UNIVERSITY OF WASHINGTON
CONSENT FORM

Title:	MECHANISTIC STUDIES OF NICOTINAMIDE RIBOSIDE IN HUMAN HEART FAILURE
Short Title:	LVAD-NR
Sponsor:	National Institutes of Health (NIH)
Principal Investigator:	Kevin O'Brien, MD 1959 NE Pacific St. Box 356422 Seattle, WA 98195 (206) 685-3930
HSD #:	STUDY00007432
Study Related Numbers:	24-hour emergency telephone number for on-call cardiologist (206) 598-6190

INTRODUCTION

We are asking you to be in a research study. The purpose of this consent form is to give you the information needed to help you decide whether to be in the study or not. Please read the form carefully. Please ask the study doctor or study staff about anything in this form that you have questions about or do not understand. Do not sign this form unless you are satisfied with the answers to your questions and decide that you want to be part of this study.

KEY INFORMATION

Participation is Voluntary	It is up to you whether you choose to participate. There will be no penalty or loss of benefits if you choose not to participate. You may change your mind at any time. You will receive a copy of this consent form for your records.
Duration of Participation	Your participation will begin after you sign this consent form and will continue for two weeks.
Duration of Trial	5 years
Purpose of the Study	To determine if NR augments mitochondrial function and decreases inflammation in subjects with advanced heart failure. Subjects receive NR or placebo (a capsule with no NR) for a minimum of 4 days prior to implantation of left ventricular assist device (LVAD). At the time of surgery, blood, and tissue is collected.
What is NR?	A nutritional supplement called nicotinamide riboside (NR) may help. NR is a form of vitamin B3 that the body can use as fuel for the mitochondria.
Risks	Study nutritional supplement: Nicotinamide riboside is a nutritional supplement and has no known side effects, but there may be unanticipated side effects. Your study doctor will provide you with any information that develops during the study that might affect your willingness to participate.
Benefits	There are no direct benefits to you for participating in this study. There may be

	benefits to patients in the future from knowledge gained in this study.
New Findings	We will notify you if we learn of new information (good or bad) during the research study that may cause you to change your mind about continuing to participate in this study.
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.	

PURPOSE OF THE STUDY

We are asking you to be in this study because you have advanced heart failure and a referral for a left ventricular assist device (LVAD) implant. An LVAD is a battery-powered pump that helps move oxygen-rich blood throughout the body to maintain life.

Your heart muscle cannot generate enough blood flow to keep up with your body's needs. A nutritional supplement called nicotinamide riboside (NR) may help. NR is a form of vitamin B_3 that the body can use as fuel for heart cells. Heart muscle cells generate more energy than any other cell in the body.

The purpose of this study is to find out how much NR reaches the heart muscle and affects cellular energy when taken orally.

The University of Washington will enroll five patients in the pilot phase of this project.

STUDY PROCEDURES

If you choose to take part in this study, we will ask you to sign this consent form before proceeding. You will be randomly assigned, like by the flip of a coin, to either placebo (sugar pill) or active drug (NR). You are three times more likely to receive NR than to receive placebo. Neither the research team nor the participants will know what group you are in until the study is over.

The UW will enroll forty in this trial (10 randomized to placebo, 30 to NR treatment).

Currently, the Food and Drug Administration (FDA) has noted that an NR dose of 180 mg/day is safe. Doses in this study build up to 2000 mg/day leading up to your surgery.

Study procedures take place over 1-2 weeks depending on scheduling of your surgery.

Screening/Enrollment (1-2 weeks pre-procedure)

- Medical record review
- Consent
- Demographics
- Passing out study supplement if you are not staying in the hospital

Day 1

- Blood draw for baseline and safety laboratory tests and experimental study.
- Take 250 mg supplement or placebo (1 tablet) twice daily

Day 2
- Blood draw for safety laboratory tests and experimental study.
- Take 500 mg supplement or placebo (2 tablets) twice daily

Day three until the day before the LVAD surgery
- Take 1000 mg supplement or placebo (4 tablets) twice daily

Day 4
- Blood draw for safety laboratory tests and experimental study.

Day of LVAD surgery (if not Day 4)
- Blood draw for experimental study.

Part of the LVAD surgery requires the doctor to remove a piece of tissue from your heart. We will collect that tissue and do experiments on it for the study.

We will access your medical records to obtain results of labs to monitor for any negative NR effects and to collect results from clinical tests done as part of your surgery.

Study Supplement Requirements

It is very important to know how you are doing with dose and frequency. Please also let us know if you have missed any doses or discarded any capsules.

RISKS AND DISCOMFORTS

NR has no known side effects, but there may be unexpected side effects. Your study doctor will provide you with any information that develops during the study that might affect your willingness to participate.

NR is a relative of nicotinamide, which, unlike niacin, does not cause flushing or itchiness and has no effect on lipid levels.

Our vegetarian capsule is made of an FDA-approved food additive known as hypromellose.

Notification of Participants and Their Physicians

Study participants and their primary cardiologists (or, if hospitalized, their inpatient cardiology attending physician) will be notified if there is clinical worsening of their heart failure. The participants' physicians will conduct clinical follow-up and treatment plans.

You will not be notified of the results of other laboratory studies performed specifically for this study.

Reproductive Risks

Women who are currently pregnant or who wish to become pregnant over the course of study follow-up cannot join this study.

Blood Draw Risk
- Discomfort

- Bruising
- Infection

ALTERNATIVES TO PARTICIPATION

You do not have to be in this study to receive treatment for your condition. The alternative is to continue your current treatment plan. You and your personal doctor can decide what treatment is best for you.

BENEFITS OF THE STUDY

There are no direct benefits to you for participating in this study. There may be benefits to LVAD patients in the future.

SOURCE OF FUNDING

The study team is receiving financial support from the National Institutes of Health.

ChromaDex Corporation, Irvine, CA is supplying us with the study supplement at no cost.

CONFIDENTIALITY OF RESEARCH INFORMATION

If you enroll in this study, we will note your participation in your UW medical record.

You will be assigned a study number linked to your name in a separate, secure electronic file. We will keep this key until the research is complete and for the retention period required by law. Use of de-identified data may continue.

All blood samples for laboratory analysis outside UWMC will be labeled by a study number, not your name. All of the information you provide will be confidential. Your will not be personally identified in any reports, studies, publications or presentations.

We have a Certificate of Confidentiality from the federal National Institutes of Health. This helps us protect your privacy. The Certificate means that we do not have to give out identifying information about you even if we are asked to by a court of law. We will use the Certificate to resist any demands for identifying information.

We cannot use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, or other person. In addition, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the federal government who needs it in order to audit or evaluate the research;
- individuals at the University of Washington, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- the federal Food and Drug Administration (FDA), if required by the FDA;
- State or local authorities, if we learn of child abuse, elder abuse, or the intent to harm yourself or others."

Government or university staff sometimes reviews studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

The U.S. Food and Drug Administration (FDA) reserve the right to review study data that may contain identifying information.

USE OF INFORMATION AND SPECIMENS

The information and/or specimens obtained from you for this study may be used for future studies without getting additional permission from you.

In the future, it is possible that we will want to use or share study information that might identify you. If we do, a review board will decide whether we need to get additional permission from you.

VOLUNTARY PARTICIPATION

You may choose not to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled.

If you stop taking NR, or decide to leave the study early, we ask that you complete remaining study visits and procedures if possible.

You will be asked to return your study nutritional supplement if you stop the study. If you agree, we will contact you 4 weeks after your last dose of study nutritional supplement to assess for safety.

COST OF PARTICIPATION

The NR supplement or placebo is provided at no charge. There are no charges for the additional visits, tests, or procedures that are required for this study. All costs not related to the study, including those related to the normal treatment of your disease, will be your responsibility.

REIMBURSMENT FOR PARTICIPATION

The UW will reimburse you $100 for your participation during study visit one.

RESEARCH-RELATED INJURY

For a life-threatening problem, call 911 right away or seek help immediately. If you think you have a medical problem or illness related to this research, contact Dr. Kevin O'Brien at (206) 685-3930, Dr. Dennis Wang at (206) 405-8223, or the 24-hour paging operator at (206) 598-6190 right away. They will treat you or refer you to treatment.

The costs of the treatment may be billed to you or your health insurance just like other medical costs, or it may be covered by the UW's discretionary Human Subjects Assistance Program (HSAP), depending on a number of factors. The researcher may request HSAP coverage by following established procedures. If you wish to request HSAP coverage yourself, contact the researcher or the UW Human Subjects Division at hsdinfo@uw.edu or 206-543-0098. You may also call collect to the UW Human Subjects Division at 206-221-5940 if you do not otherwise have access to a telephone. Ask the researcher if you would like information about the limits and conditions of the HSAP. The UW does not normally provide any other form of compensation for

injury. However, the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers. You do not waive any right to seek payment by signing this consent form. We will bill your health insurance for treating problems that result from your heart failure, LVAD implantation surgery, or standard clinical care. If you have no health insurance or your insurance refuses to pay, we will bill you.

Printed name of study staff obtaining consent	Signature	Date
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Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form or. If I have questions about my rights as a research subject, I can call the UW Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940.

I give permission to the researchers to use my medical records and biospecimens as described in this consent form. I will receive a copy of this consent form.

Printed name of subject	Signature of subject	Date
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Copies to: Researcher
Subject
Subject's Medical Record