Patient Information and Consent Form

Protocol Title: HF-ACTION – for Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing

Principal Investigator:
Address:
24-hour Telephone number:

You are being asked to take part in a research study that is being sponsored by a grant from the National Institutes on Health (NIH). Portions of Dr. [PI]'s and [his/her] research team's salaries are being paid by this grant.

INTRODUCTION/PURPOSE: Before agreeing to participate in this research study, it is important that you read and understand the information provided. This form describes the purpose, procedures, benefits, risks, discomforts and alternative treatments that are available to you, as well as your right to withdraw from the study at any time.

We know that certain patients with heart disorders can benefit from exercise training in terms of their physical fitness and sense of well-being. However, no one has conducted a study to see if an exercise program will allow patients with heart failure to live longer and decrease the need for a hospital admission. The purpose of this study is to see if a long-term exercise program affects illness and survival. To identify and understand the benefits of exercise training, we need to observe patients like you while you participate in usual care or usual care plus a regular exercise-training program.

The entire study will last about four years. The duration of your participation will be at least one year but not more than four years, with an average of 2.5 years. The study will be conducted at over eighty different centers. About 3000 patients will participate in this study. We plan to enroll about _____ patients at [INSERT STUDY SITE NAME].

PROCEDURES: If you agree to participate, you will be asked to sign this consent form. While participating in the study, you are expected to follow all study procedures. In addition, you should not take part in any other research project for the duration of this research study.

The following sequence of events will occur during the study.

Screening: If you are eligible and your physician has no objections to your participation, study personnel will speak to you about the study and your responsibilities as a research subject. If you agree to participate, a baseline clinic appointment will be made for you. If a reason(s) exist that exclude your participation in this study, you will be told why and a letter with the information will be sent to your doctor.

Baseline Visit: You will be asked a number of questions about your medical history and the medications you are currently taking. Information such as your name, phone number, social security number, and your father's last name will be collected and sent to the Duke Clinical Research Institute (DCRI) for purposes of long-term follow-up. The information will be kept confidential.

A limited physical examination will be conducted. It will include the recording of your blood pressure, pulse and an evaluation of your lung sounds.

As part of the study, you will be asked to take a 6-minute walk test. You will walk down a hallway and will be allowed to stop and rest during this test if you have symptoms preventing you from walking. You can stop the test at any time. The distance completed will be recorded. The 6-minute walk test has been found to be important in heart failure research and patient care.

Pregnant women cannot participate in this study. If you are a woman of childbearing potential, you will be asked if you are pregnant or plan to become pregnant in the next year. If you or your doctor think you could be pregnant, a pregnancy test will be required prior to enrollment. The study will not pay for the pregnancy test. About 2 teaspoons of blood will be drawn or a sample of urine will be obtained for this test. We recommend that you use contraceptive methods and immediately notify your study doctor if your pregnancy status changes.

You will be asked to complete a number of Quality of Life (QOL) questionnaires at this visit and several times throughout the study to assess your perception of the state of your health. The questionnaires will take up to 60 minutes to complete.

An echocardiogram (ECHO) may be done at no charge to you. An echocardiogram is a test that uses sound waves (ultra sound) to form a picture of the heart valves and muscle. The results will be used to determine if you are a good candidate for this study. The ECHO may not be done if you had one within the last 30 days. If there has not been a change in your treatment or health since the last ECHO, the results can be used for this study. By signing this consent form, you will be authorizing us to obtain a copy of the previous ECHO.

All echocardiograms will be sent to the HF-ACTION Echocardiogram Core Lab. The core lab will do specific measurements of your heart. These measurements will be used in our research. By signing this consent form, you will be authorizing a copy of your echocardiogram to be sent to the HF-ACTION Echocardiogram Core Lab.

A blood test will be performed during this visit, at 3 months and at 1 year, to look at proteins in your blood (biomarkers). While you rest, a nurse will put a small needle (catheter) in a vein in your arm and withdraw about 4 teaspoons (20 milliliters) of blood. The blood will be sent to the HF-ACTION Biomarker Core Lab. The core lab will store your blood indefinitely for future measurements of these proteins. We will use these measurements in our research. By signing this consent form, you will be authorizing a tube of your blood to be sent to the HF-ACTION Biomarker Core Lab. Any unused blood will be destroyed once it is determined that it is no longer needed.

Withdrawal of samples: If you decide at a later point that you do not want your blood samples kept for future research, we ask that you contact Dr. [PI] in writing and let [him/her] know you are withdrawing your permission. [His/her] mailing address is [address].

Exercise Test: During your baseline visit, you will perform an exercise test measuring gas-exchange in the [INSERT STUDY CLINIC LOCATION]. Gas-exchange is a two-part process occurring in the lungs during breathing. It allows oxygen from inhaled air to move into the blood and carbon dioxide to move out. You will exercise on a treadmill or exercise bike while breathing through a special mouthpiece. Trained personnel will administer the test and monitor your blood pressure and heart rhythm and blood flow to your heart using an electrocardiogram (ECG).

The ECG will include placing electrodes on your chest, arms and legs. You will exercise until one of the following three things happens: 1) you feel unable to continue, usually because you are too tired; 2) you develop significant shortness of breath or chest pain; or 3) the study doctor stops you because of

changes on your electrocardiogram or because of your blood pressure response to the exercise. This whole procedure will take about 1-□ hours.

If you are one of the first 100 patients enrolled in this study or one of the first five study patients performing the exercise test at this testing center, you will be asked to undergo a second exercise test. This test will be scheduled within 7 days of the first test. The purpose of the second test is to verify the results of the first test.

Copies of all exercise tests performed as part of this study will be sent to the HF-ACTION Exercise Testing Core Lab. The core lab will do specific measurements of your exercise function. We will use these measurements in our research. By signing this consent form, you will be authorizing us to send a copy of your exercise test to the HF-ACTION Exercise Testing Core Lab.

The baseline visit and exercise test will take a full day. You will have the choice of completing it over 2 days with no more than 4 weeks between the two visits. At the end of the clinic appointment, you will be given a schedule of follow-up appointments. If you are assigned to the Exercise Training group, you will receive an appointment for your first supervised training session. All enrolled patients will be scheduled for a follow-up phone call in two weeks.

RANDOMIZATION:

After completing the exercise tests, you will have a clinic visit that will last about 1 hour. At this clinic visit, you will be assigned to one of two groups by chance (like the flip of a coin). The two groups are the Usual Care Group and the Exercise Training Group**.** In order to assign you to one of these two groups, an automated voice system operated by Interactive Clinical Technologies, Inc. (ICTI) will be called and information such as your date of birth, sex, and race will be entered.

Usual Care Group:

If you are assigned to the usual care group, you will be given a patient education manual on heart failure. This education manual covers diet therapy, lifestyle changes, medication use and side effects, and activity. The contents of the manual will be reviewed with you. Every 3 months you will be given a new patient diary to keep track of all of your healthcare-related visits or hospital stays. You may be asked to write down your weight, resting heart rate, and blood pressure in your diary. By signing this consent, you agree to use your HF-ACTION patient diary.

If you are assigned to the usual care group, you will not receive supervised exercise training. You will receive follow-up phone calls at a minimum of every two weeks for the first 9 months. Follow-up phone calls will continue monthly during months 10 through 24 then every 3 months thereafter. The calls will be made to assess symptoms, to review your medications and compliance to those medications and to see if you had any tests, emergency room visits or hospital stays since the last call. You will be asked if you needed to call your health care provider about your health and if your medications were changed because of the call.

Patients in both groups will have scheduled clinic visits every 3 months for the first 24 months and yearly thereafter.

During each study clinic visit, we will perform a brief physical exam and take a history. We will also ask you to complete a number of quality of life questionnaires to assess your perception of your health and your activity level. The questionnaires will take about 60 minutes to complete. The clinic visits will be in the [INSERT STUDY CLINIC LOCATION] and will last about 2 hours.

An exercise test with gas-exchange measurements will be performed at 3 months, 12 months, and 24 months. The same methods and measures as those taken at the first/baseline test will be used and recorded.

If there are exercise-induced ECG changes during the follow-up exercise testing, are not life threatening and are tolerated by you, the exercise test will be completed. You will be allowed to continue in the trial once the results are discussed with your physician. If the exercise-induced ECG change is identified as life threatening, you will be asked to stop any exercise that you have begun. Your doctors will be notified of the results. You will still be followed as part of the trial.

Exercise Training Group:

If you are assigned to the exercise training group, you will be given a patient education manual on heart failure and an exercise training manual. The patient education manual covers diet therapy, lifestyle changes, medication use and side effects, and activity. The exercising training manual covers the benefits of exercise, the HF-ACTION exercise training program, and patient safety considerations. The contents of both manuals will be reviewed with you. Every 3 months you will be given a new patient diary to keep track of your home-exercise sessions and all of your healthcare-related visits or hospital stays. You may be asked to write down your weight, resting heart rate, and blood pressure in your diary. By signing this consent you are agreeing to use your HF-ACTION patient diary.

If you are assigned to the Exercise Training group, you will receive the same care as patients in the Usual Care group including the same schedule of exercise testing and follow-up telephone calls. During the follow-up telephone calls, clinic visits, and supervised training sessions, you will receive educational information that will help you keep up with your exercise.

You will begin an exercise program that will consist of exercising about 1 hour per day, 3 days a week for 3 months (12 weeks) with a trainer. The exercise time includes a 10-minute warm-up and a 10-minute cool down period. If you miss exercise sessions, you will have up to 6 months to complete 36 supervised training sessions. If you have not completed at least nine training sessions at the end of 6 months, you will continue the sessions with a trainer until you have completed the 9 sessions.

The supervised exercise training sessions will begin at [INSERT NAME OF EXERCISE TRAINING CENTER]. You will be given a heart rate monitor at the beginning of your exercise training. The training staff supervising your exercise will show you how to use the monitor. You will learn how to exercise safely and at the appropriate intensity. The heart rate monitor and how you are feeling will indicate how hard to exercise. The intensity of exercise that you are asked to perform will be based on your exercise test. You will exercise by walking, running, or cycling.

Following the first 18 supervised exercise training sessions, you will begin additional exercise training at home. If you do not own exercise equipment, we will provide you with an exercise bicycle or treadmill to use at home during the study. Someone will deliver the equipment to your home. If needed, it may be necessary for a service technician or study personnel from [INSERT STUDY CLINIC LOCATION] to help set-up the equipment. By signing this form, you will be authorizing this person to enter your home for this purpose.

An alternative to training in your home is to participate in unsupervised group training sessions at a cardiac rehabilitation center or other appropriate training program. Your study doctor will provide you with a list of appropriate facilities in your area and will recommend specific types of equipment you should use. The study will not pay for this alternative facility-based training.

We will ask you to keep an exercise diary that will be reviewed at follow-up clinic visits and to wear your heart rate monitor when exercising.

When you have completed 6 months of follow-up, you will be asked to return for facility-based training sessions once every three months until the end of the study. Following the exercise tests at 3 months, 12 months, and 24 months, we will look at the training program to evaluate your progress and may make changes in your exercise routine and training intensity.

RISKS/DISCOMFORTS: Any study evaluating the effect of outcomes in a patient population is subject to potential risks. The risks involved in this study of exercise training in heart failure patients include the risk of performing an exercise test.

There are no significant risks to the echocardiogram. The procedure may cause mild discomfort on the chest wall.

Exercise testing is routinely performed in patients with heart disease, but it has some risks. About one in every 10,000 patients with heart disease dies during an exercise test, and serious complications such as prolonged chest pain or serious heart rhythm problems happen in about four in every 10,000 patients. In patients with your condition, heart failure, up to 2 percent of patients undergoing an exercise test have had a serious abnormal heart rhythm, but none of these episodes caused any immediate death during the exercise testing. Personnel trained to manage such complications will supervise your exercise test.

If you have an abnormal heart rhythm or signs of abnormal blood flow to the heart, you will be asked to stop the test. If you have an abnormal blood pressure response during exercise testing, you will be asked to stop the test.

If you are asked to stop during the first exercise test, you will not be allowed to participate in this study due to concerns about your safety. If you are asked to stop during a follow-up exercise test, one of the study doctors must give approval for you to resume exercise.

A potential risk for participating in exercise training is also present. The rate of cardiac complications for all participants in cardiac rehabilitation is very low. There were only 21 cardiac arrests (sudden and often unexpected stoppage of heart action) and 8 nonfatal heart attacks among 51,303 patients during more than 2 million hours of exercise. It is unknown if this risk is increased among patients with heart failure.

There is also the risk of exercise related injuries to your body, not related to your heart, including injuries from a fall.

It is unknown if the risk of having a cardiac arrest, nonfatal heart attack or other cardiac or non-cardiac event is higher during home exercise.

During exercise, you will be asked to wear a heart rate monitor. Although there is no known serious risk to wearing the monitor, it may cause skin irritation.

Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is also possible, although unlikely.

As previously stated, you will be asked to complete a number of questionnaires to help your study doctors understand how exercise affects quality of life. Additionally, the research staff will ask you a number of questions. You may consider answering these questions stressful. We will make every attempt to make your time with the research staff as stress-free as possible.

RISKS TO WOMEN OF CHILDBEARING POTENTIAL: This research may have an adverse effect on an unborn child. If you are pregnant or you plan to become pregnant in the next year, you cannot participate in this study.

BENEFITS: There may be no benefit to you for participating in this study. However, this study will provide you and us with a detailed assessment of your heart function and exercise ability. It will also help us to understand if regular exercise affects illness and survival of heart failure patients, which may lead to better treatments in the future.

ALTERNATIVES: The only alternative is not to participate. If you choose not to participate in this study, you will continue to receive the standard therapy for heart failure. You will not be denied care based on your decision not to participate.

NEW FINDINGS: In the event any significant new findings are developed during the study that may affect you, your condition, or your willingness to participate, this information will be provided to you.

CONFIDENTIALITY:

As part of this study, Dr. [PI] and [his/her] study team will report the results of your study participation and related tests to the DCRI, the NIH, Echocardiogram Core Lab, Exercise Testing Core lab and the Biomarker Core Lab.

The staff of the [INSERT STUDY CLINIC LOCATION] and/or representatives of the HF-ACTION Economics and Quality of Life (EQOL) Coordinating Center at Duke University may contact your study doctors as well as hospitals that you have stayed at to obtain copies of your medical records, tests and bills for up to 4 years (the length of the study). This information will be used to determine the cost effects of the treatment strategies being studied in HF-ACTION. All information obtained will be kept confidential and no identifying information will be shared outside the HF-ACTION study team and your health care providers unless requested by court order. At the end of the study, all data kept by the EQOL Coordinating Center will be de-identified. By signing this form, you authorize this access.

Dr. John Spertus, a Co-Investigator participating in this study developed the quality of life instrument titled, Kansas City Cardiomyopathy Questionnaire (KCCQ). At the end of the study, he will receive a dataset from DCRI containing the questionnaire data, other quality of life data, patient demographics, and some clinical information. He will use this information to help in analyzing the KCCQ data and in further validating the KCCQ. Dr. Spertus will not use or further disclose any information about you other than what is permitted by DCRI or as required by law.

If the results of this study are published in medical journals, presented at meetings, or used for other educational purposes, your identity as a participant will remain confidential. By signing this consent, you are authorizing such access.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the NIH, [INSERT INSTITUTION NAME] Institutional Review Board (IRB) *or* Research Ethics Board (REB) the Data Safety Monitoring Board (DSMB), associates of the DCRI, [INSERT SITE SPECIFICS] and [ADD OTHERS AS APPROPRIATE]. If your research record is reviewed by any of these groups, they may also need to review your entire medical record. In addition, various HF-ACTION subcommittees responsible for certain aspects of this research study may have access to your data however; your identifying information will be removed.

The National Heart, Lung, Blood Institute (NHLBI) requires that the data collected during a research study is made available to qualified investigators and non-study researchers. However, the institute

also requires that your personal information, dates, or data that can identify you be removed or changed. The data will only be provided to investigators who agree in advance to adhere to established policies for distribution.

Please indicate below, your willingness to share your information outside of the HF-ACTION study investigators and core labs (HF-ACTION study team) commercially or non-commercially.

I am willing to have information about me shared beyond the HF-ACTION study team for non-commercial purposes (not-for-profit). ☐ Yes ☐ No _____ Patient Initials

I am willing to have information about me shared beyond the HF-ACTION study team for commercial purposes (for profit). ☐ Yes ☐ No _____ Patient Initials

The study results will be retained in your research record for at least six years or until after the study is completed, whichever is longer. The information in your medical record will be kept indefinitely.

RE-DISCLOSURES: The NIH may further disclose this information. If disclosed, the information is no longer covered by the federal privacy regulations.

COMPENSATION/COSTS:

Compensation for 3-month, 12-month and Final Visits:
Effective your date of enrollment into the HF-ACTION study, you will be eligible for compensation for completion of the 3-month, 12-month, and Final study visits and any associated study procedures due at those visits. Upon completion of each of the indicated study visits and the associated study procedures you will receive $20 compensation from Duke University.

Compensation for diary completion and return:
As previously mentioned in this informed consent, there are patient diaries for you to write down specific healthcare information, and additional exercise information if you are assigned to the exercise group. The information collected from these patient diaries is most valuable to the researchers conducting the HF-ACTION study. It is most important for you to be responsible and accountable for writing in your diary and returning it to Dr. *<insert PI's name>* or his associate on a timely basis. From the date this version of the informed consent is signed until the time your participation in this study ends, you will be eligible for compensation for the completion and return of diaries as described in the chart below.

Study Visit	Payment amount
3-month	$10 for completed and returned diary/diary packet
6-month	$10 for completed and returned diary/diary packet
9-month	$10 for completed and returned diary/diary packet
12-month	$10 for completed and returned diary/diary packet
15-month	$10 for completed and returned diary/diary packet
18-month	$10 for completed and returned diary/diary packet
21-month	$10 for completed and returned diary/diary packet
24-month	$10 for completed and returned diary/diary packet
3-year	$10 per completed and returned quarterly diary/diary packet. Up to a total of $40 for a full year of completed and returned diaries.
Final Visit	$10 per completed and returned quarterly diary/diary packet. Up to a total

	of $40 for a full year of completed and returned diaries.

For each completed and returned diary indicated above, Duke University will be notified and they will mail you your compensation. In order for your compensation to be mailed to you by Duke University, your name, address, and social security number will be released to the DCRI and the Duke Payment Office.

There will be no costs to you for any of the treatment or testing done as part of this research. If you are a Medicare patient or have other third-party insurance, that third-party insurance may be billed for certain clinical activities (e.g., tests, procedures, clinical visits) related to this study. In order to process third-party billing, we may use your name, phone number, and social security number. Otherwise, costs related to these clinical activities will be paid for from the study budget. You will not be expected to pay any amount, including co-payments, for trial related activities. Any office visits or additional lab work that is not study-related, like the pregnancy test for women, will not be paid by the study.

Immediate necessary care is available if you are injured as a direct result of taking part in this study. However, there is no provision for free medical care or for monetary compensation for such injury other than what your insurance company may provide.

CONTACT PERSONS: If at any time, you develop worsening heart failure symptoms or think you are having a medical problem, you need to call your primary care physician or cardiologist.

If you experience any discomfort, have any problems or think you have been injured as a result of your participation in this study, you need to call Dr. [REGIONAL CENTER PI] at [INSERT PHONE NUMBER].

If you have any questions or concerns about your rights as a participant in this research study, you may contact (INSERT APPROPRIATE NAME, TITLE AND CONTACT INFORMATION FOR IRB/REB REPRESENTATIVE).

VOLUNTARY PARTICIPATION/WITHDRAWAL: Your participation in this research study is voluntary. Your decision to participate or not to participate will in no way affect your current or future access to healthcare at [INSERT STUDY SITE NAME]. If you do decide to withdraw, we ask that you contact Dr. [REGIONAL CENTER PI] in writing and let [him/her] know that you are withdrawing from the study. [His/Her] mailing address is [INSERT ADDRESS].

If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. We will ask your permission to continue using all the data about you that has already been collected for this study prior to your withdrawal. You may withdraw your authorization for us to use all data (other than data needed to report an adverse event or to keep track of your withdrawal) that has already been collected, but you must do this in writing.

Your doctor may stop your participation in this study without your consent if circumstances warrant doing so. The NIH, NHLBI or the DSMB may also stop the study for any reason.

STATEMENT OF CONSENT

The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions and my questions have been answered to my satisfaction. I have been told whom to contact if I have additional questions. I have read this consent form and agree to be in this study with the understanding that I may withdraw at any time. I understand that I should report any discomforts or problems to the study doctor. I agree that any information obtained from my participation may be used in publications resulting from this study. In case of publication, my personal identity will not be revealed in any way. A signed copy of this consent form will be given to me. I will notify study personnel if my address or phone number changes.

_____ _____

Signature of Patient or Legally Authorized Representative Date

_____

Printed Name of Patient or Legally Authorized Representative

_____ _____

Investigator or designee obtaining consent Date

_____

Printed name of Investigator or designee obtaining consent