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REPORT:

FIFRA Scientific Advisory Panel Meeting, April 7, 2000, held at the Sheraton Crystal City Hotel, Arlington, Virginia

Session II - A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding:

Insect Repellent Product Performance Testing Guideline Evaluation

Mr. Larry Dorsey
Designated Federal Official
FIFRA/Scientific Advisory Panel
Date:_____

Mary Anna Thrall, DVM
FIFRA SAP Session Chair
FIFRA/Scientific Advisory Panel
Date:_____

Federal Insecticide, Fungicide, and Rodenticide Act
Scientific Advisory Panel Meeting
April 7, 2000

SESSION II - Insect Repellent Product Performance Testing Guideline Evaluation

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PUBLIC COMMENTERS

Oral statements were made by:
Mr. Marvin Bertsch, Mr. Nick Spero, and Robin Todd, Ph.D., on behalf of Insect Control and Research, Inc.
Scott Carroll, Ph.D. and Jenella Lloye, Ph.D., on behalf of Carroll-Loye Biological Research
Stephen Gettings, Ph.D., on behalf of Avon Products, Inc., Product Safety and Integrity
Peter Gray, Esq., McKenna & Cuneo, L.L.P., on behalf of the Chemical Specialties Manufacturers Association
James Hudson, Ph.D. on behalf of Pest Management Regulatory Agency, Health Canada
Daniel Lawson, Ph.D., DEET Issues Task Force, on behalf of the Chemical Specialties Manufacturers Association
Ms. Julie Spagnoli, on behalf of Bayer Corporation

Written statements were received from:
Mr. Marvin Bertsch, Mr. Nick Spero, and Robin Todd, Ph.D., on behalf of Insect Control and Research, Inc.
Scott Carroll, Ph.D. and Jenella Lloye, Ph.D., on behalf of Carroll-Loye Biological Research
Stephen Gettings, Ph.D., on behalf of Avon Products, Inc., Product Safety and Integrity
Daniel Lawson, Ph.D., DEET Issues Task Force, on behalf of the Chemical Specialties Manufacturers Association

INTRODUCTION

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Scientific Advisory Panel (SAP) has completed its review of the set of scientific issues being considered by the Agency pertaining to Insect Repellent Product Performance Testing Guideline Evaluation. Advance notice of the meeting was published in the *Federal Register* on March 16, 2000. The review was conducted in an open Panel meeting held in Arlington, Virginia, on April 7, 2000. The meeting was chaired by Mary Anna Thrall, D.V.M. Mr. Larry Dorsey served as the Designated Federal Official.

Inconsistencies have developed in product performance testing and labeling of insect repellents. In order to minimize this variance, EPA has developed draft product performance testing guidelines and appropriate label language. This guideline recommends specific methods for conducting product performance testing of insect repellents. As a guideline, it does not impose mandatory requirements. It does, however, reflect the Agency's considered recommendations for minimum steps necessary to develop reliable data on repellent product performance. In addition, the product performance testing guidelines are intended to supersede EPA, Pesticide Assessment Guidelines, Subdivision G: 95-9, ``Treatments to control pests of humans and pests" and 95-10, ``Mosquito, black fly, nonbiting midge, and biting midge."

A performance standard represents the minimum level of product performance which would normally be acceptable for protecting public health, when required, or for economic control of a pest or pest combination at a specific site. These guidelines are concerned with product performance testing for evaluation of pesticides used to repel mosquitos, biting flies, fleas, chiggers and ticks from human skin and outdoor premises. EPA intends to use the data from guideline studies to help determine the adequacy of the labeling of insect repellant products. The label language proposed by the Agency is intended to standardize and improve the information provided to the consumer. The Agency sought the Panel's advice on the adequacy of the proposed testing guidelines and protocols for human insect repellants. Ms. Robyn Rose (EPA, Office of Pesticide Programs), Mr. Kevin Sweeney (EPA, Office of Pesticide Programs), and Russell S. Jones, Ph.D. (EPA, Office of Pesticide Programs) provided an introduction and summary of insect repellent product performance testing guidelines. Mr. Larry Dorsey served as the Designated Federal Official.

CHARGE

The specific issues to be addressed by the Panel are keyed to the background document, "OPPTS 810.3700; Insect Repellents for Human Skin and Outdoor Premises" memorandum dated March 16, 2000, and are presented as follows:

FIRST BITE vs. FIRST CONFIRMED BITE vs. 95% REDUCTION IN BITES

1. First Bite (FB) vs. First Confirmed Bite (FCB): Historically, the Agency has used the First Confirmed Bite (FCB) test to assess the effectiveness of human insect repellents. However, the Agency is concerned that the FCB method will result in the loss of valuable information. The FCB method does not appear to have been developed using a statistically valid approach. For this reason and because some insect bites may be disregarded when all bites should be counted, the Agency does not currently approve of the FCB method. The Agency recommends use of the First Bite (FB) method or a 95% reduction in bites, because all bites are counted and the method provides a more "real-world" assessment of insect repellent efficacy.

Is the Panel aware of any scientifically valid justification for using the FCB method, or, conversely with using the FB or 95% reduction in bites methods. Should we use 95% and a first bite test or choose just one of these as the standard - why or why not?

GENERAL CONSIDERATIONS FOR ALL TESTING

2. If a product effectively repels a particular pest based upon the time to first bite, the Agency is considering allowing a claim of protection against potential disease vectors. For example: "May repel deer ticks which carry lyme disease."

What degree of protection is necessary to warrant allowing claims of protection from specific diseases? What rationale can the Agency use to demonstrate a high enough level of

efficacy to claim protection against potential disease vectors? What suggestions if any does the Panel have for changes to these protocols that would allow a claim for protection against potential disease vectors? Can you suggest a way to account for differences in level of repellency for different products?

3. The Agency is recommending five treated test subjects for a label claim of less than five hours of repellency and ten treated test subjects for a label claim of five or more hours of repellency.

The Agency considered the publications by Rutledge and Gupta (1999) as a resource in the development of recommendations for the numbers of replications to be used in field tests of insect repellents (Appendix I). Although the Agency believes that the data are scientifically sound, a direct and literal use of these data may not be practical (either economically or logistically) for all registrants. However, after review of Rutledge and Gupta (1999), the Agency realized that more test subjects may be necessary to test repellents with longer durations of repellency.

What number of test subjects would provide statistically-valid results? If more test subjects then currently recommended by EPA are appropriate, would it then be feasible for Registrants to conduct the test? If the number of test subjects should be different for repellents with shorter claims of duration of repellency, how many test subjects should repellents with longer claims include?

4. How should exposure testing be designed to take into account that some test organisms (e.g., mosquitoes) only bite during specific times in a day which may exceed the duration of repellency. For example, would it be acceptable to apply repellent to test subjects at varying number of hours before exposure (e.g., 1,2,4,8, and 12 hours) and then expose all subjects at once? Why, or why not? For this method, how many times should each test subject be exposed? Can you recommend an alternative way to address this problem that might be better?

5. Are the application rates proposed in "OPPTS 810.3700; Insect repellents for human skin and outdoor premises" acceptable for a scientifically sound study? If not, how should application rates be derived? Should an application rate be recommended in these protocols or left to the discretion of the registrant? If a repellent is applied as a thick layer, how will it affect the results of the efficacy test?

MOSQUITO AND STABLE FLY LABORATORY TESTS

6. How valuable are cage studies in assessing the efficacy of a repellent? If the Agency decides to require submission of the cage studies, are there better ways to perform the studies than the Agency-recommended protocols? If so, what are they? Are there advantages to the Klun and Debboun (2000) study that might justify including it as an alternative method (Appendix 2)? If so, what are they?

MOSQUITO, BLACKFLY CERATOPOGONID, SANDFLY, TABANID, AND STABLE FLY FIELD TESTS

7. What biting pressures are appropriate, e.g., five bites in ten minutes for Ceratopogonids and one bite in five minutes for Tabanids? How should biting pressure be determined, e.g., should lands be considered as well as probes and/or bites? If landing rate data collection can be justified for laboratory and/or field studies, what rates would be acceptable?

CANDLES, COILS, AND VAPORIZING MATS

8. The agency has proposed a 50% reduction in bites for a label claim that the repellent may aid in reducing bites and a 95% reduction in bites for a label claim that the product repels, e.g., mosquitoes. What level of reduction in bites is acceptable to show efficacy for candles, coils, and vaporizing mats?

FLEAS

9. What laboratory tests will provide adequate data to determine flea repellency? Of those, including the USDA test found in Appendix III, are any better than the Agency-proposed tests? How many lands should be required within three or five minutes to verify biting pressure (e.g., the Agency proposed ten)?

TICKS AND CHIGGER MITES

10. Due to the high incidence of Lyme disease in the U.S., EPA did not recommend deer tick field tests using human subjects. How adequate are the proposed laboratory tests in determining deer tick repellency? Evaluate the tick and chigger tests found in Appendix III (Smith 1955) and IV. Should these protocols be considered in lieu of or in addition to the Agency proposal?

DETAILED RESPONSE TO THE CHARGE

FIRST BITE vs. FIRST CONFIRMED BITE vs. 95% REDUCTION IN BITES

1. First Bite (FB) vs. First Confirmed Bite (FCB): Historically, the Agency has used the First Confirmed Bite (FCB) test to assess the effectiveness of human insect repellents. However, the Agency is concerned that the FCB method will result in the loss of valuable information. The FCB method does not appear to have been developed using a statistically valid approach. For this reason and because some insect bites may be disregarded when all bites should be counted, the Agency does not currently approve of the FCB method. The Agency recommends use of the First Bite (FB) method or a 95% reduction in bites, because all bites are counted and the method provides a more "real-world" assessment of insect repellent efficacy.

Is the Panel aware of any scientifically valid justification for using the FCB method, or, conversely with using the FB or 95% reduction in bites methods. Should we use 95% and a first bite test or choose just one of these as the standard - why or why not?

The consensus of the Panel was that the 95% reduction in biting should be the principal standard for testing repellents. The Panel's decision is based on the application of good science in the experimental design (including the use of an untreated control) and subsequent data analysis. In addition, several Panel members commented that the 95% reduction method provides a stronger basis for the data to be statistically analyzed. The Panel also agreed that the 95% reduction in bite method is more easily understood than either the First Confirmed Bite or First Bite. The first bite methods could be utilized to establish the time period of complete protection for a repellent. While the specific time for complete protection was discussed later in response to Question 3, a 2 hour minimum was suggested. It was also suggested that the Agency adopt a standard scientifically-based testing protocol with subsequent review and comment by the FIFRA SAP. One possible design could be a latin-square design. Development of such a protocol would dictate the standards for testing, thus helping to alleviate GLP concerns. In any case, reducing vector borne diseases should not be used as a rationale in the development of testing protocols.

GENERAL CONSIDERATIONS FOR ALL TESTING

2. If a product effectively repels a particular pest based upon the time to first bite, the Agency is considering allowing a claim of protection against potential disease vectors. For example: "May repel deer ticks which carry lyme disease."

What degree of protection is necessary to warrant allowing claims of protection from specific diseases? What rationale can the Agency use to demonstrate a high enough level of efficacy to claim protection against potential disease vectors? What suggestions if any does the Panel have for changes to these protocols that would allow a claim for protection against potential disease vectors? Can you suggest a way to account for differences in level of repellency for different products?

The consensus of the Panel was that no claim should be made regarding protection against arthropod-borne pathogens. There are several points presented by the Panel to support this position. First, most arthropods that interact with humans and/or animals are not capable of transmitting pathogens. In addition, in those instances where a potential disease vector exists, the Panel cautioned against a claim of repellency for the products. Gupta & Rutledge (1994) reported that the use of repellents to reduce human vector contact and reduce the transmission of mosquito-borne diseases has not been scientifically proven. Second, individual factors such as proper application, individual variability and susceptibility, and environmental factors (temperature, humidity, perspiration production, rain, clothing presence), also affect the degree of protection afforded by the repellent. Therefore, in order for the Agency to rely on the best scientific data for claims of insect repellency, the use of repellents for reducing arthropod-borne pathogens must be determined.

3. The Agency is recommending five treated test subjects for a label claim of less than five hours of repellency and ten treated test subjects for a label claim of five or more hours of repellency.

The Agency considered the publications by Rutledge and Gupta (1999) as a resource in the development of recommendations for the numbers of replications to be used in field tests of insect repellents (Appendix I). Although the Agency believes that the data are scientifically sound, a direct and literal use of these data may not be practical (either economically or logistically) for all registrants. However, after review of Rutledge and Gupta (1999), the Agency realized that more test subjects may be necessary to test repellents with longer durations of repellency.

What number of test subjects would provide statistically-valid results? If more test subjects then currently recommended by EPA are appropriate, would it then be feasible for Registrants to conduct the test? If the number of test subjects should be different for repellents with shorter claims of duration of repellency, how many test subjects should repellents with longer claims include?

The Panel suggests that primary emphasis regarding sample size (human test subjects) should be based on the scientific experimental design and not on formula driven guidelines. It was pointed out that there are inherent flaws in the determination of sample size in Gupta and Rutledge (1979). For example, according to Ruthledge and Gupta, for five individuals the confidence of protection is 97.5% confidence protection for 1 hour but at 2 hours it is only about 50%. In Table 4 of the Agency's Background Document (No. Subjects, Protection Periods 1-8 hours, Confidence limit 99 and 95 %) the best possible results ($P < 0.01$ with $D = 0.5$ h) for a product claiming 1 hour of protection would require 15 test subjects whereas one claiming 8 hours requires 280. This would not be feasible or practical.

In most experimental designs for the evaluation of insect repellents, gaining an adequate number of replications of the product(s) is typically stressed over using a large number of subjects. The principal objective is to ensure that tests are replicated a sufficient number of times in order to strengthen the power of associated statistical tests. Thus, for example, if four repellent concentrations and a control are tested using five individuals, the whole assessment could be repeated 5 times. In this way, the assignment of treatments to individuals over replicate assessment "rounds" would be such that each individual would eventually be evaluated on each treatment (a "round robin" or Latin Square design). This is just one of a set of equally acceptable study designs. The Panel suggested that the Agency, rather than proscribing evaluation protocols, consider a solution similar to that used in the National Institutes of Health to evaluate their assessment studies. In particular, the Panel suggested that convening an expert panel, such the FIFRA SAP, to periodically evaluate, comment on and recommend changes to industry-proposed study protocols might be the most effective way of handling testing protocol specification. Acceptable design protocols could be published and most new assessments would be performed using these protocols.

4. How should exposure testing be designed to take into account that some test organisms (e.g., mosquitoes) only bite during specific times in a day which may exceed the duration of repellency. For example, would it be acceptable to apply repellent to test subjects at varying number of hours before exposure (e.g., 1, 2, 4, 8, and 12 hours) and then expose all subjects at once? Why, or why not? For this method, how many times should each test subject be exposed? Can you recommend an alternative way to address this problem that might be better?

Since insects/arthropods seek hosts at different times of the day, it is essential that the field testing of repellents occur at those times. In addition, repellents should be applied at different times to establish efficacy. Exposing human subjects to continuous biting activity as proposed is unnecessary. It is feasible to apply repellents to human skin surfaces of all volunteers at one time and then to expose all volunteers together to coincide with arthropod activity periods. The test subjects should remain in a field environment to simulate climatic conditions that properly test efficacy under an actual use scenario. Numerous studies have indicated that repellency can be influenced by changes in temperature, humidity, rate of perspiration, physical activity, and abrasion with clothing. Each test subject should be rotated through all the treatment regimens, including the untreated control, to reduce inter-personal effects due to differential attractiveness of individuals to insects and variability of individual effectiveness of repellents. If insufficient statistical power is achieved with this approach, additional subjects could be used to increase the per test number of individuals exposed at each dose.

5. Are the application rates proposed in "OPPTS 810.3700; Insect repellents for human skin and outdoor premises" acceptable for a scientifically sound study? If not, how should application rates be derived? Should an application rate be recommended in these protocols or left to the discretion of the registrant? If a repellent is applied as a thick layer, how will it affect the results of the efficacy test?

The Panel believes that the amount of repellent to be applied to the skin could be determined by the registrant for several reasons. The proposed guidelines (OPPTS 810,3700) specifies that the applied product amount should be determined by weight. The Panel disagreed with this approach and specifically saw potential problems when dealing with application rates of aerosols. Therefore, since most repellents are liquids, creams or aerosols, the application rates should be in milliliters (or in seconds of spray time for aerosol). In addition, the test area for application of 600 cm^2 is too large an area for many arms. A test area of 250-300 cm^2 is more than adequate.

The amount of the repellent to be tested should be determined by conducting statistically valid studies that demonstrate the quantity of a given physical formulation consumers are likely to apply. Based on public comments from an industry representative at the meeting, it is apparent some of these data already exist in the cosmetic industry. If such data are not available, repellent

manufacturers should conduct such studies to provide such data to the Agency. The dose rate per unit could than be established through pre-field tests using cage tests. The rationale for this is that there are, and in the future, will be numerous new products that do not fit the synthetic chemical repellent mode of action. We are already seeing this with the increased number of natural repellents and many new products that have multiple purposes, i.e. sun-screen, moisturizers etc. This would certainly play a major role in determining the application amount. Field efficacy data could then be used by the Agency for registration.

MOSQUITO AND STABLE FLY LABORATORY TESTS

6. How valuable are cage studies in assessing the efficacy of a repellent? If the Agency decides to require submission of the cage studies, are there better ways to perform the studies than the Agency-recommended protocols? If so, what are they? Are there advantages to the Klun and Debboun (2000) study that might justify including it as an alternative method (Appendix 2)? If so, what are they?

The Panel strongly recommends that only field studies be used to establish efficacy and subsequent registration. Cage studies are not a valid substitute for repellent field studies but they can be used to compare products. Cage tests should be used only as a screening device and should not be submitted in support of a registration. They could, however, be used by the manufacturer to screen possible repellents, developing formulations, and determining a range of application rates.

The Klun & Debboun device may be an alternative to the device specified in the ASTM Standard for laboratory studies of mosquitoes (ASTM 951-94). However, it is a screening tool that was never intended as a substitute for mosquito field studies. If a test cage with an enclosed area, such as Klun & Debboun, does not provide for free flow of repellent vapors from the surface and eventual dissipation of repellent vapors into immediate environment, it is probable that some repellents may have erroneously indicated higher repellency. Any laboratory test cage selected for product testing should take the vaporous state of repellents into account before being recommended for use.

MOSQUITO, BLACKFLY CERATOPOGONID, SANDFLY, TABANID, AND STABLE FLY FIELD TESTS

7. What biting pressures are appropriate, e.g., five bites in ten minutes for Ceratopogonids and one bite in five minutes for Tabanids? How should biting pressure be determined, e.g., should lands be considered as well as probes and/or bites? If landing rate data collection can be justified for laboratory and/or field studies, what rates would be acceptable?

The recommendation of the Panel for biting pressures appropriate for testing are based primarily on what the general public perceives as a nuisance problem. The Panel would recommend the following biting rates for field-testing: mosquitoes 1 bite per minute;

ceratopogonids at 1 bite per 5 minutes; tabanids at 1 bite per 5 minutes. Since little information is available in the literature, the experience of members of the Panel coupled with a publication by Morris and Clanton (1988) titled *Quantification of a nuisance mosquito problem in Florida* were used as guidelines. It is important to remember that repellents are typically used for nuisance problems rather than for disease prevention. Therefore, it follows that the guidelines used by the Agency regarding biting pressure reflect conditions that impact the general public and not military or public health personnel.

CANDLES, COILS, AND VAPORIZING MATS

8. The Agency has proposed a 50% reduction in bites for a label claim that the repellent may aid in reducing bites and a 95% reduction in bites for a label claim that the product repels, e.g., mosquitoes. What level of reduction in bites is acceptable to show efficacy for candles, coils, and vaporizing mats?

A 50% repellency of mosquitoes and other arthropods is not appropriate. If candles, coils, vaporizing mats or other such products are to be useful, they should provide at least 95% repellency. FIFRA SAP member Robert Novak will submit to EPA a manuscript that is in press in the Journal of the American Mosquito Control Association, where coils, candles, plants etc. are tested under field conditions.

FLEAS

9. What laboratory tests will provide adequate data to determine flea repellency? Of those, including the USDA test found in Appendix III, are any better than the Agency-proposed tests? How many lands should be required within three or five minutes to verify biting pressure (e.g., the Agency proposed ten)?

Even though the proposed tests by the Agency to evaluate flea repellency is adequate, the Panel questions whether a flea repellent for humans is necessary in North America. In any event, the test proposed by the Agency is adequate to evaluate repellency. The Agency should recognize that alternative test protocols have been developed and published by laboratories throughout the world, many of which are perfectly adequate to determine flea repellency. The USDA test is somewhat lacking in detail and, as such, comparison of data from one test to another may be called into question. The Agency should have the flexibility to evaluate and allow alternative testing methods.

Flea bites can be painful, allergenic, and annoying. When first disturbed, fleas will jump and inadvertently land on hosts. However, when in the blood feeding mode, they will land and walk on a host in search of a feeding site. It is the Panel's recommendation that one landing and probable probe per minute should be the standard used to verify biting and lack of repellency.

TICKS AND CHIGGER MITES

10. Due to the high incidence of Lyme disease in the U.S., EPA did not recommend deer tick field tests using human subjects. How adequate are the proposed laboratory tests in determining deer tick repellency? Evaluate the tick and chigger tests found in Appendix III (Smith 1955) and IV. Should these protocols be considered in lieu of in addition to the Agency proposal?

The Panel does not agree with the Agency's recommendation against deer tick field tests on human subjects because of disease risk. It is precisely because of high risk of disease transmission from deer tick bites in Lyme disease endemic areas that field-testing with human subjects should be required. There are several reasons and options available to do field testing which minimize the risks to subjects. First, the black-legged tick *Ixodes scapularis* does not carry the Lyme disease spirochete throughout its range and prevalence of infection is insignificant (<1%) over most of its range. This is also true for the western black-legged tick *Ixodes pacificus* where prevalence rates in excess of 1% are rare. Under these circumstances, it seems unreasonable to identify the black-legged tick or the western black-legged tick, as species having exceptionally high risk for disease transmission to human subjects. In areas with high infection prevalence, effective measures can be taken to minimize infection and prevent disease among subjects. These include careful inspection for attached ticks following exposure. Transmission of the Lyme disease spirochete does not occur within the first 48 hours of attachment. Additionally, subjects may be offered a vaccine or prophylactic antibiotics dose prior to exposure to prevent infection. Alternatively, subjects can be tested for antibodies to tick borne infections before and two weeks following exposure to detect asymptomatic infection. Subjects should be briefed on the symptoms of tick-borne infections and seek medical treatment from any unusual symptoms following exposure to ticks. These recommendations would be appropriate for all field tests involving ticks, regardless of the species, location or perceived risk of infection.

The Panel recommends that the Agency review the scientific literature to evaluate a laboratory test method for ticks and chiggers that do not involve use of humans directly. Such studies could include a method used by Buescher et al 1984.

The Panel questions why only tick repellents are permitted to claim efficacy against certain tick species. There is no evidence to support the notion that response variability among tick species is greater than that of mosquitoes. Since nymphal stage dog ticks do not feed upon humans, the Panel concludes there is no justification for requiring testing different stages based upon disease potential. Adult "deer" ticks are equally capable of transmitting ehrlichiosis as the nymphs.

More research is needed to develop an improved field test for mites and chiggers. Laboratory tests do not seem sufficient to determine efficacy of tick or chigger repellents. The alternative methods supplied in the appendix of the Agency's background documents do not seem to be much of an improvement. There is a serious need for research on tick and mite behavioral biology that would provide critical information pertinent to the issue of repellent testing.

ADDITIONAL COMMENTS

The Panel also provided additional comments as provided below.

(1) The Panel strongly recommends that the Agency have a mathematical statistician spend some time with the problem of experimental design. There are statistical models/tools that would clarify many of the sample size/statistical power issues.
(2) The Agency should not require GLP standards for field trials. First, GLPs were designed for laboratory studies. Also, if the Agency requires a scientifically based experimental design, the standards for GLP for lab studies would be incorporated for field studies. The GLP standards that are used for field studies do not fit nor add anything to the quality of the field test except additional costs.
(3) Several Panel members suggested that both male and female test subjects be utilized in field tests to evaluate gender-related efficacy differences.

INDEPENDENT
INVESTIGATIONAL
REVIEW BOARD INC.

Study Specific Instructions

Protocol Title: (EMD-004) Test of Personal Insect Repellents

Sponsor: EMD Chemicals, Inc.
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CRO:
Contact Info:

Contact/Title	Phone/Fax	email

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

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

___ Use translations Services though IIRB (Americo Gomez)

___ We will provide our own Spanish Translations

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

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

Copies to:
Address:
Sent by: FedEX – UPS - USPS
Account #:

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

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