EXHIBIT 4-1

CONSENT TO ACT AS A SUBJECT IN AN EXPERIMENTAL STUDY

TITLE: THE RAYNAUD'S TREATMENT STUDY

INVESTIGATORS: (FILL IN APPROPRIATE INVESTIGATORS FOR EACH CLINICAL UNIT)

You are being asked to join a clinical research study. The doctors at (INSTITUTION) are studying the nature of disease and are attempting to develop improved methods of diagnosis and treatment. This is called clinical research. In order to decide whether or not you should agree to be part of this research study, you should understand enough about its risks and benefits to make an informed judgement. This process is called informed consent, and is meant to tell you about the study and answer any questions you may have.

DESCRIPTION: The (Institution) is part of a nation-wide study in which the effects of 4 treatments for Raynaud's Disease are compared. Sixty patients will be recruited from (INSTITUTION), and a total of 300 patients will be asked to join across the country. You have been asked to join this study because of your report of attacks to your fingers of numbness, tingling and color change, in which blood flow to the hands or feet almost stops, mainly during cold weather.

The study compares the effect of two unlike drug treatments and two unlike non-drug treatments. You will be assigned to one of these four treatments by chance (like the flip of a coin). It is possible that the effectiveness is different for the four treatments. It is likely that some differences in side effects will be found between the four treatments as well. The purpose of this study is to compare the four treatments to find out which, if any, works best. The drug treatments are Procardia XL (nifedipine XL), a drug which dilates the blood vessels to the fingers, or placebo, a pill that contains no drug or medication. If you are assigned to one of the two drug treatments, neither you nor your doctor will know which treatment you are receiving.

The non-drug treatments both involve biofeedback. This is a process in which people learn to change a body function with the help of a device that measures small changes in that function. The two non-drug treatments in this study are temperature biofeedback and muscle tension biofeedback (called EMG biofeedback). If you are assigned to temperature or EMG biofeedback, you will learn mental methods to

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attempt to control Raynaud's symptoms. Unlike the drug treatment conditions, where you and your doctor will not know which drug you are receiving, you and your doctor/therapist will know which biofeedback treatment you are receiving.

Before you can be assigned to one of the four treatments, the fact that you have Raynaud's Disease must be confirmed by a check-up with a doctor, as well as blood and urine tests. The blood test will require a tablespoon (15 cc) of blood to be drawn from a vein in your arm. You will also have a sample of your blood stored for future tests. This sample will require another tablespoon of blood (15 cc) of blood. Should it turn out that you have some other condition causing your Raynaud's Disease, you will not be asked to remain in the study any further. If you are a female, and of child-bearing age, a urine pregnancy test will be performed. If you are pregnant, you will not be asked to remain in this study any further. If you do have Raynaud's Disease, you will be asked to remain in the study. If you are taking drugs for Raynaud's Disease right now, you will be asked to stop taking them at this point. Your complete participation in this study after this initial visit will take about 17 months. After the initial visit, you will enter a one-month phase in which you will record your symptoms, fill out several forms, and take a "cold test" of the hands. All of these tasks will be described in more detail below.

During the four weeks before you enter treatment, you will be asked to keep a diary in which you record each attack, at the time it occurs, on a card designed for this purpose. You are asked to carry this card with you at all times. You will also be asked to record your symptoms each evening on the end-of-the-day report, a quick checklist of your Raynaud's symptoms during that day. During one visit to the clinic, you will be asked to fill out a set of forms that will take about 45 minutes of your time. These forms will ask questions about your Raynaud's symptoms, how you are coping with the symptoms, and how your life is going at this time.

For the cold test of your hands, you will go to a laboratory. You will be asked to place one finger in a cuff. The cuff will be blown up like a blood pressure cuff, and your finger will be cooled for five minutes. When your finger is cool, the pressure in the cuff will be slowly released, and the blood pressure in your finger will be measured. This will be done a total of four times at different temperatures. The temperatures

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will range from room temperature to the temperature inside a refrigerator. This testing session will require about 1-2 hours of your time.

After these tests, you will start one of the four treatments. If you are assigned to a biofeedback treatment, you will be asked to visit a biofeedback therapist twice a week for a total of 10 sessions, or about 5-10 weeks. After a few months, you may be asked to come in for another 4 sessions. If you are assigned to a drug treatment, you will be asked to visit one of the doctors once a week for about 5-10 weeks.

After this, you will continue with the treatment you receive for a little over a year. During that time, you will be asked to return for brief check-ups with a doctor or nurse about every three months. At two of these visits, a blood sample (about two tablespoons) will be taken. In addition, about three months and fifteen months after you start treatment, you will be asked to repeat the assessments that were done before you started treatment: keeping the diary, filling out forms, and taking the cold test. During your first and second winter in the study (January through March), you will again be asked to complete the end-of-the-day-report.

RISKS AND BENEFITS: Risks known to exist with nifedipine treatment include low blood pressure, dizzy spells, heart burn, and swelling of the feet. Biofeedback treatment has no known side effects. If you were taking drugs for your Raynaud's symptoms before you started the study, stopping the drug could result in an increase in these symptoms. Drawing blood from a vein may cause soreness, bruising or swelling at the site of the puncture, and very rarely, it may cause you to feel faint. The cold test of your hand may result in discomfort or return of Raynaud's symptoms from putting your hand in the cold box. Although we cannot assure that benefits will result to you for your joining this study, there is the possibility that your Raynaud's symptoms will decrease as a result of the treatment to which you are assigned.

ALTERNATIVE TREATMENTS: Other treatments used for Raynaud's Disease include avoiding things that make your symptoms worse, relaxation exercises, and drugs such as a short-acting version of nifedipine, diltiazem and prazosin.

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NEW INFORMATION: If new information, either good or bad, about the study treatments comes to your doctor's attention during the course of this study, which may relate to your desire to remain in the study, it will be given to you.

COSTS AND PAYMENTS: You will not be charged for being in this study. There will be no charge for doctor visits, study drugs, or study laboratory (blood and urine) tests. Tests done for other clinical reasons will be charged to you or to your insurance company. You will not be paid for your time in the study.

COMPENSATION FOR ILLNESS OR INJURY: You will not be paid for any injury or illness resulting from this study, but any emergency medical attention which may be necessary will be provided.

PREGNANCY: You will be asked not to become pregnant during the 18 months required to complete the study, and we ask that you use some form of birth-control during this time. There are no well controlled studies evaluating the safety of the drugs being used on pregnant women or women who are breast-feeding. If you should become pregnant, you will be asked to stop treatment while you are pregnant or breast-feeding. We will continue to assess how you are doing once you have stopped your treatment.

RIGHT TO REFUSE OR WITHDRAW: Your participation is voluntary, and you may refuse to join the study, or may stop at any time, without penalty or loss of benefits. Your doctors also have the right to withdraw you from the treatment at any time.

If you choose to withdraw from the treatment, the following procedures will be followed:

- We will contact your primary doctor, regarding your participation in the study and inform him/her of your decision to withdraw, so that he may resume your treatment.

- We will also ask you to continue to participate in brief follow-up interviews, in order to assess how you are doing once you have stopped your participation.

Some of the questions you will be asked during the course of the first meeting and follow-up meetings are of a personal nature. While we would value your full participation, you have the right to refuse to answer questions.

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CONFIDENTIALITY: Every effort will be made to maintain the confidentiality of your study records. Agents of the (Institution), National Heart, Lung and Blood Institute (NHLBI), and the Food and Drug Administration (FDA), will be allowed to inspect those sections of your medical and research records. The data from the study may be published; however, you will not be listed by name. If you desire, the results of the study will be shared with you at the end of the entire study.

INDIVIDUALS TO CONTACT: If you need more information about this study before you decide to join, or if you have any questions about your treatment, or your rights as a research subject, you can contact any of the individuals listed below:

(FILL IN THE INVESTIGATORS/CONTACT PERSONS NAMES AND PHONE NUMBERS).

In case of an emergency, please call (FILL IN THE INSTITUTION'S EMERGENCY NUMBER).

You will receive a copy of this consent form if you agree to participate in this research study.

PATIENT'S STATEMENT OF CONSENT:

I have read the description of the clinical research study in this consent form and understand it. If I have any questions I have talked it over with one of the doctors to my satisfaction. I understand that my participation is voluntary. I know enough about the purpose, methods, risks and benefits of this research study to judge that I want to take part in it. I hereby consent to participate in the Raynaud's Treatment Study.

_____
Patients Signature

_____
Patients Name (Please Print)

_____
Witness' Signature

_____
Date

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