

FOR CCI USE ONLY

**Approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations,
New Procedures and New Forms of Therapy:**

Administrator:

Date:

Protocol Number: _____ **Expiration Date:** _____

INFORMED CONSENT

- Subject's name: _____
- Title of Research Protocol: A Double Blind Phase II Trial of basic Fibroblast Growth Factor delivered via Heparin-alginate Microcapsules at Coronary Artery Bypass Surgery to Improve Ischemic Myocardium
- Principal Investigator's Name: Michael Simons, MD
- Co-Investigators: Roger J. Laham, MD, Frank W. Sellke, MD
- Protocol Number: 94-04-07-2095

D1. PURPOSE OF STUDY:

Your doctor has determined that you have severe coronary artery disease. The arteries of your heart have developed atherosclerotic ("cholesterol") blockages which may cause you to experience chest pain, angina, or even heart attacks due to decreased blood flow to your heart. After reviewing the results of your cardiac catheterization, your doctor has recommended that your heart disease be treated with coronary artery bypass surgery. You have been asked to be involved in a research study using a new medication at the time of bypass surgery called basic Fibroblast Growth Factor (b-FGF). b-FGF is a laboratory produced version of a naturally occurring substance, which acts to cause blood vessel growth and enlargement. This process can occur within the heart when there are severe blockages, to create alternate channels of blood flow around those blockages, known as collateral vessels. By creating more collateral blood vessels in areas of the heart with severe blockages, b-FGF can increase blood flow so that the heart functions better. The purpose of this research study is to compare the effects of b-FGF with standard therapy to determine its safety and ability to be tolerated in patients undergoing bypass surgery. If you decide to participate in this study, you will be assigned by chance to receive either b-FGF (50% likelihood) or standard therapy (50% likelihood). This study will involve the first use of b-FGF with heparin-alginate microcapsules in human hearts. The purpose of this consent form is to provide you with the information needed to consider in deciding whether to participate in this research study.

D3. PROCEDURE:

If you are asked to participate in this study, it means that you have severe coronary artery disease which your doctor feels should be treated with coronary artery bypass surgery. During the screening process you will undergo screening to determine your eligibility for the study, with a review of your medical history, physical examination, Electrocardiogram, chest x-ray, and blood tests. Following the completion of screening, you will

- Subject's name: _____
- Title of Research Protocol: A Double Blind Phase II Trial of basic Fibroblast Growth Factor delivered via Heparin-alginate Microcapsules at Coronary Artery Bypass Surgery to Improve Ischemic Myocardium
- Principal Investigator's Name: Michael Simons, MD

- Co-Investigators: Roger J. Laham, MD, Frank W. Sellke, MD
- Protocol Number: 94-04-07-2095

enter the initial portion of the study where you will undergo testing with thallium imaging (a radionuclide image of blood flow) with or without exercise and magnetic resonance imaging of the heart (MRI) to measure the heart's function and areas of diminished blood flow, if these tests have not been performed within the past several weeks.

If these measurements of your heart function confirm that there are areas of your heart with diminished blood flow, then you will enter the trial, where microcapsules, or pellets of heparin-alginate either incubated with b-FGF or left alone, will be placed on the surface of the heart during bypass surgery, in areas shown to suffer from decreased blood flow. The bypass operation will not otherwise change because of b-FGF administration. During your postoperative recovery, you will undergo a physical exam, and have standard blood tests, urine tests, chest x-rays, and electrocardiograms monitored by study investigators. Approximately 12 weeks after surgery, you will return for an evaluation by study investigators, where you will undergo a history and physical examination, electrocardiogram, blood tests, urinalysis, exercise test with thallium imaging, and MRI.

D4. RISKS AND DISCOMFORTS:

b-FGF has been administered to approximately 250 subjects to determine its effect on wound healing. There were no side effects or discomfort associated with its administration in that study. However, in animal studies the drug has been associated with kidney damage at high doses, as well as with a lower blood count (anemia), both of which may or may not be reversible. In our animal studies, thickening of the heart muscle has been found, and therefore there is a small risk of an inflammation of the heart, or cardiomyopathy which could result in heart failure. Other animal studies have demonstrated some thickening of the wall of arteries, which may lead to more significant blockages in some arteries.

As with any new drug, there is a small risk of allergic reaction or other previously unknown or rare side effect occurring. There is also a small possibility of infection due to the presence of foreign substances (microcapsules) in the body, and the possibility of more scarring than is normally seen around the sac of the heart after bypass surgery.

There is also a small risk that b-FGF may cause tumor formation, and patients with cancer or known tumors are excluded from the study.

D5. BENEFITS:

You may or may not benefit directly from your participation in this study. The possible benefits from participating in this study include reducing or relieving symptoms of angina, by improving blood flow to areas of the heart, which could not be bypassed. This could lead to improved overall heart muscle function, and increased survival. You may also benefit from the close follow-up by the study investigators after bypass surgery, which would be in addition to the standard care you receive from your physicians.

Other patients with angina and coronary artery disease may benefit from information obtained in this study. This study may be instrumental in developing a new treatment for angina and coronary artery disease, without the use of bypass surgery or angioplasty.

- Subject's name: _____
- Title of Research Protocol: A Double Blind Phase II Trial of basic Fibroblast Growth Factor delivered via Heparin-alginate Microcapsules at Coronary Artery Bypass Surgery to Improve Ischemic Myocardium
- Principal Investigator's Name: Michael Simons, MD
- Co-Investigators: Roger J. Laham, MD, Frank W. Sellke, MD
- Protocol Number: 94-04-07-2095

D6. ALTERNATIVE PROCEDURES:

Your alternative to participation in this study is to receive your doctor's routine medical and surgical care for coronary artery disease, including bypass surgery if necessary. Your doctor will discuss these alternative treatments with you. Standard therapy for your condition includes medicines to improve blood flow to your heart, bypass surgery or angioplasty. Whatever your decision is, your care is independent of your participation in this study. You are free to change your mind about participation in this study at any time.

D7. COST/PAYMENT:

b-FGF will be provided free of charge. There will be no cost to participants, nor payments for participation. The same billing procedures will apply for your hospital stay whether you participate in the study or not. The follow up studies will also be performed without cost to participants.

D8. CONFIDENTIALITY:

The study is monitored by representatives and/or designees of Scios Nova, Inc. (suppliers of b-FGF) and regulatory authorities and they may inspect the records of this investigation. In reports of this study, you will be identified by an assigned number only. Otherwise, all personal communication remains confidential. Your records will be kept for a minimum of 2 years following the approval of this drug marketing or the discontinuation of all clinical trials.

I understand that I have a right to privacy and that the investigators on this study will take all reasonable measures to protect the confidentiality of my records. My name and any other information which might identify me will not appear in any presentation or publication resulting from this study. My name and any other information which might identify me will not be available to any person or group other than the investigators of this study and the Committee on Clinical Investigations of the Beth Israel Hospital which oversees all studies.

- Subject's name: _____
- Title of Research Protocol: A Double Blind Phase II Trial of basic Fibroblast Growth Factor delivered via Heparin-alginate Microcapsules at Coronary Artery Bypass Surgery to Improve Ischemic Myocardium
- Principal Investigator's Name: Michael Simons, MD
- Co-Investigators: Roger J. Laham, MD, Frank W. Sellke, MD
- Protocol Number: 94-04-07-2095

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page(s) of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Chairman of the Medical Center's Committee on Clinical Investigations at (617) 667-4272

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that I may be contacted by the Beth Israel Deaconess Medical Center's Committee on Clinical Investigations during or after my participation in this study as part of its efforts to monitor the experience of subjects in clinical investigations.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

_____	_____	_____
WITNESS	STUDY SUBJECT	DATE

_____	_____
PARENT OR LEGAL GUARDIAN (If subject is a minor, or subject is unable to give consent)	DATE

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

_____	_____	_____
PRINT INVESTIGATOR'S NAME	SIGNATURE OF INVESTIGATOR (or designee)	DATE

For any questions regarding the rights of a research subject, or information regarding treatment of research-related injuries, please contact Nan Clark, Manager, Research Administration, (617) 667-3743.