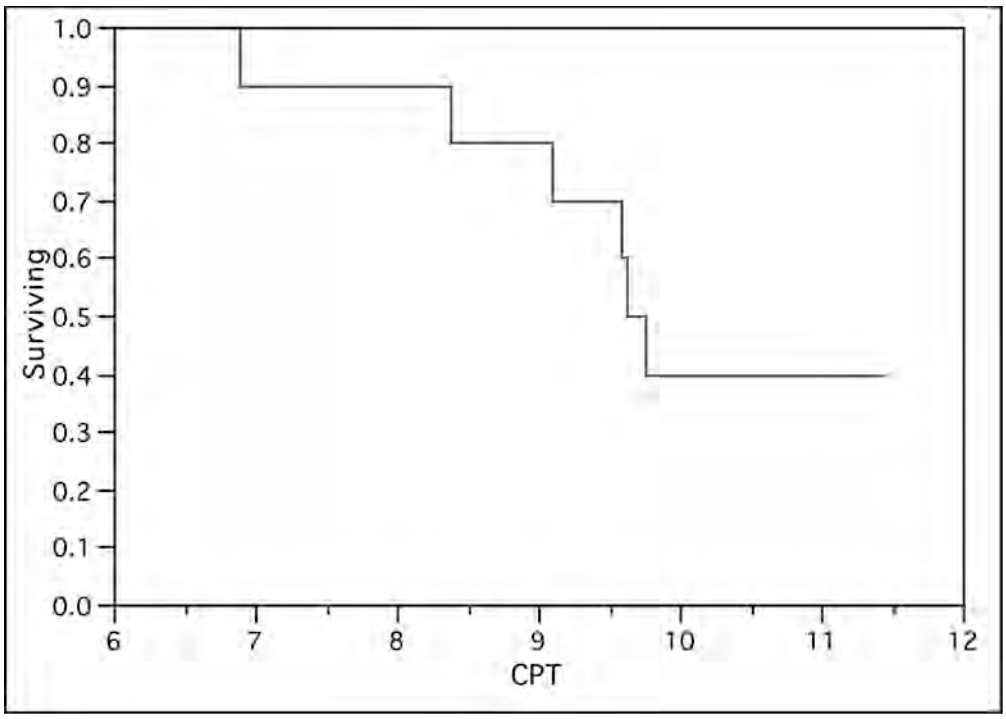


Figure 2. Survival plot of Complete Protection Time (CPT) for KBR 3023 All-Family Insect Repellent Spray (20%) against *Simulium vittatum* (black fly).

Spray protected absolutely from black fly landings with intent to bite for more than 6.5 hours.

Conclusions

Under field conditions, the repellent formulations provided substantial and prolonged protection against the black fly species *Simulium vittatum*. Mean Complete Protection Time (CPT)(±sd) for KBR 3023 All-Family Insect Repellent Cream (20% Cream) was 9.9±2.0 hours (range 6.23 to 11.58 hours). Mean CPT for KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray) was 9.9±1.5 hours (range 6.88 to 11.43 hours).

In summary, the data indicate that LANXESS Corporation KBR 3023 All-Family Insect Repellents at 20% Picaridin concentration provided unusually long periods of Complete Protection against the black fly species *Simulium vittatum*.

Reference Cited

Adler, P.H., Currie, D.C., and Wood, D.M. (2004). The Blackflies (Simuliidae) of North America. Ithaca: Cornell University Press.

Research Subject Tracking Form
(Dosimetry)

Study: LNX-002

Legend: 1 = September 26, 2009; 2 = September 27, 2009; 3 = September 28, 2009; 4 = September 29, 2009; 5 = September 30, 2009; = Measured in previous study; na = Not Applicable

Subject Number	4	15	33	37	52	53	64	83	92	99	104	105	113	114	115
Subject Gender	F	M	F	F	M	F	M	F	F	F	M	F	M	M	M
MSD Sheet(s) Provided	4	4	1	2	2	2	1	1	4	4	5	5	1	3	3
Study Synopsis Provided	4	4	1	2	2	2	1	1	4	4	5	5	1	3	3
Experimental Subject Bill of Rights Completed	4	4	1	2	2	2	1	1	4	4	5	5	1	3	3
Pregnancy Test Advisory (Females)	4	na	1	2	na	2	na	1	4	4	na	5	na	na	na
Informed Consent Form Completed	4	4	1	2	2	2	1	1	4	4	5	5	1	3	3
Limb Measurements Completed	4	*	*	*	*	*	*	*	*	*	*	*	1	3	3
Dosimetry Training Completed	4	4	1	2	2	2	1	1	4	4	5	5	1	3	3
Pregnancy Test Completed	4	na	1	2	na	2	na	1	4	4	na	5	na	na	na
Dosimetry Completed	4	4	1	2	2	2	1	1	4	4	5	5	1	3	3

Research Subject Tracking Form
(Efficacy Test)

Study: LNX-002

Legend:

1 = March 15, 2010
2 = March 16, 2010
3 = March 17, 2010
4 = March 18, 2010
5 = March 19, 2010
6 = March 20, 2010

na = Not Applicable
= Measured in previous study
* Alt. Subj. = Alternate Subject

Study LNX-002: Efficacy Test of KBR 3023 (Picaridin, Icaridin) - Based Personal Insect Repellents (20% Cream and 20% Spray) with Black Flies Under Field Conditions

Subject Number	4	5	12	14	20	24	28	35	39	40	41	52	56	60	61	71	81	84	85	86	88	92	102	104	105
Subject Gender	F	M	M	M	F	M	F	F	F	F	M	M	M	F	M	M	F	F	F	M	M	F	M	M	F
MSD Sheet(s) Provided	2	1	2	2	2	2	2	2	1	2	2	4	5	2	2	5	4	2	2	5	2	2	2	3	3
Study Synopsis Provided	2	1	2	2	2	2	2	2	1	2	2	4	5	2	2	5	4	2	2	5	2	2	2	3	3
Experimental Subject Bill of Rights Completed	2	1	2	2	2	2	2	2	1	2	2	4	5	2	2	5	4	2	2	5	2	2	2	3	3
Pregnancy Test Advisory (Females)	2	na	na	na	2	na	2	2	1	2	na	na	na	2	na	na	4	2	2	na	na	2	na	na	3
Informed Consent Form Completed	2	1	2	2	2	2	2	2	1	2	2	4	5	2	2	5	4	2	2	5	2	2	2	3	3
Limb Measurements Completed	*	1	2	*	2	*	2	2	1	2	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Arthropod Training Orientation Completed	2	1	2	2	2	2	2	2	1	2	2	4	5	2	2	5	4	2	2	5	2	2	2	3	3
Pregnancy Test Completed	6	na	na	na	6	na	6	6	6	6	na	na	na	6	na	na	6	6	6	na	na	6	na	na	6
Positive Result for Black Fly Attractiveness Assay	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Repellent Efficacy Test Day	Alt. Subj.	6	6	Alt. Subj.	6	Alt. Subj.	6	6	6	6	6	Control 1	6	6	6	6	6	Control 2	6	6	6	6	6	6	6

Carroll-Loye Biological Research Study LNX-002
Limb Measurement Data Capture Forms

Clarification Note

Limb measurement capture forms are presented in two groups:
Dosimetry Subjects' forms – Pages 32-46
Efficacy Subjects' Forms (not carried over from Dosimetry) – Pages 47-67

Note that Subject #52 limb measurements appear in both groups as different data capture form scans. For dosimetry, as per protocol specifications, older limb measurements were used (9 Nov 2007), as they were taken within two years of the day the Subject 52 participated in the dosimetry phase of this study. The efficacy phase was conducted after the 9 Nov 2007 limb measurements expired, and thus the subject was re-measured. Subjects 92, 104, and 105 participated in both phases using the same limb measurement data. Subject 4 participated in dosimetry and as an alternate in the efficacy phase. Subjects 14 and 24 were alternates in the efficacy phase whose limb measurement data had expired prior to consenting. Both subjects were thus re-measured and their measurements are reported here.

Limb Measurement Form

Study: LNX-002

Subject number: 4

Date: September 29, 2009

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	19	6.3	14	17	21	21.5	18.38	349
Right forearm	19	6.3	14	17	21	21.5	18.38	349
Left lower leg	32	10.7	20.5	26.5	32	30	27.25	872
Right lower leg	32	10.7	20.5	26.5	32	30	27.25	872

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 15

Date: November 8, 2007

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	23.5	7.8	15.5	17.5	24	27	21	494
Right forearm	23.5	7.8	15.5	17.5	24.5	27.5	21.25	499
Left lower leg	39	13	22	25	33	31	27.75	1082
Right lower leg	39	13	22	25	33.5	31	27.88	1087

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 33

Date: March 21, 2008

Data recorder name: W. K. Johnson

Data recorder signature: WK Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	22	7.3	15	18	20.5	22	18.88	415
Right forearm	22	7.3	15	18	21	22	19	418
Left lower leg	33	11	21	26	32	30	27.25	899
Right lower leg	33	11	21	26.5	32.5	30	27.5	908

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 37

Date: November 9, 2007

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	25.5	8.5	15	17.5	22	23	19.38	494
Right forearm	25.5	8.5	15	17.5	22.5	23.5	19.63	500
Left lower leg	39	13	21.5	26	32.5	30.5	27.63	1077
Right lower leg	39	13	21.5	26.5	33	30.5	27.88	1087

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 52

Date: November 9, 2007

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26	8.7	18.5	23.5	29	29.5	25.13	653
Right forearm	26	8.7	19	24	29.5	30	25.63	666
Left lower leg	32	10.7	23	32.5	41	40	34.13	1092
Right lower leg	32	10.7	23.5	32	41	40.5	34.25	1096

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 53

Date: November 9, 2007

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	22	7.3	15	20	24.5	25.5	21.25	468
Right forearm	22	7.3	15	20.5	24	26	21.38	470
Left lower leg	30.5	10.2	24	31	38	35	32	976
Right lower leg	30.5	10.2	24	31	38.5	35	32.13	980

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 64

Date: November 8, 2007

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	22	7.3	17.5	22.5	29	28	24.25	534
Right forearm	22	7.3	17.5	23	29.5	28	24.5	539
Left lower leg	37	12.3	22.5	28	38	35	30.88	1142
Right lower leg	37	12.3	22.5	28	38	35	30.88	1142

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 83

Date: May 31, 2008

Data recorder name: W. K. Johnson

Data recorder signature: William K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	22	7.3	13	16	21	22	18	396
Right forearm	22	7.3	13	16	21	21.5	17.88	393
Left lower leg	36	12	20	24	30	30	26	936
Right lower leg	36	12	20	24	29.5	29.5	25.75	927

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 92

Date: June 3, 2008

Data recorder name: W. K. Johnson

Data recorder signature: [signature]

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	20	6.7	14	16.5	20	22	18.13	363
Right forearm	20	6.7	14	16.5	21	22.5	18.5	370
Left lower leg	34	11.3	21	28.5	32	31	28.13	956
Right lower leg	34	11.3	21	28.5	32	31	28.13	956

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 99

Date: June 4, 2008

Data recorder name: W.K. Johnson

Data recorder signature: [signature]

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	24	8	16.5	18	23.5	25	20.75	498
Right forearm	24	8	16.5	18	23.5	25	20.75	498
Left lower leg	40	13.3	24	31.5	38.5	35	32.25	1290
Right lower leg	40	13.3	24	31.5	38.5	35	32.25	1290

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 104

Date: June 4, 2008

Data recorder name: W.K Johnson

Data recorder signature: WK Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	24.5	8.2	18.5	23.5	31	31	26	637
Right forearm	24.5	8.2	18.5	25	32	32	26.88	658
Left lower leg	38	12.7	25.5	35	43	42	36.38	1382
Right lower leg	38	12.7	25.5	35	43	42	36.38	1382

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 105

Date: June 4, 2008

Data recorder name: WK Johnson

Data recorder signature: WK Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	23	7.7	16	20	25	25.5	21.63	497
Right forearm	23	7.7	16	20	25.5	26	21.88	503
Left lower leg	35	11.7	22.5	30	36.5	32	30.25	1059
Right lower leg	35	11.7	22.5	30	36.5	32	30.25	1059

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 113

Date: September 26, 2009

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26.5	8.8	17	21.5	28	28.5	23.75	629
Right forearm	26	8.7	17.5	22	28.5	29	24.25	631
Left lower leg	42	14	23.5	29	37.5	34.5	31.13	1307
Right lower leg	42	14	23.5	29	37.5	34.5	31.13	1307

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 114

Date: September 28, 2009

Data recorder name: W. K. Johnson

Data recorder signature: WK John

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	27	9	18.5	22.5	29	29.5	24.88	672
Right forearm	27	9	19	23	29,5	29.5	25.25	682
Left lower leg	42	14	26	34.5	41	36	34.38	1444
Right lower leg	42	14	26	34.5	41	36	34.38	1444

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 115

Date: September 28, 2009

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	25	8.3	17.5	22.5	29	28.5	24.38	609
Right forearm	25	8.3	17.5	22.5	29.5	28.5	24.5	613
Left lower leg	36.5	12.2	24.5	29.5	38	35	31.75	1159
Right lower leg	36.5	12.2	24.5	29.5	38	35	31.75	1159

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 5

Date: March 15, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	24	8	18.5	22	27.5	29	24.25	582
Right forearm	24	8	18.5	22.5	29.5	30.5	25.25	606
Left lower leg	38	12.7	23	29	40	37	32.25	1226
Right lower leg	38	12.7	23	29	40	37	32.25	1226

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 12

Date: March 16, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	23	7.7	17.5	23	29	28.5	24.5	564
Right forearm	23	7.7	17.5	23	29.5	29	24.75	569
Left lower leg	38	12.7	23.5	32	39.5	34.5	32.38	1230
Right lower leg	38	12.7	23.5	32	40	35	32.63	1240

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 14

Date: January 21, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26	8.7	17	19	26.5	27	22.38	582
Right forearm	26	8.7	17	19	27	28	22.75	592
Left lower leg	44	14.7	22	27	36	34.5	29.88	1315
Right lower leg	44	14.7	22	27	36.5	35	30.13	1326

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 20

Date: March 16, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	20	6.7	15	19	23	25	20.5	451
Right forearm	20	6.7	15	19.5	23.5	25	20.75	457
Left lower leg	37	12.3	21.5	29	37.5	34	30.5	1129
Right lower leg	37	12.3	21.5	29	37.5	34	30.5	1129

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 24

Date: January 15, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26	8.7	17	20.5	28	28	23.38	608
Right forearm	26	8.7	17	20.5	28	28	23.38	608
Left lower leg	42	14	24.5	29	39	33	31.38	1318
Right lower leg	42	14	24.5	29	39	33	31.38	1318

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 28

Date: March 16, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	25	8.3	16	19.5	25	26	21.63	541
Right forearm	25	8.3	16	19.5	25	26	21.63	541
Left lower leg	40	13.3	22	33	39.5	36	32.63	1305
Right lower leg	40	13.3	22	33.5	40	36	32.88	1315

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 35

Date: March 16, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	23	7.7	15	19	25	25	21	483
Right forearm	23	7.7	15	19	25	25	21	483
Left lower leg	35	11.7	22	27	39.5	35	30.88	1081
Right lower leg	35	11.7	22	27	39.5	35	30.88	1081

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 39

Date: March 15, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	25	8.3	14.5	16.5	21	23	18.75	469
Right forearm	25	8.3	15	17	21	23	19	475
Left lower leg	39	13	21	27	35	31	28.5	1112
Right lower leg	39	13	21	27	35	31	28.5	1112

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study: LNX-002

Subject number: 40

Date: March 16, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	23	7.7	14.5	16	20	20.5	17.75	408
Right forearm	23	7.7	14.5	17	21	21	18.38	423
Left lower leg	35	11.7	21	25	31.5	30	26.88	941
Right lower leg	35	11.7	21	25	31.5	30	26.88	941

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 41

Date: June 10, 2008

Data recorder name: W.K. Johnson

Data recorder signature: William K. Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	23	7.7	16.5	22	28	28.5	23 75	546
Right forearm	23	7.7	17	22.5	28.5	29	24.25	558
Left lower leg	38	12.7	235	35	40.5	35.5	33.63	1278
Right lower leg	38	12.7	23 5	35.5	41.	35.5	33.88	1287

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 52

Date: January 23, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26	8.7	18.5	23.5	30	29.5	25.38	660
Right forearm	26	8.7	19	24	30	30	25.75	670
Left lower leg	32	10.7	23	32	41	40	34	1088
Right lower leg	32	10.7	23.5	32	41	40	34.13	1092

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 56

Date: June 10, 2008

Data recorder name: W. K. Johnson

Data recorder signature: W. K. Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	24	8	20	23.5	29	30.5	25.75	618
Right forearm	24	8	20	24	29.5	30.5	26	624
Left lower leg	45	15	27	34.5	39.5	37	34.5	1553
Right lower leg	45	15	27	34.5	40	37.5	34.75	1564

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 60

Date: January 20, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	21.5	7.2	14	15.5	19	21	17.38	374
Right forearm	21.5	7.2	14	15.5	19.5	21	17.5	376
Left lower leg	34	11.3	20	25	31	30	26.5	901
Right lower leg	34	11.3	20	25.5	31.5	30.5	26.88	914

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 61

Date: June 10, 2008

Data recorder name: W.K. Johnson

Data recorder signature: [signature]

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	25	8.3	19	22	28	29	24.25	606
Right forearm	25	8.3	18	22	28	29	24.25	606
Left lower leg	39	13	24	30.5	38	36	32.13	1253
Right lower leg	39	13	24	30.5	38	36	32.13	1253

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 71

Date: January 15, 2010

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	28	9.3	17.5	20	25.5	27	22.5	630
Right forearm	28	9.3	17.5	20	27	28.5	23.25	651
Left lower leg	42	14	26	34	43	37.5	35.13	1475
Right lower leg	42	14	26	34	43	37.5	35.13	1475

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 81

Date: March 21, 2008

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	22	7.3	14	16	20	21	17.75	391
Right forearm	22	7.3	14	16	20.5	21.5	18	396
Left lower leg	34	11.3	21	28	33.5	31.5	28.5	969
Right lower leg	34	11.3	21	28	33.5	32	28.63	973

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 84

Date: June 1, 2008

Data recorder name: W. K. Johnson

Data recorder signature: Wilmix. John

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	24	8	14.5	17.5	22	23.5	19.38	465
Right forearm	24	8	14.5	18	22.5	24	19.75	474
Left lower leg	38	12.7	20.5	26.5	33	32	28	1064
Right lower leg	38	12.7	20.5	26.5	33	32	28	1064

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 85

Date: June 2, 2008

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	22	7.3	14	16	22	23	18.75	413
Right forearm	22	7.3	14	17	22	23	19	418
Left lower leg	36	12	22	27.5	34.5	33	29.25	1053
Right lower leg	36	12	22	27.5	34	33	29.13	1049

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 86

Date: June 2, 2008

Data recorder name: W. K. Johnson

Data recorder signature:

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26.5	8.8	18	21.5	29	29.5	24.5	649
Right forearm	26.5	8.8	18	21	28	28.5	23.88	633
Left lower leg	43	14.3	25	30.5	36	36	31.88	1371
Right lower leg	43	14.3	25	30.5	37	36.5	32.25	1387

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 88

Date: June 2, 2008

Data recorder name: W. K. Johnson

Data recorder signature: W. K. Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	27.5	9.2	18.5	20	25	29	23.13	636
Right forearm	27.5	9.2	18.5	20	26	29	23 38	643
Left lower leg	44	14.7	27	29	39	38	33.25	1463
Right lower leg	44	14.7	27	29	39	38	33.25	1463

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

Limb Measurement Form

Study:

Subject number: 102

Date: June 5, 2008

Data recorder name: W. K. Johnson

Data recorder signature: Wallace K. Johnson

Note: all measurements in cm

			Circumference					
Limb	**Length**	**Length/3[1]**	**Lower (A)**	**Lower-mid (B)**	**Upper-mid (C)**	**Upper (D)**	**Mean circumference[2]**	**Surface area[3]**
Left forearm	26.5	8.8	18	21.5	28	29	24.13	639
Right forearm	26.5	8.8	18	21.5	28	28.5	24	636
Left lower leg	42	14	24	30	40.5	37	32.88	1381
Right lower leg	42	14	24	30	40.5	37	32.88	1381

[1] For placing dosimeters in pump spray & aerosol studies. 'B' is 1/3 Length from 'A' (wrist/ankle), 'C' is 1/3 Length from 'B' & 'D' (elbow/knee crease).

[2] Sum of the four circumferences measured per limb, divided by 4.

[3] Product of mean circumference and length

LNX-002 Lotion Dosimetry Data

Subject Number	Sex	Limb	Limb Surface Area (sq cm)	Lotion Mass Before (gm)	Lotion Mass After (gm)	Total Lotion Applied (gm)	Average Lotion Applied (gm)	Average grams of lotion / sq cm
4	F	L arm	349	96.589	95.952	0.637	0.628	0.00180
				95.952	95.313	0.639		
				95.313	94.704	0.609		
		R arm	349	94.067	93.432	0.635	0.673	0.00193
				93.432	92.748	0.684		
				92.748	92.047	0.701		
15	M	L arm	494	168.063	166.616	1.447	1.310	0.00265
				166.616	165.377	1.239		
				165.377	164.132	1.245		
		R arm	499	162.789	161.513	1.276	1.382	0.00277
				161.513	160.311	1.202		
				160.311	158.642	1.669		
33	F	L arm	415	135.984	135.257	0.727	0.663	0.00160
				135.257	134.601	0.656		
				134.601	133.995	0.606		
		R arm	418	133.408	132.635	0.773	0.701	0.00168
				132.635	131.935	0.700		
				131.935	131.306	0.629		
37	F	L arm	494	168.714	168.132	0.582	0.478	0.00097
				168.132	167.751	0.381		
				167.751	167.280	0.471		
		R arm	500	166.746	166.231	0.515	0.390	0.00078
				166.231	165.893	0.338		
				165.893	165.576	0.317		
52	M	L arm	653	155.222	154.460	0.762	0.718	0.00110
				154.460	153.739	0.721		
				153.739	153.069	0.670		
		R arm	666	151.949	151.140	0.809	0.761	0.00114
				151.140	150.421	0.719		
				150.421	149.665	0.756		
53	F	L arm	468	137.225	136.496	0.729	0.621	0.00133
				136.496	135.805	0.691		
				135.805	135.361	0.444		
		R arm	470	134.717	134.094	0.623	0.601	0.00128
				134.094	133.507	0.587		
				133.507	132.914	0.593		
64	M	L arm	534	116.691	115.299	1.392	1.278	0.00239
				115.299	113.942	1.357		
				113.942	112.857	1.085		
		R arm	539	111.075	109.963	1.112	1.356	0.00252
				109.963	108.580	1.383		
				108.580	107.007	1.573		
83	F	L arm	396	168.309	167.848	0.461	0.448	0.00113
				167.848	167.409	0.439		
				167.409	166.965	0.444		
		R arm	393	166.569	166.192	0.377	0.455	0.00116
				166.192	165.612	0.580		
				165.612	165.205	0.407		
92	F	L arm	363	110.072	109.483	0.589	0.616	0.00170
				109.483	108.760	0.723		
				108.760	108.223	0.537		
		R arm	370	107.685	107.003	0.682	0.657	0.00178
				107.003	106.405	0.598		
				106.405	105.714	0.691		
99	F	L arm	498	119.066	118.548	0.518	0.398	0.00080
				118.548	118.265	0.283		
				118.265	117.873	0.392		
		R arm	498	117.624	117.361	0.263	0.346	0.00069
				117.361	116.907	0.454		
				116.907	116.586	0.321		
104	M	L arm	637	157.002	156.093	0.909	0.945	0.00148
				156.093	155.160	0.933		
				155.160	154.168	0.992		
		R arm	658	152.819	151.853	0.966	0.925	0.00141
				151.853	150.932	0.921		
				150.932	150.044	0.888		

LNX-002 Lotion Dosimetry Data

Subject Number	Sex	Limb	Limb Surface Area (sq cm)	Lotion Mass Before (gm)	Lotion Mass After (gm)	Total Lotion Applied (gm)	Average Lotion Applied (gm)	Average grams of lotion / sq cm
105	F	L arm	497	168.845	168.394	0.451	0.466	0.00094
				168.394	167.858	0.536		
				167.858	167.447	0.411		
		R arm	503	166.930	166.478	0.452	0.428	0.00085
				166.478	166.080	0.398		
				166.080	165.645	0.435		
113	M	L arm	629	158.600	157.909	0.691	0.694	0.00110
				157.909	157.173	0.736		
				157.173	156.518	0.655		
		R arm	631	155.784	155.231	0.553	0.593	0.00094
				155.231	154.735	0.496		
				154.735	154.006	0.729		
114	M	L arm	672	118.861	117.583	1.278	1.339	0.00199
				117.583	116.167	1.416		
				116.167	114.844	1.323		
		R arm	682	113.562	112.301	1.261	1.284	0.00188
				112.301	111.087	1.214		
				111.087	109.710	1.377		
115	M	L arm	609	95.976	94.785	1.191	1.222	0.00201
				94.785	93.599	1.186		
				93.599	92.311	1.288		
		R arm	613	90.915	89.626	1.289	1.169	0.00191
				89.626	88.459	1.167		
				88.459	87.409	1.050		

KBR 3023 Lotion Specific Gravity = 0.98

Application Rate: 0.00152 / 0.98 = **0.00155 mL per sq cm**

	Overall average grams of lotion per arm	Overall average grams of lotion per sq cm
L arms only	**0.788**	**0.00153**
R arms only	**0.781**	**0.00151**
L and R arms	**0.785**	**0.00152**

LNX-002 Lotion Dosimetry Data

Subject Number	Sex	Limb	Limb Surface Area (sq cm)	Lotion Mass Before (gm)	Lotion Mass After (gm)	Total Lotion Applied (gm)	Average Lotion Applied (gm)	Average grams of lotion / sq cm
4	F	L leg	872	90.751	89.682	1.069	1.030	0.00118
				89.682	88.650	1.032		
				88.650	87.661	0.989		
		R leg	872	86.733	85.713	1.020	0.971	0.00111
				85.713	84.721	0.992		
				84.721	83.820	0.901		
15	M	L leg	1082	156.048	151.851	4.197	3.963	0.00366
				151.851	147.622	4.229		
				147.622	144.160	3.462		
		R leg	1087	130.644	127.965	2.679	2.604	0.00240
				127.965	125.122	2.843		
				125.122	122.832	2.290		
33	F	L leg	899	129.454	128.169	1.285	1.123	0.00125
				128.169	127.200	0.969		
				127.200	126.086	1.114		
		R leg	908	125.109	123.874	1.235	1.206	0.00133
				123.874	122.856	1.018		
				122.856	121.490	1.366		
37	F	L leg	1077	164.005	162.901	1.104	1.047	0.00097
				162.901	161.798	1.103		
				161.798	160.864	0.934		
		R leg	1087	159.948	158.723	1.225	1.242	0.00114
				158.723	157.488	1.235		
				157.488	156.222	1.266		
52	M	L leg	1092	148.161	146.401	1.760	1.609	0.00147
				146.401	145.087	1.314		
				145.087	143.333	1.754		
		R leg	1096	141.995	140.534	1.461	1.321	0.00121
				140.534	139.282	1.252		
				139.282	138.031	1.251		
53	F	L leg	976	131.512	129.923	1.589	1.599	0.00164
				129.923	128.430	1.493		
				128.430	126.714	1.716		
		R leg	980	124.799	123.158	1.641	1.641	0.00167
				123.158	121.547	1.611		
				121.547	119.877	1.670		
64	M	L leg	1142	104.479	101.560	2.919	2.531	0.00222
				101.560	99.465	2.095		
				99.465	96.886	2.579		
		R leg	1142	94.137	91.935	2.202	2.538	0.00222
				91.935	89.500	2.435		
				89.500	86.524	2.976		
83	F	L leg	936	164.381	163.521	0.860	0.724	0.00077
				163.521	162.783	0.738		
				162.783	162.210	0.573		
		R leg	927	161.581	160.927	0.654	0.648	0.00070
				160.927	160.286	0.641		
				160.286	159.636	0.650		
92	F	L leg	956	104.351	103.260	1.091	0.920	0.00096
				103.260	102.361	0.899		
				102.361	101.592	0.769		
		R leg	956	100.649	99.357	1.292	1.075	0.00112
				99.357	98.385	0.972		
				98.385	97.425	0.960		
99	F	L leg	1290	115.795	115.169	0.626	0.675	0.00052
				115.169	114.619	0.550		
				114.619	113.771	0.848		
		R leg	1290	113.013	112.152	0.861	0.810	0.00063
				112.152	111.415	0.737		
				111.415	110.584	0.831		
104	M	L leg	1382	147.558	145.521	2.037	1.694	0.00123
				145.521	144.053	1.468		
				144.053	142.477	1.576		
		R leg	1382	140.027	137.952	2.075	1.830	0.00132
				137.952	136.138	1.814		
				136.138	134.537	1.601		

LNX-002 Lotion Dosimetry Data

Subject Number	Sex	Limb	Limb Surface Area (sq cm)	Lotion Mass Before (gm)	Lotion Mass After (gm)	Total Lotion Applied (gm)	Average Lotion Applied (gm)	Average grams of lotion / sq cm
105	F	L leg	1059	164.501	163.797	0.704	0.757	0.00071
				163.797	162.960	0.837		
				162.960	162.230	0.730		
		R leg	1059	160.999	160.040	0.959	0.900	0.00085
				160.040	159.178	0.862		
				159.178	158.298	0.880		
113	M	L leg	1307	151.322	149.133	2.189	2.147	0.00164
				149.133	147.034	2.099		
				147.034	144.882	2.152		
		R leg	1307	142.810	140.856	1.954	2.048	0.00157
				140.856	138.756	2.100		
				138.756	136.667	2.089		
114	M	L leg	1444	108.245	106.694	1.551	1.556	0.00108
				106.694	105.188	1.506		
				105.188	103.576	1.612		
		R leg	1444	102.116	100.772	1.344	1.542	0.00107
				100.772	99.197	1.575		
				99.197	97.490	1.707		
115	M	L leg	1159	84.738	82.768	1.970	1.718	0.00148
				82.768	81.282	1.486		
				81.282	79.585	1.697		
		R leg	1159	76.952	75.429	1.523	1.615	0.00139
				75.429	73.545	1.884		
				73.545	72.106	1.439		

KBR 3023 Lotion Specific Gravity = 0.98

Application Rate: 0.00135 / 0.98 = **0.00138 mL per sq cm**

	Overall average grams of lotion per leg	Overall average grams of lotion per sq cm
L legs only	**1.539**	**0.00139**
R legs only	**1.466**	**0.00132**
L and R legs	**1.503**	**0.00135**

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 4

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	97.425	96.589

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	96.589	95.952
2	95.952	95.313
3	95.313	94.704

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	92.047	90.751

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	90.751	89.682
2	89.682	88.650
3	88.650	87.661

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 4

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	94.704	94.067

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	94.067	93.432
2	93.432	92.748
3	92.748	92.047

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	87.661	86.733

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	86.733	85.713
2	85.713	84.721
3	84.721	83.820

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 15

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	169.566	168.063

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	168.063	166.616
2	166.616	165.377
3	165.377	164.132

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	158.642	156.048

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	156.048	151.851
2	151.851	147.622
3	147.622	144.160

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 15

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	164.132	162.789

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	162.789	161.513
2	161.513	160.311
3	160.311	158.642

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	133.195	130.644

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	130.644	127.965
2	127.965	125.122
3	125.122	122.832

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 33

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	136.667	135.984

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	135.984	135.257
2	135.257	134.601
3	134.601	133.995

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	131.306	129.454

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	129.454	128.169
2	128.169	127.200
3	127.200	126.086

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 33

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	133.995	133.408

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	133.408	132.635
2	132.635	131.935
3	131.935	131.306

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	126.086	125.109

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	125.109	123.874
2	123.874	122.856
3	122.856	121.490

Lotion Dosimetry Form
Study LNX-002
Date: September 27, 2009

Subject number: 37

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	169.177	168.714

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	168.714	168.132
2	168.132	167.751
3	167.751	167.280

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	165.576	164.005

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	164.005	162.901
2	162.901	161.798
3	161.798	160.864

Lotion Dosimetry Form
Study LNX-002
Date: September 27, 2009

Subject number: 37

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	167.280	166.746

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	166.746	166.231
2	166.231	165.893
3	165.893	165.576

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	160.864	159.948

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	159.948	158.723
2	158.723	157.488
3	157.488	156.222

Lotion Dosimetry Form
Study LNX-002
Date: September 27, 2009

Subject number: 52

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	156.216	155.222

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	155.222	154.460
2	154.460	153.739
3	153.739	153.069

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	149.665	148.161

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	148.161	146.401
2	146.401	145.087
3	145.087	143.333

Lotion Dosimetry Form
Study LNX-002
Date: September 27, 2009

Subject number: 52

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	153.069	151.949

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	151.949	151.140
2	151.140	150.421
3	150.421	149.665

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	143.333	141.995

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	141.995	140.534
2	140.534	139.282
3	139.282	138.031

Lotion Dosimetry Form
Study LNX-002
Date: September 27, 2009

Subject number: 53

Data recorder name: W.K. Johnson

Data recorder signature: WK Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	138.031	137.225

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	137.225	136.496
2	136.496	135.805
3	135.805	135.361

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	132.914	131.512

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	131.512	129.923
2	129.923	128.430
3	128.430	126.714

Lotion Dosimetry Form
Study LNX-002
Date: September 27, 2009

Subject number: 53

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	135.361	134.717

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	134.717	134.094
2	134.094	133.507
3	133.507	132.914

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	126.714	124.799

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	124.799	123.158
2	123.158	121.547
3	121.547	119.877

Lotion Dosimetry Form

Study LNX-002

Date: September 26, 2009

Subject number: 64

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	118.099	116.691

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	116.691	115.299
2	115.299	113.942
3	113.942	112.857

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	107.007	104.479

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	104.479	101.560
2	101.560	99.465
3	99.465	96.886

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 64

Data recorder name: W. K. Johnson

Data recorder signature: WK Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	112.857	111.075

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	111.075	109.963
2	109.963	108.580
3	108.580	107.007

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	96.886	94.137

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	94.137	91.935
2	91.935	89.500
3	89.500	86.524

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 83

Data recorder name: W. K. Johnson

Data recorder signature: W K John

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	169.236	168.309

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	168.309	167.848
2	167.848	167.409
3	167.409	166.965

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	165.205	164.381

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	164.381	163.521
2	163.521	162.783
3	162.783	162.210

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 83

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	166.965	166.569

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	166.569	166.192
2	166.192	165.612
3	165.612	165.205

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	162.210	161.581

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	161.581	160.927
2	160.927	160.286
3	160.286	159.636

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 92

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	110.584	110.072

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	110.072	109.483
2	109.483	108.760
3	108.760	108.223

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	105.714	104.351

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	104.351	103.260
2	103.260	102.361
3	102.361	101.592

Lotion Dosimetry Form
Study LNx-002
Date: September 29, 2009

Subject number: 92

Data recorder name: W. K. Johnson

Data recorder signature: WK John

I. Practice Application		
A. Arm. Left or (Right) (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	108.223	107.685

II. Lotion Sampling		
A. Arm. Left or (Right) (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	107.685	107.003
2	107.003	106.405
3	106.405	105.714

B. Leg Left or (Right) (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	101.592	100.649

B. Leg Left or (Right) (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	100.649	99.357
2	99.357	98.385
3	98.385	97.425

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 99

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	119.525	119.066

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	119.066	118.548
2	118.548	118.265
3	118.265	117.873

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	116.586	115.795

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	115.795	115.169
2	115.169	114.619
3	114.619	113.771

Lotion Dosimetry Form
Study LNX-002
Date: September 29, 2009

Subject number: 99

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	117.873	117.624

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	117.624	117.361
2	117.361	116.907
3	116.907	116.586

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	113.771	113.013

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	113.013	112.152
2	112.152	111.415
3	111.415	110.584

Lotion Dosimetry Form
Study LNX-002
Date: September 30, 2009

Subject number: 104

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	158.298	157.002

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	157.002	156.093
2	156.093	155.160
3	155.160	154.168

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	150.044	147.558

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	147.558	145.521
2	145.521	144.053
3	144.053	142.477

Lotion Dosimetry Form
Study LNX-002
Date: September 30, 2009

Subject number: 104

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	154.168	152.819

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	152.819	151.853
2	151.853	150.932
3	150.932	150.044

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	142.477	140.027

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	140.027	137.952
2	137.952	136.138
3	136.138	134.537

Lotion Dosimetry Form
Study LNX-002
Date: September 30, 2009

Subject number: 105

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	169.407	168.845

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	168.845	168.394
2	168.394	167.858
3	167.858	167.447

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	165.645	164.501

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	164.501	163.797
2	163.797	162.960
3	162.960	162.230

Lotion Dosimetry Form
Study LNX-002
Date: September 30, 2009

Subject number: 105

Data recorder name: W. K. Johnson

Data recorder signature: WK

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	167.447	166.930

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	166.930	166.478
2	166.478	166.080
3	166.080	165.645

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	162.230	160.999

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	160.999	160.040
2	160.040	159.178
3	159.178	158.298

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 113

Data recorder name: W.K. Johnson

Data recorder signature: [signature]

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	159.603	158.600

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	158.600	157.909
2	157.909	157.173
3	157.173	156.518

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	154.006	151.322

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	151.322	149.133
2	149.133	147.034
3	147.034	144.882

Lotion Dosimetry Form
Study LNX-002
Date: September 26, 2009

Subject number: 113

Data recorder name: W.K. Johnson

Data recorder signature: W.K. Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	156.518	155.784

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	155.784	155.231
2	155.231	154.735
3	154.735	154.006

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	144.882	142.810

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	142.810	140.856
2	140.856	138.756
3	138.756	136.667

Lotion Dosimetry Form
Study LNX-002
Date: September 28, 2009

Subject number: 114

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	119.869	118.861

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	118.861	117.583
2	117.583	116.167
3	116.167	114.844

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	109.710	108.245

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	108.245	106.694
2	106.694	105.188
3	105.188	103.576

Lotion Dosimetry Form
Study LNX-002
Date: September 28, 2009

Subject number: 114

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	114.844	113.562

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	113.562	112.301
2	112.301	111.087
3	111.087	109.710

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	103.576	102.116

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	102.116	100.772
2	100.772	99.197
3	99.197	97.490

Lotion Dosimetry Form
Study LNX-002
Date: September 28, 2009

Subject number: 115

Data recorder name: W.K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	97.466	95.976

II. Lotion Sampling		
A. Arm. (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	95.976	94.785
2	94.785	93.599
3	93.599	92.311

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	87.409	84.738

B. Leg (Left) or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	84.738	82.768
2	82.768	81.282
3	81.282	79.585

Lotion Dosimetry Form
Study LNX-002
Date: September 28, 2009

Subject number: 115

Data recorder name: W. K. Johnson

Data recorder signature: W K Johnson

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	92.311	90.915

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	90.915	89.626
2	89.626	88.459
3	88.459	87.409

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	79.585	76.952

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1	76.952	75.429
2	75.429	73.545
3	73.545	72.106

Randomized Treatment Allocation Table*

Study: LNX-002 **Allocated by: W.K. Johnson** **Test Date: March 20, 2010**

Subject Number	Gender	Treated Limb (R or L)	Treatment A	Treatment B
5	M	L	X	
12	M	R		X
20	F	L		X
28	F	R		X
35	F	R	X	
39	F	R		X
40	F	R	X	
41	M	R		X
56	M	L	X	
60	F	L		X
61	M	L	X	
71	M	R		X
81	F	L	X	
85	F	L	X	
86	M	R		X
88	M	R		X
92	F	R		X
102	M	L	X	
104	M	L	X	
105	F	L	X	

* Stratified by Gender

Allocator signature and date: William K. Johnson March 17, 2010

Repellent Applications

Study: LNX-002 **Test Location: Parker Dam** **Date: March 20, 2010**

Subject Number	Sex	Arm (R or L)	Forearm Surface Area (sq cm)	Repellent Applied (A or B)	Application Rate (mL of Repellent/ sq cm of skin)	mL of Repellent Applied	Time of Application	Initials of Applicator
5	M	L	582	A	0.00194	1.13	07:25	WKJ
12	M	R	569	B	0.00097	0.55	07:30	RW
20	F	L	451	B	0.00097	0.44	07:25	RW2
28	F	R	541	B	0.00097	0.52	07:35	RW2
35	F	R	483	A	0.00194	0.94	07:27	RC
39	F	R	475	B	0.00097	0.46	07:37	WCJ
40	F	R	423	A	0.00194	0.82	07:25	WCJ
41	M	R	558	B	0.00097	0.54	07:34	YP
56	M	L	618	A	0.00194	1.20	07:28	WKJ
60	F	L	374	B	0.00097	0.36	07:35	WKJ
61	M	L	606	A	0.00194	1.18	07:30	YP
71	M	R	651	B	0.00097	0.63	07:37	RC
81	F	L	391	A	0.00194	0.76	07:29	WCJ
85	F	L	413	A	0.00194	0.80	07:31	RC
86	M	R	633	B	0.00097	0.61	07:39	RW2
88	M	R	643	B	0.00097	0.62	07:37	WKJ
92	F	R	370	B	0.00097	0.36	07:37	YP
102	M	L	639	A	0.00194	1.24	07:25	YP
104	M	L	637	A	0.00194	1.24	07:31	WKJ
105	F	L	497	A	0.00194	0.96	07:33	WCJ
52	M	R	670	None	Control 1	None	-	-
84	F	L	465	None	Control 2	None	-	-

Technician signature and date: William K. Johnson March 20, 2010

LNX-002 Black Fly LIBe Data

Sequential Exposure Intervals (1 - 37)

Subject Number	Sex	Repellent	Application Time	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	CPT (hours)	Total Landings	Confirmed Landing	Subject Number	Repellent
			Hours since first exposure					1				2				3				4				5				6				7				8				9					
5	M	A	07:25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	-	-	-	-	-	10.08	3	Yes	5	A
12	M	B	07:30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	-	-	-	-	-	-	9.75	3	Yes	12	B
20	F	B	07:25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	-	-	-	-	-	-	-	-	9.58	2	Yes	20	B
28	F	B	07:35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.42	0	No	28	B
35	F	A	07:27	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.55	0	No	35	A
39	F	B	07:37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	-	-	-	-	-	-	-	-	-	-	-	8.38	2	Yes	39	B
40	F	A	07:25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.58	0	No	40	A
41	M	B	07:34	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	11.43	2	No	41	B
56	M	A	07:28	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	-	-	-	-	-	-	-	-	9.28	3	Yes	56	A
60	F	B	07:35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.42	0	No	60	B
61	M	A	07:30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.5	0	No	61	A
71	M	B	07:37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	-	-	-	-	-	-	9.63	3	Yes	71	B
81	F	A	07:29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	11.52	1	No	81	A
85	F	A	07:31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.48	0	No	85	A
86	M	B	07:39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	-	-	-	-	-	-	-	-	9.1	3	Yes	86	B
88	M	B	07:37	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6.88	3	Yes	88	B
92	F	B	07:37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	11.38	1	No	92	B
102	M	A	07:25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	-	-	-	-	-	-	-	-	-	9.08	3	Yes	102	A
104	M	A	07:31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6.23	2	Yes	104	A
105	F	A	07:33	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6.95	2	Yes	105	A
52 (Control)	M	None	Not Applicable	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	Not Applicable	37	Yes	52 (Control)	None
84 (Control)	F	None	Not Applicable	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	Not Applicable	37	Yes	84 (Control)	None
			Hours since first exposure					1				2				3				4				5				6				7				8				9					
Subject Number	Sex	Repellent	Time	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	CPT (hours)	Total Landings	Confirmed Landing	Subject Number	Repellent

First Time Interval =10:00

Biting Fly Landings at 15 Minute Intervals

Study: LNX-002
Date: March 20, 2010

Application Time(s): 07:25-07:39
Time of First Exposure: 10:00

Time:	10:00	10:15	10:30	10:45	11:00	11:15	11:30	11:45	12:00	12:15	12:30	12:45	13:00	13:15	13:30	13:45	14:00	14:15	14:30	14:45	15:00	15:15
15 Minute Interval:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Subject Number																						
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
61	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
71	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
81	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
85	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
86	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
88	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	—	—
92	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	—	—	—	—
105	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	—	—
Control 1 (52)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Control 2 (84)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Key: 0 = Repulsion, 1 = Landing

Data Recorder Name and Signature: W. K. Johnson — William K. Johnson March 20, 2010

Biting Fly Landings at 15 Minute Intervals

Study: LNX-002

Date: March 20, 2010

Application Time(s): 07:25 – 07:39

Time of First Exposure: 10:00

Time:	15:30	15:45	16:00	16:15	16:30	16:45	17:00	17:15	17:30	17:45	18:00	18:15	18:30	18:45	19:00							
15 Minute Interval:	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44
Subject Number																						
5	0	0	0	0	0	1	0	0	1	1	—	—	—	—	—							
12	0	0	0	1	0	0	0	1	1	—	—	—	—	—	—							
20	0	0	0	0	0	0	2	—	—	—	—	—	—	—	—							
28	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
39	0	0	1	1	—	—	—	—	—	—	—	—	—	—	—							
40	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
41	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0							
56	0	0	0	0	0	1	1	—	—	—	—	—	—	—	—							
60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
61	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
71	0	0	0	1	0	0	0	1	1	—	—	—	—	—	—							
81	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0							
85	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
86	0	0	0	0	0	1	1	—	—	—	—	—	—	—	—							
88	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—							
92	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0							
102	1	0	0	0	1	1	—	—	—	—	—	—	—	—	—							
104	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—							
105	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—							
Control 1 (52)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1							
Control 2 (84)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1							

Key: 0 = Repulsion, 1 = Landing

W. K. Johnson

Data Recorder Name and Signature: William K. Johnson March 20, 2010

Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530)902-8267 http://www.carroll-loye.com/

Research Notes

CLBR Project I.D.# LNX-002

Date: 20 March 2010

This note reports that all study subjects undertook 1-minute exposures to guage their individual attractiveness to black flies. These exposures, monitored by the Study Director, took place at this study field site prior to subjects' exposing their treated or control limbs to black flies. All subject experienced at least one LIBe (Landing with Intent to Bite) during their attractiveness exposures, and were thus judged suitably attractive, as per the study protocol, for participating in the repellent efficacy test.

Signed J.R. Carll

Field Environmental Conditions

Study: LNX-002 **Test Location:** Parker Dam

Date: March 20, 2010 **Observer:** W. K. Johnson

Time	Air Temperature (degrees C)	Relative Humidity (%)	Light Intensity (lux)	Wind Speed (mph) (avr./10 min.)	Cloud Cover/ Other
09:00	17	33	417 [X10]	1.5	Clear Skys
10:00	19	26	479 [X10]	2.2	Clear
11:00	20	25	522 [X10]	1.1	Clear
12:00	22	24	616 [X10]	1.6	Clear
13:00	23	22	1077 [X10]	0.7	Clear
14:00	23	22	700 [X10]	0.6	Clear
15:00	25	20	1245 [X10]	0.5	Clear
16:00	23	21	571 [X10]	0.9	Clear
17:00	25	20	554 [X10]	0.7	Clear
18:00	21	22	250 [X10]	0.6	Clear
19:00	19	23	7 [X1]	0.5	Clear

Additional Comments:

Observer Signature: William K Johnson March 20, 2010

Biting Fly Species Identification
Field Test Samples

Carroll-Loye Biological Research
711 Oak Avenue Davis
530-902-8267

Study: LNX-002

Date Samples Collected: 20 MARCH 2010

Site: 7 IL

TREATED SUBJECTS:

Subject Number	5	12	20	39	41	56	71	81	86	88	92	102	104	105	Total Number Collected of Each Species	Total of Each Species Ctrl (#)	Total of Each Species Ctrl (#)	Total of Each Species Treated	Total of Each Species Misc.
Pool Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14					
Leptoconops carteri	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Simulium cf. vittatum	2	1	2	2	1	3	3	0	3	2	1	3	2	2	27	31	34	26	0
Number of flies / midges in Pool	2	1	2	2	1	3	3	0	3	2	1	3	2	2	of All Species 27	31	34	26	0

SR

Biting Fly Species Identification
Field Test Samples

Carroll-Loye Biological Research
711 Oak Avenue Davis
530-902-8267

p. 2 of 2

Study: LNX-002

Date Samples Collected: 20 MARCH 2010

Site: PK

CONTROL SUBJECTS:

Subject Number	52	84													Total Number Collected of Each Species	Total of Each Species Ctrl (#)	Total of Each Species Ctrl (#)	Total of Each Species Treated	Total of Each Species Misc.
Pool Number	15	16																	
Leptoconops carteri	0	0													0	0	0	0	0
Simulium cf. vittatum	31	34													65	31	34	26	0
															of All Species				
Number of flies / midges in Pool	31	34													65	31	34	26	0

JPC

Mosquito Pools Submitted to UCD by CLBR

Carroll-Loye Biological Research
711 Oak Avenue Davis
530-902-8267

Date samples received by UCD:

Date samples tested by UCD:

Study: LNX-002

Date Samples Collected: 20 MARCH 2010

Site: PLC

No: No Mosquitoes observed

Subject Number														Total Number Collected of Each Species	Total of Each Species Ctrl (#)	Total of Each Species Ctrl (#)	Total of Each Species Treated	Total of Each Species Misc.
Pool Number																		
Aedes melanimon																		
Aedes vexans																		
Aedes increpitus																		
Aedes sierrensis																		
Aedes nigromaculis																		
Culex tarsalis																		
Anopheles freeborni																		
														of All Species				
Number of Mosquitoes in Pool																		
Assay Results for West Nile Fever Virus														} Legend for viral assays of mosquito pools: + = positive 0 = negative				
Assay Results for Western Equine Encephalitis Virus																		
Assay Results for St. Louis Encephalitis Virus																		

KBR 3023 Insect Repellent Cream

Contains Bayrepel™. Long-lasting, effective protection from mosquitoes ticks, biting flies, and fleas. Not oily, greasy or sticky. It smells great, too. Repels insects for up to 8 hours.

ACTIVE INGREDIENT: Picaridin, 1-Methylpropyl-2-(2-hydroxyethyl)-1-piperidine carboxylate	20%
INERT INGREDIENTS**	80%
TOTAL	100.0%

**Other Ingredients: Purified water, glycerin, denatured alcohol, thickener, emollient, fragrance

KEEP OUT OF REACH OF CHILDREN

WARNING

STOP – Read This Entire Label Before Use

PRECAUTIONARY STATEMENTS

WARNING. HAZARDS TO HUMANS.

Causes substantial but temporary eye injury. Do not get in eyes. Wash thoroughly with soap and water after handling, returning indoors, and before eating, drinking, chewing gum, or using tobacco. Discontinue use and consult a doctor if irritation or rash occurs.

The information below describes the first aid procedures for incidents involving KBR 3023 Insect Repellent Cream:

FIRST AID

IF IN EYES:

- Hold eye open and rinse gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first five minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

IF SWALLOWED:

- Call a physician or poison control center immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to do so by a Poison Control Center or a doctor.
- Do not give anything to an unconscious person.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-410-3063 for emergency medical information.

The LANXESS Pittsburgh Emergency Response Telephone Number is 800-410-3063

PHYSICAL HAZARDS

Flammable. Do not use or store near heat sources, sparks or open flame. Do not smoke while applying.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

For best results, read and follow all label directions.

Follow these guidelines when applying KBR 3023 Insect Repellent:

- Apply evenly to skin in a thin layer
- Excessive amounts or more frequent reapplication should be unnecessary. Do not apply more than 2 times a day.
- Repels insects and ticks for up to eight hours.
- Reapply every 8 hours. Do not exceed two applications per day.
- Do not spray directly on face.
- Avoid contact with lips, cuts, wounds, or irritated skin.
- Do not apply to excessively sunburned skin.
- Do not apply under clothing.
- Apply sparingly around ears.

STORAGE AND DISPOSAL

STORAGE: Store in a cool, dry place out of the reach of children. Keep away from heat, sparks and open flame.
DISPOSAL: Do not reuse empty container. Discard in trash.
IF EMPTY: Do not reuse this container. Place in trash or offer for recycling if available.
IF PARTLY FILLED: Call your local solid waste agency or 1-800-526-9377 for disposal instructions. Never place unused product down any indoor or outdoor drain.

IN CASE OF EMERGENCY, CALL: CHEMTREC 800-424-9300
EPA REGISTRATION NUMBER: 39967-50
EPA ESTABLISHMENT NUMBER:

INTERNATIONAL 703-527-3887
Net Contents:
Lot No.:

LANXESS

LANXESS Corporation
111 RIDC Park West Drive ● Pittsburgh, PA 15275-1112

LABEL TEXT DATE: 12/19/06

KBR 3023 All-Family Insect Repellent Spray

Long-lasting, effective protection from mosquitoes, ticks, biting flies, gnats, chiggers and fleas. Use with confidence on the whole family. And your family will want to use it, too. Not oily, greasy or sticky. It smells great, too.

ACTIVE INGREDIENT: Picaridin, 1-Methylpropyl-2-(2-hydroxyethyl)-1-piperidine carboxylate ---------- 20%
INERT INGREDIENTS ---------- 80%
TOTAL ---------- 100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

STOP – Read This Entire Label Before Use

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling, returning indoors, and before eating, drinking, chewing gum, or using tobacco.

The information below describes the first aid procedures for incidents involving KBR 3023 Insect Repellent Spray:

FIRST AID

IF IN EYES:

- Hold eye open and rinse gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first five minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

IF SWALLOWED:

- Call a physician or poison control center immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to do so by a Poison Control Center or a doctor.
- Do not give anything to an unconscious person.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-410-3063 for emergency medical information.

The LANXESS Pittsburgh Emergency Response Telephone Number is 800-410-3063

IN CASE OF EMERGENCY, CALL: CHEMTREC 800-424-9300

EPA REGISTRATION NUMBER: 39967-53
EPA ESTABLISHMENT NUMBER:

PHYSICAL HAZARDS

Flammable. Do not use or store near heat sources, sparks or open flame. Do not smoke while applying.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

Follow these guidelines when applying KBR 3023 Insect Repellent:

- Hold 4 to 6 inches from skin while spraying, keeping nozzle pointed away from face. Slightly moisten skin with a slow sweeping motion.
- Excessive amounts or frequent reapplication is unnecessary.
- Apply on face by first spraying small amounts in palms of hands and spreading on face and neck.
- Do not apply to the hands of small children.
- Repels insects and ticks for up to eight hours.
- Reapply every 8 hours. Do not exceed two applications per day.
- Do not spray directly on face.
- Avoid contact with lips, cuts, wounds, or irritated skin.
- Do not apply to excessively sunburned skin.
- Do not apply under clothing.
- Apply sparingly around ears.

STORAGE AND DISPOSAL

Store in a cool, dry place out of the reach of children. Keep away from heat, sparks and open flame.
IF EMPTY: Do not reuse this container. Place in trash or offer for recycling if available.
IF PARTLY FILLED: Call your local solid waste agency or 1-800-526-9377 for disposal instructions. Never place unused product down any indoor or outdoor drain.

INTERNATIONAL 703-527-3887
Net Contents:
Lot No.:

LANXESS

LANXESS Corporation
111 RIDC Park West Drive • Pittsburgh, PA 15275-1112

LABEL TEXT DATE: 12/19/06

saltigo
customized competence

Dr. B-Koch
Saltigo GmbH, Leverkusen,
Germany
phone: ++49/214/30-43872

KBR 3023 ALL-FAM.INSECT REPELL.CREAM MUS

Lot.Nr.: XKOC 0712

Auftr.Nr.: 7700011222 / 10 / 1

A company of the LANXESS Group

gross: 168,3g net: 140g tare: 28,3g
Art.Nr.: 56154780

[redacted]

saltigo
customized competenc

Dr. B-Koch
Saltigo GmbH, Leverkusen,
Germany
phone: ++49/214/30-43872

KBR 3023 ALL-FAM.INSECT REPELL.SPRAY MUS

Lot.Nr.: XKOC 0331

Auftr.Nr.: 7700011222/ 20 / 1

company of the LANXESS roup

gross: 111g net: 90g tare: 21g
Art.Nr.: 56115181

[redacted]

Test Substance Information*

LANXESS CORPORATION

Date Shipped: 2009.08.12 Quantity Shipped: 560g

Test Substance: 56154780

Product Name: KBR 3023 All-FAMILY INSECT REPELLENT CREAM

CAS #: of the Active Ingredient 119515-38-7

Source: Saltigo GmbH, Building Q 18, 51369 Leverkusen, Germany

Batch / Lot / Reference No.: XKOC 00712

Secondary Reference No.:

Appearance: white cream

% Active Ingredient (COA) / Date of Analysis: mean value:20.9% KBR 3023 / 2009-07-21

Expiration Date: 2011-07-09

Analysis Reference Number: CURRENTA GmbH & Co. OHG No. 2009/0070/01

Storage Conditions: store at temperature not more than 30°C

Room Temperature: x Refrigerator: Freezer: Light Sensitive:

Safety Information - Attach copy of MSDS or list known information:

Hazards -

Health & Safety Data -

* This questionnaire should be completed and shipped with all materials to be used for testing. This requested information is needed for implementation of GLP studies and to protect personnel conducting studies. The sponsor is required to maintain this technical information / data in order to comply with the GLP regulations.

Test Substance Information*

LANXESS CORPORATION

Date Shipped: 2009.08.12 Quantity Shipped: 500ml

Test Substance: 56115181

Product Name: KBR 3023 All-FAMILY INSECT REPELLENT SPRAY

CAS #: of the Active Ingredient 119515-38-7

Source: Saltigo GmbH, Building Q 18, 51369 Leverkusen, Germany

Batch / Lot / Reference No.: XKOC 00331

Secondary Reference No.:

Appearance: clear solution

% Active Ingredient (COA) / Date of Analysis: mean value:21.% KBR 3023 / 2009-08-06

Expiration Date: 2011-08-06

Analysis Reference Number: CURRENTA GmbH & Co. OHG No. 2008/0078/03

Storage Conditions: store at temperature not more than 30°C

Room Temperature: x Refrigerator: Freezer: Light Sensitive:

Safety Information - Attach copy of MSDS or list known information:

Hazards -

Health & Safety Data -

* This questionnaire should be completed and shipped with all materials to be used for testing. This requested information is needed for implementation of GLP studies and to protect personnel conducting studies. The sponsor is required to maintain this technical information / data in order to comply with the GLP regulations.

CURRENTA

Study Title

Identity and Content of KBR 3023 in KBR 3023 All Family Insect Repellent Cream 20 %

AUTHOR

Michael Prüm

Data requirement

Analytical method M01166-01 for the determination of the active ingredient KBR 3023 (Icaridin) in the formulation KBR 3023 All Familiy Repellent Cream 20 % (validated and reported under Study No. 2008/0120/02)

Study completion date: 2009-07-23

PERFORMING LABORATORY

CURRENTA GmbH & Co. OHG
Services Analytik
D-51368 Leverkusen
Federal Republic of Germany

Sponsor:

Saltigo GmbH
HSEQ-PS&RA
Katzbergstrasse 1
D-40764 Langenfeld
Germany

LABORATORY PROJECT ID

Study No. 2009/0070/01

This page is intentionally left blank for the purpose of submitting administrative information that is required by regulations promulgated by various countries.

1. Statement of compliance with GLP (SOC) Claim

This study was conducted in compliance with the OECD principles of Good Laboratory Practice (GLP, as revised in 1997) and with the Principles of Good Laboratory Practice according to Annex 1, German Chemical Law (Änderung des Anhanges 1 vom 8 Mai 2001).

STUDY DIRECTOR
CURRENTA GmbH & Co. OHG
Services Analytik
Building Q 18
D-51368 Leverkusen
Federal Republic of Germany

Michael Prüm

Date: 2008-07-23

FOR THE HEAD OF TEST FACILITY
CURRENTA GmbH & Co. OHG
Services Analytik
Building Q 18
D-51368 Leverkusen
Federal Republic of Germany

Prof. Dr. [illegible]

Date: 2008-07-27

2. Archiving

The original report, the study plan and all raw data pertaining to this study are stored in the "GLP Archiv, Services Analytik, Building Q 18, Currenta GmbH & Co. OHG, D-51368 Leverkusen". A sample of the test substance is stored in "GLP-Probenlager, Services Analytik, Building Da 1, Currenta GmbH & Co. OHG, D-41538 Dormagen".

This page is intentionally left blank for the purpose of submitting administrative information that is required by regulations promulgated by various countries.

3. GLP CERTIFICATE

Ministerium für Umwelt und Naturschutz, Landwirtschaft und Verbraucherschutz des Landes Nordrhein-Westfalen

Postanschrift: 40190 Düsseldorf Aktenzeichen: VI-3- 31.11.65.05

Gute Laborpraxis/Good Laboratory Practice

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 88/320/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 88/320/EEC at

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

Bayer Industry Services GmbH & Co OHG
Prüfeinrichtung BIS-SUA-Analytics
D-51368 Leverkusen

(unverwechselbare Bezeichnung und Adresse/Unequivocal name and address)

Prüfungen nach Kategorien (gemäß ChemVwV-GLP Nr. 5.3/OECD guidance)	Areas of Expertise (according ChemVwV-GLP Nr. 5.3/OECD guidance)
Kategorie 1	category 1
Prüfungen zur Bestimmung der physikalisch-chemischen Eigenschaften und Gehaltsbestimmungen	physical-chemical testing
Kategorie 4	category 4
Ökotoxikologische Prüfungen zur Bestimmung der Auswirkungen auf aquatische und terrestrische Organismen	environmental toxicity studies on aquatic and terrestrial organisms
Kategorie 5	category 5
Prüfungen zum Verhalten im Boden, im Wasser und in der Luft; Prüfungen zur Bioakkumulation und zur Metabolisierung	studies on behaviour in water, soil and air; bioaccumulation
Kategorie 8	category 8
Analytische Prüfungen an biologischen Materialien	analytical and clinical chemistry testing

Datum der Inspektion (Tag,Monat,Jahr)	Date of Inspection (day,month,year)
14. bis 16. September und 26. bis 28. Oktober 2005	on 14 until 16 September and on 26 until 28 October 2005
Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.	The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.
Auf der Grundlage des Inspektionsberichts wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt worden können.	Based on the inspection report it can be confirmed, that this test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Düsseldorf, den 11. Januar 2008
Im Auftrag

(Prof. Dr. David)

Dienstsiegel/official-seal

Please note: Effective January 1st, 2008, the company name Bayer Industry Services GmbH & Co. OHG was changed to CURRENTA GmbH & Co. OHG.

4. Quality Assurance Statement

This report was audited by the Quality Assurance Unit Currenta, Services Analytik, Quality Maragement at Currenta GmbH & Co. OHG and this statement confirms that the final report reflects the raw data.

The dates of Quality Assurance inspections and audits are given below

Audits	Dates of QAU Inspections	Dates of Reports
Study plan inspection	2009-07-17	2009-07-17
Inspection of experimental phase	2009-07-20	2009-07-20
Report inspection	2009-07-27	2009-07-27

FOR THE HEAD OF QUALITY ASSURANCE

Dr Neupert

Date: 2009-07-27

5. Study Time Table

Study initiation date:	2009-07-17
Study completion date:	2009-07-23
Start of Experimental Tests:	2009-07-20
End of Experimental Tests:	2009-07-21

Table of contents

6. Summary

Report: Prüm, Michael: Identity and Content of KBR 3023 in KBR 3023 All Family Insect Repellent Cream 20 %, CURRENTA, report No.: 2009/0070/01

Guidelines: --

GLP: yes (certified laboratory)

Time of experimental tests: 2009-07-20 – 2009-07-21

Materials and Determinations:
With the test substance KBR 3023 All Family Insect Repellent Cream 20 %, Batch no.: XKOC00712, the following analytical determinations were performed:

Identity of the active ingredient in KBR 3023 All Family Insect Repellent Cream 20 %

The identity of the active ingredient KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %, batch no. XKOC00712, was confirmed by comparison with the retention time of the external standard KBR 3023 (Icaridin) determined by HPLC.

Content of KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %

The content of KBR 3023 was determined by the HPLC – method M01166-01 (validated and reported under study no.: 2008/0120/02)

Test	KBR 3023 All Family Insect Repellent Cream 20 % Batch no.: XKOC00712 sample-no.: 994
Identity	Was confirmed
Content of KBR 3023	20.9 %

7. Methods and Documents

7.1 Methods, guidelines and documents

Identity by comparison of retention times of KBR 3023 (Icaridin) determined by HPLC.
HPLC-method with quantification by external standardization is described in Point 9.1.
The content was determined by the HPLC – method M01166-01.
(validated and reported under Study No. 2008/0120/02)

7.2 Principle of the test

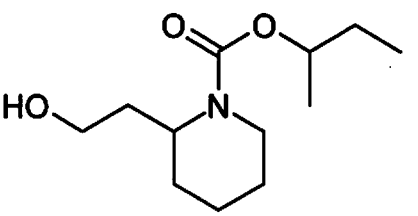
High Performance Liquid Chromatography (HPLC)

The content of the active ingredient KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 % was determined by HPLC on a reversed phase column with UV-detection and quantified by external standardization. The identity was performed by comparison the retention time of the external standard KBR 3023 (Icaridin) with the retention time of the active ingredient KBR 3023 (Icaridin) in KBR 3023 All-Family Insect Repellent Cream, batch no. XKOC00712.

8. Test and Calibration Material

8.1 Test item

Test substance:	KBR 3023 All Family Insect Repellent Cream 20%
Active ingredient:	KBR 3023 (Icaridin)
Chemical name of a.i.:	1-methylpropyl 2-(2-hydroxyethyl)piperidine-1-carboxylate
Empirical formula of a.i:	$C_{12}H_{23}NO_3$
Molecular mass of a.i:	229.3 g/mol
CAS no. of a.i.:	119515-38-7
Batch no.:	XKOC00712
Sample no.:	994
Date of receipt:	2009-07-13
Expiry date:	2011-07-09
Structural Formula:	KBR 3023 (Icaridin)



8.2 KBR3023 (Icaridin), analytical standard

Bayer CropScience

Certificate of Analysis

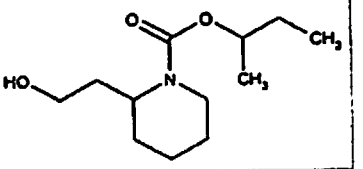
Bayer CropScience GmbH
Product Technology-Analytics Frankfurt
Industriepark Höchst, G 864
65926 Frankfurt am Main, DEU
TEL.: +49(0)69-305-2520, FAX: +49(0)69-305-80323

A GLP Testing Facility Certificate No.: AZ 13506

This Certificate of Analysis fulfills the requirement for characterization of a test/reference item prior to a study according to GLP - regulations. It documents the identity, purity/content and the stability of the test/reference item.

1. Certification of a Reference Substance

Project:	KBR3023 (Icaridin / AE 1228957)
Intended use:	Primary reference substance PS
Batch code:	AE 1228957 00 1B99 0001
Material:	icaridin; pure substance
Common name:	icaridin
Chemical name:	1-methylpropyl 2-(2-hydroxyethyl)piperidine-1-carboxylate
Report Name:	KBR3023-a.i.
Cas. No.:	119515-38-7
Molecular form.:	C12 H23 N O3
Molar mass:	229.32 g/mol
Origin Batch No.:	M22098
LIMS No.:	0616528



2. Analytical Summary

Composition

Substance	Name	Content	Method
AE 1228957	icaridin content a.i. was determined as 100% minus impurities.	98.9 % w/w	various

Physical properties

Parameter	Value	Method
Appearance	light yellow clear viscous liquid	

Identity

The identity of the certified material was established by use of the following method(s):

MS 1H-NMR 13C-NMR

Comment:

Substance in hand is hygroscopic. Please keep away from moisture.

3. Storage and Stability

Storage conditions: +5± 5 °C

Date of analysis: 02-AUG-2006 Expiry date if stored as recommended: 02-AUG-2010

Bayer CropScience

Certificate of Analysis

Bayer CropScience GmbH
Product Technology-Analytics Frankfurt
Industriepark Höchst, G 864
65926 Frankfurt am Main, DEU
TEL.: +49(0)69-305-2520, FAX: +49(0)69-305-80323

A GLP Testing Facility

Certificate No.: AZ 13506

Origin of the Certified Material
Bereich Pflanzenschutz
Bayer AG
40789 Monheim, DEU

Certificate Timetable

Experimental start date:	03-JUL-2006
Experimental termination date: (= Date of analysis)	02-AUG-2006
Completion date:	03-AUG-2006

Archiving

Report and raw data are archived at the testing facility.

A retained sample of the certified material is archived at the testing facility.

Records of the preparation of the certified material are retained at the origin.

General Information

Storage

The recommended storage temperature applies for storage over prolonged periods of time. Unless otherwise stated, during shipment or use the substance may be kept at room temperature for a period of several days.

Samples stored at low temperatures should be removed from these conditions of storage as infrequently as possible. A number of small aliquots should be requested when the substance will be used at regular intervals. The number of times each aliquot is brought to room temperature is therefore reduced.

Substances which are easily degraded in the presence of light, moisture or air need to be carefully handled. Dark glass containers should be used to store photolytically unstable substances. Self indicating silica gel or another suitable material should be stored along with moisture sensitive materials. Those substances which are easily oxidized should be stored under an atmosphere of dry-nitrogen.

Handling

Whenever the container is opened for removal of portions of the substance the integrity of the substance must be maintained. Special care must be taken to avoid contamination or adulteration of the test substance. Proper records of the handling and use of the substance must be kept.

Recertification

If this material is to be used after the specified expiry date it will require re-validation and re-certification. The user must then request a new certificate of analysis or can be advised as to the availability of an alternative material.

Responsible Scientist:

3.8.06

Date, Signature

Dr. Michael Cichy for Rüdiger Weilbächer

Head of the Testing Facility:

7.8.2006

Date, Signature

Dr. Thomas Müller for Dr. Martin Feyerabend

9. Methods and Results

9.1 Identity and Assay

Test:	Identity and content of KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %
Method no.:	M01166-01 (validated and reported under Study No. 2008/0120/02)
Supervisor:	Dr. Königer
Procedure:	High Performance Liquid Chromatography
Column type:	Length: 250 mm, inner diameter: 4.0 mm
Stationary phase:	LiChrosorb RP-8, particle diameter: 10 µm
Supplier of HPLC-column:	Merck KgaA, 64271 Darmstadt, Germany
Mobile Phase:	60 % demineralized water, 30 % acetonitrile, 10 % tetrahydrofuran (v/v/v)
Flow rate:	1.5 ml/min
Analysis time:	7 minutes
Column temperature:	25 °C (Room temperature)
Detection:	UV, 210 nm
Injection volume:	20 µl

The quantification was performed by external standardization.

The following external standard was used:
KBR 3023 (Icaridin), Bayer CropScience, certificate of analysis AZ13506, 98.9 %

Identity of KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %, determined by HPLC:

The identity of the active ingredient KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %, batch no. XKOC00712 was confirmed by comparison with the retention time of the external standard KBR 3023 (Icaridin) determined by HPLC. The relative retention time of KBR 3023 (Icaridin) for the sample solution should not deviate by more than 2 % from that for the calibration solution.

Retention time of the calibration sample KBR 3023 (Icaridin)	= 5.04 minutes
Retention time of KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %, batch no. XKOC00712	= 5.04 minutes

9.1.1 Preparation of the analytical standard solution for the determination of the active ingredient.

About 125 mg of the external standard KBR 3023 (Icaridin) was weighed to the nearest 0.1 mg into a 50 ml measuring flask. After addition of methanol the mixture was sonicated for two minutes to dissolve the substance and than filled up to the mark with methanol.

9.1.2 Preparation of the test solution for the determination of the active ingredient.

After mechanical homogenization about 650 mg of the test item was weighed to the nearest 0.1 mg into a 50 ml measuring flask. After addition of methanol the mixture was sonicated for two minutes to dissolve the substance and than filled up to the mark with methanol.

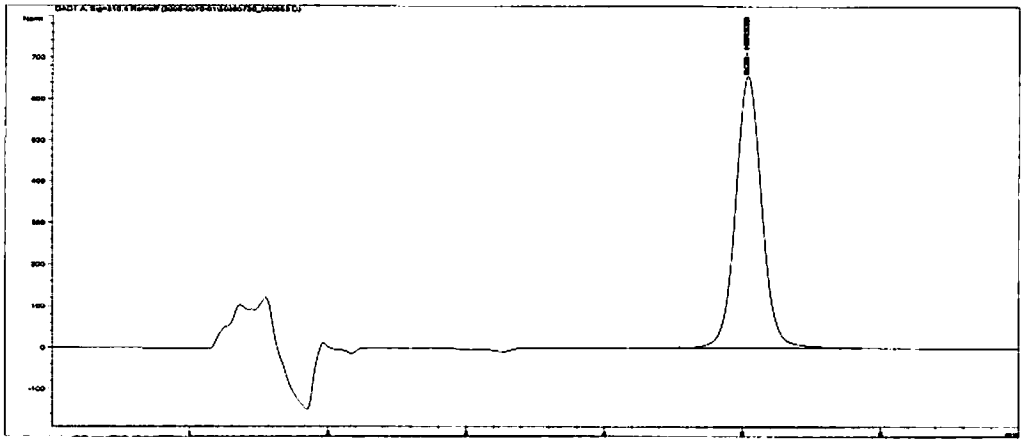
HPLC-chromatogram of the analytical standard KBR 3023 (Icaridin)

9.1.3 Results:

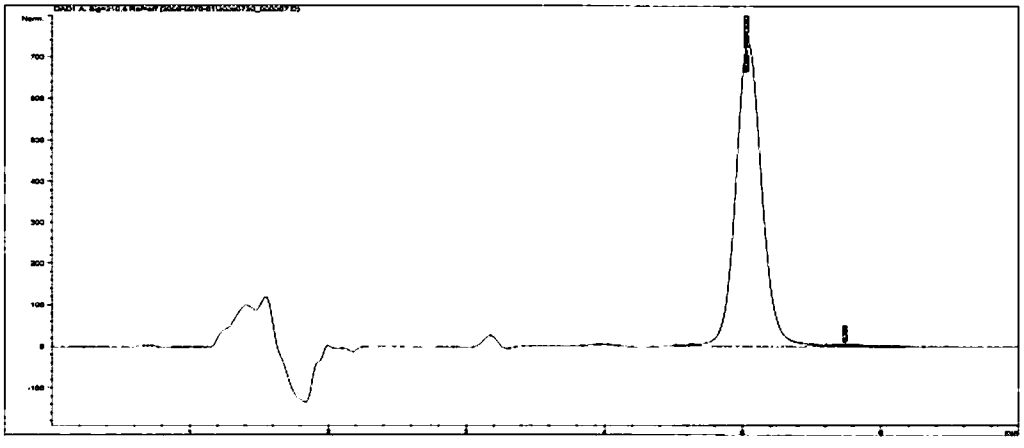
Test	KBR 3023 All Family Insect Repellent Cream 20 % Batch no.: XKOC00712 sample-no.: 994
Identity	Was confirmed
Content of KBR 3023 Mean value of two determinations	20.9 %
Single values	20.9 % / 20.9 %

9.1.4 Example chromatograms

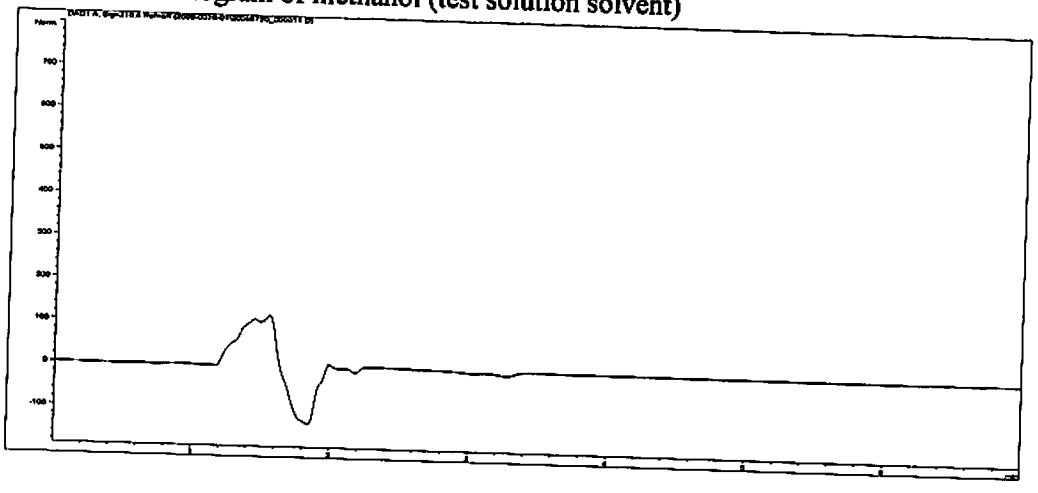
HPLC-chromatogram of the analytical standard KBR 3023 (Icaridin)



HPLC-chromatogram of KBR 3023 (Icaridin) in KBR 3023 All Family Insect Repellent Cream 20 %, batch no. XKOC00712



HPLC-chromatogram of methanol (test solution solvent)



CURRENTA

Study Title

Identity and Content of KBR 3023 in KBR 3023 All-Family Insect Repellent Spray

AUTHOR

Rainer Jungheim

Study completion date: 2009-08-07

PERFORMING LABORATORY

CURRENTA GmbH & Co. OHG
Services Analytik
D-51368 Leverkusen
Federal Republic of Germany

Sponsor:

Saltigo GmbH
HSEQ-PS&RA
Katzbergstrasse 1
D-40764 Langenfeld
Germany

LABORATORY PROJECT ID

Study No. 2008/0078/03

This page is intentionally left blank for the purpose of submitting administrative information that is required by regulations promulgated by various countries.

1. Statement of compliance with GLP (SOC) Claim

This study was conducted in compliance with the OECD principles of Good Laboratory Practice (GLP, as revised in 1997) and with the Principles of Good Laboratory Practice according to Annex 1, German Chemical Law (Änderung des Anhanges 1 vom 8.Mai 2001).

STUDY DIRECTOR
CURRENTA GmbH & Co. OHG
Services Analytik
Building Q 18
D-51368 Leverkusen
Federal Republic of Germany

Mr. Rainer Jungheim: R. Jungheim

Date: 2009-08-07

FOR THE HEAD OF TEST FACILITY
CURRENTA GmbH & Co. OHG
Services Analytik
Building Q 18
D-51368 Leverkusen
Federal Republic of Germany

Prof. Dr. Norbert Caspers: Caspers

Date: 2009-08-11

2. Archiving

The original report, the study plan and all raw data pertaining to this study are stored in the "GLP Archiv, Services Analytik, Building Q 18, Currenta GmbH & Co. OHG, D-51368 Leverkusen". A sample of the test item is stored in "GLP-Probenlager, Services Analytik, Building Da 1, Currenta GmbH & Co. OHG, D-41538 Dormagen".

3. GLP CERTIFICATE

Ministerium für Umwelt und Naturschutz, Landwirtschaft und Verbraucherschutz
des Landes Nordrhein-Westfalen

Postanschrift: 40190 Düsseldorf Aktenzeichen: VI-3- 31.11 63.05

Gute Laborpraxis/Good Laboratory Practice

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 88/320/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 88/320/EEC st

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

Bayer Industry Services GmbH & Co OHG
Prüfeinrichtung BIS-SUA-Analytics
D-51368 Leverkusen

(unverwechselbare Bezeichnung und Adresse/Unequivocal name and address)

Prüfungen nach Kategorien (gemäß ChemVwV-GLP Nr. 5.3/OECD guidance)	Areas of Expertise (according ChemVwV-GLP Nr. 5.3/OECD guidance)
Kategorie 1	category 1
Prüfungen zur Bestimmung der physikalisch-chemischen Eigenschaften und Gehaltsbestimmungen	physical-chemical testing
Kategorie 4	category 4
Ökotoxikologische Prüfungen zur Bestimmung der Auswirkungen auf aquatische und terrestrische Organismen	environmental toxicity studies on aquatic and terrestrial organisms
Kategorie 5	category 5
Prüfungen zum Verhalten im Boden, im Wasser und in der Luft; Prüfungen zur Bioakkumulation und zur Metabolisierung	studies on behaviour in water, soil and air; bioaccumulation
Kategorie 8	category 8
Analytische Prüfungen an biologischen Materialien	analytical and clinical chemistry testing

Datum der Inspektion (Tag.Monat.Jahr)	Date of Inspection (day.month.year)
14. bis 16. September und 26. bis 28. Oktober 2005	on 14 until 16 September and on 26 until 28 October 2005

Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Based on the inspection report it can be confirmed, that this test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Düsseldorf, den 11. Januar 2006
Im Auftrag

(Prof. Dr. David)

Dienstsiegel/official-seal

Please note: Effective January 1st, 2008, the company name Bayer Industry Services GmbH & Co. OHG was changed to CURRENTA GmbH & Co. OHG.

4. Quality Assurance Statement

This report was audited by the Quality Assurance Unit Currenta, Services Analytik, Quality Management at Currenta GmbH & Co. OHG and this statement confirms that the final report reflects the raw data.

The dates of Quality Assurance inspections and audits are given below:

Audits	Dates of QAU Inspections	Dates of Reports
Study plan inspection	2008-08-04	2008-08-04
Inspection of experimental phase	---	---
Process based inspection	2009-07-20	2009-07-20
Report inspection	2009-08-10	2009-08-10

FOR THE HEAD OF QUALITY ASSURANCE

Mrs. Alexandra Senic A. Senic

Date: 2009-08-10

5. Study Time Table

Study initiation date:	2009-08-05
Study completion date:	2009-08-07
Start of Experimental Tests:	2009-08-05
End of Experimental Tests:	2009-08-06

Table of contents

6. Summary

Report: Jungheim, Rainer: Identity and Content of KBR 3023 in KBR 3023 All-Family Insect Repellent Spray, CURRENTA, report No.: 2008/0078/03, 2009-08-07

Guidelines: --

GLP: yes (certified laboratory)

Time of experimental tests: 2009-08-05 – 2009-08-06

Materials and Determinations:

With the test substance KBR 3023 All-Family Insect Repellent Spray, Batch no.: XKOC00331 the following analytical determinations were performed:

Identity of the active ingredient KBR 3023 in KBR 3023 All-Family Insect Repellent Spray:

The identity of the active ingredient KBR 3023 in KBR 3023 All-Family Insect Repellent Spray, batch no. XKOC00331, was confirmed by comparison with the retention time of the external standard KBR 3023, certified by BayerCropScience GmbH, certification number AZ13506 , determined by HPLC.

Content of KBR 3023 in KBR 3023 All-Family Insect Repellent Spray:

The content of KBR 3023 was determined by the internal method M01166-01 (Saltigo) – HPLC-method for determination of the active ingredient Icaridin in the formulation KBR 3023 All Family Repellent Spray. The method M01166-01 corresponds to the method ANR- 02397 (described in Currenta study no.: 2008/0078/02) and was validated and reported under study no.: 2008/0120/01.

Test	KBR 3023 All Family Insect Repellent Spray Batch no.: XKOC0331 Sample-no.: 808
Identity	Identity confirmed
Content of KBR 3023	21.0 %

Expiry Date

With the results of the identity test and the assay, the stipulated expiry date is: **2011-08-06**

7. Methods and Documents

7.1 Guidelines, guidelines and programs

Identity by comparison of retention times of KBR 3023 determined by HPLC.
HPLC-method with quantification by external standardization is described in Point 9.1.
The content of KBR 3023 was determined by the internal method M01166-01 (Saltigo) – HPLC-method for determination of the active ingredient Icaridin in the formulation KBR 3023 All Family Repellent Spray. The method M01166-01 corresponds to the method ANR- 02397 (described in Currenta study no.: 2008/0078/02) and was validated and reported under study no.: 2008/0120/01.

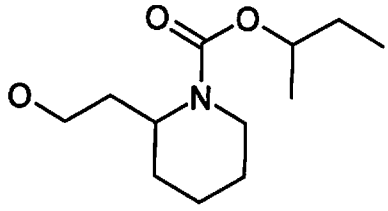
7.2 Principle of the test

High Performance Liquid Chromatography (HPLC)
The content of the active ingredient KBR 3023 in KBR 3023 All-Family Insect Repellent Spray is determined by HPLC on a reversed phase column with UV-detection and quantified by external standardization. The identity was performed by comparison the retention time of the external standard KBR 3023, certified by BayerCropScience GmbH, certification number AZ13506 with the retention time of the active ingredient KBR 3023 in KBR 3023 All-Family Insect Repellent Spray, batch no. XKOC00331.

8. Test and Calibration Material

8.1 Test item

Test substance:	KBR 3023 All family insect repellent Spray
Active ingredient:	KBR 3023
Chemical name of a.i.:	1-methylpropyl 2-(2-hydroxyethyl)piperidine-1-carboxylate
Empirical formula of a.i:	$C_{12}H_{23}NO_3$
Molecular mass of a.i:	229.3 g/mol
CAS no. of a.i.:	119515-38-7
Batch no.:	XKOC00331
Sample no.:	808
Sampling date:	2008-06-30
Expiry date:	2011-08-06
Structural Formula:	KBR 3023



8.2 KBR3023 (analytical standard)

Bayer CropScience

BAYER

Certificate of Analysis

Bayer CropScience GmbH
Product Technology-Analytics Frankfurt
Industriepark Höchst, G 864
65926 Frankfurt am Main, DEU
TEL: +49(0)69-305-2520, FAX: +49(0)69-305-80323

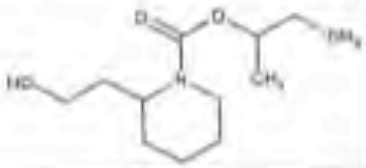
A GLP Testing Facility

Certificate No.: AZ 13506

This Certificate of Analysis fulfils the requirement for characterization of a test/reference item prior to a study according to GLP - regulations. It documents the identity, purity/content and the stability of the test/reference item.

1. Certification of a Reference Substance

Project:	KBR3023 (Icaridin / AE 1228957)
Intended use:	Primary reference substance PS
Batch code:	AE 1228957 00 1899 0001
Material:	icaridin; pure substance
Common name:	icaridin
Chemical name:	1-methylpropyl 2-(2-hydroxyethyl)piperidine-1-carboxylate
Report Name:	KBR3023-a.i.
Cas No.:	119515-38-7
Molecular form.:	C12 H23 N O3
Molar mass:	229.32 g/mol
Origin Batch No.:	M32098
LIMS No.:	0016128



2. Analytical Summary:

Composition

Substance	Name	Content	Method
AE 1228957	icaridin	98.9 % w/w	various
	content a.i. was determined as 100% minus impurities		

Physical properties

Parameter	Value	Method
Appearance	light yellow clear viscous liquid	

Identity

The identity of the certified material was established by use of the following method(s):

MS, 1H-NMR, 13C-NMR

Comment:

Substance in hand is hygroscopic. Please keep away from moisture.

3. Storage and Stability

Storage conditions: +5± 5 °C

Date of analysis: 02-AUG-2006 Expiry date if stored as recommended: 02-AUG-2010

Bayer CropScience

Certificate of Analysis

Bayer CropScience GmbH
Product Technology-Analytics Frankfurt
Industriepark Höchst, G 864
65926 Frankfurt am Main, DEU
TEL.: +49(0)69-305-2520, FAX: +49(0)69-305-69323

A GLP Testing Facility

Certificate No.: **AZ 13506**

Origin of the Certified Material
Biotech Pflanzenschutz
Bayer AG
40789 Monheim, DEU

Certificate Timetable

Experimental start date:	03-JUL-2006
Experimental termination date: (= Date of analysis)	02-AUG-2006
Completion date:	03-AUG-2006

Archiving

Report and raw data are archived at the testing facility.

A retained sample of the certified material is archived at the testing facility.

Records of the preparation of the certified material are retained at the origin.

General Information

Storage

The recommended storage temperature applies for storage over prolonged periods of time. Unless otherwise stated, during shipment or use the substance may be kept at room temperature for a period of several days.

Samples stored at low temperatures should be removed from these conditions of storage as infrequently as possible. A number of small aliquots should be requested where the substance will be used in regular intervals. The number of times each aliquot is brought to room temperature is therefore reduced.

Substances which are easily degraded in the presence of light, moisture or air need to be carefully handled. Dark glass containers should be used to store photochemically unstable substances. Self-indicating silica gel or another suitable material should be stored along with moisture sensitive materials. Those substances which are easily oxidized should be stored under an atmosphere of dry nitrogen.

Handling

Whenever the container is opened for removal of portions of the substance the integrity of the substance must be maintained. Special care must be taken to avoid contamination or adulteration of the test substance. Proper records of the handling and use of the substance must be kept.

Recertification

If this material is to be used after the specified expiry date it will require re-validation and re-certification. The user must then request a new certificate of analysis or can be advised as to the availability of an alternative material.

Responsible Scientist:

3.8.06

Date: Signature

Dr. Michael Cichy for Rüdiger Weilbächer

Head of the Testing Facility:

3.8.2006

Date: Signature

Dr. Thomas Müller for Dr. Martin Feyerabend

9. Methods and Results

9.1 Identity and Assay

Test:	Identity and content of KBR 3023 (Icaridin) inKBR 3023 All Family Insect Repellent Spray
Method no.:	M01166-01 (validated and reported under Study No. 2008/0120/01)
Supervisor:	Dr. Königer
Procedure:	High Performance Liquid Chromatography
Column type:	Length: 250 mm, inner diameter: 4.0 mm
Stationary phase:	LiChrosorb RP-8, particle diameter: 10 µm
Supplier of HPLC-column:	Merck KgaA, 64271 Darmstadt, Germany
Mobile Phase:	60 % demineralized water, 30 % acetonitrile, 10 % tetrahydrofuran (v/v/v)
Flow rate:	1.5 ml/min
Analysis time:	7 minutes
Column temperature:	25 °C (Room temperature)
Detection:	UV, 210 nm
Injection volume:	20 µl

The quantification was performed by external standardization.

The following external standard was used:
KBR 3023, Bayer CropScience, certificate of analysis AZ13506, 98.9 %

Identity of KBR 3023 in KBR 3023 All Family Insect Repellent Spray, determined by HPLC:

The identity of the active ingredient KBR 3023 in KBR 3023 All Family Insect Repellent Spray, batch no. XKOC0331 was confirmed by comparison with the retention time of the external standard KBR 3023 determined by HPLC. The relative retention time of KBR 3023 for the sample solution should not deviate by more than 2 % from that for the calibration solution.

Retention time of the calibration sample KBR 3023	= 4.41 minutes
Retention time of KBR 3023 in KBR 3023 All Family Insect Repellent Spray, batch no. XKOC0331	= 4.42 minutes

9.1.1 Preparation of the analytical standard solution for the determination of the active ingredient.

About 125 mg of the external standard KBR 3023 was weighed to the nearest 0.1 mg into a 50 ml measuring flask. After addition of methanol the mixture was sonicated for two minutes to dissolve the substance and than filled up to the mark with methanol.

9.1.2 Preparation of the test solution for the determination of the active ingredient.

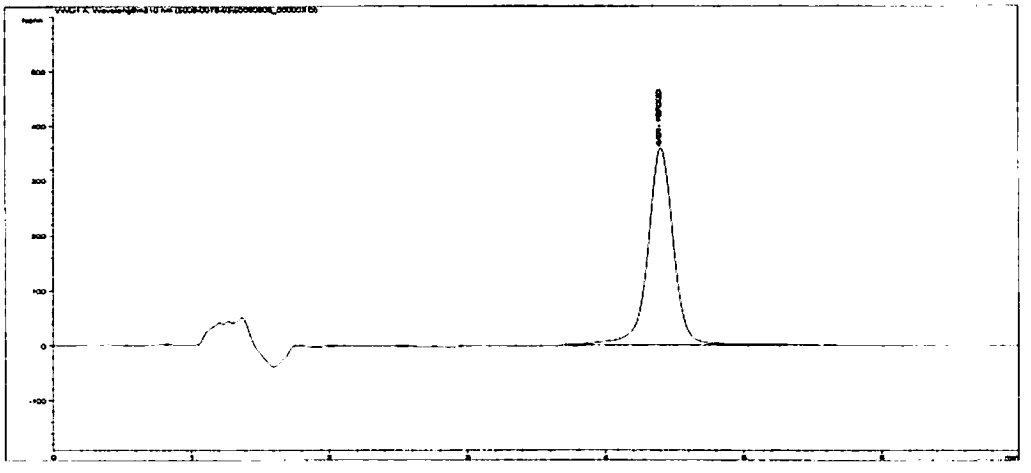
After mechanical homogenization about 625 mg of the test item was weighed to the nearest 0.1 mg into a 50 ml measuring flask. After addition of methanol the mixture was sonicated for two minutes to dissolve the substance and than filled up to the mark with methanol.

9.1.3 Results:

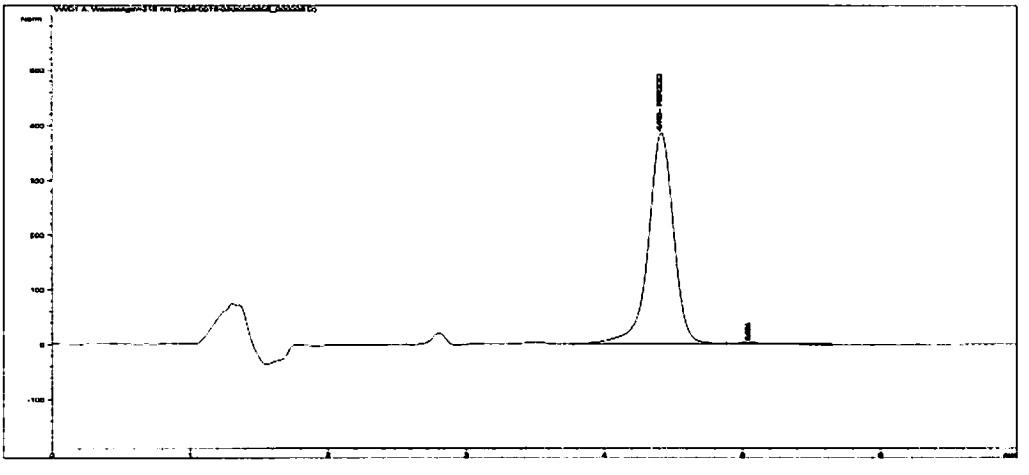
Test	KBR 3023 All Family Insect Repellent Spray Batch no.: XKOC0331 sample-no.: 808
Identity	Identity confirmed
Content of KBR 3023	20.9 % / 21.0 %
Mean value	21.0 %

9.1.4 Example chromatograms

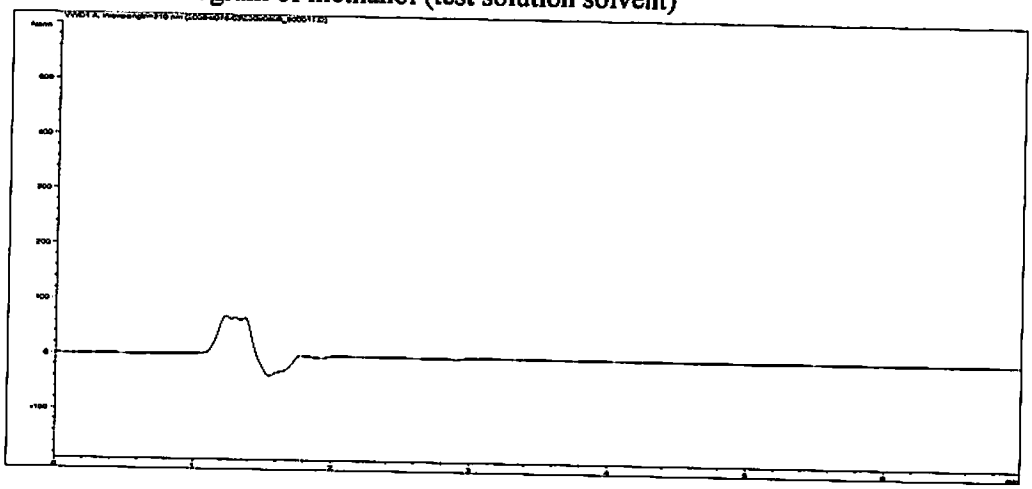
HPLC-chromatogram of the analytical standard KBR 3023



HPLC-chromatogram of KBR 3023 in KBR 3023 All Family Insect Repellent Spray, batch no. XKOC0331



HPLC-chromatogram of methanol (test solution solvent)



LANXESS CORPORATION/Saltigo GMBH
Test Material Shipment
Chain-Of-Custody

Sent To: _Scott P. Carroll. Ph.D. **Date Sent:** 2009.08.12

Address: Carroll-Loye,Biological Research, 711 Oak Avenue, Davis, CA 95616 USA

Signature: Dr. Burkhard Koch **Date:**2009.08.10

Description Of Shipment

Test Substance	Batch / Lot / Reference No.	Amount	Number of Containers	Container Type
KBR 3023 ALL-FAMILY INSECT REPELLENT CREAM	XKOC 00712 (batch Nr) 56154780 (article code)	500 ml	4	Plastic container
KBR 3023 ALL-FAMILY INSECT REPELLENT Spray	XKOC 00331 (batch Nr) 56115181 (article code)	500 ml	5	Plastic container

Received By: Shawn B. King **Date:** 24 August 2009

Signature: B. Z

Condition at Receipt: Excellent – as described in table above

Comments:

Please return copy of the Chain-of-Custody to:

Stan Oslosky
LANXESS Corporation

Carroll-Loye Biological Research

711 Oak Avenue Davis, California Tel (530) 902-8267 http://www.carroll-loye.com/

CHAIN-OF-CUSTODY, MATERIALS RECEIVED

Sponsor reference (Study #): LNX-002

Date Received: 24 August 2009

Courier: Fed Ex

Courier delivery information: International Priority fo door

Vendor/Source: Lanxess Germany

Vendor Shipment ID Number:

☑ Vendor Packing List Received?:

☑ Study Monitor notified by email that materials have been received (if appl.)?: also By phone

Sight (Label) Inventory of Materials Received:

Name (description):	Code no.	Lot (batch) no.	Quantity
KBR 3023 ALL-FAMILY INSECT REPELLENT CREAM	56154780	XKOC 0712	Total of ≈560g (≈500 ml) in 4 Containers
KBR 3023 ALL-FAMILY INSECT REPELLET Spray	56115181	XKOC 0331	Total of ≈450g (≈500 ml) in 5 Containers

Deviations of Sight Inventory from Packing List?:

None Observed

Other (e.g., notes on condition, references to information recorded elsewhere):

Signature of Custodian, date: B. Z. 24 August 2009

Management Approval:
Signature B. Z. Date 19 May 2009

Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530)902-8267 http://www.carroll-loye.com/

Research Notes

CLBR Project I.D.# LNX-002

Date: 19 March 2010

This note records storage temperatures and humidity min/max values for the test materials after receipt from the sponsor until the present, at which time they are being removed for transport to the field site.

Temperature range 19-23°C

Relative humidity range 30-50%.

Signed J.R. Carroll

Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530)902-8267 http://www.carroll-loye.com/

Research Notes

CLBR Project I.D.# LNX-002
Date: 20 March 2010

THIS NOTE records storage temperature & relative humidity during TRANSPORT OF TEST MATERIALS from CLBR laboratory to LNX-002 field site. Storage vessel is an insulated plastic box. Recorded conditions cover period between removal from storage and time of application.

Instrument: control Company 'Thermo-Hygro' 4096, S/N 91228888. Calibrated: 12/09 – 11/09/11.

Min/Max Temperature range: 21-24 °C.
Min/Max Relative humidity range: 24-65 %.

Signed

Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530)902-8267 http://www.carroll-loye.com/

Research Notes

CLBR Project I.D.# LNX-002
Date: 31 March 2010

This note concerns test material accounting.

Test materials were returned to storage, after having been transported back from the site of field efficacy testing, on 22 March 2010.

Signed [signature]

Conforms to 91/155/EEC - 2001/58/EC - Europe

SAFETY DATA SHEET

KBR 3023 ALL-FAM.INSECT REPELLENT CREAM

saltigo
customized competence
A company of the LANXESS Group

56154772

1. Identification of the substance/preparation and of the company/undertaking

Identification of the substance or preparation

Product name : KBR 3023 ALL-FAM.INSECT REPELLENT CREAM

Use of the substance/preparation : Repellent

Company/undertaking identification

Supplier/Manufacturer : Saltigo GmbH
51369 Leverkusen, Germany
Phone: +49 214 30 65109
Fax: +49 214 30 55787
E-mail: infosds@lanxess.com

Emergency telephone number : +49 214 30 99300 (Sicherheitszentrale Chemiepark Leverkusen)

2. Composition/information on ingredients

Preparation of
sec-butyl 2-(2-hydroxyethyl)piperidine-1-carboxylate CAS No.: 119515-38-7 ELINCS No.: 423-210-8

Substance/preparation : Preparation

Ingredient name	CAS number	%	EC Number	Classification
Perfume floral 12889G		0.5		N; R51/53

*** Occupational Exposure Limit(s), if available, are listed in Section 8**

3. Hazards identification

The preparation is classified as dangerous according to Directive 1999/45/EC and its amendments.

Physical/chemical hazards : Flammable.

See section 11 for more detailed information on health effects and symptoms.

4. First aid measures

First aid measures

Inhalation : If inhaled, remove to fresh air. If breathing is difficult, give oxygen. If not breathing, give artificial respiration. Obtain medical attention.

Ingestion : Wash out mouth with water. If affected person is conscious, give a copious amount of water to drink. Seek medical attention.

Skin Contact : Wash skin thoroughly with soap and water or use recognised skin cleanser.

Eye contact : In case of contact with eyes, rinse immediately with a copious amount of water. Seek medical attention.

See section 11 for more detailed information on health effects and symptoms.

5. Fire-fighting measures

Extinguishing media : In case of fire, use water spray (fog), foam, dry chemical or CO_2 extinguisher or spray.

Special exposure hazards : Flammable liquid and vapour. Vapour may cause flash fire. Vapours may accumulate in low or confined areas, travel a considerable distance to a source of ignition and flash back. Runoff to sewer may create fire or explosion hazard.

Hazardous thermal decomposition products : These products are carbon oxides (CO, CO_2), nitrogen oxides (NO, NO_2...).

Special protective equipment for fire-fighters : Fire fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.

6. Accidental release measures

Personal Precautions : Immediately contact emergency personnel. Eliminate all ignition sources. Keep unnecessary personnel away. Use suitable protective equipment (Section 8). Do not touch or walk through spilled material.

Environmental precautions : Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers.

Methods for cleaning up : If emergency personnel are unavailable, contain spilled material. For small spills add absorbent (soil may be used in the absence of other suitable materials) and use a non-sparking or explosion proof means to transfer material to a sealed, appropriate container for disposal. For large spills dike spilled material or otherwise contain material to ensure runoff does not reach a waterway. Place spilled material in an appropriate container for disposal.

7. Handling and storage

Handling : Keep container closed. Use only with adequate ventilation. Keep away from heat, sparks and flame. To avoid fire or explosion, dissipate static electricity during transfer by earthing and bonding containers and equipment before transferring material. Use explosion-proof electrical (ventilating, lighting and material handling) equipment.

Storage : Store in a segregated and approved area. Keep container in a cool, well-ventilated area. Keep container tightly closed and sealed until ready for use. Avoid all possible sources of ignition (spark or flame) .

Packaging materials

Recommended : Use original container.

8. Exposure controls/personal protection

Exposure limit values : Not available.

Exposure controls

Occupational exposure controls : Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapours below their respective occupational exposure limits. Ensure that eyewash stations and safety showers are close to the workstation location.

Respiratory protection : No special measures required.

Hand protection : No special measures required.

Eye protection : No special measures required.

Skin protection : No special measures required.

9. Physical and chemical properties

General information

Appearance

Physical state : Liquid.

Important health, safety and environmental information

Boiling point : >35°C

Flash point : Closed cup: 23 - 61°C

Vapor pressure : <1100 hPa (20°C)

Density : 0.98 - 1 kg/l

Solubility : Soluble in cold water

10. Stability and reactivity

Stability : The product is stable.

Materials to avoid : Flammable liquid and vapour. Vapour may cause flash fire. Vapours may accumulate in low or confined areas, travel a considerable distance to a source of ignition and flash back. Runoff to sewer may create fire or explosion hazard.

11. Toxicological information

Potential acute health effects

Inhalation : No known significant effects or critical hazards.

Ingestion : No known significant effects or critical hazards.

Skin Contact : No known significant effects or critical hazards.

Eye contact : No known significant effects or critical hazards.

Potential chronic health effects

Carcinogenicity : No known significant effects or critical hazards.

Mutagenicity : No known significant effects or critical hazards.

Reproductive toxicity : No known significant effects or critical hazards.

Over-exposure signs/symptoms

Inhalation : No known significant effects or critical hazards.

Ingestion : No known significant effects or critical hazards.

Skin : No known significant effects or critical hazards.

Remarks : Ames-test: negative
Micronucleus test: no clastogenic effect. (sec-butyl 2-(2-hydroxyethyl)piperidine-1-carboxylate)

12. Ecological information

Other adverse effects : No known significant effects or critical hazards.

Other adverse effects : Not available.

Special remarks on the products of biodegradation

13. Disposal considerations

Methods of disposal : Examine possibilities for re-utilisation. Product residues and uncleaned empty containers should be packaged, sealed,labelled, and disposed of or recycled according to relevant national and local regulations. Where large quantities are concerned, consult the supplier. When uncleaned empty containers are passed on, the recipient must be warnedof any possible hazard that may be caused by residues. For disposal within the EC, the appropriate code according to the European Waste List (EWL) should be used. It is

among the tasks of the polluter to assign the waste to waste codes specific to industrial sectors and processes according to the European Waste List (EWL).

Hazardous waste : The classification of the product may meet the criteria for a hazardous waste

14. Transport information

Regulation	UN number	Proper shipping name	Class	Packing group	Label	Additional Information
ADR/RID	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Hazard identification number** 30 **Limited quantity** LQ7
GGVSE	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Hazard identification number** 30 **Limited quantity** LQ7
ADNR	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Hazard identification number** 30 **Limited quantity** LQ7
IMDG	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Emergency schedules (EmS)** F-E, _S-E_
IATA	UN1993	Flammable liquid, n.o.s. (CONTAINS ETHANOL)	3	III		**Passenger Aircraft** 309: 60 L **Cargo Aircraft** 310: 220 L

Combustible
Flash point (Closed cup): 23 - 61°C
Keep separated from foodstuffs

15. Regulatory information

EU Regulations

Classification and labelling have been performed according to EU directives 67/548/EEC, 1999/45/EC, including amendments and the intended use.
- Industrial applications.

Risk Phrases : R10- Flammable.

Safety Phrases : S3- Keep in a cool place.

Other EU regulations

16. Other information

Full text of R phrases referred to in sections 2 and 3 - Europe : R10- Flammable.
R51/53- Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

History

Date of printing : **7/19/2006**

Date of issue : **7/19/2006**

Date of previous issue : **6/7/2006**

Version : **0.02**

Prepared by : Not available.

Notice to reader

The data given here is based on current knowledge and experience. The purpose of this Safety Data Sheet is to describe the products in terms of their safety requirements. The above details do not imply any guarantee concerning composition, properties or performance.

Conforms to 91/155/EEC - 2001/58/EC - Europe

SAFETY DATA SHEET

KBR 3023 ALL-FAMILY INSECT REPELLENT SPRAY

saltigo
customized competence
A company of the LANXESS Group

56115173

1. Identification of the substance/preparation and of the company/undertaking

Identification of the substance or preparation

Product name : KBR 3023 ALL-FAMILY INSECT REPELLENT SPRAY

Use of the substance/preparation : Repellent

Company/undertaking identification

Supplier/Manufacturer : Saltigo GmbH
51369 Leverkusen, Germany
Phone: +49 214 30 65109
Fax: +49 214 30 55787
E-mail: infosds@lanxess.com

Emergency telephone number : +49 214 30 99300 (Sicherheitszentrale Chemiepark Leverkusen)

2. Composition/information on ingredients

contains
sec-butyl 2-(2-hydroxyethyl)piperidine-1-carboxylate CAS No.: 119515-38-7 ELINCS No.: 423-210-8

Substance/preparation : Preparation

Ingredient name	CAS number	%	EC Number	Classification
Perfume floral 12889G		1		N; R51/53

*** Occupational Exposure Limit(s), if available, are listed in Section 8**

3. Hazards identification

The preparation is classified as dangerous according to Directive 1999/45/EC and its amendments.

Physical/chemical hazards : Flammable.

See section 11 for more detailed information on health effects and symptoms.

4. First aid measures

First aid measures

Inhalation : If inhaled, remove to fresh air. If breathing is difficult, give oxygen. If not breathing, give artificial respiration. Obtain medical attention.

Ingestion : Wash out mouth with water. If affected person is conscious, give a copious amount of water to drink. Seek medical attention.

Skin Contact : Wash skin thoroughly with soap and water or use recognised skin cleanser.

Eye contact : In case of contact with eyes, rinse immediately with a copious amount of water. Seek medical attention.

See section 11 for more detailed information on health effects and symptoms.

5. Fire-fighting measures

Extinguishing media : In case of fire, use water spray (fog), foam, dry chemical or CO_2 extinguisher or spray.

Special exposure hazards : Flammable liquid and vapour. Vapour may cause flash fire. Vapours may accumulate in low or confined areas, travel a considerable distance to a source of ignition and flash back. Runoff to sewer may create fire or explosion hazard.

Hazardous thermal decomposition products : These products are carbon oxides (CO, CO_2), nitrogen oxides (NO, NO_2...).

Special protective equipment for fire-fighters : Fire fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.

6. Accidental release measures

Personal Precautions : Immediately contact emergency personnel. Eliminate all ignition sources. Keep unnecessary personnel away. Use suitable protective equipment (Section 8). Do not touch or walk through spilled material.

Environmental precautions : Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers.

Methods for cleaning up : If emergency personnel are unavailable, contain spilled material. For small spills add absorbent (soil may be used in the absence of other suitable materials) and use a non-sparking or explosion proof means to transfer material to a sealed, appropriate container for disposal. For large spills dike spilled material or otherwise contain material to ensure runoff does not reach a waterway. Place spilled material in an appropriate container for disposal.

7. Handling and storage

Handling : Keep container closed. Use only with adequate ventilation. Keep away from heat, sparks and flame. To avoid fire or explosion, dissipate static electricity during transfer by earthing and bonding containers and equipment before transferring material. Use explosion-proof electrical (ventilating, lighting and material handling) equipment.

Storage : Store in a segregated and approved area. Keep container in a cool, well-ventilated area. Keep container tightly closed and sealed until ready for use. Avoid all possible sources of ignition (spark or flame) .

Packaging materials

Recommended : Use original container.

8. Exposure controls/personal protection

Exposure limit values : Not available.

Exposure controls

Occupational exposure controls : Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapours below their respective occupational exposure limits. Ensure that eyewash stations and safety showers are close to the workstation location.

Respiratory protection : Use a properly fitted, air-purifying or air-fed respirator complying with an approved standard if a risk assessment indicates this is necessary.Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the selected respirator.

Hand protection : Chemical-resistant, impervious gloves or gauntlets complying with an approved standard should be worn at all times when handling chemical products if a risk assessment indicates this is necessary.

Eye protection : Safety eyewear complying with an approved standard should be used when a risk assessment indicates this is necessary to avoid exposure to liquid splashes, mists or dusts.

Skin protection : Personal protective equipment for the body should be selected based on the task being performed and the risks involved and should be approved by a specialist before handling this product.

9. Physical and chemical properties

General information

Appearance

Physical state : Liquid.

Important health, safety and environmental information

Boiling point : >35°C

Flash point : Closed cup: 26°C

Density : 0.96 kg/l

Solubility : Easily soluble in cold water

10. Stability and reactivity

Stability : The product is stable.

Materials to avoid : Flammable liquid and vapour. Vapour may cause flash fire. Vapours may accumulate in low or confined areas, travel a considerable distance to a source of ignition and flash back. Runoff to sewer may create fire or explosion hazard.

11. Toxicological information

Potential acute health effects

Inhalation : No known significant effects or critical hazards.

Ingestion : No known significant effects or critical hazards.

Skin Contact : No known significant effects or critical hazards.

Eye contact : No known significant effects or critical hazards.

Acute toxicity

Product/ingredient name	Test	Result	Route	Species

Potential chronic health effects

Carcinogenicity : No known significant effects or critical hazards.

Mutagenicity : No known significant effects or critical hazards.

Reproductive toxicity : No known significant effects or critical hazards.

Over-exposure signs/symptoms

Inhalation : No known significant effects or critical hazards.

Ingestion : No known significant effects or critical hazards.

Skin : No known significant effects or critical hazards.

Remarks :

12. Ecological information

Other adverse effects : No known significant effects or critical hazards.

Other adverse effects : Not available.

Special remarks on the products of biodegradation

13. Disposal considerations

Methods of disposal : Examine possibilities for re-utilisation. Product residues and uncleaned empty containers should be packaged, sealed,labelled, and disposed of or recycled according to relevant national and local regulations. Where large quantities are concerned, consult the supplier. When uncleaned empty containers are passed on, the recipient must be warnedof any possible hazard that may be caused by residues. For disposal within the EC, the appropriate code according to the European Waste List (EWL) should be used. It is among the tasks of the polluter to assign the waste to waste codes specific to industrial sectors and processes according to the European Waste List (EWL).

Hazardous waste : The classification of the product may meet the criteria for a hazardous waste

14. Transport information

Regulation	UN number	Proper shipping name	Class	Packing group	Label	Additional Information
ADR/RID	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Hazard identification number** 30 **Limited quantity** LQ7
GGVSE	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Hazard identification number** 30 **Limited quantity** LQ7
ADNR	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Hazard identification number** 30 **Limited quantity** LQ7
IMDG	UN1993	FLAMMABLE LIQUID, N.O.S. (CONTAINS ETHANOL)	3	III		**Emergency schedules (EmS)** F-E, _S-E_
IATA	UN1993	Flammable liquid, n.o.s. (CONTAINS ETHANOL)	3	III		**Passenger Aircraft** 309: 60 L **Cargo Aircraft** 310: 220 L

Combustible
Flash point (Closed cup): 26°C
Keep separated from
foodstuffs

15. Regulatory information

EU Regulations

Classification and labelling have been performed according to EU directives 67/548/EEC, 1999/45/EC, including amendments and the intended use.
- Industrial applications.

Risk Phrases : R10- Flammable.

Safety Phrases : S3- Keep in a cool place.
S60- This material and its container must be disposed of as hazardous waste.

Other EU regulations

16. Other information

Full text of R phrases referred to in sections 2 and 3 - Europe : R10- Flammable.
R51/53- Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

History

Date of printing : **8/29/2006**

Date of issue : **8/29/2006**

Date of previous issue : **No Previous Validation**

Version : **2**

Prepared by : Not available.

Notice to reader

The data given here is based on current knowledge and experience. The purpose of this Safety Data Sheet is to describe the products in terms of their safety requirements. The above details do not imply any guarantee concerning composition, properties or performance.

TOXICOLOGY PROFILE OF KBR 3023 (page 1 of 2)

The toxicological profile of KBR 3023 is well characterized. All toxicology data were developed using the dermal route of exposure, the most relevant route based on the use pattern of the product (insect repellent for dermal application). The rationale of product development using the dermal route of exposure was considered at the suggestion of the USEPA and in agreement with USEPA and Bayer/Miles. All study protocols, scientific issues, methodology for dermal dosing for extended periods of time and rationale for dose selection were discussed with the EPA. Agreements regarding use of dermal route of exposure were also made with BGA (German authorities) and Health & Welfare Canada. A complete toxicology package required for the registration of an insecticide including acute and subchronic neurotoxicity and metabolism studies was conducted. Additionally, 14-day, 5-week and 14-week dietary feeding studies were conducted to assess any hazard associated with hand-to-mouth transfer from dermal use of KBR 3023. The highest dermal dose for long-term studies was 200mg/kg/day. Dermal absorption studies were conducted both in rats and human volunteers to assess the human risk on the absorbed dose analysis associated with the consumer use of the product.

KBR 3023 and its formulated products have low acute toxicity by oral, dermal or inhalation routes of exposure. They were not irritating to the skin nor sensitizers in the animal studies. A slight to moderate ocular irritation was observed in the animal studies.

KBR 3023 has no demonstrable neurological or developmental toxicity by dermal route of exposure. KBR 3023 shows no evidence of genotoxicity. Subchronic dermal dosing at 500 mg/kg/day produced no clinical pathology and only slight histopathology changes in the liver, and all changes were reversible after four weeks. Chronic dermal dosing in mice, rat and dogs produced no evidence of adverse toxicity changes and it was not oncogenic in mice or rats. In the oral toxicity studies (14-day, 5-weeks and 14-weeks), only kidney effects were seen in the male rats and were attributed to α_{2u} globulin accumulation. The toxicology profile by oral route of exposure did not reveal any new targets compared to the dermal route. Cumulative effects were not evident in dermal or oral studies. The systemic NOAEL in the subchronic studies by oral route were similar (308mg/kg/day for oral/200mg/kg/day- the highest dose tested).

TOXICOLOGY PROFILE OF KBR 3023 (page 2 of 2)

The safety of KBR 3023 was further established by dermal absorption studies conducted in rats and in human volunteers. The dermal absorption study in human volunteers showed that KBR 3023 is poorly absorbed through the human skin. Only 1.66% of the material (AI) was absorbed compared to 19 – 60% for the rat. A conservative dermal penetration factor of 11.5 was used by the EPA for risk assessment. The excretion half-life in humans was 8.2 hours compared to 23.3 hours in the rat. The qualitative pattern of excretion is similar in humans and rats (primary urinary excretion) with similar metabolites. KBR 3023 has good skin feel and is odorless. No significant complaints have been reported over years of use.

In summary:

KBR 3023 has complete toxicology data supported by State-of-the–Art testing
KBR 3023 showed no foreseeable public health risks, including in children and is alternative to DEET
It has no end points of concern
Low acute toxicity
No irritant or sensitizing potential
No specific effects in rats or dogs in short-term and long-term studies
NOAEL = 200 mg/kg (dermal); NOAEL = 308 mg/kg (oral)
Not mutagenic
Not tumorigenic
No effects on reproduction
No neurotoxicity
No photo-sensitisation or irritation
It is poorly absorbed through the human skin
Does not bio-accumulate and is rapidly excreted

Carroll-Loye Biological Research
711 Oak Avenue Davis, California 95616 Tel (530) 902-8267 http://www.carroll-loye.com/

EFFICACY TEST PROTOCOL LNX-002

EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Original Date:	23 March 2009
Initial IRB Approval:	24 March 2009
Federal EPA/HSRB Review:	25 June 2009
California EPA Review:	Initial: 2 June 2009 Final:
Date Amended:	13 August 2009
Final IRB Approval:	
Standards Applied	U. S. EPA Good Laboratory Practice Regulations (40 CFR 160); 40 CFR 26 subparts K, L and M; FIFRA § 12(a)(2)(P); California State EPA Department of Pesticide Regulation study monitoring (California Code of Regulations Title 3, Section 6710).

SYNOPSIS

This biting fly repellent study was commissioned by the sponsor to provide efficacy data for purposes of US/EPA registration. The test materials, based on the active ingredient Picaridin, consist of KBR 3023 All-family Insect Repellent Cream (20% Cream) and KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray).

KBR 3023 (Icaridin; Picaridin) is a new generation of synthetic repellent developed as an alternative to DEET. It was developed by molecular modeling techniques.

From more than 800 substances, KBR 3023 showed the best performance regarding efficacy against a variety of arthropods (Boeckh, et al., 1996) and had the most desired attributes regarding safety, low skin penetration, compatibility with skin, and plastic materials. It was developed by Bayer and is now owned by Saltigo GmbH (LANXESS Group) and in the USA it is handled by LANXESS Corporation (previously a Division of Bayer Corporation).

Icaridin (US EPA Registration Name Picaridin), the current common name, was developed under the Code Name KBR 3023 and the registered trade name Bayrepel™ and was sold under the Brand name Autan. The chemical name for Icaridin is 1-PIPERIDINECARBOXYLIC ACID, 2- (HYDROXY-ETHYL), 1-METHYLPROPYLESTER. However, the INCI (International Nomenclature of Cosmetic Ingredients) name was given as HYDROXY METHYL ISOBUTYL PIPERIDINE CARB. The product was submitted to US EPA under the common name Picaridin. However, the common name, Picaridin, was rejected by ISO (International Organization for Standards) as it was not considered a pesticide. The common name Picaridin was also rejected by WHO/INN (World Health Organization/International Non-proprietary Name) but the common name, Icaridin, was accepted by WHO/INN

The study pursuant to this insect repellent efficacy protocol is intended to provide data under the Data-Call-In requirements (EPA Reg. No. 3126-LRN0) of United States Environmental Protection Agency Guideline OPPTS 810.3700.

Investigator (Study Director) and Performing Laboratory:

Dr. Scott P. Carroll, Ph. D.
Carroll-Loye Biological Research
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Davis, CA 95616
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CV on file with Carroll-Loye Biological Research

Sponsor:

Rainer Eischeid, Vice President
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Study Monitor:

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913-638-3968

IRB:

Independent Investigational Review Board, INC.
6738 West Sunrise Blvd. Suite 102
Plantation Florida 33313
954-327-0778

Quality Assurance Unit:

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Modesto, CA 95357
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CV on file with Carroll-Loye Biological Research

TABLE OF CONTENTS

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1 Justification for Research

1.1 Objective of Research and Endpoints:

1.1.1 Dosimetry

The objective is to determine the amount of repellent a consumer might typically apply using the lotion (cream) formulation, and to determine the dosage to be applied during the repellency phase of the study. The endpoint will be a standard rate of application expressed in ml/cm^2.

1.1.2 Repellency

The objective is to determine the duration and efficacy of the Test Material(s), when applied at a typical consumer dose, in repelling black flies, as well as other biting flies that may be present at the field site;

Shawn King User 6/28/09 2:56 PM
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Arthropod	Species	Disease risk	Study location
Black fly	*Simulium* cf. *vittatum*	None	Sierra and Coast Range foothills, CA
No-see-um fly	*Leptoconops carteri*	None	Central Valley, California
Horse, deer flies	Family Tabanidae	None	Pasture
Stable flies	*Stomoxys calcitrans*	None	Agricultural – near stables

The study will primarily target black flies, but may include other flies listed above depending on seasonal availability in nature. Individual subject dosage will be determined using the standard application rates from the dosimetry completed for related Carroll-Loye Biological Research (CLBR) mosquito repellency study LNX-001 (MRID 47506401).

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Efficacy and duration will be measured as Complete Protection Time, or CPT, defined herein as the time between application of test material and the First Confirmed Probing called 'Landing with Intent to Bite', or 'LIBe', defined as when a biting fly lands on the treated test skin of a subject and ceases locomotion. A 'First Confirmed LIBe' is that which is followed by another within 30 minutes.

The endpoint will be the time of failure expressed as the time of the first confirmed LIBe for each subject.

The resulting data set will be suitable for submission to US/EPA to comply with the conditions of the registration.

1.2 Importance of the Research

Insect repellents are commonly used in the United State to reduce both nuisance biting and disease risk. Traditional DEET-based repellents are highly effective, but are cosmetically inferior and relatively more likely to produce mild to serious side effects. Picaridin-based repellents are cosmetically superior and have a better safety profile. They have been marketed around the world for a decade, but only recently in the US, where they were introduced in 2005. The US Centers for Disease Control (CDC) has acknowledged the existence of substantial consumer interest in new and effective insect repellent products, including the choice of a variety of formulations, delivery systems, and concentrations of active ingredient. Of the three DEET-alternatives currently considered by CDC to have public health value, Picaridin probably has the highest broad-spectrum efficacy. However, few Picaridin products are currently available to US consumers. US EPA has requested new, US-based efficacy data as condition of registration for the test products. The purpose of this study is to provide those efficacy data. The information will also be used in product labeling.

Human subjects are required because they represent the target system for the test material, and sufficiently reliable models for repellency testing have not been developed. Repellent efficacy can only be measured in the presence of biting insects. In addition, the duration of repellency recorded is likely a function of the number of host-seeking insects active during the study. The US/EPA uses a standard minimum rate of insect attack on untreated subjects to ensure that the repellents under study are sufficiently challenged to provide meaningful data. Traditionally, the measure rate is termed the ‘ambient biting pressure’. We adopt that value, but use LIBes (‘Landing with Intent to Bite’) rather than bites, to minimize risks to subjects.

1.3 Balance of Risks and Benefits:

The study-associated risks are of five types: exposure to the test materials themselves, exposure to biting arthropods, possible exposure to vectors of arthropod-borne diseases, physical stress from test conditions, and psychological stress associated with a breach in confidentiality concerning pregnancy test results. As described below, subject health and safety are unlikely to be impacted by any study-associated risks during or after the study.

Subject health and safety are also safeguarded by medical monitoring, assistance, and management.

1.3.1 Risks from Exposure to Test Material(s)

The repellent active ingredient has a low acute and chronic risk profile (§2), established both through experimentation and through a history of consumer use. EPA regulates use of inert ingredients (also termed "other" ingredients) by toxicology profiles in animal tests and by their inclusion in EPA lists of "approved" other ingredients. The insect-repellent products proposed for testing have been tested on animals for potential oral and dermal toxicity (§2). The active ingredient (Picaridin) has an extensive toxicity data base, has been previously registered by EPA and has a positive safety record in consumer use.

Subjects with known allergic reactions to insect repellents and common cosmetics are excluded from participating (§3.3.3). 'Repeat' exposures during dosimetry are all of brief duration before the product is washed off, and the likely total exposure time is much shorter than a typical single consumer application. Risks associated with inhalation and ingestion would only ensue from serious mishandling by subjects, a scenario that the study methods preclude.

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1.3.2 Risks from Exposure to Biting Arthropods

The risk of skin reactions to a bite is reduced by excluding candidate subjects who are aware of having a history of such reaction (§3.3.3). Stopping Rules (§4.7.7) and Medical Management practices (§1.3.6) specify removing any treated limb from the study when the repellent begins failing or the subject shows signs of reacting to a bite or to a Test Material. Treated subjects will expose small areas of untreated skin only once for a maximum of 2 minutes (see following paragraph) to assay subject attractiveness to the target insects immediately prior to beginning exposures of treated skin for 1 minute every 15 minutes for evaluation of repellent efficacy. Untreated subjects with special inclusion criterion (§3.3.2) will participate in the same assay of subject attractiveness to target insects, and expose untreated skin for up to 1 minute every 15 minutes for evaluation of biting pressure during the efficacy test. Other parts of the body will be protected with provided gloves, headnets and full body suits made of Tyvek, through which insects do not bite. Subjects will be teamed with a partner for joint observation and experienced technical personnel will be present at all times for assistance.

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The small biting flies we are targeting are not readily studied in the laboratory. Accordingly, subjects will be shown how to handle them at the field site prior to exposures. Technicians will show subjects how to observe landing flies and

quickly remove them with a small artists' paint brush. After partnering, treated subjects will also briefly expose, only once, an untreated limb to test for individual attractiveness to biting flies, with each partner in the pair assisting the other in preventing bites. As soon as a single fly lands within a one-minute exposure period (or two flies within a two-minute period should no flies land in the first minute), the subject or a technician will remove any flies with a small artists' paint brush and cover the untreated limb immediately.

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Mosquitoes may also be present at the field site. They may land on exposed skin and attempt to bite during biting fly trials. A technician will quickly remove them with an aspirator. Nuisance landings by mosquitoes will be uncommon due to choice of field site, season, and active control (see §1.3.3 for detail). For treated subjects, the Test Materials' repellency towards mosquitoes, previously documented in study LNX-001 (MRID 47506401), will provide additional protection.

1.3.3 Risks from Exposure to Disease Vectors

Disease risk from biting fly bites in California is nil. Disease risk from mosquitoes present during biting fly studies is very low, for several reasons. In our central California biting fly field sites, mosquitoes are far less abundant than in our 'mosquito test' field sites. Moreover, biting fly populations suitable for testing are mainly active in spring and early summer before pathogens such as West Nile virus (WNV) are detected in mosquito populations by state surveillance. Added risk from Western Equine Encephalitis and St. Louis Encephalitis, which present with similar pathology, is basically nil.

The techniques we employ to minimize exposure to insects and insect bites further minimize the possibility of contracting an insect-vectored virus. Field tests are conducted in an area where such viruses have not been detected by county and state health or vector control agencies for at least two weeks, so the risk is probably low that any individual mosquito present carries a disease. Untreated subjects with special inclusion criterion (§3.3.2) will expose untreated skin for a maximum of only 1 minute every 15 minutes over the duration of the test.

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However, because subjects in field tests of biting flies may attract some mosquitoes, they will be instructed to be alert for the presence of these pests and to prevent them from landing or biting. Technicians will attempt to capture any mosquitoes that land on subjects with a mechanical aspirator (or net). Such mosquitoes will be submitted for viral screening as described in §4.7.3.

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

1.3.4 Physical Stress in the Test Environment

Subjects judged to be in poor physical health are excluded from participation (§3.3.3). Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. In addition to providing protection from biting insect pressure, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (ca. 1-3 minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 meters of the screen house.

CLBR staff are trained to watch for and recognize early stages of dehydration, heat, or cold stress in subjects and offer assistance immediately. CLBR staff have advanced first aid training.

1.3.5 Maintaining Privacy of Pregnancy Test Results

Section 3.3.3 lists the exclusion criterion detailing pregnancy test procedures. Results of a subject's test are only observed by one female CLBR staff technician and never recorded to minimize stress on a female subject testing positive, and minimize the possibility that other staff or subjects may become aware of the results of that test.

1.3.6 Medical Monitoring, Assistance, and Management

Subjects are clearly and repeatedly informed that they may remove themselves for any reason from the study at any time, without penalty to their compensation. All subjects are asked to contact the Study Director and a physician of their own choice at any time should they develop a rash (a delayed hypersensitivity reaction) within seven days of the conclusion of the test day.

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On the test day, staff will immediately communicate all subject concerns about health, safety, or comfort to the Study Director for assessment. The Study Director will also assess skin condition of affected subjects should any bites inadvertently occur during efficacy testing, or any subject reports any discomfort in treated areas. Subjects are instructed to inform the Study Director (i.e., the 'Principal Investigator'), or any other staff member if at any time during the study a subject suffers a skin reaction, such as redness, edema, itching or pain, or feels ill. Such subjects will be immediately withdrawn from testing and insect exposure, and medical management will be implemented. When a subject completes the study or is removed for any reason, treated skin areas will be gently washed with clean water and mild soap, rinsed with a 35% ethanol in water solution, then gently dried with a towel to remove test materials.

When medical management is implemented, the Study Director will contact the On-Call physician for the study and comply with the physician's instructions. On the day of testing, a physician who has read the protocol and discussed the research with the Study Director will be on call. Contact information for the nearest medical facilities and maps from the test site to the facilities will be prepared and on file before the day of testing. In unlikely event of a Type 1 allergic reaction (anaphylaxis), we will contact 9-1-1 by cellular or satellite telephone and cooperate as instructed with emergency personnel. Epi-Pens will be on-site. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject. We will be prepared to instruct emergency personnel on how to reach our site via multiple routes. In addition, we will personally transport affected persons to the nearest hospital if so advised by emergency personnel. There is sufficient redundancy in personnel that in such a case subjects remaining at the study site will still receive appropriate technical, scientific and safety guidance.

Subjects may also request access to standard first aid materials (such as bandages, antiseptics, and mild topical and oral antihistamines) and request qualified first aid assistance at any time.

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

1.3.7 Summary of Risks and Benefits

The combination of technical precautions and natural factors means that the chances that any subject will contract disease, suffer an injury, or suffer a severe reaction from an insect bite are extremely small. There is probably less

risk to subjects than they would experience when engaged in normal outdoor activities in a similar rural area at the same time of year.

Against these slight risks are balanced substantial and reasonably likely benefits. The principle beneficiary will likely be the Sponsor, for whom new data and new labeling will meet current US EPA registration standards. Because EPA registration requires efficacy data, a test such as that proposed here is the only path toward further product development, greater availability, and increased consumer acceptance of new repellent formulations in the United States. For the general public, insect-borne disease is of growing significance in the United States and around the world where U.S. citizens are active. Moreover, discomfort associated with nuisance biting restricts many work and pleasure activities.

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355
356 ## 2 Test Material(s): Description and Control
357
358 The following table summarizes all information about the test material(s)
359 relevant to this study.
360

Test Materials as referred to in this Protocol:

	Cream 20%	Spray 20%
Test Material name (Picaridin conc.)	KBR 3032 All-Family Insect Repellent Cream (20%)	KBR 3023 All-Family Insect Repellent Spray (20%)
Manufacturer	LANXESS Corporation	LANXESS Corporation
Manufacturing Standards Applied	Good Manufacturing Practice standards, with records available to EPA.	Good Manufacturing Practice standards, with records available to EPA.
Transport	Commercial Courier, express, insulated container	Commercial Courier, express, insulated container
Chain of Custody	Documented	Documented
Specific gravity	0.98	0.96
Delivery system	Lotion	Pump Spray
Active ingredient(s) (%)	Picaridin 20%	Picaridin 20%
Inert ingredients	Proprietary, available to US EPA	Proprietary, available to US EPA
Stability	Stable	Stable
Storage conditions specified	Room temperature, max 30° C (86° F)	Room temperature, max 30° C (86° F)
Storage conditions applied	Locking, closed cabinet at room temperature (19-24°C) protected from light and moisture sources	Locking, closed cabinet at room temperature (19-24°C) protected from light and moisture sources
Description of cosmetic properties	White cream	Clear solution
NOAELs for Picaridin	NOAEL = 200 mg/kg (dermal); 308 mg/kg (oral)	NOAEL = 200 mg/kg (dermal); 308 mg/kg (oral)
Irritation and sensitization class	(Picaridin) No irritant or sensitizing potential	(Picaridin) No irritant or sensitizing potential
Hazard label requirements	Substantial but temporary eye injury. Do not get in eyes. Wash thoroughly with soap & water after handling, returning indoors, and before eating, drinking, chewing gum, or using tobacco. Discontinue use and consult a doctor if irritation or rash occurs; Flammable.	Moderate eye irritation, avoid contact with eyes or clothing, wash thoroughly with soap & water after handling, returning indoors, and before eating, drinking, chewing gum, or using tobacco. Flammable.
Reference materials	Sample labels in Appendix 3, page 71 MSDS and Toxicology documents in Appendix 4, page 73	

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The sponsor is responsible for completing all toxicological screening, compositional analysis, and stability studies for the test material(s) and providing the results to Carroll-Loye Biological Research prior to providing the test material(s) to Carroll-Loye.

3 Research Subjects: Recruitment, Screening, Consent, Privacy

3.1 Candidate Recruitment: Population, Sampling Frame, Representativeness

For reasons of practicality and control, we work with people associated with the community in which our business is located (Davis, CA). Davis is a university-dominated community, and so the population demography differs somewhat from non-university communities. Compared to the Population of Concern (the US population - all potential repellent users), our sampling frame tends to under-represent blacks and over-represent Asians. It is also young, well educated, and slanted towards Life Science researchers and students.

Over time, we have developed a Volunteer Database of individuals who have expressed interest in participating in future repellency tests, provided contact information, and asked us to contact them. Initial recruiting is from this database, then from word-of-mouth of volunteers. The size and composition of the database varies over time as new individuals volunteer and old volunteers move out of the Davis area, but is now typically over 100 individuals, with the following average ethnic (self-identified) and gender distribution (averaged over 3 years):

Male	52%
Female	48%
Caucasian	74%
Asian	12%
Hispanic	7%
African-American	4%
Arabic	3%

In general, about three-quarters of the subjects are age 20-40, with the remainder between 40 and 55. Final composition is not determined until enrollment is completed. The relevant demographics of the participants will be reported.

There are few published studies of repellent affects on biting flies, in contrast to mosquitoes, thus considerations of how attributes of the arthropod or the

repellent test design affect repellent performance are best inferred from studies of mosquito repellents. Carroll (2006) reviewed the factors that influence the performance of insect repellents and concluded that there is no ready *a priori* means of predicting an individual's attractiveness to a particular mosquito population. Likewise, there are few clear patterns permitting us to predict which individuals might be at relatively greater risk from participating in this study. Pregnant and lactating women are excluded on general medical principals, and persons over 55 are excluded due to slightly elevated health risks from West Nile Fever (above), even though the likelihood of contracting the causal agent during a biting fly repellent test is very low.

We conclude that this study's deviations from the ideal frame will not influence the representativeness of the results, or their generalizability to the greater population. In addition, because our Volunteer Database cohort is comprised by individuals who regularly spend time in outdoor settings (and thereby may have relatively frequent encounters with biting arthropods), this group is probably appropriate for insect repellent users in general.

3.2 Candidate Recruitment Procedures

Recruitment for the Dosimetry study is conducted within a 60-day period prior to the repellency field test day. Recruitment for the Repellency study begins as soon as the test dates are determined.

Potential candidates are initially contacted by phone from our Volunteer Database and queried about interest and availability. Individuals are chosen using a random number table to choose subject numbers from the database and contacted. During the phone interview, we also inform potential candidates that they are permitted to refer others to us by having them contact us. Recruitment continues until the roster of subjects and alternates is full.

Two or more candidate subjects believed to meet the inclusion criteria will be asked if they are willing to consider serving as untreated control subjects. All such subjects currently in our Volunteer Database have participated as treated subjects in at least three previous repellent efficacy trials and thus have observed procedures for untreated controls. They are informed during initial recruitment that the Study Director will discuss with them the relative risks of participating as an untreated (versus treated) subject in greater detail during the consenting process. It is emphasized that participation as an untreated control, while construable as an indication of the Study Director's assessment of their

personal experience and ability, in no way alters their right to withdraw from the study at any time.

3.3 Candidate Screening

3.3.1 Inclusion Criteria, all subjects

Age: 18-55 years

Sex: Male/female

Race: Any race

Completed Consent Process (§3.4) including providing Written Consent (defined as having read, initialed, dated and signed Informed Consent Form and Experimental Subject Bill of Rights)

Language: Speak and read English

3.3.2. Inclusion criteria specific to the two untreated subjects

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.

3.3.3 Exclusion criteria, all subjects:

1. Known to be hypersensitive to biting fly bites or exhibiting hypersensitivity during testing.
2. Phobic of biting insects or insect bites.
3. Known to be allergic to insect repellents or common cosmetics.
4. Known to be sensitive or showing sensitivity to any of the test product ingredients after application.
5. Poor physical condition.
6. Unwilling to submit to brief query about personal condition.
7. Use of insect repellent within one day preceding the efficacy test.
8. Unwilling to refrain from use of perfumed products, alcoholic beverages or smoking after 9 PM the evening preceding the efficacy test and throughout that test.
9. Known to be pregnant or lactating. Each female volunteer of child-bearing potential will self-check for pregnancy using an OTC test kit provided by a technician on the day of any study visit in which repellent will be applied or in which a subject will be exposed to biting insects. Results of each such test will be immediately verified by direct inspection by a female technician experienced in making that assessment.

Information regarding pregnancy test results will be kept in confidence. Only volunteers scored as nonpregnant will be allowed to participate.

10. Unable to see biting flies on skin or otherwise effectively monitor and remove flies that alight on skin.
11. Student or employee of the Study Director.
12. Does not regularly spend time in outdoor settings.
13. Withdraws from testing before receiving a confirming LIBe, when the total exposure duration is less than 90% of the mean of subjects who did not withdraw, and when not more than 2 of 10 subjects have so withdrawn. If more that 2 of 10 subjects withdraw prematurely, those with the briefest participation will be replaced first. This exclusion factor is not automatically invoked if the Study Director ends exposures due to other factors, such as darkness; in such cases the data collected before termination may be sufficient to meet the study goals.

3.4 Obtaining Subjects' Consent

All candidates are screened or re-screened for suitability for each test in a private, one-on-one conversation with the Study Director, at which time the Exclusion Criteria (§3.3.3) are exercised by asking each candidate to address them. It is explained to female candidates of child bearing potential that pregnancy will be assessed directly on the day of any study visit in which repellent will be applied or in which the subject will be exposed to biting insects in the field.

Untreated control subjects are consented first, so that candidate individuals who wish not to serve as controls do not face the option of being excluded from the entire study. For candidate untreated control subjects, the practices to be followed during the field study are reviewed in detail. The relative probability of receiving a bite, compared to a treated subject, is discussed in relation to the precautions inherent in the study design, and to the required behavior for untreated control subjects. Optionality for serving in this role is emphasized.

The Study Director encourages candidates to ask questions and ask for clarification at any time during the interview and in all activities that follow. To candidates that pass screening, the Study Director describes the test purpose in plain language (in English), and the procedures and comportment to be followed are described. Candidates are then asked if they would like to retire from consideration at that point. If they wish to remain in consideration, it is emphasized that they may withdraw from the test at any time during the test without penalty to their compensation. This freedom is especially re-emphasized in cases in which

considerable effort or expense has been required to include a subject (e.g., travel to a distant site), to discourage the subject from believing that the considerable effort or expense creates an added obligation to participate.

If the candidate indicates he or she wishes to proceed, the Study Director provides a copy of this study's IRB-approved Informed Consent Form (ICF) and State of California Department of Pesticide Regulation 'Experimental Subjects' Bill of Rights' (BOR) for review (Appendix 1). The candidate is also offered their own copy of the protocol itself, and supporting documents (MSDSs, toxicology study results, compositional analysis of the Test Materials) for review. In a private session, a senior CLBR staff member certified in protecting human research participants by the National Institute of Health (NIH) will read the ICF and BOR documents out loud with the candidate, offering to take questions and answering any that arise. The amount and form of compensation is described.

Candidates are again encouraged to ask any questions they have about the test, which may include understanding its purpose more fully, understanding risks and discomforts more fully, and understanding treatment and compensation for injury more fully. While the majority of our subjects have worked with us on an occasional basis for a number of years, we encourage them to personally evaluate their interests and concerns about participation seriously each time. We ask them not to sign on immediately but to give the situation due consideration (normally at least one day, sometimes less for those who have participated in multiple prior studies). Because most of the volunteers are researchers and/or have advanced degrees in life sciences, or work directly with or otherwise regularly encounter biting insects in infested habitats, we regard their motivations and decisions to participate as being well considered and well informed. Accordingly, we normally accept their decisions to participate if they so choose following due consideration. Nonetheless, the Study Director retains the final right to refuse participation to any candidate.

When all screening procedures are complete, the candidate is asked to sign, initial, and date the ICF and BOR for this study, both of which are then cosigned by an NIH certified staff member of CLBR. The candidate, now a subject, is then asked to complete a contact and emergency medical form.

3.5 Protecting Subjects' Privacy

Screening interviews are conducted in private and one-on-one. All written records containing names, contact information, medical information, and

signatures are kept in a locked, fire-proof cabinet. Access to these files is restricted to CLBR staff with the Study Director's permission. All subjects are assigned a unique number to identify them on all data forms and to staff and other subjects during testing activities. Although many subjects interact socially during the tests, and may voluntarily share names or other personal information, subjects are never asked, required, or encouraged to do so. Individual data will be entered into the computer for retention and analysis with reference to individual number, not name. Records relating individual names to individual numbers will be retained separately. The Study Director will retain records indefinitely. Subjects may obtain their own records from the Study Director at any time.

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

The possibility that any subject may be designated as an alternate will assist in protecting the privacy of any subject that must withdraw in or near the presence of other subjects at the start of the test day (i.e., before treatment and testing begins), for reasons such as a positive pregnancy test result, or for any other personal circumstance.

4 Study Design

4.1 Number of Subjects

In the dosimetry phase of the study, 15 subjects will be engaged to apply the cream repellent. In the efficacy testing phase, the number of treated subjects per test material will remain at 10, the original justification for which remains unchanged (see text beginning with the next paragraph). Subjects may be asked to participate in one or both phases of the study. The existing dosimetry data set for Cream is from 10 subjects, and was collected in the conduct of the mosquito repellent study LNX-001 (MRID 47506401, reported in 2008). Dosimetry data from the additional 15 unique subjects will supplement those earlier data. The purpose of supplementing existing dosimetry data for Cream is to meet the sponsor's request to improve the accuracy of the mean dosing rate estimate we use for Cream efficacy testing. Given the scientific novelty of dosimetry

studies, it is inevitable that our intentionally conservative sample sizes for human exposure trials will sometimes generate highly variable results, as noted in our discussions with responsible EPA personnel following the formal review of the prior version of this protocol during the June 2009 HSRB meeting. That is the case in the existing Cream dosimetry data set. Methods used to collect the supplementary data (§4.6 & Appendix 9) will be the same as those in the earlier study. Picaridin's dermal safety profile is relatively benign, and we know it to have comparatively low dermal absorption rates. We anticipate that we will have both logical and statistical justification to pool data from the total of 25 subjects to generate single mean and variance statistics based on that augmented sample size.

In efficacy testing, we will use 10 subjects per treatment and 2 untreated control subjects per field trial. Each subject is a replicate. Ten subjects are two-thirds more than the historical EPA requirement of six subjects. EPA is currently working on more precise guidance on sample size, but that remains forthcoming.

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The number of subjects is chosen as a compromise among multiple factors. The goal is to meet regulatory requirements to provide an estimation of the true mean CPT, and so from a scientific standpoint an appropriate response under such circumstances is to increase size, but ethical and economic considerations demand the opposite in the present study, particularly during the efficacy-testing phase.

Importantly, under the historical guidelines, there seem to have been few problems with EPA registering repellents failing to meet their labeled performance specification. Nonetheless, there are clear risks in using a very small sample, and conspicuous among them in this study is that the probability of over-representing subjects inherently unattractive to the target species is rather large. We reduce this risk by confirming subject attractiveness to biting flies before they participate in the phase of the test where efficacy data is collected. In addition, two negative controls are used for a more robust baseline comparison. Those facts should decrease the probability of certain sampling errors substantially.

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For calculating EPA-required mean and variance data, estimating the power associated with a given sample size is constrained by three factors, namely, little knowledge of the magnitude of individual CPT values in a biting fly study, little information regarding the distribution of CPT values in insect repellent studies in general, and, the first consideration notwithstanding, a reasonably

high chance that there will be a number of censored values. If a minority of values is censored, and particularly if the range of values is not great (as in related mosquito repellent study LNX-001), a sample size of 10 should give excellent estimates of mean, median, and variation around those values, relative to historical standards. Still, 10 is sufficiently small, from both statistical and biological perspectives, that we are confident that we are not oversampling.

EPA has expressed interest in refining how CPT data are assessed and analyzed. We judge that such improvements are best made in the context of a further formalization of how EPA makes its labeling decisions from CPT data sets. The central ideas stem from types of survival analysis. One suggestion is to use, e.g., the time to 25% failure (among subjects) as the labeled protection time (when censoring is not too frequent). Another would require the Agency to specify acceptable Type I error probabilities for estimates of minimum CPTs *exceeding* a specified value. With the latter approach, EPA would also have to judge how to label with respect to the confidence interval around such probability estimates. Like the typical estimation of means and standard deviations, the soundness of such alternative statistical judgments will hinge on the accuracy of assumptions regarding the nature of the population distribution.

Given the success of past practices in application, and our clear improvements in sample size, it is premature for us to suggest further substantial change in how the EPA assesses repellent efficacy data. The basic philosophy, and therefore methodology, of how these data are analyzed should be based on a clear and stable agency strategy regarding the information content of product labels.

4.2 Number of Controls

The controls function to assay ambient biting pressure. Recognizing that individual subjects differ in their inherent attractiveness to biting insects, US/EPA science reviewers have recommended that we use two untreated control subjects for field studies in order to improve the likelihood of sampling ambient biting pressure in a representative fashion, while still exposing a very small number of untreated subjects to risks from foraging insects. Having separate untreated subjects also avoids the problem of interaction between treated and untreated limbs that may arise when subjects serve as their own simultaneous controls.

4.3 Controls for Matrix Materials

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

4.4 Controls with Comparison Materials

There are no comparison materials in this study. Questions of comparison between the Test Materials and other repellents are external to the objective.

4.5 Subject Measurements

We will measure length and circumference of the forearms and lower limbs of subjects. Circumference will be measured at four points (upper forearm/calf, lower forearm/calf, and two equally spaced points in between). This data will be averaged for mean circumference, which will be multiplied by length to calculate surface area. This data will be kept on file for each subject. Subjects will be re-measured every two years or if, when asked, they indicate they may have gained or lost weight or muscle mass on their limbs since their measurements were last taken. This practice reduces the frequency of potentially invasive repeated measurement procedures for subjects.

4.6 Standard Dose as Determined by Dosimetry

Dosimetry data collection will take place in the main laboratory building and on the terrace at the letterhead address of Carroll-Loye Biological Research. Dosimetry data is collected for multiple trials on each limb (both arms and both legs). When 15 unique subjects have completed dosimetry for the Cream 20% formulation, the resulting data will be used to determine dosing for the efficacy testing. Some or all of the subjects in the dosimetry trial may participate in efficacy testing. Appendix 9 details conduct of dosimetry and subject training. A summary is provided in the table below. See Appendix 2 for data forms.

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Delivery System	Variables Measured	Key Details of procedure
Cream 20%	Weight[1] of dispensing container before and after subject use	3 trials for average, wash and dry limb between applications.

[1] traceably calibrated Sartorius GC 2502 (measurement increment 0.001 g, 500 g capacity)

4.6.1 Dosimetry Analysis

Statistics will be computed with SAS's JMP software, Version 5.0.1.2 (SAS Institute, Cary, NC). The individual subject will be the experimental unit.

The following table summarizes values that will be calculated:

Delivery system	Value calculated (per trial)	Formula
Cream 20%	Dosage Test Material applied in g/cm^2 skin	Δ weight of dispensing container ÷ surface area of subject's limb

Data will be pooled with dosimetry data from related study LNX-001 (MRID 47506401). Subject means and standard deviations will be calculated for all measures. We will use subject dose means for the Test Material to calculate the dosing grand mean (± SD). That mean, expressed as repellent weight per unit skin surface area, will be converted to volume and used to determine individual subject doses in the efficacy test. To accomplish that, the specific gravity of the test material will be used to convert the dosage weight data to volumes, prepared for each subject on the basis of their skin surface area.

Dosimetry data are thus used to determine individual dosing for efficacy testing. Dosing rates are calculated on a per square cm basis. Spray 20% rates were obtained in a dosimetry study in 2007 during our conduct of an earlier study reported as LNX-001 (MRID 47506401).

The dosing rate for each Test Material is the grand mean rate calculated from 10 subjects (converted from weight to volume by reference to the specific gravity of each test material)

Dosing Rates, by Test Material

	arms	legs
Cream 20%	TBD	TBD
Spray 20%	0.97 μl/cm^2	0.83 μl/cm^2

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4.7 Efficacy – Components of the test

The efficacy study will consist of one field trial in which each Test Material is tested with 10 subjects. There will be two untreated control subjects. The individual subject will be the experimental unit. A single field site is sufficient because the test is for efficacy against a single arthropod taxon that is habitat specific.

Using a mean application rate derived from dosimetry (§4.6), individual dosages will be prepared for each subject volumetrically such that for each Test Material, all subjects receive the same amount of Test Material per unit skin area exposed. Skin surfaces of both treated and untreated control subjects are first cleansed with water and a low-fragrance cleanser, rinsed with a 35% ethanol in water solution, and then towel-dried. Test Material are dispensed from tuberculin (1 ml) syringes by technicians wearing surgical gloves who apply it to treated subjects by spreading it evenly over the area to be treated using one finger and a light rubbing motion. Application of each Test Material is considered a treatment.

All subjects that are not untreated controls will be assigned to the treated group, which will be blocked by gender. The treatments will be allocated in sequence ('A', then 'B', then 'A', etc.). Within each gender, the treatments will be allocated at random excepting minor adjustments needed to constrain the numbers treated with a particular Test Material to 10. The treatment each subject receives and the time of application for each subject will be recorded on a data capture form (Appendix 2). Multiple technicians will make the applications, and each application will take only about three minutes to complete, so that subjects receiving 'A', for example, will not be treated on average significantly earlier than those treated with 'B'.

Whether arms, legs or both are tested at a given site will depend on the behavior of the biting fly population employed. That decision will be made by the Study Director based on reconnaissance of the field sites prior to data collection. Treatments will be balanced between arms and legs if both limbs are used.

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

Subject	Cream 20%	Spray 20%	Untreated
1	Left limb		
2	Left limb		
3	Left limb		
4	Left limb		
5	Left limb		
6	Right limb		
7	Right limb		
8	Right limb		
9	Right limb		
10	Right limb		
11		Left limb	
12		Left limb	
13		Left limb	
14		Left limb	
15		Left limb	
16		Right limb	
17		Right limb	
18		Right limb	
19		Right limb	
20		Right limb	
21			Left limb
22			Right limb

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4.7.1 Blinding of Study

Because the treated condition will be evident to CLBR staff (researchers, technicians) and subjects, neither group will be effectively blinded. However, within the treated group, the two treatments will be indistinguishable to test subjects and technicians based on their physical properties. Accordingly, the two treatments will be coded 'A' or 'B' by a technician. That technician will dispense the Test Materials so labeled for efficacy test treatments. That technician will not be involved in judging LIBe events during efficacy data collection.

The treatment code key will be recorded in hardcopy by the technician and maintained in a locked file drawer to which only he/she has the key. As a backup, the key will also be recorded in a password protected computer file. For backup access, two technicians will be charged with memorizing and privately maintaining the password offsite from the laboratory. Technicians will be charged not to reveal the code or the specific identity of Test Materials at any time during application or data collection, unless needed for medical or legal reasons. The Study Director will retrieve the code key from the technician(s) after the conclusion of data collection.

This moderate level of blinding security is appropriate because the performance difference between untreated and treated conditions is unlikely to be ambiguous, and in which the performances of the Test Materials are not specifically being compared.

4.7.2 Choice of Field Site

Field tests are conducted with large populations of arthropods. This permits the analysis of the replicates (data by subject) as independent values. Also, conditions of use strongly influence repellent performance. Thus we intentionally limit our testing to places and times where large numbers of biting flies are active. We expose subjects as uniformly as possible to the biting flies, and choose sites where subjects may safely engage in behaviors resembling common outdoor activities (walking, sitting, reaching) that may be attractive to biting insects. Subjects are monitored to prevent exposure of treated areas to external moisture or abrasion. We also restrict locations to areas where screen shelters may be effectively erected and maintained for subject comfort and safety.

Locations are in or adjacent to the Central Valley of California. More detailed test site information will be available once it is clear when testing will be permitted, since season influences the availability of test arthropods on both regional and local scales.

4.7.3 Target Arthropods

We will test repellency against either biting midges (*Leptoconops carteri*) or black flies (*Simulium* cf. *vittatum*.) Biting midges occur in and around seasonally flooded grasslands and pastures, while black flies occur near and around flowing streams. This test will be conducted against one, but not both, of these pests. The target pest will be chosen on the basis of availability. We take this approach because a) they do not reliably co-occur, b) EPA has requested that at least one taxon be tested, c) in comparison to mosquitoes, suitable populations of these biting flies are more ephemeral, and d) the techniques used to conduct tests with either are identical.

Specimens will be collected from both treated and untreated (control) subjects and from the protective clothing of all subjects during testing and identified in the laboratory using taxonomic keys and stereomicroscopy. Any specimens of mosquito species known to vector human diseases will be appropriately handled in the field then submitted to a laboratory for viral screening. Results from the assays will be reported by subject in the report, and each subject's results will

be provided to them individually once the screening laboratory provides them to CLBR.

4.7.4 Measuring Ambient Biting Pressure

Traditionally, the US/EPA minimum attack rate for challenging a repellent under testing is termed the 'ambient biting pressure'. We propose to define the minimum ambient biting pressure as 1 LIBe ('Landing with Intent to Bite') per minute.

A mean study LIBe ('Landing with Intent to Bite') rate of ≥ 1 LIBe per untreated (negative control) lower leg or lower arm per minute is required. No more than 10% '0' values for individual exposure periods are permitted. For stable flies, draft EPA repellency test guidelines recommend an ambient biting pressure of one per 5 minutes with exposures every 30 minutes. Since the focus of the study will be black flies, whereas data collected for stable flies, if it occurs, will be incidental, we propose to use the one LIBe per minute minimum. Ambient LIBe pressure is measured from continuous exposure during 1-minute exposure periods commencing once every 15 minutes, beginning at the onset of data collection. Because the test material has been shown to have very long duration efficacy against mosquitoes (approximately 12 hours; Carroll-Loye Biological Research (CLBR) mosquito repellency study LNX-001 [MRID 47506401]), and in our experience repellents with long-duration efficacy against mosquitoes generally also display long duration efficacy against other biting arthropods, we expect data collection to continue for up to about 12 hours after repellent applications. Data will be tabulated for each control subject (Appendix 2)

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4.7.5 Measuring Repulsion

The number of LIBes on each subject's exposed treated area will be recorded (Appendix 2) as they occur during 1-minute exposure periods commencing once every 15 minutes, beginning at the onset of data collection and ending when the subject receives the First Confirmed LIBe, a stopping rule is invoked for the subject, or the Study Director stops the test for all subjects.

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4.7.6 Environmental Conditions – Data

Records (Appendix 2) of presence/absence and general rate/quality data for environmental conditions (temperature, relative humidity, wind speed, light intensity, general cloud cover description, and precipitation) will be made at approximately one-hour intervals throughout the course of the field trial.

4.7.7 Stop Rules

All subjects

Consented duration reached

Test site becomes unsafe for subjects for any reason

Biting/foraging pressure falls below threshold needed to challenge the test materials

Biting/foraging pressure rises to levels unacceptable in terms of subject comfort or safety

Sustained wind speed exceeds 10 mph

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Individual subjects

Subject asks to withdraw

Subject proves unattractive to target species

Subject's treated limb receives Confirming LIBe for all species for which repellency data is being collected on the test day.

Medical management is invoked for the subject (§1.3.6)

4.8 Sequence of efficacy test procedures

4.8.1 Within 60 days preceding Test Day

Candidate screening and subject consenting will occur.

4.8.2 Week prior to Test Day

The Field Manager and logistics staff travel to the field site, mitigate or remove all hazards from areas that will be accessed by staff and subjects, and erect and stock the screen house in preparation for the test day.

4.8.3 One day prior to Test Day (travel day, if the field site is more than about 3 hours travel time from the laboratory) or the Test Day (3 hours or less travel time)

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Subjects gather at the Carroll-Loye Biological Research laboratory. The technicians and other researchers who will assist subjects during the test will be introduced or reintroduced to the subjects. Subjects are instructed to call on them whenever they have questions. Subjects are also reminded of procedures for the repellency test day.

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4.8.4 Test Day

Treatments may be applied at the laboratory, at the field site, or shortly before travel from accommodations to the field site. Subjects will gather to clean limbs for applications, put on protective Tyvek suits, and have boundaries of treated areas bandaged for protection from biting insects. If the Test Material is already

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known to remain effective for many hours, applications may be made up to three hours in advance of the first exposure period if that reduces the probability of subjects needing to withdraw due to exhaustion before receiving a confirmed LIBe. In order not to inflate protection times recorded due to such 'pre-treatment', for any subject treated more than one hour in advance of initial exposure who receives a confirmed LIBe within the first five exposures, the limb will be withdrawn and another limb treated. Exposures of the second treated limb will begin at the next exposure period, in order to produce a replacement estimate of Complete Protection Time. All treated limbs are monitored to minimize abrasion with clothing from the time of application.

At the field site, the subjects and technicians will gather in an area without biting insects. Subjects are instructed not to leave this area until guided by a technician.

In addition to Tyvek coveralls, each subject is given and must wear a head net and latex, nitrile or vinyl gloves in their size, and is given a small artists' paintbrush to remove any biting insects that land on treated skin and attempt to bite (LIBe) once formal exposures begin. A technician will remind subjects about how to identify LIBes. Subjects will be further instructed about protecting themselves from insect bites during the test, and about reporting when an insect that lands on skin treated with repellent exhibits biting behavior.

Treated subjects will be partnered into groups of two, and untreated control subjects will each be accompanied by two technicians. A technician will then guide subjects into the area of the field site in which members of the target species are active. Each subject will briefly expose one time only an untreated limb to verify his or her attractiveness to the target species (detailed in §1.3.2).

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A technician will then advise untreated and treated subjects when their respective timed exposure periods begin and end. To assay biting pressure, the untreated control subjects will each expose one limb by uncovering the limb for 1 minute, then covering the limb. If biting insects are too abundant to permit ready removal, the controls may protect the exposed limb as soon as a LIBe by the target species occurs. Immediately following LIBes on the controls, members of a treated partner pair will watch their own one-minute-exposed limbs and those of their partner for biting flies that land and exhibit biting behavior. During exposure, subjects will immediately remove any LIBing insects from the exposed skin. Partners will assist one another in removing biting insects as needed, and technicians will assist control subjects in removing LIBing insects.

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At the end of the one-minute exposure period, subjects move away from the area with biting insect activity. To reduce abrasion of the treated skin by shifting the sleeves/legs of the protective garments, subjects may leave the skin uncovered between exposure periods if they immediately enter a protected site (e.g., a screen house) and if Study Director determines that they may do so without risk of uncontrolled additional exposure to biting insects.

Each subject will report the number of target species that attempted to bite their own treated skin during that one-minute period when asked by a technician who will record it on a data sheet (Appendix 2).

The preceding sequence will be repeated at 15 minute intervals until the Study Director stops the test.

For perspective, note that in a typical test of a reasonably effective repellent, dozens of '0' LIBe values will be recorded for each '1' or '2'. In other words, during most exposure periods, potentially for the first several hours, subjects may not experience close contact with biting flies. The probability of eventual direct contact, if any occurs before the cessation of exposure due to darkness or subject withdrawal, increases at a slow rate.

4.9 Efficacy – Statistical design and analysis

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

The hypothesis that the test material will significantly reduce the number of biting flies LIBing on treated versus untreated skin is not the objective of this study. The objective is to compute, for each test material, a reasonable estimate of mean and standard deviation for the duration between application and repellency breakdown sufficient such that two biting flies LIBe on a subject within a one-hour period ("Complete Protection Time" or CPT). That pattern is here assessed at a resolution of 15 minutes. The untreated limbs serve to monitor whether the ambient biting pressure remains at or above the EPA standard.

For each control, we will record the number of LIBes occurring within a 1-minute exposure at the beginning of each interval.

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For each treated subject, we will measure (data form Appendix 2):

- Exposure delay (min) – time between application and first exposure
- Minutes in field to First Confirmed LIBe (FCLIBe) or end
- Complete Protection Time (CPT) – time between application and FCLIB

CPT is measured as a single time value for each subject. Based on the requirements for such estimates in the EPA draft repellent efficacy testing guidelines (1999; OPPTS 810.3700), we will calculate mean CPT across all 10 subjects, with standard deviation and 95% confidence interval information. Data will be normalized as possible to enhance the value of confidence interval calculations. Ambient LIBing pressure as measured by untreated subjects will be presented tabulated by individual and exposure period. Mean LIBing pressure will be calculated as the number of LIBes received per untreated control subject and per period and span of exposure.

As described in §4.74, we anticipate that protection may span up to about 12 hours after application. By treating subjects early in the day, and testing under long day length conditions, we will minimize the number of subjects for whom sampling is truncated prematurely by darkness. To examine the temporal pattern of failure further, we will employ Kaplan-Meier survival analyses by subject. Kaplan-Meier survival analysis accommodates some data censoring in the event that any subjects withdraw or are withdrawn before failure. In addition, we will estimate the Kaplan-Meier median, and the time until 25% failure, for each test product. In the presence of a high frequency of censoring, median (and mean) values will be underestimated.

Our chosen sample size of 10 subjects will improve precision in estimating test material performance. This sample, which is larger than that traditionally required by US EPA, is implemented at considerable expense to the study sponsor, but is consistent with suggestions from HSRB advisors to EPA. The resulting data set will provide values suitable for any additional statistical characterizations of repellent performance that EPA may wish to employ in developing labeling language for the Test Materials.

5 Quality Assurance

A separate, professional Quality Assurance Unit (QAU) will inspect the study. The QAU will report to the Study Director. Protocol Review and Comments must take place before data collection commences. In-Life Inspection must include observing the measurement and recording of key variables by subjects and

technicians. In addition, the Final Report will be audited for completeness and accuracy. A QAU Statement will address compliance and noncompliance or any omissions in auditing. Findings from the In-Life Inspection and the Final Report, as well as the QAU Statement will be transmitted to both the Study Director and to the Sponsor Study Monitor.

6 Amendments and Deviations to the Protocol

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

7 LITERATURE CITED AND SELECTED REFERENCES

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8 PROTOCOL APPROVAL SIGNATURES

Scott P. Carroll, Ph. D.
Study Director

23 March 2009
Date

G. K. Sangha, Ph. D.
Study Monitor

March 23, 2009
Date

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INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in lotion (cream) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study

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laboratory. At a later date, we will go to a field site to test the insect repellents against biting flies in nature. You may be asked to participate in one or both parts of the study.

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.
- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellency testing.

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NUMBER OF SUBECTS PARTICIPATING

Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test. 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 asked to participate later if needed. If you are designated as an alternate, you will be compensated for your participation up to that point and for your inconvenience.

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STUDY INTRODUCTION AND DURATION

Schedule of visits and time required to participate in the study

Activity	Visit 1	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	12 hours to 3 days

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Visit 1 for Orientation and Cream Dosage Determination

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form. You may also work with a researcher to determine how much of the cream repellent you apply.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

This part of the study will also require one visit to the field site of the study. The field site visit will most likely require one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to accommodations, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

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STUDY PROCEDURES

Visit 1

At the laboratory, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken.

If you are participating in the dosage determination part of the study, you will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory, at the field site, or shortly before travel from accommodations to the field site.

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A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. A technician will then apply insect repellent to your forearm or lower leg to give even, complete skin coverage. The amount of repellent applied on any one arm or leg will be no more than about 1/2 teaspoon, and is typical of what people commonly use. You will be randomly (like the flip of a coin) chosen to receive either 20% Picaridin spray or 20% Picaridin cream. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

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Two experienced subjects will also participate to record the activity of biting flies by exposing their own arms or legs without repellent. Experienced subjects are pre-qualified by the Principal Investigator, and designated before the field test begins.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent application, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be partnered with another subject so that each of you can help the other observe your treated limbs for biting flies. You and your partner will watch your exposed arms or legs and those of your partner for biting flies that land during a one-minute period. As a treated subject, you will be asked to expose untreated skin only once, for up to two minutes, at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or your partner will remove the fly using a small artists' paintbrush and you will cover your untreated limb immediately. A technician will let you know when the exposure period begins and ends. If no biting flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience. Once this single attractiveness test is completed, you and the other treated subjects will continue with exposures of treated skin, in partnered pairs, going to the area where biting flies are active for one-minute exposures every 15 mintues.

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For each exposure, a technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, you or your partner will remove them immediately with a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. A technician will record the number of biting flies that attempted to bite your exposed skin during the one-minute period (normally 1 or 0). Every 15 minutes, a project leader will announce the beginning of the next one-minute period for exposures for data collection. If more than one biting fly of each species in the test attempts to bite you on your treated skin during one of the one-minute

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periods, or in two consecutive exposure periods (that is, 30 minutes apart), you should cover the skin and not expose it again.

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RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

The cream repellent will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed. You may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 7 days after the day of testing. The first-aid kit at the field site contains 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.

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In addition, there is a very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing repellent and/or 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.

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The U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 and a technician will work to quickly remove mosquitoes before they have an opportunity to bite, and since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. If you are a woman of childbearing potential, it is important that you do not participate

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in this study if you are, or if you think you may be pregnant, or if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks and discomforts listed above, there may be some unknown or infrequent and unforeseeable risks associated with using 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, or change the nature of the risks associated with participating.

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 healthcare 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 that covers you. 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

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) 902-8267 at any time.

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If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

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

For participation in the study, each research study participant will receive a cash payment of $20 per hour for research activities, and $125 for each full travel day. 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 your travel days and $20 per hour for your time at the field site.

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CONFIDENTIALITY
Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING
Right to withdraw or removal from study
You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time. You understand that the distance or time you travel to participate does not increase

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your obligation to participate or restrict in any way your right to withdraw at any time.

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

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)
Independent Investigational Review Board, Inc. Approved:

Version:
Protocol: LNX-002
TREATED Subjects

APPROVED BY
Independent IRB

Signature Date

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INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in cream (lotion) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study laboratory. At a later date, we will go to a field site to test the insect repellents

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against biting flies in nature. You may be asked to participate in one or both parts of the study. If you are asked to participate in the field test, your role will be to serve as a carefully protected, but untreated, control subject. Periodically throughout the test, you will expose skin of your lower arm or lower leg to biting flies, with no repellent applied. You and technicians attending you will remove the flies as quickly as possible, normally before you are bitten.

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The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

To be considered as a subject who exposes untreated skin, you 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.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.

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- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellent testing.

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NUMBER OF SUBECTS PARTICIPATING

Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test. 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 asked to participate later if needed. If you are designated as an alternate, you will be compensated for your participation up to that point and for your inconvenience.

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STUDY INTRODUCTION AND DURATION

Schedule of visits and time required to participate in the study

Activity	Visit 1	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	12 hours to 3 days

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Visit 1 for Orientation and Cream Dosage Determination

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form. You may also work with a researcher to determine how much of the cream repellent you apply.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

This part of the study will also require one visit to the field site of the study. The field site visit will most likely require one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to

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accommodations, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

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STUDY PROCEDURES

Visit 1

If you are participating in the dosage determination part of the study, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken. You will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

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You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory prior to departure to the field site, or at the site after arrival.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

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At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent applications to treated subjects, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be asked to expose untreated skin once for up to two minutes at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or a technician will remove the fly using a small artists' paintbrush. If no flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience.

If you are asked to continue participating, you and two technicians will watch your exposed arm or leg for biting flies that land during one-minute periods every 15 minutes for the duration of the test day. A technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, a technician or you will remove them immediately using a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. When the one-minute exposure period ends, or if biting flies are too numerous for you and your attending technicians to remove effectively, you will immediately cover your exposed skin with the fabric (sleeve or leg) of the coveralls. A technician will record the number of biting flies that attempted to bite your exposed skin during each one-minute exposure period (normally 1 or 0). Every 15 minutes, a project leader will announce the beginning of the next one-minute period for exposing your untreated skin and watching for biting flies attempting to bite it.

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RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

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Although you will not have repellent applied to you during the field test, you may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels. The cream repellent applied to treated subjects and subjects participating in dosage determination will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed.

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In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 7 days after the day of testing. The first-aid kit at the field site contains 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.

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In addition, there is a very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing protective clothing, 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 U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands or a rash on the trunk of the body. About 1 in 150 infected people will develop more serious symptoms, including neck stiffness, stupor, disorientation and possibly coma and paralysis.

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To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

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study. If you are designated as an 'alternate subject,' you will be paid for your travel days and $20 per hour for your time at the field site.

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CONFIDENTIALITY

Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time. You understand that the distance or time you travel to participate does not increase your obligation to participate or restrict in any way your right to withdraw at any time.

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

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

APPROVED BY
Independent IRB

Signature Date

Initials: _____
Date: _____

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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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)

Independent Investigational Review Board, Inc.
Approved:

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

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

1. Be informed of the nature and purpose of the study.
2. Be given an explanation of the procedures to be followed in the experiment, and any drug or device to be used.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the study may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of a signed and dated written consent form and Experimental Subject's Bill of Rights when one is required.
10. Be given the opportunity to decide to consent or not to consent to an experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

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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) 902-8267 at any time.

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) between 6AM and 2PM, Pacific Time, Monday through Friday. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study.

_____ _____
Signature of Subject Date

_____ _____
Signature of Witness Date

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APPROVED BY
Independent IRB

_____ _____
Signature Date

Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530) 902-8267 http://www.carroll-loye.com/

CLBR Training Manual

Practicing and performing dosimetry with Lotion/Cream delivery systems

A. Goals of exercise

1. Determine your preferred practices for applying lotion repellents to your arms or arms and legs.
2. Assist technicians in measuring the amounts of such repellents that you apply when using your practices

B. General information

1. A technician will measure the surface area of your forearms and lower legs. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken. He or she will introduce you to the repellent(s) and their containers
2. You will work in the laboratory, practicing applying the repellent(s).
3. You will thoroughly wash your limbs with a gentle skin cleaner between each application of repellent.

C. Materials and equipment needed

1. Test materials
2. Latex or vinyl gloves (various sizes)
3. Temperature and humidity measuring devices
4. Written copy of the procedures for subjects to read
5. Flexible metric rule

D. Practicing the methods and performing the measurements

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

[1] **Limb dimensions and surface area (technical details):**

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

Lotion sampling

The amount of lotion applied to limbs will be quantified in a series of three applications. The amount applied is the weight difference in the dispensing container before and after application.

The instructions are as follows:

"Put a new latex or vinyl glove on each hand. You will apply lotion to one arm only. The technician will tell you to which arm to apply. You will begin with an amount that you suppose is about one half of what you will need to achieve thorough and uniform coverage. After spreading that around the lower part of your arm, you will apply more as needed to the area closer to your elbow. Begin by gently squeezing lotion from a container with the cap open directly onto the horizontally-held surface of the opposite arm. Hand the container to the technician. Using the tips of the index and middle fingers, spread the lotion as evenly as possible on all surfaces of the lower arm. Do not spread it onto the hand or beyond the marking on your wrist. If you have sufficient lotion left to spread it evenly and thoroughly toward the elbow, continue in the direction. Do not spread it beyond the elbow or past the marking near the elbow. If you need more lotion to achieve thorough and even coverage, make sure you have wiped all repellent from your fingertips onto the skin and ask the technician to hand you the container. Apply as much additional as you think you need, as before, but to complete the coverage. If you decide that you have applied more repellent that you would normally use to achieve thorough and even coverage, immediately have the technician wash and dry the treated arm so that none of the repellent you have applied is visible on close inspection, and begin again. Likewise, be careful to avoid dropping any lotion off of the arm, and if this happens, begin again as you would if you applied too much.

After you have completed an application successfully, the technician will ask you to wash and dry the treated arm so that none of the repellent you have applied is visible on close inspection, and he or she will reweigh the container. You will continue until you have completed three successful applications. Then you will repeat the entire procedure above, but with the lower leg."

Lotion Dosimetry Form
Study
Date:

Subject number:

Data recorder name:

Data recorder signature:

I. Practice Application		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1		

II. Lotion Sampling		
A. Arm. Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1		
2		
3		

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1		

B. Leg Left or Right (circle 1)		
Trial number	Mass before (g)	Mass after (g)
1		
2		
3		

Subject Number	Sex	Limb	Limb Surface Area (sq cm)	Lotion Mass Before (gm)	Lotion Mass After (gm)	Total Lotion Applied (gm)	Average Lotion Applied (gm)	Average grams of lotion / sq cm
		L				0	0	#DIV/0!
						0		
						0		
		R				0	0.000	#DIV/0!
						0		
						0		
		L				0	0	#DIV/0!
						0		
						0		
		R				0	0.000	#DIV/0!
						0		
						0.000		
		L				0	0.000	#DIV/0!
						0		
						0.000		
		R				0	0.000	#DIV/0!
						0		
						0		
		L				0	0	#DIV/0!
						0		
						0		
		R				0	0.000	#DIV/0!
						0		
						0		
		L				0	0.000	#DIV/0!
						0.000		
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		R				0	0	#DIV/0!
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		L				0	0.000	#DIV/0!
						0		
						0		
		R				0	0	#DIV/0!
						0		
						0		
		L				0	0	#DIV/0!
						0		
						0		
		R				0.000	0	#DIV/0!
						0		
						0		
		L				0	0.000	#DIV/0!
						0		
						0		
		R				0	0	#DIV/0!
						0		
						0		

	Overall average grams of lotion per	Overall average grams of lotion per sq cm
L s only	0.000	#DIV/0!
R s only	0.000	#DIV/0!
L and R s	0.000	#DIV/0!

Lotion Specific Gravity =

Application Rate: / sp grav = **mL per sq cm**

Repellent Applications

Study: **Test Location:** **Date:**

	Subject Number	Sex	Limb (R or L)	Lower Limb Surface Area (square cm)	Repellent Applied (A, B, C)	Application Rate (mL of Repellent / square cm of skin)	mL of Repellent Applied	Time of Application	Initials of Technician

RepApplMaster.xls

Biting Fly LIBes at 15 Minute Intervals

Study: **Application Time(s):**

Date: **Time of First Exposure:**

Time:																				
15 Minute Interval:	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
Subject Number																				
Control 1																				
Control 2																				

Key: 0 = Repulsion, Number = LIBe(s) **BitingflyLIBeDataSheet15min.xls** **Data Recorder Name and Signature:** _____ **Page 1 of ____**

Biting Fly LIBes at 15 Minute Intervals

Study: **Application Time(s):**

Date: **Time of First Exposure:**

Time:																				
15 Minute Interval:	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**
Subject Number																				
Control 1																				
Control 2																				

Key: 0 = Repulsion, Number = LIBe(s) **BitingflyLIBeDataSheet15min.xls** **Data Recorder Name and Signature:** _____ **Page 2 of ____**

Biting Fly LIBes at 15 Minute Intervals

Study: **Application Time(s):**

Date: **Time of First Exposure:**

Time:																				
15 Minute Interval:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56				1
Subject Number																				
Control 1																				
Control 2																				

Key: 0 = Repulsion, Number = LIBe(s) **BitingflyLIBeDataSheet15min.xls** **Data Recorder Name and Signature:** _____ **Page 3 of ____**

Efficacy Data, Study ______________

Hours in field, sequential exposure period

						0				1				2				3				4				5				6				7				8				9				10				etc				
Site	**Date**	**Subject**	**Sex**	**Product**	**Exposure delay (min)**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**etc**	Min in field to FCLIBe* or end	CPT (min)	CPT (hrs)	Total # LIBes** per subject
1				A																																																0	0.00	
1				A																																																0	0.00	
1				A																																																0	0.00	
1				A																																																0	0.00	
1				A																																																0	0.00	
1				A																																																0	0.00	
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1				A																																																0	0.00	
1				B																																																0	0.00	
1				B																																																0	0.00	
1				B																																																0	0.00	
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1				B																																																0	0.00	
1				B																																																0	0.00	
1				B																																																0	0.00	
1				Control	–																																																	
1				Control	–																																																	

* = First Confirmed Landing with intent to bite
** = Landing with Intent to Bite

Amendment 1, Carroll-Loye Protocol LNX-002

Version Date: 13 August 2009

Introduction

This document is Amendment 1 for CLBR Protocol LNX-002: EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS. In addition to detailed annotations of amendments to the protocol and its support documents, it includes both the subject training document for dosimetry and dosimetry data collection and entry sheets.

The amendment is prepared in response to California EPA reviews, HSRB reviews at the 25 June, 2009 meeting at US EPA in Crystal City, VA, as well as the Sponsor's request for additional dosimetry data. For changes to the body of the protocol, consent documents, and pre-existing data forms, the amendment is prepared as a list of entries. For all edits, the location of the change in the protocol and the exact change of wording are given. Where helpful, an explanation for the change is also provided. Adjustments that apply to multiple points in the body of the Protocol are grouped by the topic of the change. Single-instance adjustments are organized in the order they appear in the Protocol, where possible. Adjustments to Consent documents follow as above, and adjustments that are editorial or typographic, with no change to meaning, are listed last, in the order they appear in the body of the Protocol and in consent forms.

Protocol

The Sponsor has requested additional dosimetry data to improve the statistical power of the mean dosing rate estimate used for the Cream 20% Test Material. The Protocol has been amended to specify how subjects will be included in dosimetry, how the data will be collected, and how it will be used for dosage determination in the repellency field test.

Section 1.1 Objective of Research and Endpoints is amended with the addition of subsection 1.1.1 Dosimetry, containing in its entirety the following paragraph: "The objective is to determine the amount of repellent a consumer might typically apply using the lotion (cream) formulation, and to determine the dosage to be applied during the repellency phase of the study. The endpoint will be a standard rate of application expressed in ml/cm^2."

Section 1.3.1 Risks from Exposure to Test Material(s) second paragraph, is amended with the addition of a new sentence added as the second sentence reading as follows: " 'Repeat' exposures during dosimetry are all of brief duration before the product is washed off, and the likely total exposure time is much shorter than a typical single consumer application."

Section 3.2 Candidate Recruitment Procedures first paragraph is amended with the addition of a new sentence at the beginning, which reads: "Recruitment for the Dosimetry study is conducted within a 60-day period prior to the repellency field test day."

Section 4.1 Number of Subjects is amended with the addition of a new first paragraph which reads: "In the dosimetry phase of the study, 15 subjects will be engaged to apply the cream repellent. In the efficacy testing phase, the number of treated subjects per test material will remain at 10, the original justification for which remains unchanged (see text beginning with the next paragraph). Subjects may be asked to participate in one or both phases of the study. The existing dosimetry data set for Cream is from 10 subjects, and was collected in the conduct of the mosquito repellent study LNX-001 (MRID 47506401, reported in 2008). Dosimetry data from the additional 15 unique subjects will supplement those earlier data. The purpose of supplementing existing dosimetry data for Cream is to meet the sponsor's request to improve the accuracy of the mean dosing rate estimate we use for Cream efficacy testing. Given the scientific novelty of dosimetry studies, it is inevitable that our intentionally conservative sample sizes for human exposure trials will sometimes generate highly variable results, as noted in our discussions with responsible EPA personnel following the formal review of the prior version of this protocol during the June 2009 HSRB meeting. That is the case in the existing Cream dosimetry data set. Methods used to collect the supplementary data (§4.6 & Appendix 9) will be the same as those in the earlier study. Picaridin's dermal safety profile is relatively benign, and we know it to have comparatively low dermal absorption rates. We anticipate that we will have both logical and statistical justification to pool data from the total of 25 subjects to generate single mean and variance statistics based on that augmented sample size."

Section 4.6 Standard Dose as determined by Dosimetry is amended by adding a new initial paragraph, a new table, and a new subsection: 4.6.1 Dosimetry Analysis, with its own table. The original text paragraph of the original section is amended adding "thus" before "used to determine" in the first sentence, "Spray

20%" replaces "those" at the beginning of the second sentence, and the phrase "of each material" is deleted from the second sentence. The "Dosing Rates, by Test Material" table first row Cream 20% values are replaced with "TBD"

The rewritten section 4.6 in its entirety now reads:
"Dosimetry data collection will take place in the main laboratory building and on the terrace at the letterhead address of Carroll-Loye Biological Research. Dosimetry data is collected for multiple trials on each limb (both arms and both legs). When 15 unique subjects have completed dosimetry for the Cream 20% formulation, the resulting data will be used to determine dosing for the efficacy testing. Some or all of the subjects in the dosimetry trial may participate in efficacy testing. Appendix 9 details conduct of dosimetry and subject training. A summary is provided in the table below. See Appendix 2 for data forms.

Delivery System	**Variables Measured**	**Key Details of procedure**
Cream 20%	Weight[1] of dispensing container before and after subject use	3 trials for average, wash and dry limb between applications.

[1] traceably calibrated Sartorius GC 2502 (measurement increment 0.001 g, 500 g capacity)

4.6.1 Dosimetry Analysis
Statistics will be computed with SAS's JMP software, Version 5.0.1.2 (SAS Institute, Cary, NC). The individual subject will be the experimental unit.

The following table summarizes values that will be calculated:

Delivery system	**Value calculated (per trial)**	**Formula**
Cream 20%	Dosage Test Material applied in g/cm^2 skin	Δ weight of dispensing container ÷ surface area of subject's limb

Data will be pooled with dosimetry data from related study LNX-001 (MRID 47506401). Subject means and standard deviations will be calculated for all measures. We will use subject dose means for the Test Material to calculate the dosing grand mean (± SD). That mean, expressed as repellent weight per unit skin surface area, will be converted to volume and used to determine individual subject doses in the efficacy test. To accomplish that, the specific gravity of the test material will be used to convert the dosage weight data to volumes, prepared for each subject on the basis of their skin surface area.

Dosimetry data are thus used to determine individual dosing for efficacy testing. Dosing rates are calculated on a per square cm basis. Spray 20% rates were obtained in a dosimetry study in 2007 during our conduct of an earlier study reported as LNX-001 (MRID 47506401).

The dosing rate for each Test Material is the grand mean rate calculated from 10 subjects (converted from weight to volume by reference to the specific gravity of each test material)

Dosing Rates, by Test Material

	arms	**legs**
Cream 20%	TBD	TBD
Spray 20%	0.97 µl/cm^2	0.83 µl/cm^2

Appendix 9, Subject training document entitled "Practicing and performing dosimetry with Lotion/Cream delivery systems", is added.

Appendix 2 is amended with the addition of Dosimetry data collection and data entry sample data sheets, removal of subject names from the repellent application data sheet (see below) and changing repellency data and data entry forms to reflect 15 minute exposure intervals, not 30 minute exposure intervals (see below).

Federal EPA and the Sponsor have indicated a clear preference for testing against black flies, with data collection for other species only as they may occur at the chosen field site.

Section 1.1 Objective of Research and Endpoints is amended such that in the first sentence of what is now subsection 1.1.2 Repellency, formerly the beginning of Section 1.1, the word "biting" is replaced with the word "black" and the phrase "of one of the following types" is replaced with the phrase "as well as other biting flies that may be present at the field site" and the phrase "when applied at a typical consumer dose" is moved to just after "Test Material(s)". The full sentence now reads: "The objective is to determine the duration and efficacy of the Test Material(s), when applied at a typical consumer dose, in repelling black flies, as well as other biting flies that may be present at the field site" In the second sentence, the phrase "substitute or" is deleted so that the second sentence now reads: "The study will primarily target black flies, but may include other flies listed above depending on seasonal availability in nature." References to "biting flies" and "species" throughout the protocol, where generic, are now understood as black flies and any member of the other genera listed in Section 1.1 that may be actively foraging at the field test location.

Section 4.8.3 Test Day is amended by splitting into sections, Section 4.8.3 One Day Prior to Test Day and 4.8.4 Test Day. The content in Section 4.8.3 describes procedures in the event of the field site being a day's travel from Carroll-Loye Biological Research's laboratory. To provide a complete description, the phrase "Subjects gather at the Carroll-Loye Biological Research laboratory" becomes a stand-alone sentence beginning section 4.8.3. The second, third, and fourth sentences remain the same, except the phrase "day's test" at the end of the fourth sentence is replaced with "repellency test day." Section 4.8.3 now reads as follows:

"4.8.3 One day prior to Test Day (travel day, if the field site is more than about 3 hours travel time from the laboratory) or the Test Day (3 hours or less travel

time) Subjects gather at the Carroll-Loye Biological Research laboratory. The technicians and other researchers who will assist subjects during the test will be introduced or reintroduced to the subjects. Subjects are instructed to call on them whenever they have questions. Subjects are also reminded of procedures for the repellency test day."
Section 4.8.4 Test Day (formerly section 4.8.3), in the first sentence, the phrase "laboratory, at the" is added before "field site", a comma is added after "field site", and the phrase "the lab" is replaced with "accommodations". This sentence is then followed by the original phrase "Subjects will gather to clean limbs for applications, put on protective Tyvek suits, and have boundaries of treated areas bandaged for protection from biting insects", now a stand-alone sentence. Thus the first two sentences of section 4.8.4 (formerly of 4.8.3) now read:
"Treatments may be applied at the laboratory, at the field site, or shortly before travel from accommodations to the field site. Subjects will gather to clean limbs for applications, put on protective Tyvek suits, and have boundaries of treated areas bandaged for protection from biting insects."

The Protocol specifies an assay to verify treated subjects' attractiveness to the target insects prior to repellent challenge exposures, but neglects to mention the assay for untreated subjects.
Section 1.3.2, Risks from Exposure to Biting Arthropods First Paragraph, fourth sentence is amended, adding after the word "will" the phrase "participate in the same assay of subject attractiveness to target insects, and…" such that the sentence now reads: "Untreated subjects with special inclusion criterion (§3.3.2) will participate in the same assay of subject attractiveness to the target insects, and expose untreated skin for up to 1 minute every 15 minutes for evaluation of biting pressure during the efficacy test."
Section 4.8.3 Test Day, (now Section 4.8.4) fifth Paragraph, third sentence is amended with the deletion of the word "treated" and now reads: "Each subject will briefly expose an untreated limb to verify his or her attractiveness to the target species (detailed in §1.3.2)." Second to last paragraph is amended by deleting the phrase "except for the once only assay of attractiveness mentioned above, where each subject briefly exposes an untreated limb" so that the paragraph now reads: "The preceding sequence will be repeated at 15 minute intervals until the Study Director stops the test."

Ambient biting pressure, length of exposure period, and time between exposures were all selected to accommodate draft EPA repellency testing guidelines as they apply to stable flies. Prior to the US EPA review of this Protocol, the Sponsor requested that the experimental design remain open to include a test focused on stable flies. Subsequent to the Federal EPA review of this Protocol, the Sponsor has developed a clear preference for a test targeting black flies. Shorter duration exposures, as they relate to biting pressure, are now preferable. Accordingly, with the exception of the brief discussion of exposure duration and frequency as related to stable flies in section 4.7.4 (see below), language has been amended throughout the protocol and data forms as follows:

"half-hour" and "30 minutes" become "15 minutes"
"10 minutes" becomes "2 minutes"
"5 minutes" becomes "1 minute"

Section 4.7.4 Measuring Ambient Biting Pressure, second paragraph is amended with the addition of new third and fourth sentences that read: "For stable flies, draft EPA repellency test guidelines recommend an ambient biting pressure of one per 5 minutes with exposures every 30 minutes. Since the focus of the study will be black flies, whereas data collected for stable flies, if it occurs, will be incidental, we propose to use the one LIBe per minute minimum." A new sixth sentence reads: "Because the test material has been shown to have very long duration efficacy against mosquitoes (approximately 12 hours: Carroll-Loye Biological Research (CLBR) mosquito repellency study LNX-001 [MRID 47506401]), and in our experience repellents with long-duration efficacy against mosquitoes generally also display long duration efficacy against other biting arthropods, we expect data collection to continue for up to about 12 hours after repellent applications." Section 4.7.4 in its entirety, as amended, now reads as follows:

"Traditionally, the US/EPA minimum attack rate for challenging a repellent under testing is termed the 'ambient biting pressure'. We propose to define the minimum ambient biting pressure as 1 LIBe ('Landing with Intent to Bite') per minute.

A mean study LIBe ('Landing with Intent to Bite') rate of ≥ 1 LIBe per untreated (negative control) lower leg or lower arm per minute is required for black flies. No more than 10% '0' values for individual exposure periods are permitted. For stable flies, draft EPA repellency test guidelines recommend an ambient biting pressure of one per 5 minutes with exposures every 30 minutes. Since the focus of the study will be black flies, whereas data collected for stable flies, if it occurs, will be incidental, we propose to use the one LIBe per minute minimum. Ambient LIBe pressure is measured from continuous exposure during 1-minute exposure periods commencing once every 15 minutes, beginning at the onset of data collection. Because the test material has been shown to have very long duration efficacy against mosquitoes (approximately 12 hours: Carroll-Loye Biological Research (CLBR) mosquito repellency study LNX-001 [MRID 47506401]), and in our experience repellents with long-duration efficacy against mosquitoes generally also display long duration efficacy against other biting arthropods, we expect data collection to continue for up to about 12 hours after repellent applications. Data will be tabulated for each control subject (Appendix 2)"

Protocol does not correctly account for the possible delay period of a hypersensitivity reaction by subjects.
Section 1.3.6 Medical Monitoring, Assistance, and Management, Paragraph 1, sentence two is amended to replace "48 hours" with "7 days" such that sentence two now reads: "All subjects are asked to contact the Study Director and a physician of their own choice at any time should they develop a rash (a delayed hypersensitivity reaction) within seven days of the conclusion of the test day."

The Protocol inadequately describes the balance of risks and benefits of the research.
Section 1.3.7, Summary of Risks and Benefits, second paragraph. The last two sentences are deleted, and the remaining sentences reorganized, along with the addition of the following sentence: "The principle beneficiary will likely be the

Sponsor, for whom new data and new labeling will meet current US EPA registration standards." The second paragraph now reads in its entirety:
"Against these slight risks are balanced substantial and reasonably likely benefits. The principle beneficiary will likely be the Sponsor, for whom new data and new labeling will meet current US EPA registration standards. Because EPA registration requires efficacy data, a test such as that proposed here is the only path toward further product development, greater availability, and increased consumer acceptance of new repellent formulations in the United States. For the general public, insect-borne disease is of growing significance in the United States and around the world where U.S. citizens are active. Moreover, discomfort associated with nuisance biting restricts many work and pleasure activities."

Section 2, table, Test Material(s): Test Description and Control. The table contains an ambiguous reference to LD50 data. "LD50s (rat oral, dermal)" is replaced with "NAOELs" in the first column, row 14.

Section 4.7.1 Blinding of Study, first Paragraph, first sentence is amended to correct an ambiguous language reference to "experimenters." The word "experimenters" is replaced with the phrase "CLBR staff (researchers, technicians)".

Section 4.7.7 Stop Rules: Fifth statement on the "all subjects" list appears inappropriately, and is redundant with the third item in the "individual subjects" list. The fifth statement "More than one biting insect attempts to bite during any exposure period" is deleted. The third item in the "individual subjects" list should account for data collection for more than one biting fly species. This statement is amended by adding "s" to the end of "LIBe" and the addition of the phrase "from all species for which repellency data is being collected on the test day" to now read as follows:
"Subject's treated limb has received Confirming LIBes from all species for which repellency data is being collected on the test day."

The description of expected test duration and details concerning withdrawal of subjects required elaboration for clarity in the Statistical Design and Analysis section.
Section 4.9 Efficacy – Statistical design and analysis Paragraph six is amended by the addition of two new sentences at the beginning, and the phrase "or are withdrawn" is added after the word "withdraw" in the third to last sentence, such that Paragraph six in its entirety now reads:
"As described in §4.74, we anticipate that protection may span up to about 12 hours after application. By treating subjects early in the day, and testing under long day length conditions, we will minimize the number of subjects for whom sampling is truncated prematurely by darkness. To examine the temporal pattern of failure further, we will employ Kaplan-Meier survival analyses by subject. Kaplan-Meier survival analysis accommodates some data censoring in the event that any subjects withdraw or are withdrawn before failure. In addition, we will estimate the Kaplan-Meier median, and the time until 25% failure, for each test product. In the presence of a high frequency of censoring, median (and mean) values will be underestimated."

Informed Consent Forms for both Treated and Untreated Subjects

Global change to both informed consent forms:
Exposure times are changed from 5 minutes to 1 minute, and intervals between exposures are changed from 30 minutes to 15 minutes, to match the amended Protocol. The attractiveness assay exposure is similarly adjusted. Descriptions of target species for the test are clarified. For the addition of dosimetry, the number of subjects participating is adjusted, and scheduling of dosimentry activities is described. Details about scheduling, duration of test activities, and compensation as related to the possibility of a field site that is one full day of travel from the laboratory are added.

Nature and Purpose, second paragraph, first line is amended with the addition of "(cream)" after "lotion" and in the second line, "biting midges and black flies" is changed to "biting flies" to match the amended Protocol. In the third sentence, the phrase "we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study laboratory. At a later date," is inserted after the phrase "During the study". In the fifth sentence in the Untreated Subject Informed Consent Form, a new sentence and phrase, "You may be asked to participate in one or both parts of the study. If you are asked to participate in the field test," are added before "Your role". In the Treated Subject Informed Consent Form, a similar change is made by simply adding the sentence "You may be asked to participate in one or both parts of the study" to the end of the second paragraph. The relevant paragraphs as amended read as follows:
Treated Subject's ICF: "The purpose of the study is to test how well this insect repellent, in lotion (cream) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study laboratory. At a later date, we will go to a field site to test the insect repellents against biting flies in nature. You may be asked to participate in one or both parts of the study."
*UnTreated Subject's ICF: "*The purpose of the study is to test how well this insect repellent, in cream (lotion) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study laboratory. At a later date, we will go to a field site to test the insect repellents against biting flies in nature. You may be asked to participate in one or both parts of the study. If you are asked to participate in the field test, your role will be to serve as a carefully protected, but untreated, control subject. Periodically throughout the test, you will expose skin of your lower arm or lower leg to biting flies, with no repellent applied. You and technicians attending you will remove the flies as quickly as possible, normally before you are bitten."

Number of Subjects Participating first paragraph, first sentence is amended by adding at the beginning the phrase: "Up to about 40 subjects will be enrolled in the study.

Fifteen subjects will participate in dosimetry, and.." Also, the phrase "be enrolled" is replaced by "participate in the field test". The relevant sentences as amended now read: "Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test." Also, in the second to last sentence of the paragraph, the word "contacted" is replaced with the word "asked" so that it now reads: "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 asked to participate later if needed."

Study Introduction and Duration table, total time for Visit Two is amended by being changed from "8-16 hours" to "12 hours to 3 days".

Visit 1 for Orientation is amended by being renamed "Visit 1 for Orientation and Cream Dosage Determination" and having a new sentence added to the end "You may also work with a researcher to determine how much of the cream repellent you apply."

Visit 2 for the Field Test against Biting Flies First sentence is amended by replacing the word "the" with the phrase "this part of" and the word "field" is moved back three words so that the amended sentence now reads: "This part of the study will require one visit to the field site of the study." Also, beginning in the second sentence, the paragraph is amended by replacing the phrase: "…approximately 10 hours of your time. However, it may require as few as 8 hours (including travel time) or as many as about 16 hours plus return travel time." with the phrase: "one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to accommodations,…"

Study Procedures section, Visit 1 subsection is amended by making the paragraph beginning "You will also be given a verbal orientation…" the last paragraph of the section, and by inserting before it a new paragraph as follows:

"If you are participating in the dosage determination part of the study, you will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply."

Treated Subject's Consent Form Study Procedures section, Visit 2 subsection first paragraph last sentence is amended by replacing the phrase "prior to departure to the

field site, or at the field site after arrival" with the phrase "at the field site, or shortly before travel from accommodations to the field site" such that the amended sentence now reads: "Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory, at the field site, or shortly before travel from accommodations to the field site."

UnTreated Subject's Consent Form Risks/Discomforts section, second paragraph first sentence is amended by replacing "testing" with the phrase "the field test". Third sentence is amended by changing the word "lotion" to "cream" and adding the phrase "and subjects participating in dosage determination" after the phrase "applied to treated subjects". The amended second paragraph how reads:
"Although you will not have repellent applied to you during the field test, you may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels. The cream repellent applied to treated subjects and subjects participating in dosage determination will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed."

Costs and Reimbursement, second paragraph; first sentence is amended by adding the phrase "for research activities, and $125 for each full travel day" after the phrase "$20 per hour". The last sentence is amended by adding the phrase "for your travel days and" after the word "paid", and replacing the phrase "$50 to compensate you for being inconvenienced" with the phrase "$20 per hour for your time at the field site".
The amended second paragraph now reads:
"For participation in the study, each research study participant will receive a cash payment of $20 per hour for research activities, and $125 for each full travel day. 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 your travel days and $20 per hour for your time at the field site."

Statements of Understanding, first paragraph is amended with the addition of the following new sentence at the end: "You understand that the distance or time you travel to participate does not increase your obligation to participate or restrict in any way your right to withdraw at any time."

Treated Subject Informed Consent Form does not properly describe stopping rule if data is collected for more than one biting fly species.
Study Procedures Visit 2, Paragraph 6, last sentence is amended by moving the phrase "of each species in the test" to come after "If more than one biting fly" and now reads:
"If more than one biting fly of each species in the test attempts to bite you on your treated skin during one of the one-minute periods, or in two consecutive exposure periods (that is, 30 minutes apart), you should cover the skin and not expose it again."

Forms do not properly describe how the assay of subject attractiveness to the target insects affects participation and compensation.

Treated Subject Consent Form, Study Procedures Visit 2, Paragraph 5 is amended with the addition of new second and third to last sentences that read: "If no biting flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience". Also, the word "treated" is added before "subject" in the last sentence so that it now reads:

"Once this single attractiveness test is completed, you and the other treated subjects will continue with exposures of treated skin, in partnered pairs, going to the area where biting flies are active for one-minute exposures every 15 minutes."

Untreated Subject Consent Form, Study Procedures Visit 2, Paragraph 4, is amended by splitting it into two paragraphs, with the second sentence of the first paragraph to its end, and the beginning of first sentence of the paragraph that follows amended with the addition of the following text:

"You will be asked to expose untreated skin once for up to two minutes at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or a technician will remove the fly using a small artists' paintbrush. If no flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience." "If you are asked to continue participating,…" then the phrase "…for the duration of the test day" added to the end of that sentence.

The relevant amended paragraphs four and five now read:

"After repellent applications to treated subjects, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be asked to expose untreated skin once for up to two minutes at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or a technician will remove the fly using a small artists' paintbrush. If no flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience.

If you are asked to continue participating, you and two technicians will watch your exposed arm or leg for biting flies that land during one-minute periods every 15 minutes for the duration of the test day. A technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, a technician or you will remove them immediately using a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. When the one-minute exposure period ends, or if biting flies are too numerous for you and your attending technicians to remove effectively, you will immediately cover your exposed skin with the fabric (sleeve or leg) of the coveralls. A technician will record the number of biting flies that attempted to bite your exposed skin during each one-minute exposure period (normally 1 or 0). Every 15 minutes, a project leader will

announce the beginning of the next one-minute period for exposing your untreated skin and watching for biting flies attempting to bite it."

Forms do not correctly account for the possible delay period of a hypersensitivity reaction by subjects.
Risks/Discomforts, third Paragraph, fourth sentence is amended by replacing "48 hours" with "7 days".

Forms incompletely identify the subject as removing nuisance mosquitoes that may land.
Risks/Discomforts, Paragraph 6, second line in the Untreated Subject Consent Form and Paragraph 7, second line in the Treated Subject Consent "Since you will work to remove mosquitoes…" is amended by replacing the word "you" with the phrase "you and a technician".

Forms contain an ambiguous reference regarding health insurance. Research Related Injuries, both consent forms, third sentence, "third party" is changed to "third party that covers you" for clarity.

Informed Consent Form, UnTreated Subjects, Restrictions, last item on the list, the word "mosquito", a transcription error, is replaced with the word "repellent".

Experimental Subject's Bill of Rights

The word "medical" is deleted where it appeared inappropriately.

The clarification "at any time" is added after the Study Director's phone number to clarify contact hours.

Item number nine: Statement does not indicate the subject will receive a copy of the signed and dated Bill of Rights document when needed. The statement now reads "Be given a copy of a signed and dated written consent form and Experimental Subject's Bill of Rights when one is required."

Forms

The Repellent Applications form currently includes a column for the subjects' names. For confidentiality, this column is made blank.

Data entry forms referring to a 30-minute interval between exposure events are edited to now refer to 15-minute intervals.

Editorial Corrections:

Protocol

§4.1, first paragraph (now second paragraph), “is” is replaced with “are” after “ten subjects”; third paragraph (now fourth paragraph) “than” is replaced with “there” after “Nonetheless”

§4.7, Chart, last two rows, replaced 31 and 32 with 21 and 22

§4.9, inserted “e” at the end of “FCLIB”

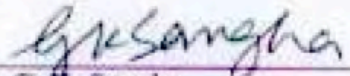
Informed Consent Form, Treated Subjects, Study Procedures, Paragraph 2, line 6: removes “e” from “randomly”

SPONSOR AND STUDY DIRECTOR APPROVAL, AMENDMENT 1, CARROLL-LOYE STUDY LNX-002

13 August 2009

Dr. Scott P. Carroll
Study Director

Date



August 13, 2009

Dr. G. K. Sangha
Study Monitor for Sponsor

Date

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in lotion (cream) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study

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Independent IRB
Julie Blasingame 8/18/09
Signature Date

Initials: _____
Date: _____

laboratory. At a later date, we will go to a field site to test the insect repellents against biting flies in nature. You may be asked to participate in one or both parts of the study.

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.
- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellency testing.

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NUMBER OF SUBECTS PARTICIPATING

Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test. 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 asked to participate later if needed. If you are designated as an alternate, 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	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	12 hours to 3 days

Visit 1 for Orientation and Cream Dosage Determination

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form. If you are asked and agree to participate in the "dosimetry" portion of the study, you will work with a researcher to determine how much of the cream repellent you would normally apply.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

This part of the study will also require one visit to the field site of the study. The field site visit will most likely require one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to accommodations, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

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Signature Date

Initials: _____
Date: _____

STUDY PROCEDURES

Visit 1

At the laboratory, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken.

If you are participating in the dosage determination part of the study, you will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory, at the field site, or shortly before travel from accommodations to the field site.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. A technician will then apply insect repellent to your forearm or lower leg to give even, complete skin coverage. The amount of repellent applied on any one arm or leg will be no more than about 1/2 teaspoon, and is typical of what people commonly use. You will be randomly (like the flip of a coin) chosen to receive either 20% Picaridin spray or 20% Picaridin cream. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

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Two experienced subjects will also participate to record the activity of biting flies by exposing their own arms or legs without repellent. Experienced subjects are pre-qualified by the Principal Investigator, and designated before the field test begins.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent application, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be partnered with another subject so that each of you can help the other observe your treated limbs for biting flies. You and your partner will watch your exposed arms or legs and those of your partner for biting flies that land during a one-minute period. As a treated subject, you will be asked to expose untreated skin only once, for up to two minutes, at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or your partner will remove the fly using a small artists' paintbrush and you will cover your untreated limb immediately. A technician will let you know when the exposure period begins and ends. If no biting flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience. Once this single attractiveness test is completed, you and the other treated subjects will continue with exposures of treated skin, in partnered pairs, going to the area where biting flies are active for one-minute exposures every 15 mintues.

For each exposure, a technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, you or your partner will remove them immediately with a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. A technician will record the number of biting flies that attempted to bite your exposed skin during the one-minute period (normally 1 or 0). Every 15 minutes, a project leader will announce the beginning of the next one-minute period for exposures for data collection. If more than one biting fly of each species in the test attempts to bite you on your treated skin during one of the one-minute periods, or in two consecutive exposure periods (that is, 30 minutes apart), you should cover the skin and not expose it again.

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RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

The cream repellent will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed. You may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 7 days after the day of testing. The first-aid kit at the field site contains 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 very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing repellent and/or 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.

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Julie Blassingame 8/18/09
Signature Date

Initials: _____
Date: _____

The U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 and a technician will work to quickly remove mosquitoes before they have an opportunity to bite, and since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

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PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. 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 if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks and discomforts listed above, there may be some unknown or infrequent and unforeseeable risks associated with using 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, or change the nature of the risks associated with participating.

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 healthcare 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 that covers you. 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

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

TREATMENT ALTERNATIVE

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

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.

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Date: _____

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) 902-8267 at any time.

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

COSTS AND REIMBURSEMENT

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

For participation in the study, each research study participant will receive a cash payment of $20 per hour for research activities, and $125 for each full travel day. 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 $125.00 for your travel days and $20 per hour for your time at the field site.

CONFIDENTIALITY

Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you

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Julie Blasingame 8/18/09
Signature Date

Initials: _____
Date: _____

are otherwise entitled. You may withdraw from this study at any time. You understand that the distance or time you travel to participate does not increase your obligation to participate or restrict in any way your right to withdraw at any time.

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

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name
Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative	

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)

Independent Investigational Review Board, Inc.
Approved: 3/24/09; Revised: 8/18/09

APPROVED BY
Independent IRB
Julie B. Lasinger 8/18/09
Signature Date

Initials: _____
Date: _____

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in cream (lotion) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study

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laboratory. At a later date, we will go to a field site to test the insect repellents against biting flies in nature. You may be asked to participate in one or both parts of the study. If you are asked to participate in the field test, your role will be to serve as a carefully protected, but untreated, control subject. Periodically throughout the test, you will expose skin of your lower arm or lower leg to biting flies, with no repellent applied. You and technicians attending you will remove the flies as quickly as possible, normally before you are bitten.

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

To be considered as a subject who exposes untreated skin, you 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.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.

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Date: _____

- You must not have used repellents within a day prior to the start of the study.
- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellent testing.

NUMBER OF SUBECTS PARTICIPATING

Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test. 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 asked to participate later if needed. If you are designated as an alternate, 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	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	12 hours to 3 days

Visit 1 for Orientation and Cream Dosage Determination

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form. If you are asked and agree to participate in the "dosimetry" portion of the study, you will work with a researcher to determine how much of the cream repellent you would normally apply.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

This part of the study will also require one visit to the field site of the study. The field site visit will most likely require one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory

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facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to accommodations, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

STUDY PROCEDURES

Visit 1

If you are participating in the dosage determination part of the study, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken. You will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory prior to departure to the field site, or at the site after arrival.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent applications to treated subjects, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be asked to expose untreated skin once for up to two minutes at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or a technician will remove the fly using a small artists' paintbrush. If no flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience.

If you are asked to continue participating, you and two technicians will watch your exposed arm or leg for biting flies that land during one-minute periods every 15 minutes for the duration of the test day. A technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, a technician or you will remove them immediately using a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. When the one-minute exposure period ends, or if biting flies are too numerous for you and your attending technicians to remove effectively, you will immediately cover your exposed skin with the fabric (sleeve or leg) of the coveralls. A technician will record the number of biting flies that attempted to bite your exposed skin during each one-minute exposure period (normally 1 or 0). Every 15 minutes, a project leader will announce the beginning of the next one-minute period for exposing your untreated skin and watching for biting flies attempting to bite it.

RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

Although you will not have repellent applied to you during the field test, you may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels. The cream repellent applied to treated subjects and subjects participating in dosage determination will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 7 days after the day of testing. The first-aid kit at the field site contains 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 very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing protective clothing, 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.

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Julie Blasingame 8/18/09
Signature Date

Initials: _____
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The U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 and a technician will work to quickly remove mosquitoes before they have an opportunity to bite, and since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. 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 if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

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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 healthcare 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 that covers you. 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

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

TREATMENT ALTERNATIVE

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

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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.

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Julie Blasiyo 8/18/09
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Date: _____

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) 902-8267 at any time.

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

COSTS AND REIMBURSEMENT

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

For participation in the study, each research study participant will receive a cash payment of $20 per hour for research activities, and $125 for each full travel day. 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 $125.00 for your travel days and $20 per hour for your time at the field site.

CONFIDENTIALITY

Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical

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Signature 8/18/09 Date

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Date: _____

care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time. You understand that the distance or time you travel to participate does not increase your obligation to participate or restrict in any way your right to withdraw at any time.

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

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)

Independent Investigational Review Board, Inc.
Approved: 3/24/09; Revised: 8/18/09

APPROVED BY
Independent IRB
Julie Blasingame 8/18/09
Signature Date

Initials: _____
Date: _____

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

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

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

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

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

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

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

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

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

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

9. Be given a copy of a signed and dated written consent form and Experimental Subject's Bill of Rights when one is required.

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

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) 902-8267 at any time.

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) between 6AM and 2PM, Pacific Time, Monday through Friday. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study.

_____ _____

Signature of Subject Date

_____ _____

Signature of Witness Date

APPROVED BY
Independent IRB

Julie Blasingi 8/18/09

Signature Date

Carroll-Loye Biological Research Study LNX-002
Summary of Protocol Deviations

A deviation was noted in the electronically scanned data capture form files for the final report of study LNX-002. A reformat of an older version of the data capture (recording) form for repellency data was printed and used at the field site instead of the intended version as provided in Amendment 1, Version 13 August 2010. This older version is titled "Biting Fly Landings at 15 Minute Intervals" instead of "Biting Fly LIBes at 15 Minute Intervals." The data collected were LIBEs, as specified in the protocol. The title of the corresponding data entry spreadsheet (MS Excel electronic document) was corrected prior to final report assembly. This deviation had no effect on data quality or subject safety.

S.P. Carroll — 1 April, 2010

Dr. Scott Carroll, Ph.D.
Study Director

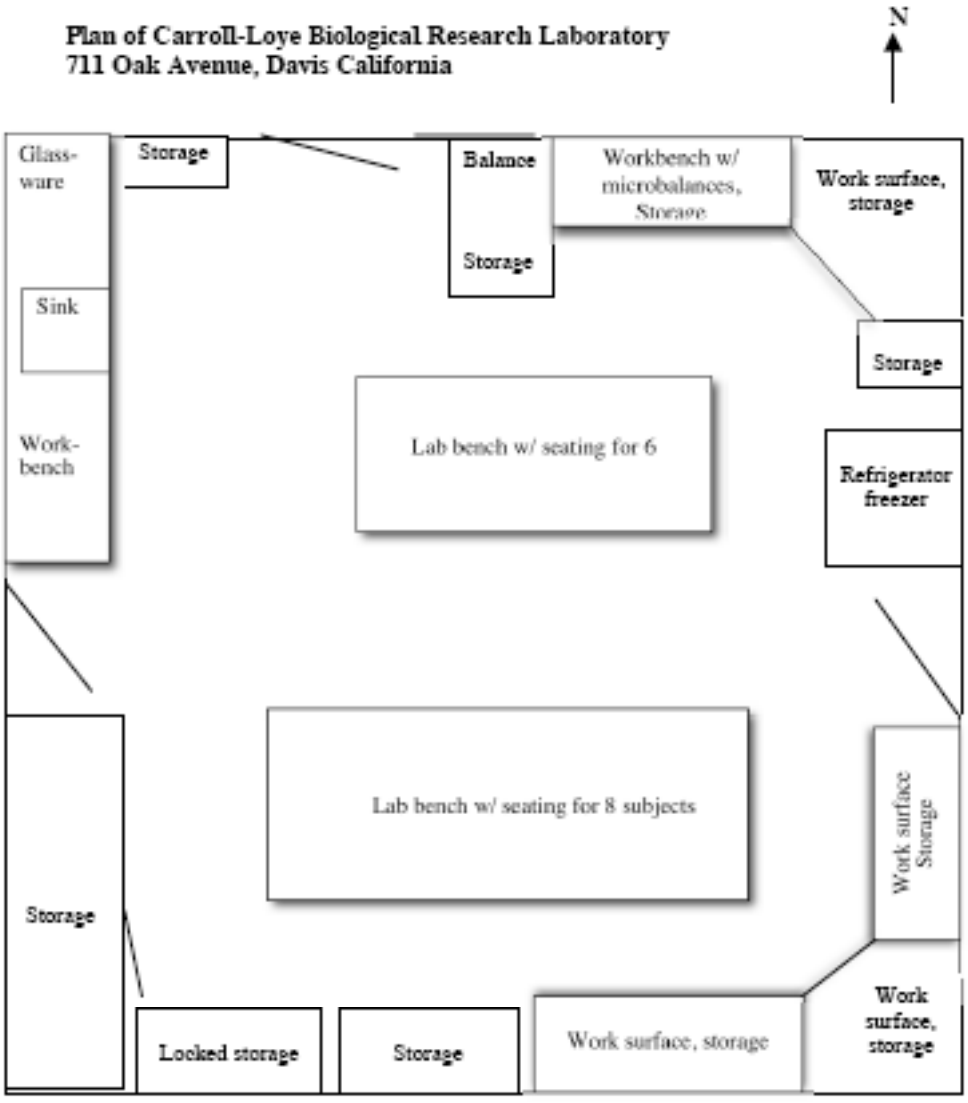
Date

G K Sangha — April 1, 2010

Dr. G. K. Sangha, Ph.D.
Study Monitor

Date

Appendix 9. Physical plan of Carroll-Loye Biological Research Laboratory



Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530)902-8267 http://www.carroll-loye.com/

Research Notes

CLBR Project I.D.# LNX-002
Date: April 1, 2010

This note describes in general terms the field site of the study.

The study site encompassed approximately 5 hectares of open vegetation containing biodiverse low (1-4 m) shrubs, as well as tall (3-10) m shrubs and trees along watercourses and planted in a small park.

The aspect was mainly northerly, with several hundred square meters of level, largely devegetated land at the southern edge on which were placed the screenhouse complex and toilet areas. Dense peripheral plantings of woody species to 12 m in height sheltered these facilities from wind and sun.

The remainder of the study site consisted of slight to moderate slopes, and sandy bottom lands with natural shelter from wind and an abundance of black flies.

Signed

dpr

Department of Pesticide Regulation

Mary-Ann Warmerdam
Director

Arnold Schwarzenegger
Governor

September 14, 2009

Dr. Scott Carroll
711 Oak Avenue
Davis, California 95616

Dear Dr. Carroll:

In accordance with the provisions of the California Code of Regulations, Title 3 (3CCR), Chapter 3, Section 6710, the Director of the Department of Pesticide Regulation (DPR) grants final approval of the pesticide study protocol entitled, **"Efficacy Test of KBR 3023 (Picaridin; Icaridin) - Based Personal Insect Repellents (20% Cream and 20% Spray) with Biting Flies Under Field Conditions"** on September 10, 2009. This study protocol and associated consent form were reviewed and unanimously approved by the Independent Investigational Review Board of Plantation, Florida on August 18, 2009, in accordance with 40 CFR Part 26. This study approval will expire on August 17, 2010.

Please note that Section 6710 of 3CCR authorizes DPR staff to observe your study. Site visits may include observing subject recruitment and the informed consent procedures. This section also authorizes an official observer from DPR or the county agricultural commissioner's office to terminate any study activity that jeopardizes the safety of the study subjects, the public, or the environment.

This study must be conducted according to the approved protocol and consent forms. All protocol and consent form amendments that may impact the health of the human participants must have DPR and Institutional Review Board approval prior to implementing such changes (3CCR 6710, subsection g).

The revised and approved Informed Consent Forms contain a typographical error: "amrs" instead of "arms" in the Study Procedures, Visit 1 section (treated: paragraph 2, line 6; untreated: paragraph 1, line 11).

If during the study, problems should arise related to the safety of the study subjects, please notify our office immediately. If you have any questions, please feel free to contact Don Richmond of my staff at (916) 445-4192, or by e-mail at: drichmond@cdpr.ca.gov.

Sincerely,

George Farnsworth, Environmental Program Manager I
Worker Health and Safety Branch
(916) 445-4163

cc: Anna M. Fan, Ph.D., Chief, Pesticide and Environmental Toxicology Branch (PETB), OEHHA
Joy Wisniewski, Ph.D., Pesticide Epidemiology Section, PETB, OEHHA
Susan Edmiston, Environmental Program Manager II, WHS Branch, DPR
Joseph P. Frank, D.Sc., Senior Toxicologist, WHS Branch, DPR
Roger Cochran, Ph.D., D.A.B.T., Staff Toxicologist, WHS Branch, DPR
Don Richmond, Research Scientist II, WHS Branch, DPR

LNX-002 IRB <-> CLBR Correspondence
Post-Submission of Protocol for HSRB Review

Amendment 1 submission by CLBR to IIRB, Inc. 17 August 2009

Amendment 1 submission IIRB, Inc. Acknowledgements that all needed documents have been received 18 August 2009

from **Shawn King** <sbkingster@gmail.com>
to Robert Roogow <rroogow@iirb.com>
cc Scott P Carroll <spcarroll@ucdavis.edu>,
Yesenia Crespo <ycrespo@iirb.com>
date Mon, Aug 17, 2009 at 1:11 AM
subject LNX-002 Amendment 1 submission for review

Dear Robert,

Please find enclosed for IIRB, INC review Carroll-Loye Protocol LNX-002 Amendment 1 and support documents. The enclosures are described as follows:

LNX-002 Amendment 1 (as PDF, includes introduction with explanations for the amendment, amendment body and study director/study monitor approval signatures, and new dosimetry-related documents)
LNX-002 Protocol amended (as MS Word with track changes showing)
LNX-002 Untreated subject ICF (as MS Word with track changes showing)
LNX-002 Treated subject ICF (as MS Word with track changes showing)
LNX-002 ESBOR (as MS Word with track changes showing)
LNX-002 biting fly LIBe data collection form (interval changed from half-hour to 15 minutes)
LNX-002 biting fly efficacy data entry form (interval changed from half-hour to 15 minutes)
LNX-002 repellent application data sheet (subject name column header removed)

The ICF and ESBOR documents are track change edited from the 3/24/09 versions, with dates cleared in formatting. Please confirm receipt and readability of all files at your earliest convenience. Thanks!

from **Robert Roogow** <RRoogow@iirb.com>
to Shawn King <sbkingster@gmail.com>
cc Scott P Carroll <spcarroll@ucdavis.edu>,
Yesenia Crespo <YCrespo@iirb.com>
date Mon, Aug 17, 2009 at 6:22 AM
subject RE: LNX-002 Amendment 1 submission for review

Dear Shawn,

Do to the change in the number of possible participants and the changes to the study design, this must go for full board review. It will be placed on the agenda for tomorrow. I will let you know if we need any clarifications. If you need the documents out sooner than the end of the week, let me know.

Regards,

Robert Roogow, MS, CIM
Chief Operating Officer
Independent Investigational Review Board, Inc.

from	**Yesenia Crespo** <YCrespo@iirb.com>
to	Shawn King <sbkingster@gmail.com>
cc	Scott P Carroll <spcarroll@ucdavis.edu>
date	Mon, Aug 17, 2009 at 8:45 AM
subject	RE: LNX-002 Amendment 1 submission for review

Dear Shawn,
I am not able to open the consent forms, can you please submit it in a word document. Also I attached the most recent approved consent forms just in the case that you didn't use those to make your changes.

Regards,
Yesenia Crespo
Project Leader
Independent Investigational Review Board INC.

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in lotion and pump spray formulations, works outdoors against biting midges or black flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will go to a field site to test the insect repellents against biting flies in nature.

APPROVED BY
Independent IRB

_____ 3/24/09_
Signature Date

Initials: _____
Date: _____

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.
- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellency testing.

NUMBER OF SUBECTS PARTICIPATING

Two untreated plus up to about 23 treated subjects will be enrolled. 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

APPROVED BY
Independent IRB

_____ 3/24/09_
Signature Date

Initials: _____
Date: _____

participate, but will instead be an 'alternate subject' who may be contacted to participate later if needed. If you are designated as an alternate, 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	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	8-16 hours

Visit 1 for Orientation

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

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) or as many as about 16 hours plus return travel time, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

STUDY PROCEDURES

Visit 1

At the laboratory, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken.

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory prior to departure to the field site, or at the site after arrival.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. A technician will then apply insect repellent to your forearm or lower leg to give even, complete skin coverage. The amount of repellent applied on any one arm or leg will be no more than about 1/2 teaspoon, and is typical of what people commonly use. You will be randomely (like the flip of a coin) chosen to receive either 20% Picaridin spray or 20% Picaridin cream. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

Two experienced subjects will also participate to record the activity of biting flies by exposing their own arms or legs without repellent. Experienced subjects are pre-qualified by the Principal Investigator, and designated before the field test begins.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent application, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be partnered with another subject so that each of you can help the other observe your treated limbs for biting flies. You and your partner will watch your exposed arms or legs and those of your partner for biting flies that land during a five-minute period. As a treated subject, you will be asked to expose untreated skin only once, for up to 10 minutes, at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a five-minute exposure period (or two flies land within 10 minutes), you or your partner will remove the fly using a small artists' paintbrush and you will cover your untreated limb immediately. A technician will let you know

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Independent IRB

3/24/09
Signature Date

Initials: _____
Date: _____

when the exposure period begins and ends. Once this single attractiveness test is completed, you and the other subjects will continue with exposures of treated skin, in partnered pairs, going to the area where biting flies are active for 5 minute exposures every half hour.

For each exposure, a technician will let you know when the five-minute period begins and ends. If any biting flies land and attempt to bite, you or your partner will remove them immediately with a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. A technician will record the number of biting flies that attempted to bite your exposed skin during the five-minute period (normally 1 or 0). Every 30 minutes, a project leader will announce the beginning of the next five-minute period for exposures for data collection. If more than one biting fly attempts to bite you on your treated skin during one of the five-minute periods, or if one biting fly attempts to bite in two consecutive exposure periods (that is, 30 minutes apart), you should cover the skin and not expose it again.

RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

The cream repellent will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed. You may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 48 hours after the day of testing. The first-aid kit at the field site contains treatments to reduce allergic symptoms from bites. Inform the Principal investigator if you are allergic to any

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Independent IRB

_____ 3/24/09_
Signature Date

Initials: _____
Date: _____

nonprescription medicines. At least one technician with current first-aid training will be present during the field test.

In addition, there is a very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing repellent and/or 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 U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. 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 if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks and discomforts listed above, there may be some unknown or infrequent and unforeseeable risks associated with using 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, or change the nature of the risks associated with participating.

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 healthcare 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

APPROVED BY
Independent IRB

_____ 3/24/09_
Signature Date

Initials: _____
Date: _____

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) 902-8267 at any time.

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

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

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

CONFIDENTIALITY
Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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

APPROVED BY
Independent IRB

_____ 3/24/09_
Signature Date

Initials: _____
Date: _____

confidentiality cannot be guaranteed. Any information or reports published as a result of this study will not identify you by name, or by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time.

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

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

_____	_____	_____
Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)

Independent Investigational Review Board, Inc.
Approved: 3/24/09

Version: 3/24/09
Protocol: LNX-002
TREATED Subjects

APPROVED BY
Independent IRB

_____ 3/24/09_
Signature Date

Initials: _____
Date: _____

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in lotion and pump spray formulations, works outdoors against biting midges or black flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will go to a field site to test the insect repellents against biting flies in nature. Your role will be to serve as a carefully protected, but untreated, control subject. Periodically throughout the

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Independent IRB
_____ 3/24/09
Signature Date

Initials: _____
Date: _____

test, you will expose skin of your lower arm or lower leg to biting flies, with no repellent applied. You and technicians attending you will remove the flies as quickly as possible, normally before you are bitten.

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

To be considered as a subject who exposes untreated skin, you 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.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.
- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.

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Independent IRB
3/24/09
Signature Date

Initials: _____
Date: _____

- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during mosquito testing.

NUMBER OF SUBECTS PARTICIPATING

Two untreated plus up to about 23 treated subjects will be enrolled. 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, 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	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	8-16 hours

Visit 1 for Orientation

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

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) or as many as about 16 hours plus return travel time, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

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Signature 3/24/09 Date

Initials: _____
Date: _____

STUDY PROCEDURES

Visit 1

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory prior to departure to the field site, or at the site after arrival.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent applications to treated subjects, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You and two technicians will watch your exposed arm or leg for biting flies that land during a five-minute period. A technician will let you know when the five-minute period begins and ends. If any biting flies land and attempt to bite, a technician or you will remove them immediately using a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. When the five-minute exposure period ends, or if biting flies are too numerous for you and your attending technicians to remove effectively, you will immediately cover your exposed skin with the fabric (sleeve or leg) of the coveralls. A technician will record the number of biting flies that attempted to bite your exposed skin during each five-minute exposure period (normally 1 or 0). Every 30 minutes, a project

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Independent IRB
3/24/09
Signature Date

Initials: _____
Date: _____

leader will announce the beginning of the next five-minute period for exposing your untreated skin and watching for biting flies attempting to bite it.

RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

Although you will not have repellent applied to you during testing, you may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels. The lotion repellent applied to treated subjects will cause substantial but temporary injury to eyes on contact. The pump spray repellent applied to treated subjects will cause moderate irritation to eyes on contact. Both are harmful if swallowed.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 48 hours after the day of testing. The first-aid kit at the field site contains 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 very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing protective clothing, 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.

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3/24/09
Signature Date

Initials: _____
Date: _____

The U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. 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 if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

UNKNOWN / UNFORESEEABLE RISKS

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, or change the nature of the risks associated with participating.

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 healthcare 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

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

TREATMENT ALTERNATIVE

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

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) 902-8267 at any time.

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Date: _____

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

COSTS AND REIMBURSEMENT

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

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

CONFIDENTIALITY

Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time.

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

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3/24/09
Signature Date

Initials: _____
Date: _____

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)

Independent Investigational Review Board, Inc.
Approved: 3/24/09

APPROVED BY
Independent IRB
3/24/09
Signature Date

Initials: _____
Date: _____

from **Shawn King** <sbkingster@gmail.com>
to Yesenia Crespo <YCrespo@iirb.com>
cc Scott P Carroll <spcarroll@ucdavis.edu>
date Mon, Aug 17, 2009 at 10:18 AM
subject Re: LNX-002 Amendment 1 submission for review

Hi Yesenia,

All attempts to send as MS Word with tracked changes showing have failed. Please find enclosed versions with tracked changes accepted, and versions as PDFs showing tracked changes. I have confirmed the versions are correct. If it is helpful, I will FedEx a CD-R with the tracked changes versions. How should the FedEx be addressed? Thanks!

Best, Shawn King
Director of Operations
Carroll-Loye Biological Research

Ed Note: The two attached ICF documents with track changes accepted appear below. The other two enclosed documents are re-sends, in MS Word and PDF versions, of the Treated and UnTreated Subject ICF documents that appear on pages 195-214 of this report.

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in lotion (cream) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study

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Signature Date

Initials: _____
Date: _____

laboratory. At a later date, we will go to a field site to test the insect repellents against biting flies in nature. You may be asked to participate in one or both parts of the study.

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.
- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellency testing.

NUMBER OF SUBECTS PARTICIPATING

Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test. 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 asked to participate later if needed. If you are designated as an alternate, 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	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	12 hours to 3 days

Visit 1 for Orientation and Cream Dosage Determination

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form. You may also work with a researcher to determine how much of the cream repellent you apply.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

This part of the study will also require one visit to the field site of the study. The field site visit will most likely require one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to accommodations, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

STUDY PROCEDURES

Visit 1

At the laboratory, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken.

If you are participating in the dosage determination part of the study, you will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory, at the field site, or shortly before travel from accommodations to the field site.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. A technician will then apply insect repellent to your forearm or lower leg to give even, complete skin coverage. The amount of repellent applied on any one arm or leg will be no more than about 1/2 teaspoon, and is typical of what people commonly use. You will be randomly (like the flip of a coin) chosen to receive either 20% Picaridin spray or 20% Picaridin cream. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

Two experienced subjects will also participate to record the activity of biting flies by exposing their own arms or legs without repellent. Experienced subjects are pre-qualified by the Principal Investigator, and designated before the field test begins.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent application, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be partnered with another subject so that each of you can help the other observe your treated limbs for biting flies. You and your partner will watch your exposed arms or legs and those of your partner for biting flies that land during a one-minute period. As a treated subject, you will be asked to expose untreated skin only once, for up to two minutes, at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or your partner will remove the fly using a small artists' paintbrush and you will cover your untreated limb immediately. A technician will let you know when the exposure period begins and ends. If no biting flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience. Once this single attractiveness test is completed, you and the other treated subjects will continue with exposures of treated skin, in partnered pairs, going to the area where biting flies are active for one-minute exposures every 15 mintues.

For each exposure, a technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, you or your partner will remove them immediately with a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. A technician will record the number of biting flies that attempted to bite your exposed skin during the one-minute period (normally 1 or 0). Every 15 minutes, a project leader will announce the beginning of the next one-minute period for exposures for data collection. If more than one biting fly of each species in the test attempts to bite you on your treated skin during one of the one-minute

periods, or in two consecutive exposure periods (that is, 30 minutes apart), you should cover the skin and not expose it again.

RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

The cream repellent will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed. You may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 7 days after the day of testing. The first-aid kit at the field site contains 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 very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing repellent and/or 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 U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 and a technician will work to quickly remove mosquitoes before they have an opportunity to bite, and since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. 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 if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks and discomforts listed above, there may be some unknown or infrequent and unforeseeable risks associated with using 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, or change the nature of the risks associated with participating.

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 healthcare 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 that covers you. 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

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

TREATMENT ALTERNATIVE

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

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) 902-8267 at any time.

APPROVED BY
Independent IRB

_____
Signature Date

Initials: _____
Date: _____

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

COSTS AND REIMBURSEMENT

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

For participation in the study, each research study participant will receive a cash payment of $20 per hour for research activities, and $125 for each full travel day. 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 your travel days and $20 per hour for your time at the field site..

CONFIDENTIALITY

Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time. You understand that the distance or time you travel to participate does not increase

your obligation to participate or restrict in any way your right to withdraw at any time.

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

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)
Independent Investigational Review Board, Inc. Approved:

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE AS A RESEARCH STUDY SUBJECT

Title of Study: **LNX-002** EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Principal Investigator: Scott P. Carroll, Ph.D.
Carroll-Loye Biological Research
711 Oak Avenue
Davis, CA 95616
(530) 902-8267

Site of Investigation: Carroll-Loye Biological Research
711 Oak Avenue, Davis, CA 95616

Sponsor: LANXESS Corporation

Participant's Name: _____

INTRODUCTION

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 to think about before making your decision. If you request, we will also provide you with a copy of the study Protocol, which details all the procedures of the study, and contains details about product safety. 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 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 improved formulations of the ingredient Picaridin. More studies are needed to determine how well such new insect repellents work.

The purpose of the study is to test how well this insect repellent, in cream (lotion) and pump spray formulations, works outdoors against biting flies. The information gained from the study will assist in developing these repellents for commercial marketing. During the study, we will first study how much of the cream repellent subjects put on their own arms and legs ('dosimetry') during a visit to the study laboratory. At a later date, we will go to a field site to test the insect repellents

against biting flies in nature. You may be asked to participate in one or both parts of the study. If you are asked to participate in the field test, your role will be to serve as a carefully protected, but untreated, control subject. Periodically throughout the test, you will expose skin of your lower arm or lower leg to biting flies, with no repellent applied. You and technicians attending you will remove the flies as quickly as possible, normally before you are bitten.

The sponsor, LANXESS Corporation, has contracted Carroll-Loye Biological Research to conduct the study. Scott Carroll, Ph.D., of Carroll-Loye Biological Research is the Principal Investigator (Study Director) 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 old.

If you are a female of child-bearing potential, you cannot be pregnant or breastfeeding. Using an over-the-counter (OTC) pregnancy kit supplied by a technician, you will perform a pregnancy test at the laboratory on the day of any study visit in which repellent will be applied or in which you will be exposed to biting insects. Your test results will be verified by a female technician experienced in making that assessment. 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. If you decide to withdraw from the study after taking the pregnancy test you do not need to show a positive result.

To be considered as a subject who exposes untreated skin, you 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.

RESTRICTIONS

- You must not be a student or employee of the Principal Investigator.
- You must not be hypersensitive (allergic) to mosquito bites, or phobic of bites or biting insects.
- You must not be sensitive to any of the test product ingredients, or allergic to common cosmetics.
- You must regularly spend time in outdoor settings.
- You must be able to see and remove biting insects that come in contact with your skin.
- You must not have used repellents within a day prior to the start of the study.

- You must not use perfumed products after 9 p.m. the night before and throughout the tests. To meet this restriction, you may need to purchase fragrance-free cosmetics prior to the test days. If you do, you will be reimbursed for your expenses.
- You must refrain from smoking or consuming alcoholic beverages after 9 p.m. the night before and throughout the tests.
- You must wear specified protective clothing during repellent testing.

NUMBER OF SUBECTS PARTICIPATING

Up to about 40 subjects will be enrolled in the study. Fifteen subjects will participate in dosimetry, and two untreated plus up to about 23 treated subjects will participate in the field test. 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 asked to participate later if needed. If you are designated as an alternate, 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	Visit 2
1. Orientation visit	X	
2. Field study visit		X
Total time	1-2.5 hours	12 hours to 3 days

Visit 1 for Orientation and Cream Dosage Determination

Within 60 days before the field study visit, you will meet with a researcher to perform orientation activities for the repellent study. The researcher will tell you more about what you will experience while participating and what is expected of you and you will sign this consent form. You may also work with a researcher to determine how much of the cream repellent you apply.

The total time for Visit 1 activities will be about 1-2.5 hours.

Visit 2 for the Field Test against Biting Flies

This part of the study will also require one visit to the field site of the study. The field site visit will most likely require one to three days of your time. The site may be from about 2 to up to about 10 hours driving time from the Carroll-Loye laboratory. If the field site requires prolonged travel within California, the first and third days will be travel days to and from the site. Hotel, motel, or dormitory facilities will be provided for the nights before and after the test day. The day of the test may require as few as 8 hours (including travel time from accommodations) or as many as about 16 hours plus return travel time to

accommodations, depending on how long the repellents remain effective. Bathrooms are available, and meals, drinks and snacks will be provided. A screened shelter will also be provided for shade, seated rest, and protection from biting insects between exposure events. 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.

STUDY PROCEDURES

Visit 1

If you are participating in the dosage determination part of the study, a researcher will measure the length and circumference of your forearm and/or lower leg. If you have participated in a Carroll-Loye Biological Research study within the last two years, and were measured for that study, we will use your on-file limb measurements unless, when asked, you indicate that you think you have gained or lost weight or muscle mass on your limbs since the previous measurements were taken. You will then practice using the cream product to decide how you best like to apply it 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 amrs and/or lower legs with soap and water and dry them with a towel. The researcher will then ask you to apply an amount of repellent product to your skin that you think gives complete and even coverage. We will use the amounts you and other subjects apply in this part of the study to determine how much repellent people normally apply.

You will also be given a verbal orientation to the activities of the field test day, with an opportunity to ask the researcher questions or share your concerns about any aspect of the research activities.

Visit 2

Before the field testing, the subjects and researchers will gather in an area that is free of biting insects. You should not leave this area until instructed by a researcher. You will be introduced to the technicians and other researchers who will assist you and directed to ask them any questions you may have. Depending on conditions on the day of the test, limb washing, donning of protective clothing, and repellent applications to treated subjects may be completed at the laboratory prior to departure to the field site, or at the site after arrival.

A technician will guide you in washing the lower arms and/or legs with mild, low-fragrance cleanser, rinsing them with a spray of 35% ethyl alcohol, then drying them with a clean towel. You will be given protective coveralls and gloves to prevent bites on other parts of your arms and legs, plus a head net. Vulnerable areas around wrists, elbows, ankles, and knees will be provided with extra protection.

At the field site, you will be given a small artists' paintbrush to use to brush off or lightly crush any biting flies that land on your skin and attempt to bite you once the test begins. A researcher or technician will show you how to use it. You will also be introduced or reintroduced 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 protecting yourself from biting insects or reporting a biting fly that lands on your skin.

After repellent applications to treated subjects, introductions, and provision of small artists' paintbrushes, a researcher or technician will guide you to an area of the field site in which biting flies are active. You will be asked to expose untreated skin once for up to two minutes at the beginning of the field test, to assess your attractiveness to biting flies. As soon as a single biting fly lands within a one-minute exposure period (or two flies land within two minutes), you or a technician will remove the fly using a small artists' paintbrush. If no flies land on you during this initial exposure, you may be asked to withdraw from the test. If you are asked to withdraw, you will be compensated for your time up to that point and for your inconvenience.

If you are asked to continue participating, you and two technicians will watch your exposed arm or leg for biting flies that land during one-minute periods every 15 minutes for the duration of the test day. A technician will let you know when the one-minute period begins and ends. If any biting flies land and attempt to bite, a technician or you will remove them immediately using a small artists' paintbrush. There is a chance that mosquitoes may be present in low numbers. If any mosquitoes land and attempt to bite, a technician will remove them immediately with an aspirator. When the one-minute exposure period ends, or if biting flies are too numerous for you and your attending technicians to remove effectively, you will immediately cover your exposed skin with the fabric (sleeve or leg) of the coveralls. A technician will record the number of biting flies that attempted to bite your exposed skin during each one-minute exposure period (normally 1 or 0). Every 15 minutes, a project leader will announce the beginning of the next one-minute period for exposing your untreated skin and watching for biting flies attempting to bite it.

RISKS / DISCOMFORTS

If at any time you feel ill, inform the Principal Investigator (or anyone else who is assisting to direct the study) immediately. You will be taken to receive medical attention at the nearest healthcare facility. 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 any time without penalty to your compensation. At least one qualified researcher will remain with the other test subjects if other researchers depart with an injured or ill subject.

Although you will not have repellent applied to you during the field test, you may obtain more information about the safety of the repellents by asking a technician at any time. You will be given the Material Safety Data Sheets, which list product safety details similar to those found on commercial product labels. The cream repellent applied to treated subjects and subjects participating in dosage determination will cause substantial but temporary injury to eyes on contact. The pump spray repellent will cause moderate irritation to eyes on contact. Both are harmful if swallowed.

In addition, even if you have not previously had a serious skin reaction to a biting fly bite, it is possible that such a reaction could occur if you receive any bites during this study. Swelling, redness and itching near the bite are all symptoms of an allergic reaction to a bite. You should inform the Principal Investigator or one of his technicians if you are having such a reaction. Contact a physician and the Principal Investigator if you develop a rash within 7 days after the day of testing. The first-aid kit at the field site contains 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 very 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 will be conducted in an area in which such viruses have not been detected by state health or mosquito-control agencies for at least two weeks, and at a time of year when such viruses are rarely present in mosquito populations in the test area. The risk is probably very low that any individual mosquito that might bite you carries a disease. In addition, since you are wearing protective clothing, 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 U.S. 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 2 weeks after the test, be alert for any flu-like symptoms (unusual tiredness or unusually severe headaches, body aches, fever), swollen glands 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 and a technician will work to quickly remove mosquitoes before they have an opportunity to bite, and since 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.

To provide additional information about your disease risk during the field test, we will check mosquitoes that land on you and other subjects for the presence of West Nile and similar viruses. That information will be available within one week of the test, and we will inform you both verbally and in writing if any disease organisms were found. Even if you are not aware of receiving any mosquito bites during the field test, 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.

Physical stresses on subjects are minimized by careful preparation and provisioning at the field site. There will be a screen house on site to provide relief from biting insect pressure between exposure periods. In addition, the screen house provides shade, is equipped with fans and evaporative coolers for environmental control, is maintained free of tripping hazards, and is stocked with food, water, beverages, and seating for all subjects. Screened and private bathroom facilities are also provided on site. Paths between the screen house and exposure areas, as well as between the screen house and bathroom facilities, are cleared of hazards by staff prior to the arrival of subjects. The screen house is located within brief (several minutes) walking distance of the exposure areas. The bathroom facilities will be within 25 yards of the screen house.

PREGNANCY RISKS

The risks to the unborn are unknown and may be hazardous. 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 if you are lactating.

If you are a female subject who is tested for pregnancy, and you test positive, there is some risk of psychological stress from the surprise of the result. Only a single female technician will evaluate the results, and no record will be made of the results, to maximize your privacy by minimizing the small but present risk that other staff or subjects may become aware of the results.

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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 healthcare 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 that covers you. 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, volunteers should call the Carroll-Loye Biological Research office at (530) 902-8267.

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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) 902-8267 at any time.

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1- (877) 888-iirb (4472) between 6:00 AM and 2:00 PM, Pacific time, Monday through Friday. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

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

For participation in the study, each research study participant will receive a cash payment of $20 per hour for research activities, and $125 for each full travel day. 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 your travel days and $20 per hour for your time at the field site.

CONFIDENTIALITY

Carroll-Loye Biological Research will retain records of this study indefinitely. You may access your own records by contacting the Study Director. Representatives from the sponsor (LANXESS Corporation), the U.S. Environmental Protection Agency (EPA), the California Department of Pesticide Regulation and the Independent Investigational Review Board, Inc. (an independent committee that reviewed this study's ethical aspects 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 by any other personal identification.

STATEMENTS OF UNDERSTANDING

Right to withdraw or removal from study

You understand that you are free to withdraw from this study at any time, and you agree to inform the Principal Investigator immediately if you intend to withdraw. It is understood that your decision to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of compensation or benefits to which you are otherwise entitled. You may withdraw from this study at any time. You understand that the distance or time you travel to participate does not increase your obligation to participate or restrict in any way your right to withdraw at any time.

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

a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
b. Your failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or Principal Investigator 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 that 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 (MM/DD/YY)	Time	**Print** Subject Name	**Sign** Subject Name

_____	_____	_____
Date	**Print** Carroll-Loye Biological Research Representative	**Sign** Carroll-Loye Biological Research Representative

Copy of signed/dated consent form given to subject on (date)_____ by_____ (initials)

Independent Investigational Review Board, Inc.
Approved:

APPROVED BY
Independent IRB

Signature Date

Initials: _____
Date: _____

from **Shawn King** <sbkingster@gmail.com>
to Robert Roogow <rroogow@iirb.com>
cc Yesenia Crespo <ycrespo@iirb.com>,
Scott P Carroll <spcarroll@ucdavis.edu>
date Mon, Aug 17, 2009 at 11:15 AM
subject LNX-002 ICF files one more attempt

Hi Robert,

Please find enclosed, hopefully, both MS Word versions with tracked changes and PDF versions showing tracked changes.

Ed Note: The four enclosed documents are re-sends, in MS Word and PDF versions, of the Treated and UnTreated Subject ICF documents that appear on pages 195-214 of this report.

from **Yesenia Crespo** <YCrespo@iirb.com>
to Shawn King <sbkingster@gmail.com>
date Tue, Aug 18, 2009 at 6:13 AM
subject RE: LNX-002 Amendment 1 submission for review

Thanks Shawn this will work

from **Yesenia Crespo** <YCrespo@iirb.com>
to Shawn King <sbkingster@gmail.com>
date Tue, Aug 18, 2009 at 6:14 AM
subject RE: LNX-002 ICF files one more attempt

Perfect this is what I needed.

Thanks,

Regards,
Yesenia Crespo
Project Leader

Independent Investigational Review Board INC.

from **Shawn King** <sbkingster@gmail.com>
to Yesenia Crespo <ycrespo@iirb.com>
cc Robert Roogow <rroogow@iirb.com>,
Scott P Carroll <spcarroll@ucdavis.edu>
date Tue, Aug 18, 2009 at 10:44 AM
subject LNX-002 amendment dated front pages

Hi Yesenia,

Please find enclosed as requested substitute front pages, as both MS Word and PDF files (protocol) and as a PDF file (amendment document), for the Amendment One and Protocol documents submitted yesterday (17 August 2009). Note the Protocol substitutions are for the title page and synopsis, for a total of 2 pages, since the addition of an amendment date line to the title page shifted the synopsis text down.
If you have any questions, please feel free to contact me. Thanks!

Amendment 1, Carroll-Loye Protocol LNX-002

Version Date: 13 August 2009

Introduction

This document is Amendment 1 for CLBR Protocol LNX-002: EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS. In addition to detailed annotations of amendments to the protocol and its support documents, it includes both the subject training document for dosimetry and dosimetry data collection and entry sheets.

The amendment is prepared in response to California EPA reviews, HSRB reviews at the 25 June, 2009 meeting at US EPA in Crystal City, VA, as well as the Sponsor's request for additional dosimetry data. For changes to the body of the protocol, consent documents, and pre-existing data forms, the amendment is prepared as a list of entries. For all edits, the location of the change in the protocol and the exact change of wording are given. Where helpful, an explanation for the change is also provided. Adjustments that apply to multiple points in the body of the Protocol are grouped by the topic of the change. Single-instance adjustments are organized in the order they appear in the Protocol, where possible. Adjustments to Consent documents follow as above, and adjustments that are editorial or typographic, with no change to meaning, are listed last, in the order they appear in the body of the Protocol and in consent forms.

Carroll-Loye Biological Research

711 Oak Avenue Davis, California 95616 Tel (530) 902-8267 http://www.carroll-loye.com/

EFFICACY TEST PROTOCOL LNX-002

EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

Original Date:	23 March 2009
Initial IRB Approval:	24 March 2009
Federal EPA/HSRB Review:	25 June 2009
California EPA Review:	Initial: 2 June 2009 Final:
Date Amended:	13 August 2009
Final IRB Approval:	
Standards Applied	U. S. EPA Good Laboratory Practice Regulations (40 CFR 160); 40 CFR 26 subparts K, L and M; FIFRA § 12(a)(2)(P); California State EPA Department of Pesticide Regulation study monitoring (California Code of Regulations Title 3, Section 6710).

SYNOPSIS

This biting fly repellent study was commissioned by the sponsor to provide efficacy data for purposes of US/EPA registration. The test materials, based on the active ingredient Picaridin, consist of KBR 3023 All-family Insect Repellent Cream (20% Cream) and KBR 3023 All-Family Insect Repellent Spray (20% Pump Spray).

KBR 3023 (Icaridin; Picaridin) is a new generation of synthetic repellent developed as an alternative to DEET. It was developed by molecular modeling techniques.

From more than 800 substances, KBR 3023 showed the best performance regarding efficacy against a variety of arthropods (Boeckh, et al., 1996) and had the most desired attributes regarding safety, low skin penetration, compatibility with skin, and plastic materials. It was developed by Bayer and is now owned by Saltigo GmbH (LANXESS Group) and in the USA it is handled by LANXESS Corporation (previously a Division of Bayer Corporation).

Icaridin (US EPA Registration Name Picaridin), the current common name, was developed under the Code Name KBR 3023 and the registered trade name Bayrepel™ and was sold under the Brand name Autan. The chemical name for Icaridin is 1-PIPERIDINECARBOXYLIC ACID, 2- (HYDROXY-ETHYL), 1-METHYLPROPYLESTER. However, the INCI (International Nomenclature of Cosmetic Ingredients) name was given as HYDROXY METHYL ISOBUTYL PIPERIDINE CARB. The product was submitted to US EPA under the common name Picaridin. However, the common name, Picaridin, was rejected by ISO (International Organization for Standards) as it was not considered a pesticide. The common name Picaridin was also rejected by WHO/INN (World Health Organization/International Non-proprietary Name) but the common name, Icaridin, was accepted by WHO/INN

The study pursuant to this insect repellent efficacy protocol is intended to provide data under the Data-Call-In requirements (EPA Reg. No. 3126-LRN0) of United States Environmental Protection Agency Guideline OPPTS 810.3700.

from **Yesenia Crespo** <YCrespo@iirb.com>
to Shawn King <sbkingster@gmail.com>
date Tue, Aug 18, 2009 at 12:09 PM
subject RE: LNX-002 amendment dated front pages

Thanks

from **Robert Roogow** <RRoogow@iirb.com>
to Shawn King <sbkingster@gmail.com>,
Scott P Carroll <spcarroll@ucdavis.edu>
date Tue, Aug 25, 2009 at 1:29 PM
subject LNX-002 Minutes

Dear Shawn,

Per request, I have included the Minutes for last weeks meeting regarding the LNX-002 protocol. There have been no revisions to our Membership Roster or HRPP Plan since your last submission. Let me know if you need anything additional.

Regards,
Robert

Robert Roogow, MS, CIM
Chief Operating Officer
Independent Investigational Review Board, Inc.

Tuesday, August 18, 2009
MINUTES

ATTENDANCE:

PRESENT	ALSO PRESENT
Shari Somerstein, RPh	Glenn Moran, MD
Edward Wiederhorn	David Wells, MD
Julie Blasingim alternate for George Garbarino	
Marcos Rejtman, DO	GUEST
Rabbi Akiva Mann	Katy Kysela, Director of Research, IRB Liaison
Kim Lerner	
Frances Conway, RN	NOT PRESENT
	George Garbarino

I. CALL TO ORDER

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

determined to be present and all attendees affirmed that no significant financial or non-financial conflicts of interest existed with review of any of the items listed on the agenda.

II. APPROVAL OF THE 9/11/2009 and 8/14/2009 MINUTES (The order of the Minutes does not reflect the order in which they were reviewed.)

The minutes of the meetings held 8/11/2009 and 8/14/2009 were reviewed and unanimously approved as reviewed.

III. REVIEW PROTOCOLS

IV. OTHER BUSINESS

E Revised Protocol including Protocol Amendment ; LNX-002; Scott P. Carroll, PhD;

- Treated Informed Consent Form version 8/18/2009
- Untreated Informed Consent Form version 8/18/2009
- California Experimental Subject's Bill of Rights
- Efficacy Test Protocol dated 8/13/2009
- Amendment 1 dated 8/13/2009
- CLBR Training Manual
- Lotion dosimetry recording form
- Lotion dosimetry data entry
- Biting Fly LIBes at 15 Minutes Intervals Form
- Efficacy Data Form
- Repellent Applications Form

The Independent Investigational Review Board, Inc. had an opportunity to review the above referenced Treated Informed Consent Form, Untreated Informed Consent Form, California Experimental Subject's Bill of Rights, Efficacy Test Protocol, Amendment 1, CLBR Training Manual, Lotion dosimetry recording form, Lotion dosimetry data entry, Biting Fly LIBes at 15 Minutes Intervals Form, Efficacy Data Form and Repellent Applications Form for the above noted research study. The Protocol was revised to include the California Department of Pesticide Regulation and HSRB requests as well as the Sponsor's request for additional dosimetry data to be added. In addition, other administrative changes were made throughout the document.

Motion was made, seconded and the Committee approved the Treated Informed Consent Form, Untreated Informed Consent Form, California Experimental Subject's Bill of Rights, Efficacy Test Protocol and Amendment 1. The CLBR Training Manual, Lotion dosimetry recording form, Lotion dosimetry data entry, Biting Fly LIBes at 15 Minutes Intervals Form, Efficacy Data Form and Repellent Applications Form are acceptable for use with a favorable opinion. The Treated Informed Consent Form and Untreated Informed Consent Form have been revised to accommodate the Protocol. The approved revised Treated Informed Consent Form and approved revised Untreated Informed Consent Form are both identified as Version 8/18/2009 and are both stamped, "Approved 8/18/2009". The California Experimental Subject's Bill of Rights has been revised to accommodate the California Department of Pesticide Regulation. The approved revised California Experimental Subject's Bill of Rights is stamped, "Approved 8/18/2009". All current subjects and future research participants must sign the revised consent forms. Based on analysis using the Criteria for Approval Guidance Sheet, the submission does not alter the criteria for approval.

The results of the voting for the action taken was as follows: 7 Votes for; 0 Votes against; 0 Abstained

from **Scott P Carroll** <spcarroll@ucdavis.edu>
to Robert Roogow <RRoogow@iirb.com>
cc sbkingster@gmail.com
date Tue, Aug 25, 2009 at 2:13 PM
subject Re: LNX-002 Minutes

Thank you very much, Robert.

from **Robert Roogow** <RRoogow@iirb.com>
to Shawn King <sbkingster@gmail.com>,
Scott P Carroll <spcarroll@ucdavis.edu>
date Wed, Aug 26, 2009 at 12:47 PM
subject LNX-002 Minutes

Sorry for the inconvenience. There are some minor changes to the minutes in reference to the attendance. Please see attached.

Robert Roogow, MS, CIM
Chief Operating Officer
Independent Investigational Review Board, Inc.

Tuesday, August 18, 2009
MINUTES

ATTENDANCE:

PRESENT
Shari Somerstein, RPh
Edward Wiederhorn
Julie Blasicngim alternate for George Garbarino
Marcos Rejtman, DO left 12:00 PM
Rabbi Akiva Mann
Kim Lerner
Frances Conway, RN

ALSO PRESENT
Glenn Moran, MD arrived at 12:00 PM alternate for Marcos Rejtman, DO when Dr. Rejtman left.
David Wells, MD

GUEST
Katy Kysela, Director of Research, IRB Liaison

NOT PRESENT
George Garbarino

V. CALL TO ORDER

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

determined to be present and all attendees affirmed that no significant financial or non-financial conflicts of interest existed with review of any of the items listed on the agenda.

VI. APPROVAL OF THE 9/11/2009 and 8/14/2009 MINUTES (The order of the Minutes does not reflect the order in which they were reviewed.)
The minutes of the meetings held 8/11/2009 and 8/14/2009 were reviewed and unanimously approved as reviewed.

VII. REVIEW PROTOCOLS

VIII. OTHER BUSINESS Dr. Moran voted in Dr. Rejtman's absence

E Revised Protocol including Protocol Amendment ; LNX-002; Scott P. Carroll, PhD;

- Treated Informed Consent Form version 8/18/2009
- Untreated Informed Consent Form version 8/18/2009
- California Experimental Subject's Bill of Rights
- Efficacy Test Protocol dated 8/13/2009
- Amendment 1 dated 8/13/2009
- CLBR Training Manual
- Lotion dosimetry recording form
- Lotion dosimetry data entry
- Biting Fly LIBes at 15 Minutes Intervals Form
- Efficacy Data Form
- Repellent Applications Form

The Independent Investigational Review Board, Inc. had an opportunity to review the above referenced Treated Informed Consent Form, Untreated Informed Consent Form, California Experimental Subject's Bill of Rights, Efficacy Test Protocol, Amendment 1, CLBR Training Manual, Lotion dosimetry recording form, Lotion dosimetry data entry, Biting Fly LIBes at 15 Minutes Intervals Form, Efficacy Data Form and Repellent Applications Form for the above noted research study. The Protocol was revised to include the California Department of Pesticide Regulation and HSRB requests as well as the Sponsor's request for additional dosimetry data to be added. In addition, other administrative changes were made throughout the document.

Motion was made, seconded and the Committee approved the Treated Informed Consent Form, Untreated Informed Consent Form, California Experimental Subject's Bill of Rights, Efficacy Test Protocol and Amendment 1. The CLBR Training Manual, Lotion dosimetry recording form, Lotion dosimetry data entry, Biting Fly LIBes at 15 Minutes Intervals Form, Efficacy Data Form and Repellent Applications Form are acceptable for use with a favorable opinion. The Treated Informed Consent Form and Untreated Informed Consent Form have been revised to accommodate the Protocol. The approved revised Treated Informed Consent Form and approved revised Untreated Informed Consent Form are both identified as Version 8/18/2009 and are both stamped, "Approved 8/18/2009". The California Experimental Subject's Bill of Rights has been revised to accommodate the California Department of Pesticide Regulation. The approved revised California Experimental Subject's Bill of Rights is stamped, "Approved 8/18/2009". All current subjects and future research participants must sign the revised consent forms. Based on analysis using the Criteria for Approval Guidance Sheet, the submission does not alter the criteria for approval.

The results of the voting for the action taken was as follows: 7 Votes for; 0 Votes against; 0 Abstained

from **Scott P Carroll** <spcarroll@ucdavis.edu>
to Robert Roogow <RRoogow@iirb.com>
cc sbkingster@gmail.com
date Wed, Aug 26, 2009 at 12:53 PM
subject Re: LNX-002 Minutes

Got it, thanks Robert.

From: Andrea Lettman [mailto:ALettman@iirb.com]
Sent: Thursday, February 18, 2010 6:40 AM
To: sangha8@roadrunner.com
Cc: Yesenia Crespo
Subject: Protocol LNX-002 Dr. Carroll

The above study is due for a progress/closeout report prior to your expiration date of 3/23/2010.

Please choose either the Progress Report Form or Closeout Report Form and complete all sections. Provide attachments where necessary.

1. Include a copy of the most recent consent form(s) which is **VERSION 8/18/09** and stamped **APPROVED 8/18/09.** Include any additional applicable forms (i.e. Assent Form, Addendum, DNA form Photography Release Form). If the most recent consent form has not been used yet, please explain why it has not been used on the report.
2. Include a copy of the Principal Investigator's current medical license.
3. Include documentation of the Principal Investigator's completion of Human Research Protection Training.
4. Please provide your name and number where you can be reached if we have any questions.
5. Please have the Principal Investigator sign the form.
6. Please fax these items to **954-327-5778** or email a scanned copy to ycrespo@iirb.com NO LATER THAN 3/12/2010.

Thank You

from **Shawn King** <sbkingster@gmail.com>
to Andrea Lettman <ALettman@iirb.com>
cc Yesenia Crespo <ycrespo@iirb.com>,
Robert Roogow <rroogow@iirb.com>,
Scott P Carroll <spcarroll@ucdavis.edu>
date Tue, Mar 2, 2010 at 6:37 PM
subject Study LNX-002 Progress Report

Hi Andrea,

Please find enclosed the completed Progress Report, and associated support documents, for Carroll-Loye Biological Research study LNX-002. If you have any questions or concerns, please contact us at your earliest convenience.

Best, Shawn King
Director of Operations
Carroll-Loye Biological Research

Ed Note: Enclosures follow except for the sample Informed Consent Form completed by a test subject, which is withheld from this report to ensure subject privacy. A copy of the completed ICF, with subject signature and initial lines partially redacted as submitted to IIRB, Inc., will be made available to EPA/HSRB reviewers on request.

[redacted]

Progress Report Form

Thank you for choosing Independent Investigational Review Board, Inc. for your IRB services. A Progress Report Form is required prior to the expiration of the study's approval (indicated on your Initial Approval Letter). Additional documentation may be requested if further clarification is required.

DOCUMENTATION TO INCLUDE WITH REPORT

- Signed copy of the most current informed consent form(s) –subject's name should be "blacked out." [include copies of translated consent forms, and additional consents (i.e. DNA ICF, Addendum etc.) if applicable].
- Current medical license of Principal Investigator

Protocol Number: **LNX-002**	
Title of Protocol: **Efficacy Test of KBR 3023 (Picaridin; Icaridin) - Based Personal Insect Repellents (20% Cream and 20% Spray) with Biting Flies under Field Conditions**	
Principal Investigator: **Dr. Scott P. Carroll**	After Hours or 24 Hour Phone Number: (emergency contact for subjects) **530-902-8267**
Sub Investigator(s): **None**	
Site Name and Address: **Carroll-Loye Biological Research 711 Oak Avenue Davis CA 95616**	Principal Investigator's Mailing Address: (If different)
Regulatory/Study Coordinator: **Dr. G.K. Sangha**	Phone: **913-638-3968**
Fax Number: **253-840-8047**	Main Office Phone: **913-638-3968**
Email: **sangha8@roadrunner.com**	
Initial Approval date of site: **3/24/09**	Ongoing Approval (prior continuing reviews) date of site: (if applicable)
Anticipated Date of completion: **July 15 2010** (tentative date of completion of study at site)	

A. RESEARCH STATUS (Enrollment)

1. Indicate the current status of this research (choose only those that apply):
   - ☒ Subjects have been enrolled and will continue to be enrolled in the next approval period.
   - ☐ The research is closed to the enrollment of new subjects at the site; the research remains active only for follow-up of subjects.
   - ☐ No subjects have been enrolled to date; enrollment is anticipated in the next approval period.
   - ☐ This study has been placed on clinical hold.
   - ☐ Other (specify):

B. HUMAN SUBJECTS

1. Number of subjects:

***Please note D through F = C and B + C = A ***

A.	# of Subjects Signed Consent	**15**
B.	# of Screen Failures	**15**
C.	# of Subjects Enrolled/Randomized	**0**
D.	# of Subjects Active	**0**
E.	# of Subjects Completed	**0**
F.	Total Number of Subjects Withdrawn From the Study*	**0**

**Please list why each subject withdrew from the study.*

2. Have there been any subject complaints during this period? **If yes, please provide the number, nature of the complaints, and outcome.*	☐ Yes*	☒ No
3. Were the participants selected in an equitable way and in accordance to the approved research protocol to participate in this study? **If no, explain:*	☒ Yes	☐ No*
4. Were there any subjects from vulnerable populations enrolled in this study (i.e. children, prisoners, pregnant women, etc.) **If yes, identify the number in each category:* ** If yes, identify if any of the vulnerable populations enrolled required an independent monitor (e.g., a qualified individual not involved in the research study who determines the subject's capacity to provide voluntary informed consent).* ☐ Yes ☐ No	☐ Yes*	☒ No
5. Have any Non-English speaking subjects been enrolled?	☐ Yes	☒ No

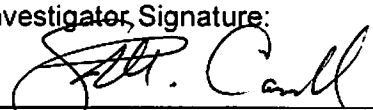
C. CHANGES IN RESEARCH AND NEW INFORMATION

1. Since previous approval, indicate the following: ☐ All problems that require reporting to the Independent IRB have been reported ☒ No problems have occurred that require reporting by the Independent IRB ☐ No problems have occurred that require reporting by the Independent IRB however, problems were reported due to a Site policy or Sponsor requests. Review the Investigator's Guidebook to verify problems that require reporting. **If no, attach information.*		
2. Have there been any changes to this research study? ** If yes, have the changes been approved by the IIRB, Inc.?* ☐ Yes ☐ No** ***If no, submit these changes with this form.*	☐ Yes*	☒ No
D. RISK/BENEFIT		
1. Have any subjects experienced any unexpected benefit from participating in this research? **If yes, provide a description of the benefits.*	☐ Yes*	☒ No
2. Has anything occurred that has altered the risk/benefit ratio? **If yes, provide a description.*	☐ Yes*	☒ No
E. AUDITS		
1. Since the previous approval, have there been any audits? (i.e. FDA/OHRP/EPA) **If Yes, submit documentation of summary of findings, and any FDA Form 483s that have been issued.*	☐ Yes*	☒ No
F. OTHER		
1. Have there been any recent publications in scientific/medical literature, or any interim findings specifically pertaining to this research study that the subject should be notified that may alter their willingness to continue to participate in the study? **If yes, explain*	☐ Yes*	☒ No
2. Have there been any changes in regards to conflict of interest since the initial approval? See Investigator's Guidebook for list of conflict of interest criteria. **If yes, submit summaries of change in conflict of interest.*	☐ Yes*	☒ No

3. Does the Principal Investigator have a current medical license (i.e., no sanctions or suspension)? **If yes, attach current medical license.* ***If no, explain:* **NA - Insect repellent research, non-medical in nature**	☐ Yes*	☒ No**
4. Have there been any changes to your human research protection program (HRPP), consenting process, or recruitment process since the initial approval? ** If yes, explain and provide updated documentation (i.e. updated standard procedures for consenting process/recruiting process).*	☐ Yes*	☒ No
5. Have there been any change in any state or local laws or the community attitude with regard to clinical research? ** If yes, provide explanation.*	☐ Yes	☒ No
6. Have there been any changes to your site qualifications including emergency equipment, distance from hospital, qualifications of staff, and security of data and investigational products? ** If yes, provide explanation.*	☐ Yes*	☒ No
7. Do the investigators and research staff remain adequately trained on the research protocol, human research protection, and Good Clinical Practice? ** If no, provide explanation.*	☒ Yes	☐ No*

G. SIGNATURE (*Signature on this Progress Report by the Principal Investigator is required.*)

I attest that I have thoroughly reviewed the information provided on this progress report form, and to the best of my knowledge all of the information provided is true and accurate.

Person Completing the form: **Shawn King**	Phone Number: **916-832-9593**
Principal Investigator Signature: 	Date: 2/26/2010

You may email this report along with any applicable documents to submissions@iirb.com, fax to (954) 327-5778, or send by mail to 6738 West Sunrise Boulevard, Suite 102, Plantation Florida 33313.

CITI Collaborative Institutional Training Initiative

Human Research Curriculum Completion Report
Printed on Thursday, October 30, 2008

Learner: Scott Carroll (username: scottpcarroll)
Institution: University of California, Davis
Contact Information 711 Oak Avenue
Davis, CA 95616 United States
Department: Entomology
Phone: 530 297 6080
Email: spcarroll@ucdavis.edu

Group 1.: This course is suitable for **Students, Investigtors and staff** conducting BIOMEDICAL RESEARCH with human subjects. The VA module must be completed if you plan to work with subjects at a VA facillity.

Stage 2. Refresher 2 Course Passed on 04/10/08 (Ref # 1120376)

Required Modules	Date Completed
History and Ethical Principles.	07/05/07
Regulations and Process, Part 1	10/24/07
Regulations and Process, Part 2	10/24/07
Informed Consent.	10/24/07
Social & Behavioral Research (SBR)	10/24/07
Genetics Research, Part 1	10/24/07
Genetics Research, Part 2	10/24/07
Records-Based Research, Part 1	04/08/08
Records-Based Research, Part 2	04/08/08
Records-Based Research, Part 3	04/08/08
Research with Protected Populations - Vulnerable Subjects: A Definition.	04/09/08
Vulnerable Subjects - Prisoners, Part 1	04/09/08
Vulnerable Subjects - Prisoners, Part 2	04/09/08
Studies With Minors, Part 1	04/09/08
Studies With Minors, Part 2	04/09/08
Studies With Minors, Part 3	04/09/08
Studies with Pregnant Women and Fetuses, Part 1	04/09/08
Studies with Pregnant Women and Fetuses, Part 2	04/09/08
Group Harms: Research with Culturally or Medically Vulnerable Groups.	04/09/08
FDA Regulated Research, Part 1	04/09/08
FDA Regulated Research, Part 2	04/10/08
Human Subjects Protections at the VA, Part 1	04/10/08
Human Subjects Protections at the VA, Part 2	04/10/08
HIPAA and Human Subjects Research.	04/10/08
Conflicts of Interest in Research Involving Human Subjects.	04/10/08
How to Complete the CITI Refresher Course and Receive a Completion Report	04/10/08

For this Completion Report to be valid, the learner listed above must be affiliated with a CITI participating institution. Falsified information and unauthorized use of the CITI course site is unethical, and may be considered scientific misconduct by your institution.

Paul Braunschweiger Ph.D.
Professor, University of Miami
Director Office of Research Education
CITI Course Coordinator

Return

from **Yesenia Crespo** <YCrespo@iirb.com>
to Shawn King <sbkingster@gmail.com>
date Wed, Mar 3, 2010 at 6:04 AM
subject RE: Study LNX-002 Progress Report

Since I received the Progress Report already is it OK if we review it this upcoming Tuesday, and if so you would lose 1 week of approval. Unless you prefer for us to review it the following Tuesday the 16th. Please let me know.

Regards,
Yesenia Crespo
Independent Investigational Review Board INC.

from **Shawn King** <sbkingster@gmail.com>
to Yesenia Crespo <YCrespo@iirb.com>
date Wed, Mar 3, 2010 at 6:50 AM
subject Re: Study LNX-002 Progress Report

Hi Yesenia,

Thanks for the reminder. Please review as soon as possible. Current study approval ends on the 18 of March 2010, but we are not concerned about "loosing" a week of duration for our total study approval period by having an new approval date before the 18th. At this time, we expect to complete the study well within the 2010 calendar year.

Best, Shawn King
Director of Operations
Carroll-Loye Biological Research.

from **Yesenia Crespo** <YCrespo@iirb.com>
to Shawn King <sbkingster@gmail.com>
date Wed, Mar 3, 2010 at 11:23 AM
subject lnx002

Please see attached

Regards,
Yesenia Crespo
Independent Investigational Review Board INC.

[redacted]

Progress Report Form

Full Accreditation

Thank you for choosing Independent Investigational Review Board, Inc. for your IRB services. A Progress Report Form is required prior to the expiration of the study's approval (indicated on your Initial Approval Letter). Additional documentation may be requested if further clarification is required.

DOCUMENTATION TO INCLUDE WITH REPORT
- Signed copy of the most current informed consent form(s) -subject's name should be blacked out- [include copies of translated consent forms, and additional consents (i.e. DNA ICF, Addendum etc) if applicable].
- Current medical license of Principal Investigator

Protocol Number: **LNX-002**	
Title of Protocol: **Efficacy Test of KBR 3023 (Picaridin; Icaridin) - Based Personal Insect Repellents (20% Cream and 20% Spray) with Biting Flies under Field Conditions**	
Principal Investigator: **Dr. Scott P. Carroll**	After Hours or 24 Hour Phone Number: (emergency contact for subjects) **530-902-8267**
Sub Investigator(s): **None**	
Site Name and Address: **Carroll-Loye Biological Research 711 Oak Avenue Davis CA 95616**	Principal Investigator's Mailing Address: (If different)
Regulatory/Study Coordinator: **Dr. G.K. Sangha**	Phone: **913-638-3968**
Fax Number: **253-840-8047**	Main Office Phone: **913-638-3968**
Email: **sangha8@roadrunner.com**	
Initial Approval date of site: **3/24/09**	Ongoing Approval (prior continuing reviews) date of site: (if applicable)
Anticipated Date of completion: **July 15 2010** (tentative date of completion of study at site)	

Study mentor

A. RESEARCH STATUS (Enrollment)

1. Indicate the current status of this research (choose only those that apply):
   - ☒ Subjects have been enrolled and will continue to be enrolled in the next approval period.
   - ☐ The research is closed to the enrollment of new subjects at the site; the research remains active only for follow-up of subjects.
   - ☐ No subjects have been enrolled to date; enrollment is anticipated in the next approval period.
   - ☐ This study has been placed on clinical hold.
   - ☐ Other (specify):

B. HUMAN SUBJECTS

1. Number of subjects:

***Please note D through F = C and B + C = A ***

A.	# of Subjects Signed Consent	15
B.	# of Screen Failures	15
C.	# of Subjects Enrolled/Randomized	0
D.	# of Subjects Active	0
E.	# of Subjects Completed	0
F.	Total Number of Subjects Withdrawn From the Study*	0

**Please list why each subject withdrew from the study.*

2. Have there been any subject complaints during this period? **If yes, please provide the number, nature of the complaints, and outcome.*	☐ Yes*	☒ No
3. Were the participants selected in an equitable way and in accordance to the approved research protocol to participate in this study? **If no, explain:*	☒ Yes	☐ No*
4. Were there any subjects from vulnerable populations enrolled in this study (i.e. children, prisoners, pregnant women, etc.) **If yes, identify the number in each category:* ** If yes, identify if any of the vulnerable populations enrolled required an independent monitor (e.g., a qualified individual not involved in the research study who determines the subject's capacity to provide voluntary informed consent).* ☐ Yes ☐ No	☐ Yes*	☒ No
5. Have any Non-English speaking subjects been enrolled?	☐ Yes	☒ No

C. CHANGES IN RESEARCH AND NEW INFORMATION

1. Since previous approval, indicate the following: ☐ All problems that require reporting to the Independent IRB have been reported ☒ No problems have occurred that require reporting by the Independent IRB ☐ No problems have occurred that require reporting by the Independent IRB however, problems were reported due to a Site policy or Sponsor requests. Review the Investigator's Guidebook to verify problems that require reporting. *If no, attach information.*		
2. Have there been any changes to this research study? * If yes, have the changes been approved by the IIRB, Inc.? ☒ Yes ☐ No** **If no, submit these changes with this form.*	☒ Yes*	☒ No
D. RISK/BENEFIT		
1. Have any subjects experienced any unexpected benefit from participating in this research? *If yes, provide a description of the benefits.*	☐ Yes*	☒ No
2. Has anything occurred that has altered the risk/benefit ratio? *If yes, provide a description.*	☐ Yes*	☒ No
E. AUDITS		
1. Since the previous approval, have there been any audits? (i.e. FDA/OHRP/EPA) *If Yes, submit documentation of summary of findings, and any FDA Form 483s that have been issued.*	☐ Yes*	☒ No
F. OTHER		
1. Have there been any recent publications in scientific/medical literature, or any interim findings specifically pertaining to this research study that the subject should be notified that may alter their willingness to continue to participate in the study? *If yes, explain*	☐ Yes*	☒ No
2. Have there been any changes in regards to conflict of interest since the initial approval? See Investigator's Guidebook for list of conflict of interest criteria. *If yes, submit summaries of change in conflict of interest.*	☐ Yes*	☒ No

per Shawn K

3. Does the Principal Investigator have a current medical license (i.e., no sanctions or suspension)? *If yes, attach current medical license. **If no, explain: **NA - Insect repellent research, non-medical in nature**	☐ Yes*	☒ No**
4. Have there been any changes to your human research protection program (HRPP), consenting process, or recruitment process since the initial approval? * If yes, explain and provide updated documentation (i.e. updated standard procedures for consenting process/recruiting process).	☐ Yes*	☒ No
5. Have there been any change in any state or local laws or the community attitude with regard to clinical research? * If yes, provide explanation.	☐ Yes	☒ No
6. Have there been any changes to your site qualifications including emergency equipment, distance from hospital, qualifications of staff, and security of data and investigational products? * If yes, provide explanation.	☐ Yes*	☒ No
7. Do the investigators and research staff remain adequately trained on the research protocol, human research protection, and Good Clinical Practice? * If no, provide explanation.	☒ Yes	☐ No*

G. SIGNATURE (Signature on this Progress Report by the Principal Investigator is required)

I attest that I have thoroughly reviewed the information provided on this progress report form, and to the best of my knowledge all of the information provided is true and accurate.

Person Completing the form: **Shawn King**	Phone Number: **916-832-9593**
Principal Investigator Signature: Scott. Call	Date: 2/26/2010

You may email this report along with any applicable documents to submissions@iirb.com, fax to (954) 327-5778, or send by mail to 6738 West Sunrise Boulevard, Suite 102, Plantation Florida 33313.

from **Yesenia Crespo** <YCrespo@iirb.com>
to Shawn King <sbkingster@gmail.com>
date Tue, Mar 9, 2010 at 1:58 PM
subject LNX

Please see attached

Regards,
Yesenia Crespo
Independent Investigational Review Board INC.

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

Association for the Accreditation of Human Research Protection Programs, Inc. — Full Accreditation

DATE: March 09, 2010

TO: Scott P. Carroll, PhD
Principal Investigator

FROM: Authorized Signatory
Independent Investigational Review Board, Inc.

SUBJECT: Approval for Ongoing Research;

PROTOCOL: (LNX-002) EFFICACY TEST OF KBR 3023 (PICARIDIN; ICARIDIN) - BASED PERSONAL INSECT REPELLENTS (20% CREAM AND 20% SPRAY) WITH BITING FLIES UNDER FIELD CONDITIONS

At the meeting held on March 09, 2010 the Independent Investigational Review Board, Inc. had an opportunity to review the above referenced Progress Report and current consent form in use for the above noted research study. The information provided in the Study Progress Report is found to be consistent with the information on file. The Committee verified that all new information regarding the study risks and changes to procedures have been reported. Utilizing this information, the Committee has conducted a risk-benefit assessment and is satisfied that there have been no significant changes that would alter the criteria for approval.

The research approval extends from 3/9/2010 to 3/8/2011. The Progress Report is approved. If the study is completed prior to that time period, the Independent Investigational Review Board is to be advised of the completion of the study and the Investigator is to provide a final Progress Report. If there are any changes to the protocol (amendments), changes in risks to subjects, significant protocol deviations, or other unanticipated problems involving risks to the human subjects, the Investigator is to notify the IIRB as soon as possible. Serious adverse reactions must be reported in accordance with protocol requirements.

Thank you for your cooperation.

FC/JB/yc/rr:

CITI Collaborative Institutional Training Initiative

Human Research Curriculum Completion Report
Printed on Thursday, October 30, 2008

Learner: Scott Carroll (username: scottpcarroll)
Institution: University of California, Davis
Contact Information 711 Oak Avenue
Davis, CA 95616 United States
Department: Entomology
Phone: 530 297 6080
Email: spcarroll@ucdavis.edu

Group 1.: This course is suitable for **Students, Investigtors and staff** conducting BIOMEDICAL RESEARCH with human subjects. The VA module must be completed if you plan to work with subjects at a VA facillity.

Stage 2. Refresher 2 Course Passed on 04/10/08 (Ref # 1120376)

Required Modules	Date Completed
History and Ethical Principles.	07/05/07
Regulations and Process, Part 1	10/24/07
Regulations and Process, Part 2	10/24/07
Informed Consent.	10/24/07
Social & Behavioral Research (SBR)	10/24/07
Genetics Research, Part 1	10/24/07
Genetics Research, Part 2	10/24/07
Records-Based Research, Part 1	04/08/08
Records-Based Research, Part 2	04/08/08
Records-Based Research, Part 3	04/08/08
Research with Protected Populations - Vulnerable Subjects: A Definition.	04/09/08
Vulnerable Subjects - Prisoners, Part 1	04/09/08
Vulnerable Subjects - Prisoners, Part 2	04/09/08
Studies With Minors, Part 1	04/09/08
Studies With Minors, Part 2	04/09/08
Studies With Minors, Part 3	04/09/08
Studies with Pregnant Women and Fetuses, Part 1	04/09/08
Studies with Pregnant Women and Fetuses, Part 2	04/09/08
Group Harms: Research with Culturally or Medically Vulnerable Groups.	04/09/08
FDA Regulated Research, Part 1	04/09/08
FDA Regulated Research, Part 2	04/10/08
Human Subjects Protections at the VA, Part 1	04/10/08
Human Subjects Protections at the VA, Part 2	04/10/08
HIPAA and Human Subjects Research.	04/10/08
Conflicts of Interest in Research Involving Human Subjects.	04/10/08
How to Complete the CITI Refresher Course and Receive a Completion Report	04/10/08

For this Completion Report to be valid, the learner listed above must be affiliated with a CITI participating institution. Falsified information and unauthorized use of the CITI course site is unethical, and may be considered scientific misconduct by your institution.

Paul Braunschweiger Ph.D.
Professor, University of Miami
Director Office of Research Education
CITI Course Coordinator

Return

Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that **William Johnson** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 10/03/2008

Certification Number: 110234

Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that **Shawn King** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 10/21/2008

Certification Number: 121628