November 21, 1997

CAVEAT TO IRB

Please note that this sample language does not preempt or replace local IRB review and approval. Investigators are required to provide the local IRB with a copy of this sample language along with the language intended for local use. Local IRBs are required to weigh the unique risks, constraints, and population considerations as a condition of any approval.

Any deletion or substantive change of information concerning risks or alternative treatments must be justified by the investigator, approved by the local IRB, and noted in the IRB minutes. Justification and IRB approval of such changes must be forwarded to the PEACE Clinical and Statistical Coordinating Center. Sponsor approved changes in the PEACE Protocol must be approved by the Local IRB before use unless intended for the elimination of apparent immediate hazard. New information shall be shared with existing subjects at next encounter, with all new subjects prior to involvement, or as the local IRB may otherwise additionally require.

SAMPLE CONSENT LANGUAGE

INFORMED CONSENT FORM
RESEARCH STUDY

Prevention of **E**vents with **A**ngiotensin **C**onverting **E**nzyme Inhibition
The PEACE Trial

INTRODUCTION

You are being asked to take part in a research study. Before you decide to take part, you need to understand the risks and benefits so that you can make an informed decision. This is known as informed consent. This consent form provides information about the research study which has been explained to you. Once you understand the study and the tests it requires, you will be asked to sign this form if you want to take part. You are entirely free to choose if you will take part.

PURPOSE

(Local Institution) and the National Heart, Lung and Blood Institute are carrying out a research study to determine whether trandolapril, a drug used to treat high blood pressure and heart failure, can also prevent heart attacks and death in patients with coronary heart disease. The PEACE study will enroll about 8,100 participants at 160 or more sites in the U.S., Canada and Italy. It will last 4-7 years depending on when you join the study.

Trandolapril is one of a group of drugs called angiotensin converting enzyme inhibitors, or ACE inhibitors. Trandolapril has been approved by the US Food & Drug Administration for use in the United States for use as an anti-hypertensive. A reduction in heart attacks has been observed in research studies looking at the effect of ACE inhibitors in patients with heart failure, but the ability of ACE inhibitors to prevent heart attack and coronary death has not previously been studied directly.

To be eligible for this research study, you must have coronary heart disease and your heart's ability to pump blood must be normal or near normal. If you cannot take ACE inhibitors or should definitely be taking ACE inhibitors for health reasons, you should not participate in PEACE. Also if you have abnormal kidney function, high blood potassium, or are pregnant, you may not join the study.

DESCRIPTION OF PROCEDURES

To identify candidates for PEACE, medical staff of this clinic reviewed hospital or office medical records for patients with coronary heart disease, and discussed study participation with potential candidates' physicians. Medical staff of this clinic then contacted PEACE candidates such as yourself to find out if they were interested in joining the PEACE study.

If you agree to participate, your height, weight and blood pressure will be measured, a blood sample (approximately 2 tablespoons) and a urine sample will be collected in order to measure cardiovascular risk factors (such as clotting functions, lipid values and homocysteine), you will be asked some questions about your health and medications, and you will be given a 20-day supply of trandolapril capsules (2 mg taken once daily) to see if you are able to take the medication. This visit will take about 1 hour.

You will be asked to return for a second visit which will last about 1 hour. If you have no problems with the study medication, you will be randomly assigned (like flipping a coin) to receive either trandolapril or placebo (inactive) capsules at this second visit. You have an equal chance of being assigned to trandolapril (2 mg) or placebo, and neither you nor the investigators will know which you are receiving.

Thereafter, you will be asked to return to the clinic every 6 months for the duration of the study to update your health records and receive a new supply of study medication. These visits will take about ½ hour. The dose of study medication may be increased to 4 mg (placebo or trandolapril) at the first semi-annual visit.

After PEACE is completed, the results will be analyzed and reported. If you wish, you will be notified of the results of PEACE.

BENEFITS AND RISKS

You may receive no direct benefit for participating in the research study. If trandolapril reduces heart attacks and coronary death, and you are assigned to trandolapril, you may benefit from the reduced chance of having a heart attack or coronary death. Benefits to others include an improved understanding of the effectiveness of trandolapril for protection against heart attack and coronary death.

There is a risk with drawing blood. You may feel discomfort as the needle goes through the skin. There may be some bruising at the site where blood is drawn. Pressing hard on the spot for 1 or 2 minutes after the needle is removed will help to prevent a bruise. Very rarely, the arm may become infected. Occasionally a person may feel lightheaded or even faint when blood is drawn.

Side effects associated with trandolapril in European studies are similar to other ACE inhibitors such as enalapril (Vasotec), captopril (Capoten), and lisinopril (Zestril) which are approved for use in the United States. Among 1049 participants in a research study of trandolapril, these side effects included cough (3.9%), wheezing or shortness of breath (2 patients), dizziness (5), headache (2), fatigue (2), rash (2), palpitations (2), impotence (2), insomnia (1), abdominal pain (1), diarrhea (1), swelling (1), low white blood cell count (1), and worse kidney function (1).

ACE INHIBITORS MUST NOT BE TAKEN BY WOMEN WHO ARE PREGNANT OR WHO MIGHT BECOME PREGNANT while taking the drug, because ACE inhibitors can cause serious birth defects. If you are a premenopausal woman, have not been surgically sterilized (hysterectomy or tubes tied) and wish to participate in this research study, you must not be pregnant and must use a reliable birth control method for the duration of your participation in the study and for at least 60 days after stopping the study drug. Acceptable ways to prevent pregnancy are barrier methods (sponge with spermicide, diaphragm with spermicide, cervical cap with spermicide), birth control pills, intrauterine device (IUD), injectable or implantable contraceptives (Depo-Provera, Norplant) or abstinence. Pregnancy tests are not required at the outset or during the study. If, during the study, you believe that you may be pregnant, immediately contact the study coordinator and stop taking study medication until such time as the pregnancy is or is not confirmed.

ALTERNATE TREATMENTS

Usual actions to prevent coronary heart disease include maintaining a healthful lifestyle, control of risk factors such as smoking, diabetes and high blood pressure, coronary angioplasty or bypass surgery. In middle-aged and older men, aspirin has been shown to reduce the risk of coronary heart disease. Your participation in this research study does not affect your ability to receive any of these interventions.

COSTS

The tests and visits that are a part of this study will cost only your time and travel.

PAYMENT FOR INJURY OR HARM

As the description of risks shows, taking part in this research study may result in injury or harm to you. If you require medical care, you should go to an emergency room. Otherwise the doctor in charge of this study will take care of you or help you get the care you need. You will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance. Neither The George Washington University nor the National Heart, Lung, and Blood Institute will pay for your care. You should not expect anyone to pay you for pain, worry, lost income, or non-medical care costs that occur from taking part in the study. This position does not prevent you from pursuing whatever appeals may be available under the law.

PRIVACY
The results of this research study will be given to the research study's Coordinating Center at the George Washington University, and to the National Heart, Lung and Blood Institute, and may be asked for by the Food and Drug Administration or the United States Department of Health and Human Services. Except for these people, records from this study will be kept private unless required by law. Any reports on this study will not use your name or identify you.

RIGHT TO WITHDRAW
You may decide to stop this study at any time. Your care and relations with the doctors and nurses working on this research study will not be changed in any way if you decide not to participate in the study or to stop the study.

VOLUNTARY CONSENT
Your participation in this research study is voluntary. If you have any questions about the study, you should contact (the Clinical Principal Investigator), the person in charge of the study. Also, if you have any questions about your rights as a participant in this study, please call (local IRB contact), who is not affiliated with this research study.

SIGNATURES
By signing this consent form you are agreeing that you understand this consent form, have had an opportunity to ask questions, have had your questions answered to your satisfaction, and agree to take part. You will be given a copy of this consent form.

_____ _____
Signature of Participant Date

_____ _____
Signature of person obtaining consent Date

_____ _____
Signature of Principal Investigator or Designee Date