COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT 200 FR. 4 (2016-2)

YALE SCHOOL OF MEDICINE
YALE-NEW HAVEN HOSPITAL: YORK STREET AND SAINT RAPHAEL CAMPUSES

Study Title: Mechanism and Effects of Manipulating Chloride Homeostasis in Acute Heart Failure

Principal Investigator: Jeffrey M. Testani, MD, MTR, Associate Professor of Medicine: Cardiology

Funding Source: National Institutes of Health (NIH)

Description of the Research Study

You are being asked to take part in a research study at Yale School of Medicine (YSM) and Yale New Haven Hospital (YNHH) involving people with heart failure who take a diuretic, or "water pill." We would like to talk to you about the study because you have heart failure and are taking a diuretic. The study will focus on the effects of supplementing lysine chloride in your diet. Lysine is an essential amino acid that is currently used as a dietary supplement and is a relatively inert way to supplement your chloride intake. We believe lysine chloride may also help people with heart failure. Recent studies have shown that higher levels of salt intake (salt is made of sodium and chloride) are not always detrimental in heart failure. One possibility for this surprising finding is that the chloride part of salt is actually helpful while the sodium part is harmful. This will be the primary focus of this study, to determine if supplementation of lysine chloride can help with managing your heart failure.

This study will investigate how lysine chloride may help treat heart failure by helping to remove excess fluid from the body. If you choose to take part in the study, you will be given medications and tracers, including lysine chloride, solely for research purposes (more information below). The other medications you will be given during the study will provide information about how diuretics affect the kidneys and fluid retention in heart failure, and how the body's total water and blood content changes with heart failure.

This is a multi-site study with study locations at Yale New Haven Hospital, Yale School of Medicine, and St. Francis Hospital. We will collect medical information, blood and urine samples, as well as genetic material (DNA and RNA) during the study. Genetic sequencing of these samples will hopefully reveal variations in the human genome that influence both someone's risk of developing heart failure, and their response to treatment for heart failure. Samples obtained from 200 study participants at multiple sites will be collected over the course of 6 years. These samples will be frozen, and stored in our confidential sample database, AVA-HF biorepository, and tested for biological markers called "biomarkers."

Biomarkers are pieces of information used to evaluate and predict the health of one person, or an entire population. Your doctor uses biomarkers, like your blood pressure or cholesterol level, to see how healthy you are. Biomarkers will help researchers design tests to predict how well someone will respond to treatments for heart failure, and develop new treatments. We hope to find biomarkers in your samples providing important information about how cardiovascular disease begins and worsens, and what risk factors contribute to someone developing these diseases. If you do not want your samples frozen for future use, you will not be able to take part in the study.

Your samples will be frozen and stored for future research for an unlimited time. We will investigate how best to diagnose, prevent, treat, and predict the severity of heart failure, and also explain why some people with heart failure respond poorly to treatment with diuretics. Future research may look at your genes, which contain packets of genetic information passed down from parents to children. Genes are responsible for many things about you such as eye and hair color, blood type and thousands of other traits. Future genetic analysis may study how DNA is put together, and may look at other parts of your genome other than those associated with a particular disease like heart failure. Study samples, and data gained from them, will most likely be shared with a wide range of researchers.

We will work very hard to protect your identity from discovery by others by immediately giving your samples and information a unique code. Other researchers will only receive coded samples and information, and will not be able to link the code to you. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information.

To make an informed decision about whether or not you want to take part in the study, you need to know about its risks and benefits. We will discuss this consent form with you, as it gives detailed study information, including the study's purpose, what will specifically happen during the study, and any possible risks and/or benefits involved. Once you understand the study, we will ask if you wish to take part; if so, you will be asked to sign this form.

What will I be asked to do if I decide to take part in the Research Study?

a. Complete 2 eight hour visits during the 7-day study and be seen up to every day by the study team for safety tests depending on your laboratory results. The study timing is very important. If you agree to take part, you need to complete all of the study visits:

b. If you are a female under the age of 65 who has not had a hysterectomy, we will perform a pregnancy test at each visit.

c. The first longer visit will take place today (while you are admitted to the hospital) if you agree to participate in the study.

If you are admitted at YNHH for the duration of the study, your study visits including "check in visits" will be completed while you are admitted. There may be some instances when the study would be required to be completed while you are still hospitalized. This may result in less days that you are required to participate in the study or take the study medication, the study team will keep you fully informed of any study related changes.

If you are discharged from the hospital and you are still participating in the study, you would then need to return every other day (except for weekends) for the short "check-in" visits.

You would return seven days (may vary and could be less than five days or up to eight days) following the first study visit to complete the second study visit to complete the study or, if admitted, we will conduct this visit in the hospital.

d. The final study visit or follow up visit, will take place 1 week after the second study visit. This visit would consist of asking how you are feeling, measuring your weight, checking your vital signs, 10cc blood collection and collecting a urine sample. If you are not able to come in for the follow up visit, we can contact you by telephone to assess how you are feeling and ask you what your weight is.

e. Be randomly assigned (like flipping a coin) to add lysine chloride or placebo to your regular diuretic during the study. A placebo is an inactive powder that contains no medication. It works as a control for the study to show how lysine works compared to someone not taking this medication.

f. Take the study medication powder (lysine chloride or placebo) twice a day mixed with a beverage of your choice (such as Gatorade™ or Ginger Ale).

g. Lysine chloride/placebo can cause abdominal pain, gas and loose or unformed stools. If you experience any loose stool during the randomization portion of the study, you may have the option of taking Imodium AD or Imodium(loperamide) to relieve that symptom.

h. Give access to your medical record (medical history, medications, blood and imaging results, etc.). Answer health questions to clarify information in your chart that may be unclear. Data will help researchers understand how heart failure affects the body, and discover better treatments in the future. Data stays strictly confidential, accessible only to researchers directly involved in the study.

i. Provide blood samples (6 tablespoons and 2 teaspoons (100 ml) for each Study Visit(1 and 2), less than one teaspoon each day for the daily safety test, and 2 teaspoons for each "Check-In" Visit) and urine samples (all urine produced during Study visits and one sample during "Check-In" Visits). Samples will be securely stored for future research on heart disease. If you do not want your samples stored this way, you will not be able to take part in the study.

j. Perform 24-hour Urine Collections for the 7 days of the study. You will start collecting urine after Study Visit 1 and continue until Study Visit 2, which may be five to eight days later. Urine containers will need to be refrigerated for 24 hours while you are collecting, before being returned to the research group.

k. Be scanned with an ultrasound machine to measure how much urine is in your bladder. Bladder scanning is simple, only takes about 5 minutes, and is done at the bedside. The test is non-invasive and does not involve

any risk or radiation. This will be done prior to receiving the lysine chloride and after the timed urine samples are collected throughout the study period.

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l. If you are taking metformin, you will be asked to stop taking metformin while you are taking the study medication.

- The study team will contact your treating doctor and the study doctor determine that it is safe for you to stop the medication.
- If you do stop metformin while you are in the study, and you are admitted to the hospital, your treating physician will monitor your blood glucose levels and provide an alternative to metformin if they feel this is needed.
- If you are discharged from the hospital and you are still taking the study medication, you will be asked to check your blood sugar based on your current schedule, or at least two times a day.
- If you do not own a glucometer, the study team will provide you with a glucose monitoring kit.
- Any glucometer readings that are consistently greater than 200 mg/dL, you will be asked to contact the study physician.

m. If you experience abdominal upset as loose or unformed stools, you will be given the option of taking over the counter Imodium AD or Imodium(loperamide) to try to relieve those symptoms while you are still admitted to the hospital by your treating physician. If you are discharged from the hospital and still taking the study lysine chloride/ placebo , the study team will closely monitor your episodes of unformed or loose stools Please inform the study team of any abdominal upset, once the study PI or sub I have been contacted and it is deemed safe for you. The study team will provide the Imodium for you.

- Imodium dosage: Take 2 tablets/ capsules (4 mg) once
- May take 1 additional tablet/ capsules after another episode of unformed stool.
- Up to a maximum of (8) 2 mg tablets or capsules or 16mg daily.
- The study team will provide the Imodium and the study team will record the number of doses taken per day.

n. Take medications specifically for the study. (Please see a brief table of these study medications below, and Appendix 1 for more information on these medications):

Medications Administered during the Research Study

	Effect	**Route**	**Purpose**
Lysine Chloride	Believed to help remove excess fluid from the body *Can cause abdominal pain and unformed/ loose stools	By Mouth (powder)	Study medication
Placebo	Inactive powder containing no medicine	By Mouth (powder)	Study control to compare to how Lysine Chloride works
Volumex	FDA-approved radio-pharmaceutical for the determination of total blood & plasma volumes & protein turnover studies.	IV	Determines the body's total blood & plasma volumes
Iothalamate(for participants without a contrast allergy)	Non-radioactive "tracer" version commonly used in human research studies	IV	Measures how well the kidneys are working
Iohexol(for participants without a contrast allergy)	Non-radioactive "tracer" version commonly used in human research studies and CT imaging	IV	Measures how well the kidneys are working

Deuterium Oxide	-Stable, non-radioactive type of water -Well-tolerated & naturally in everyone's tap water -Also known as "heavy water" Common "tracer" in human research	By Mouth (liquid)	Measures the body's total water content
Dextrose 5% Fluid	Salt free IV fluid given to maintain the patency of the IV line and used to flush the IV line after blood draws	IV	To keep the IV line patent during blood draws and during the study visit
Imodium AD or Imodium (Loperamide)	Slows intestinal mobility, reduces incontinence and urgency of stool. Indicated for the control and symptomatic relief of acute nonspecific diarrhea (loose Stools).	By Mouth	To decrease or relieve acute nonspecific diarrhea (loose stools)

Benefits

We do not expect you to directly or immediately benefit by taking part in this study. Information gained from this research may help explain if lysine chloride can help control fluid volume in participants with heart failure, why people develop heart failure, and how diuretics help treat people with heart failure. This knowledge may help improve future treatments for heart failure.

Risks and Inconveniences

Data Collection: There is minimal risk associated with collecting data from your electronic medical record, though there is a possible risk of loss of confidentiality. To help keep your information safe, data will be stored on a password-protected, secure server.

Blood Draws: There are minor risks associated with having blood drawn. These include a small chance of bleeding, bruising, or irritation at the site where blood is drawn, and a remote risk of infection or fainting. If possible, we will draw blood from the IV already placed at YNHH to avoid sticking you with any extra needles. If a suitable IV is not available, we will place one. The amount of blood we are drawing may present a risk, although we believe a small risk.

Urine Collection: There are no risks involved with collecting your urine

Ultrasound of your Bladder: There are no known risks involved with having an ultrasound of the bladder, aside from possible mild discomfort from the ultrasound probe pressing on your abdomen.

Study Medications:

Side effects of Study Medications:

Lysine chloride: Lysine chloride is freely available to the public as a dietary supplement and food additive and is on the FDA Generally Recognized As Safe (GRAS) list. Every day we eat large quantities of lysine and chloride in our normal diet. Furthermore, lysine chloride has been found to be safe in several human and animal studies. There are rare occasions of lysine chloride causing nausea, abdominal pain or diarrhea reported. The doses of lysine chloride administered in this study are higher than the majority of prior studies, which did not study patients with heart failure. As a result, new, unexpected, or exaggerated side effects are possible.

One possible side effect that we will follow closely will be the buildup of acid in your blood, a condition that in very severe cases can cause illness or even be fatal. This condition would slowly develop if it were to happen and thus we will closely monitor the acid levels in your blood over the course of the study to be sure this does not occur. Importantly, we did not see any evidence of acid buildup in our pilot study of heart failure patients were similar doses were used.

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An additional possibility is that lysine chloride will work "too well" in removing fluid from your body which could cause dehydration and possible damage to your kidney. As a result, we will closely follow your kidney function throughout the course of the study and adjust levels of your diuretics (water pills) and the study medication if too much fluid is removed

Placebo: If you are randomized to take the placebo as the study medication, you will not be receiving lysine chloride, and your condition may become worse, stay the same, or improve. You may retain more fluid. If you feel that your symptoms are getting worse, call the study doctor, or go immediately to the emergency room for medical attention, or call an emergency number depending on how severe your symptoms are.

Iothalamate (for participants without a contrast allergy):): You will receive either iothalamate intravenously or Iohexol intravenously. You will not receive both. They are both tracers to measure your kidney function Before taking this medication, tell your study doctor if you have a known allergy to contrast media, are pregnant or breastfeeding, or are unable to make urine. You should also tell your doctor if you have a history of pheochromocytoma, sickle cell disease, or hyperthyroidism, as these conditions may exacerbate additional reactions. Allergic reactions are possible, and may be severe. Tell your doctor right away if you have a skin rash, itching, shortness of breath, sweating, swelling of the face, tongue or throat, or tightness in the chest after you receive this medicine.

Less common side effects: short-term unpleasant after-taste, headache, dizziness, low blood pressure, nausea, vomiting, chills, sweating, flushed/warm feeling, local IV injection site reactions, chest tightness or heaviness, You should also tell your doctor if you have a history of pheochromocytoma, sickle cell disease, or hyperthyroidism, as these conditions may exacerbate additional reactions.

Iohexol (for participants without a contrast allergy): You will receive either iothalamate intravenously or Iohexol intravenously. You will not receive both. They are both tracers to measure your kidney function . Tell your study doctor if you have a known allergy to contrast media are pregnant or breastfeeding, or are unable to make urine. You should also tell your doctor if you have a history of pheochromocytoma, sickle cell disease, or hyperthyroidism, as these conditions may exacerbate additional reactions. Allergic reactions are possible, and may be severe. Tell your doctor right away if you have a skin rash, itching, shortness of breath, sweating, swelling of the face, tongue or throat, or tightness in the chest after you receive this medicine.

Less common side effects: pain, blurred vision, headache, abnormal heart rhythms, chest pain, and nausea, vomiting, chills, sweating, flushed/warm feeling, local IV injection site reactions, chest tightness or heaviness. Uncommon and serious side effects may occur including include hypotension (low blood pressure), shock, cardiac arrest, and severe cutaneous(skin) reactions.

The above risks are minimized by the very small dose of contrast injected. The study team will inject a very small dose (1 ml) through your IV. The usual dose for adults is 50-200 ml, depending on the indication for use.

Volumex: Presently, there are no known side effects or adverse reactions associated with the use of iodinated albumin as a diagnostic aid. However, as with any imaging contrast containing proteins, allergic reactions are possible. Participants who are sensitive to human serum albumin-containing products may also be sensitive to Volumex. Women of reproductive age, or women who may be pregnant should not take Volumex, as it is may cause harm to the fetal thyroid. Components of Volumex are excreted in breast milk during lactation, and thus formula feedings should be substituted for breast feedings while taking Volumex.

Deuterium Oxide: Deuterium oxide occurs naturally and is a stable, non-radioactive type of water that is well tolerated by humans. It is also known as "heavy water," and is in everyone's tap water. It is very commonly used as a "tracer" in research studies in humans.

Dextrose 5% Fluid: There is risk of fluid retention, hyperglycemia or hyperosmolar hyperglycemic state, hyponatremia, hypophosphatemia, hypersensitivity reactions and refeeding syndrome. Tell your doctor right away if you experience any symptoms of increased thirst, increased urination, tiredness, blurred vision.

Imodium AD or Imodium (loperamide)

Before taking Imodium tell your doctor if you are allergic to this medication, if you are pregnant or breastfeeding or if you have any liver impairments, fever, mucus in your stool or a heart arrhythmia. Allergic reactions are possible and may be severe. Tell your study doctor right away if you develop constipation or abdominal distention or bulging. May

cause dizziness, tiredness and drowsiness, use caution when operating heavy machinery. If clinical improvement is not observed in 48 hours, the Imodium may be stopped by the study PI or sub I.

Exposure to Radiation: This study involves exposure to a very small amount of radiation from 2 doses of medicine used during the study (Volumex). Please note this radiation exposure is **not** necessary for your medical care, and is for research purposes only. Although each organ will receive a different dose, the amount of radiation exposure you will receive from this study is equivalent to the whole body being uniformly exposed to 0.2 rem. This calculated value is known as the "effective dose," and helps relate the dose received by each organ to a single number. This level is much lower than the dose included in guidelines established by the federal government, and adhered to by the YNHH Radiation Safety Committee for research subjects. To give you an idea about how much radiation you will get, we will compare it to an every-day situation. Everyone receives a small amount of unavoidable radiation each year. This radiation comes from space and from naturally-occurring radioactive forms of water and minerals. If you participate in the study, you will receive about 8 extra months' worth of this natural radiation.

Participating in Genetic Research: Your genetic information is unique to you, though some of it is shared with family members. Although rare, there are examples of health insurers or employers denying insurance or employment based on genetic test results. Insurers or employers will not be authorized to view any research records. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers, except those with fewer than 15 employees, to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Study Locations

Depending on space availability and other logistics, you may be asked to complete any daytime study procedures (either study visits or follow-up visits) at either the YNHH Hospital Research Unit (HRU) or at the research group's outpatient clinic space at 135 College Street in New Haven, CT.

Economic Considerations

To thank you for you taking part in the research study, and to make up for any inconveniences and time spent in the study, you will be compensated by the research staff at the end of each visit you complete. No additional compensation will be given for transportation to, or parking at the study. Completion of all standard study visits will be compensated up to $1105. If you are discharged before your second visit and have to return to the outpatient clinic, you will be compensated $1,000 for that visit, up to $1605 in total compensation. If additional safety visits must take place, you will be compensated $25 per safety visit.

-$500 for first study visit (8 hours)
-$25 for each Safety Visit (up to 5)
-$15 for each 24 Hour Urine Collection (x7)
-$500 for last study visit (8 hours) if in the hospital, $1,000 if the study takes place outpatient
-$25 for follow up visit or $10 for follow up phone call
- $50 for an incomplete visit (meaning some study medication was given, but the full study was not able to be completed)

If you are withdrawn from the study after screening, you will be compensated **$20**.

All medications and laboratory or diagnostic tests that are performed for the research study will be provided by the research group at no cost to you or your insurance company. You will still be responsible for co-pays required by your insurance company for standard treatments.

For your participation in this study you will receive payments via a Bank of America pre-paid debit card. Please note that your name, address, and telephone number will be shared with Bank of America for e-payments. After your first study visit you will receive a card in the mail that you will need to activate over the phone; any subsequent visit payments will automatically add additional funds to your card. Information about card activation will be provided with the bankcard.

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According to the rules of the Internal Revenue Service (IRS), payments made to you as compensation for taking part in the study may be considered taxable income. It is up to you to report these earnings when you file your taxes as we will not report this to the IRS.

In the rare event that a laboratory abnormality arises, we will need to draw an additional sample of blood (approximately 1 teaspoon) to repeat the lab test. In this event, we will either request you either return to the study site to have the blood drawn or go to YNHH or your local Quest draw site to have the blood drawn. For this inconvenience and additional blood draw, you will be compensated an additional $50.

Treatment Alternatives

You may choose to continue with the standard clinical care as determined by your doctor, without participating in the research study.

Confidentiality

Any identifiable information obtained during the study will remain confidential, disclosed only with your permission, or as permitted by U.S. or state law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Your samples will be assigned a special code so that those viewing them will not be able to identify you. The key to this code will be kept in a locked file, separate from research data, with access controlled by the research doctor. If your information is shared with collaborators, such as government, corporate and/or academic entities in the future, your samples will remain anonymous. When research results are published or discussed at conferences, information that could reveal your identity will not be disclosed unless you specifically give your consent for this to occur.

We understand your health information is personal, and are committed to protecting your privacy. If you decide

to be in this study, research staff will collect information about your health that may directly identify you, including your name, address, and medical record number. Any identifying information will remain confidential and stored on a password- protected, secure server. The research team will only give this coded information to others to conduct this research study. The link to your personal information will be kept for 50 years and then destroyed, making the data anonymous.

Anonymous study data will be kept for another 50 years.

Health information collected for this study:

-Name, address, phone number
-Medical Record Number
-Medical history and allergies, medications, and treatment (past and present)
-Physical exam data, including blood pressure, heart rate, breathing rate, and temperature
-Family medical history
-Results of blood, urine and imaging tests, including x-rays, CT scans, MRIs, or ultrasound, and pathology tests (biopsies)
-DNA, tissue and blood

Health information may be used by or given to:

- The U.S. Department of Health and Human Services agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Providers using the EPIC Electronic Medical Record system
- Food and Drug Administration
- Individuals at Yale responsible for overseeing research finances, billing, and payments
- The study doctors, research coordinator, and members of the research team

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- Laboratories, organizations, and individuals analyzing your health information collected during this study, according to the study plan
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study
- Any third-party and any Sponsor's affiliate involved will have to comply with state of the art privacy standards.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at YSM and YNHH is required to comply with HIPAA, and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies requiring they keep your information confidential.

Representatives from the Yale Human Research Protection Program, and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects) may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential.
You have the right to review and copy your health information in your medical record in accordance with YNHH's medical records policies. This authorization to use and disclose your health information collected during your participation in this study will never expire.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects. The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law such as child abuse and neglect, or harm to self or others.

In Case of Injury

If you are injured during the study, seek treatment and contact the study doctor as soon as you can. YSM and YNHH do not provide funds for the treatment of a research-related injury. However, if you are injured as a result of participating in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this consent form.

Voluntary Participation and Withdrawing from the Study

Taking part in this study is voluntary, and you are free to choose to decline. If you do take part, you are also free to withdraw from the study at any point. Refusing to be in the study, or choosing to withdraw from the study, will not harm your relationship with your doctors or YNHH. You will not lose any benefits you are otherwise entitled to, including health care outside the study, payment for your health care, or health care benefits. If you do not want to be in the study or have your information used for this research, you will not be enrolled in the study, and will not receive study documents or procedures.

Withdrawing Authorization to Use and Disclose Your Health Information

You may withdraw your permission to use and disclose your health information at any time by contacting the study doctor, Jeffrey M. Testani, at Yale University, 135 College Street, Suite 230, New Haven, CT 06510, or by phone (203) 737-6227. If you withdraw your permission, no new information identifying you will be collected

after that date. Information already collected may still be used and given to other researchers until the end of the study to ensure the integrity of the study and/or study oversight.

Interest in Other Heart Failure Research Studies

If you would like to hear about future heart failure studies you may be eligible to take part in, please check "opt in." If you are not interested, please check "opt out."

☐ OPT IN ☐ OPT OUT

Questions

Feel free to ask about anything you do not understand or any technical terms used in this form. Please consider this research and the consent form carefully. Take as long as you need to make your decision.

Authorization and Permission

I have read this form (or someone has read it to me) and have decided to take part in the study described above. Its general purposes, specifics of my participation and possible risks and inconveniences involved have been explained to my satisfaction. My signature indicates that I have received a copy of this form, and give the researchers permission to use and give out information about me for the purposes described in this consent form. By refusing to give permission, I understand I will not be able to be enrolled in this study.

_____

Name of Subject

_____ _____

Signature of Subject *Date*

_____ _____

Signature of Principal Investigator or Person Obtaining Consent *Date*

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919. If you have more questions about this study, or if you have a research-related problem, you may contact the study doctor, Jeffrey M. Testani, at Yale University, 135 College Street, Suite 230, New Haven, CT 06510, or by phone at (203) 737-6227. If you would like to talk with someone other than the researchers to discuss problems, concerns or questions you may have concerning this research, or to discuss your rights as a research participant, you may contact the Yale Human Investigation Committee at (203) 785-4688.

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