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Keck School of Medicine
University of Southern California

Department of
Preventive Medicine

September 8, 2004

Nigel Fields
Environmental Health Research Program Manager
Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Ave, N.W.
Washington, D.C. 20460

Dear Nigel:

Enclosed please find the IRB application for Dr. David Diaz-Sanchez' "Pollution-Enhanced Allergic Inflammation and Phase II Enzymes" project, which will be reviewed September 20 at UCLA. The child assent is included.

Also enclosed is a statement from Drs. Rob McConnell and Frank Gilliland regarding the collection of buccal cells.

Please let me know if there is anything else needed from us. We are looking forward to receiving the award!

Thanks again,

(b) (6) [redacted]

Tracy de Villiers, MPH
Project Manager
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Division of Clinical Immunology and Allergy
UCLA School of Medicine

CONSENT FOR PARTICIPATION IN RESEARCH: Pollution-enhanced allergic inflammation & Phase II enzymes

You are asked to participate in a research study conducted by Dr. David Diaz-Sanchez and Adrian Casillas from the Division of Clinical Immunology and Allergy at the University of California, Los Angeles. This study is sponsored by the National Institutes of Health (NIH) and the Environmental Protection Agency. You have been asked to participate in this study because you are a person who can make responses to pollutants. Your participation in this study is entirely voluntary. You should read the information below and ask questions about anything you do not understand before deciding whether or not to participate. The number of subjects at UCLA that are expected to enroll in this study is approximately 60. The duration of your participation if you complete all the study should last approximately twelve weeks.

Disclosure: Your health care provider may be an investigator of this research protocol, and as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way associated with this project. You are not under any obligation to participate in any research project offered by your physician.

PURPOSE OF THE STUDY

The purpose of this study is to compare the ability of adults and children in producing natural chemicals (antioxidants) that protect against pollution.

PROCEDURES

If you volunteer to participate in this study, you will be asked to do the following:

1) **Nasal Challenge**
The nasal challenge, involves placing several small mists of fluid into the nasal cavity. Each challenge will consist of between one and five small samples (0.1cc, or about three drops) of fluid applied to the nasal cavity through a sprayer and will contain soot from a diesel truck (diesel exhaust particles).

The diesel exhaust particles will be administered in small mists of fluid containing different amounts of particles. The highest amount of particles you may be given is equal to two day's average urban exposure in Los Angeles. This is less than you would receive from passing behind a diesel bus as it starts its engine. There have been no reported adverse reactions to this procedure, other than the possible uncomfortable feeling of fluid being sprayed into your nose.

2) **Nasal Lavage.** Samples of nasal lavage fluid will be obtained which involves tilting the head back, holding your breath for a short period of time, having one teaspoon of sterile salt water placed in one nostril, and then recovering the fluid by repositioning your head down and catching the fluid as it exits your nose.

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3. Overall. On day 1, you will do a nasal lavage and then be challenged with diesel exhaust particles. Next day you will do another nasal lavage. You will perform the same schedule after a period of four weeks, eight weeks or 12 weeks. Each time you will be challenged with a different amount of diesel exhaust particles.

POTENTIAL RISKS AND DISCOMFORTS

During the nasal lavage, there is a possibility of swallowing this fluid which has a salt water taste but contains no other substances. Additional potential complications of nasal lavage include aspiration (inhalation) of the fluid which is uncomfortable, but the amount of fluid is so small that there is no known possibility of any respiratory complication.

Diesel exhaust particles contain "polycidic aromatic hydrocarbons" which are known cancer-causing agents (called carcinogens) in laboratory animals and man when repeatedly exposed in high enough concentrations over years. Men regularly exposed to diesel exhaust at work for many years have shown slightly higher rates of cancer than similar men in "clean" jobs. For these reasons the State of California has classified diesel exhaust as a carcinogen. The excess cancer risk from one or a few diesel exposures like the one used on this study, if any, is very small. Certainly no more than the risk from spending a few days in a city like Los Angeles. You may experience some irritation (itchiness) in your nose for a few moments.

ANTICIPATED BENEFITS TO SUBJECTS

This study is not being done to improve your condition or health. You have the right to refuse to participate in this study. Your only benefit is that you may learn how well your body makes antioxidants in response to pollutants

ANTICIPATED BENEFITS TO SOCIETY

This study may benefit society by increasing our understanding of the mechanisms that induce allergic disease, and why children are more susceptible to pollution effects than adults..

ALTERNATIVES TO PARTICIPATION

The alternative to participation is not to participate.

PAYMENT FOR PARTICIPATION

You will be paid $20.00 per lab visit (total of 8 visits). This amount will be paid whether you complete the session or withdraw for any reason. After your participation you will not be required to return for a follow-up visit. The total payment for this study is $160. Parking will also be reimbursed ($7/visit) if applicable.

POSSIBLE COMMERCIAL PRODUCTS

All tissue and/or fluid samples are important to this research study. Your sample will be owned by the University of California or by a third party designated by the University (such as another university or a private company). If a commercial product is developed from this research project, the commercial product will be owned by the

University of California or its designee. You will not profit financially from such a product.

INFORMATION ABOUT YOUR SAMPLE
On the checklist below, you are asked to let us know if you would like to receive information about the results of this study. There are two types of information you may receive:

1. general information about what this study found (or conclusions of the study)
2. specific information about what the study found about your individual sample.

You may also choose not to receive any information. Research is a long and complicated process. Obtaining general information from a project may take years. Even if there is general information from a project, there may not be personal information for every participant.

FINANCIAL OBLIGATION
Neither you nor your insurance company will be billed for your participation in this research.

EMERGENCY CARE AND COMPENSATION FOR INJURY
If you are injured as a direct result of research procedures not done primarily for your own benefit, you will receive treatment at no cost. The University of California does not provide any other form of compensation for injury.

PRIVACY AND CONFIDENTIALITY
The only people who will know that you are a research subject are members of the research team and, if appropriate your physicians and nurses. No information about you, or provided by you during the research, will be disclosed to others without your written permission, except:

- if necessary to protect your rights or welfare (for example, if you are injured and need emergency care); or
- if required by law.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

Authorized representatives of the National Institute of Allergy and Infectious Disease (NIAID) and the Public Health Service (PHS) may need to review records of individual subjects. As a result, they may see your name; but they are bound by rules of confidentiality not to reveal your identity to others.

Your samples will be kept private and a code will be assigned to them, known only by the investigators.

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PARTICIPATION AND WITHDRAWAL
Your participation in this research is VOLUNTARY. If you choose not to participate, that will not affect your relationship with UCLA (or UCLA Medical Center), or your right to health care or other services to which you are otherwise entitled. If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without prejudice to your future care at UCLA.

WITHDRAWAL OF PARTICIPATION BY THE INVESTIGATOR
The investigator may withdraw you from participating in this research if circumstances arise which warrant doing so. If you become ill during the research, you may have to drop out, even if you would like to continue. The investigator, Dr. Andrew Saxon, will make the decision and let you know if it is possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of research plan that people who develop certain conditions may not continue to participate.

If you must drop out because the investigator asks you to (rather than because you have decided on your own to withdraw), you will be paid the appropriate amount for completed procedures.

NEW FINDINGS
During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternative to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

IDENTIFICATION OF INVESTIGATORS
In the event of a research related injury or if you experience an adverse reaction, please immediately contact one of the investigators listed below. If you have any questions about the research, please feel free to contact David Diaz-Sanchez, Ph.D., at 310-825-9261; 10833 Le Conte Avenue, Room 52-175, Center for Health Sciences, UCLA, Los Angeles, CA 90095-1680. Dr. Diaz-Sanchez can be reached 24 hours a day/7days a week by calling 310 709 1459. Additionally, you can reach the co-PI, Dr. Adrian Casillas at 310 825 1153.

RIGHTS OF RESEARCH SUBJECTS
You may withdraw your consent at any time and discontinue participation without penalty. You are not waiving any legal claims, rights or remedies because of your participation in this research study. If you have questions regarding your rights as a research subject, you may contact the Office for Protection of Research Subjects, 2107 Ueberroth Building, UCLA, Box 951694, Los Angeles, CA 90095-1694, (310) 825-8714.

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SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE
I have read (or someone has read to me) the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been given a copy of this form, as well as a copy of the Subject's Bill of Rights.

BY SIGNING THIS FORM, I WILLINGLY AGREE TO PARTICIPATE IN THE RESEARCH IT DESCRIBES.

_____
Name of Subject

_____ _____
Signature of Subject Date

_____
Name of Parent or Legal Guardian (if applicable)

_____ _____
Signature of Parent or Legal Guardian Date

INFORMATION ABOUT MY SAMPLE
Please indicate by checking and initialing the category below what type of information you want to receive. It is your responsibility to let the investigator know if your address and/or telephone number changes. The contact information is in this informed consent form under "Identification of Investigators."

- ☐ _____General Information about what the study found
- ☐ _____Specific Information about what the study found about my sample
- ☐ _____I do not want any information about my sample

SIGNATURE OF INVESTIGATOR
I have explained the research to the subject and answered all of his/her questions. I believe that he/she understands the information described in this document and freely consents to participate.

_____
Name of Investigator

_____ _____
Signature of Investigator Date (must be the same as subject's)

DATE OF PREPARATION: 05-08-04
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EXPIRATION DATE:

DEPARTMENT OF MEDICINE
Division of Clinical Immunology and Allergy
UCLA School of Medicine

ASSENT TO PARTICIPATE IN RESEARCH

Pollution-enhanced allergic inflammation & Phase II enzymes

1. My name is David Diaz-Sanchez.

2. We are asking you to take part in a research study because we are trying to learn more about pollution and why it causes children to be more likely to have hay fever. Hay fever is when you sneeze and have a runny nose when you are near certain weeds or plants.

3. If you agree to be in this study:
   a) We will ask you to put a small amount of salty water in your nose. You will keep it there for 5 seconds and then blow it into a cup.

   b) We will spray the inside of your nose with salty water or salty water mixed with some diesel soot. This may cause you to have a runny or itchy nose for a few minutes.

   c) The next day we will ask you to come back and we will again put a small amount of salty water in your nose. You will keep it there for 5 seconds and then blow it into a cup.

   d) We will ask you to come back 3 other times to repeat the experiment.

   e) The number of visits you will make may be as few as one or as many as 8.

4. Some of the following things could happen to you from being in this study:

   a) Your eyes and throat may become itchy and you may get a headache. Breathing diesel soot over a long time is bad for you and may cause illness. However, you will only receive a small bit during this study, less than what you would get if you passed behind a bus.

   b) You may swallow some salty water when we place it in your nose.

   c) You may sneeze and have a runny or stuffy nose when we spray your nose.

5. There is no direct benefit from you performing this study except for learning how well your body can cope with pollution.

6. Please talk this over with your parents before you decide whether or not to participate. We will also ask your parents to give their permission for you to take part in this study. But even if your parents say "yes" you can still decide not to do this.

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7. If you don't want to be in this study, you don't have to participate. Remember, being in this study is up to you and no one will be upset if you don't want to participate or even if you change your mind later and want to stop.

8. You can ask any questions that you have about the study. If you have a question later that you didn't think of now, you can call me at (310) 825 9261 or ask me next time. If you have hay fever, you may call me at any time to ask questions about your hay fever.

9. Signing your name at the bottom means that you agree to be in this study. But remember you can change your mind at any time. You and your parents will be given a copy of this form after you have signed it.

Name of Subject _____ Date _____

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HS-1(a) HIPAA Research Application

UCLA IRB

Pollution-enhanced allergic inflammation & Phase II enzymes

P.I. David Diaz-Sanchez

I. Identify the Information that will be collected

A. We will not review, collect information from or put information into MEDICAL RECORDS.

B. We will obtain nasal lavage as specimens from the research subjects. The only data attached to the specimens will be a code. This code will be available only to the PI and co-PI and will be used to identify the subjects name, address, date of birth and telephone number.

II

A. We will obtain the HIPAA authorization of the subjects.