RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

STUDY TITLE: **Unsaturated Fatty Acids to Improve Cardiorespiratory Fitness in Patients with Obesity and Heart Failure with preserved Ejection Fraction**

VCU INVESTIGATOR: **Salvatore Carbone, PhD, FHFSA**

SPONSOR: ***American Heart Association***

ABOUT THIS CONSENT FORM

You are being invited to participate in a research study. It is important that you carefully think about whether being in this study is right for you and your situation. This consent form is meant to assist you in thinking about whether or not you want to be in this study. Please ask the investigator or the study staff to explain any information in this consent document that is not clear to you. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. Your participation is voluntary. You may decide not to participate in this study. If you do participate, you may withdraw from the study at any time. Your decision not to take part or to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

AN OVERVIEW OF THE STUDY AND KEY INFORMATION

Obesity is a condition characterized by excess fat in the body. Obesity can make it hard for people to exercise and is highly associated with heart failure. *Heart failure* is a disease in which the heart struggles to pump the blood effectively and results in tiredness (fatigue) and difficulty breathing (dyspnea). You are being asked to participate in this research study because you are affected by *both* obesity and heart failure, and you may meet the requirements for study participation.

WHY IS THIS STUDY BEING DONE?

This study has been funded by the American Heart Association and is designed to evaluate the effects of a diet rich in unsaturated fatty acids (UFA)—also known as 'healthy fats'—in patients with *obesity* and *heart failure*. If you participate in this study, we will evaluate your food consumption during 2 different 12-week periods. During one of the 12-week periods, you will receive specific counseling and instructions on how to increase the consumption of food rich in healthy fats; during the other 12-week period you will receive general dietary recommendations following the Dietary Guidelines for Americans. There will be a minimum of a 6-week break that can last for up to 1 year (washout) between the 12-week periods for a total of study period of approximately 30 weeks, depending on the duration of the washout period. During each 12-week periods, we will measure the effects of these dietary recommendations on your ability to exercise, on your body composition (body water, fat mass, muscle mass), on your cardiac function (how your heart contracts and relaxes), and on the fatty acids in your blood. Approximately 100 subjects will be enrolled in the study. We expect to complete the study in about 3 years.

WHAT WILL HAPPEN IF I PARTICIPATE?

If you decide to participate in this research study, you will be asked to sign this consent form after you have had all your questions answered. After you sign this consent form, the investigators will perform a thorough evaluation. This evaluation will consist of an interview about your medical history, followed by a brief physical exam and a pregnancy test (if indicated). If the result of the pregnancy test is positive, the medical responsible investigator will notify you and you will not qualify to participate in the study. If you meet all the initial study requirements to participate in this study, you will be asked to schedule a baseline study visit at the Clinical Research Unit (CRU) or at Kinesiology and Health Sciences building (KHS).

For the purpose of this consent form, Visit 1 refers to a baseline visit. Every 4±2 weeks for the next 12±2 weeks, there will be 3 additional visits (Visit 2, Visit 3 and Visit 4). After the washout period that can last from 6 weeks to up to 1 year, there will be a Visit 5, and then every 4±2 weeks for the next 12±2 weeks, there will be 3 additional visits (Visit 6, Visit 7 and Visit 8)

Visits Screening, 1, 4, 5 and 8

The screening visit will be conducted at the CRU or through televisit using online web apps. The duration will be around 1 hour. This will include the informed consent process as above and an interview about your medical history and health. For the purposes of the screening visit, after undergoing informed consent and medical history interview, a brief physical exam and pregnancy test will be performed. If the screening visit is conducted through televisit, the pregnancy test will be performed at the first in person visit. If the result of the pregnancy test is positive, the medical responsible investigator will notify you and you will not qualify to participate in the study.

The baseline assessment (Visit 1) may be divided in two sessions, one at CRU and one at KHS. However, it may also be completed in just one session at CRU. The total duration including both sessions is about 3 hours.
Upon arrival to the assessment, we will measure your body weight, height, waist circumference and blood pressure. You will undergo a blood draw (5-6 tablespoons of blood).

You will then undergo an ultrasound of your heart (transthoracic echocardiogram). To perform this ultrasound, you will lie down in a bed while a technician applies a small amount of gel to your chest and abdomen and uses a probe on your skin to take pictures of your heart. You will be asked to remain still and to hold your breath for approximately 10 seconds. During the ultrasound, we will also measure your pulse. These procedures will last approximately 30 minutes.

We will measure your body composition (water, fat mass, muscle mass) using a procedure called bio-electrical impedance analysis (BIA). This procedure involves placing small adhesive patches on your skin that can measure electricity running through the body. You will not be able to sense the electricity being delivered or running through the body. This test will last approximately 10 min, and it allows us to determine your body's fluid, fat, and muscle content.

A test that will measure the strength of the muscles in your upper arm will be performed. You will do this test while lying flat on your back with your arm slightly away from your body. You will be instructed to squeeze a small handgrip device as hard as possible for 2-3 seconds. This test will be repeated 3-5 times with a short break (1-2 minutes) given between each squeeze.

The investigators will then ask you some questions about your diet, particularly regarding what you ate during the 24 hours prior to the visit. You will be then asked to complete ten surveys to evaluate your heart failure symptoms and physical activity. The Duke Activity Status Index (DASI) questionnaire contains 12 questions to which you will answer "yes" or "no". Each question asks you to describe your ability to perform different activities. The Minnesota Living with Heart Failure Questionnaire (MLHFQ) contains 21 questions that ask you to mark how often you experience symptoms of heart failure (i.e. swelling in your legs, shortness of breath). The International Physical Activity Questionnaire-short (IPAQ-short) is a 7-question questionnaire that asks you about amount and intensity of your daily physical activity. The Kansas City Cardiomyopathy Questionnaire has 23-questions and asks about your physical and social health as well as your quality of life. The Subjective social status I – The MacArthur Scale of Subjective Social Status consists of a single pictorial question will be administered to assess your perceived social status at the community level. The Self-efficacy questionnaire – The Exercise Self-Efficacy Scale (EXSE) consists of 8 questions. EXSE is designed to assess an individual's beliefs in their ability to continue exercising on a three time per week basis at moderate intensities for >40 minutes

per session in the future. The Exercise outcome expectation questionnaire – The Multidimensional Outcome Expectations for Exercise Scale (MOEES) consists of 15 questions. MOEES is designed to assess three related outcome expectations for exercise (physical, social, and self-evaluative outcome expectations). The Health literacy – Health literacy will be assessed using 3 questions about your perceived ability and confidence in understanding medical information in addition to 2 questions about current physical activity guidelines. The Personal social capital (short-version) – The Personal Social Capital Scale (PSCS) consists of 16 questions. PSCS is designed to assess bonding and bridging social capital at an individual level. Sedentary time – Daily time spent in sedentary behaviors such as watching television, video or DVDs, using a computer for leisure will be assessed using the structured questions. These procedures will last approximately 40 minutes.

Upon completion of the questionnaires, a physician-supervised maximal aerobic exercise test will be conducted using a treadmill. During the test, you will breathe through a tube attached to a mouthpiece which will allow us to measure how much oxygen you are consuming while walking on the treadmill. Monitoring with non-invasive blood pressure, heart rate and 12-lead electrocardiogram (ECG) will also be conducted. We will place an additional larger electrode on your thigh called near infrared spectroscopy (NIRS). This allows us to measure how saturated your thigh muscle is with oxygen while you exercise. This procedure will last approximately 60 minutes. If you experience any chest discomfort or pain, abnormal blood pressure and heart rate response, or ECG signs of poor blood flow to the heart that limit your ability to complete the exercise test, you will not be permitted to continue the study.

You will also undergo a low-intensity X-ray routinely used to measure the composition of the bones (dual-energy X-ray absorptiometry, DEXA). DEXA can also measure the content of fat and muscle in your body. You will be asked to lie flat on a table and a machine will take pictures of different areas of the body. This test will last 15 minutes and the DEXA is located in the Ambulatory Care Center, 4th Floor as well as KHS.

At the end of the Visit 1 and Visit 5, you will be assigned to one of the two groups: the "healthy fats" group for 12±2 weeks or to the "control" group for 12±2 weeks. The decision to start with one group or the other will be random (like a flip of a coin). For the "healthy fats" group, we will provide you with detailed information about the consumption of food rich in UFA (healthy fats) like extra-virgin olive oil, canola oil, mixed nuts, seeds, avocado and fatty fish (salmon, trout, mackerel). Based on your diet, we will give you advice on how to incorporate such food in your diet, such as encouraging the use of extra-virgin olive oil or canola oil or avocado as dressing for your salads. For the "control group", we will provide you with general information related to a healthy diet, as recommended by the Dietary Guidelines for Americans 2015-2020, with a focus on controlling sodium intake and saturated fats (fats deriving from animal products) in your diet. This discussion typically lasts about 30 minutes.

After Visit 1 or Visit 5, if you are assigned to the "healthy fats" group, the investigators will give you a weekly phone call to assure that the dietary recommendations given at Visit 1 or Visit 5 were clear and that you were able to integrate the suggestions in your daily diet. If needed, the investigators will give you additional advice to help you implement the dietary recommendation. You will be also provided with a shopping list that we will ask you to complete when you purchase the foods rich in healthy fats included in the list for the duration of the study.

At the end of Visit 1 and Visit 5, we will ask you to wear two accelerometers, a wrist-band accelerometer on your non-dominant hand and a waist-worn accelerometer on your belt or directly on your pants. The weight of each device is of approximately 14 grams (half ounce). The wrist-band needs to be worn for 24 hours during the next 7 consecutive days, while the waist-worn accelerometer only during the waking hours (i.e., from waking up until bedtime). We will give you a remind call in the morning at the 1st, 3rd, 5th, and 7th days of

monitoring period. The accelerometers record your body movements while you wear them, but we will not be able to tell what kind of specific activity is happening. There is nothing you need to do other than wearing them properly every day. After 7 days, you will need to safely place the devices and return them at your next in-person visit.

Except for the exercise test and the ultrasound of the heart, the procedures listed above may be performed at KHS, depending on the availability of the devices and the investigators. The investigators will also collect information from your complete medical records during your participation in the study and for 5 years after you finish participating. Of note, this study will not use your samples to sequence all or part of your DNA. There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value.

Visit 2, 3, 6 and 7

At these visits, you will be seen in the CRU or KHS, for a shorter visit (approximately 60 minutes) that will include a medical examination, a measure of your body weight, height, waist circumference and blood pressure. You will undergo a blood draw (5-6 tablespoons of blood) and BIA. At Visit 2 and Visit 6, we will ask you to bring back the accelerometers we gave you at Visit 1 and Visit 5, respectively. If not able to come to the hospital for these visits, we will conduct them through televisits, without checking for body weight, height, waist circumference, blood pressure and blood draw and ask to keep the accelerometers with you and bring them back to us at your next in-person visit.

WHAT ALTERNATIVE TREATMENTS OR PROCEDURES ARE AVAILABLE?

You do not have to participate in this study. You will still receive the standard medical treatments for obesity and heart failure, whether or not you choose to participate in this study.

WHAT ARE THE RISKS AND BENEFITS OF PARTICIPATING?

Risks related to procedures:

- Blood draw: the discomfort may derive from minor bruising (occasional), bleeding (rare, less than 1 in 100), and infection (extremely rare, less than 1 in 1,000) at the puncture site. To minimize the potential discomforts, all blood samples will be taken by trained personnel. There may be pain at the site where the catheter is inserted for session 2, and some bruising and very rarely infection may occur. Some people may experience nausea or faint when the catheter is inserted. Please inform the study personnel if you have experienced any of these reactions before. Although unlikely, Band-Aids used to cover the catheter site can cause a skin rash (dermatitis) in some people who are allergic or sensitive to adhesive or latex.
- Cardiopulmonary exercise test: there is extremely low risk of serious complications such as heart attack or stroke (less than 1 in 1,000). Abnormal cardiovascular response during exercise testing (i.e. markedly elevated blood pressure or heart rate) may occur (approximately 1 in 10), which may require you to stop the test early and/or rest for a few minutes to catch your breath. At all times, a physician will supervise the cardiopulmonary exercise test. Minor arm or discomfort/pressure may occur during blood pressure measurement.
- Echocardiogram: there are no known risks related to the echocardiogram. Minor discomfort is associated with the applying the probe to the chest wall and the placement and removal of the electrodes on your skin.
- Bioelectrical Impedance Analysis (BIA): there are no known risks or discomforts related to the BIA. Minor discomfort is associated with the placement and removal of the electrodes on your skin.
- Other than the inconvenience of answering questions, there are no known risks or discomforts related to the dietary recall or questionnaires.

- Handgrip Test: The handgrip test is considered a low heart risk test due to the small amount of muscle mass being used and the short duration (2-3 seconds) of each repetition. This test may result in your upper arm muscles feeling tired and sore after the test is over and this might last for few days.
- Dietary recommendations: although unlikely, a diet rich in fat may give you temporary bloating and fullness, which resolves by reducing portions. Since the typical American diet has already a high content of fat, the risk of these events to occur is even lower.
- Dual-energy X-ray Absorptiometry (DEXA): as a participant in this study, you will receive extra radiation exposure from the scans that are for research purposes only (not for your direct clinical benefit). The radiation dose from these procedures is minimal, less than 1% of the annual permissible occupational exposure level for radiation workers. These limits are defined as the dose of radiation that, in light of present knowledge, is not expected to cause appreciable bodily injury to a person at any time during his/her lifetime. The risk of this amount of occupational exposure to radiation is, thus, considered to be very small and less than that associated with normal everyday activities.
- Accelerometers: there are no known risks or discomforts related to the use of the accelerometer, however, if you experience any discomfort at the accelerometers' site, you can stop wearing the devices at any time.
- There is a social/psychological risk of breaching confidentiality and having your diagnosis discovered, which may be stressful. The likelihood of this occurring is, however, very low.

REPRODUCTIVE RISKS

As the study procedures might injure an unborn child, pregnant women may not participate. Women who might become pregnant should use a medically accepted form of birth control such as total abstinence, birth control pills, an IUD, diaphragm, progesterone injections or implants, or condoms plus a spermicide. Methods of birth control other than total abstinence are not 100% effective, and should a woman become pregnant there is a risk of injury to an unborn child. For similar reasons, women who are nursing an infant may not participate. For men, the study procedures might increase the risks for birth defects of any child conceived during treatment and several months after treatment is stopped. Men in this study who have the potential of fathering children should be aware of this possibility and consider using a medically accepted form of birth control. For men this would include total abstinence and condoms plus a spermicide, or for the female partner, birth control pills, an IUD, diaphragm, progesterone injections or implants. Methods of birth control other than total abstinence are not 100% effective, and should a woman become pregnant there is a risk of injury to an unborn child.

BENEFITS TO YOU AND OTHERS

There is no guarantee that you will receive any benefit from being in this study. However, it is possible that increasing the consumption of UFA (healthy fats) in your diet may improve or even worsen your ability to exercise. The information obtained from this research study may help identify abnormalities in your laboratory tests or body composition. The information from this study may also lead to a better treatment in the future for people with obesity and heart failure.

WILL I BE PAID TO PARTICIPATE IN THE STUDY?

To compensate for your time, travel related expenses (transportation, parking fees, etc.), and for the purchase the recommended foods, you will be paid as follows: $100 for the Visits 1, 4, 5 and 8, and $50 dollars for the Visits 2, 3, 6 and 7, for a total amount of $600. Total payments within one calendar year that exceed $600 will require the University to annually report these payments to the IRS and you. This may require you to claim the compensation you receive for participation in this study as taxable income. VCU is required by federal law to collect your social security number. Your social security number will be kept confidential and will only be used to process payment.

WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THE STUDY?

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health System). Your study doctor will arrange for short-term emergency care at the VCU Health System or for a referral if it is needed. Fees for such treatment may be billed to you or to appropriate third-party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study. To help avoid research-related injury or illness it is very important to follow all study directions.

CAN I STOP BEING IN THE STUDY?

Your participation in this study is voluntary. You may decide to not participate in this study. If you do participate, you may freely withdraw from the study at any time. Your decision not to take part or to withdraw from the study will involve no penalty or loss of benefits to which you are otherwise entitled. You can decide to forgo any study procedures that make you uncomfortable or you wish not to complete. The study doctor or the investigator may however stop your participation in this study at any time for reasons including *(but not limited to)* the study doctor or the investigator think it is necessary for your health or safety, you have not followed study instructions, or administrative reasons require your withdrawal. If you withdraw from the study, data that has already been collected about you will remain part of the study database and may not be removed.

HOW WILL INFORMATION ABOUT ME BE PROTECTED?

VCU and the VCU Health System have established secure research databases and computer systems to store information and to help with monitoring and oversight of research. Your information may be kept in these databases but are only accessible to individuals working on this study or authorized individuals who have access for specific research related tasks.

Identifiable information in these databases are not released outside VCU unless stated in this consent or required by law. Although results of this research may be presented at meetings or in publications, identifiable personal information about participants will not be disclosed.

Personal information about you might be shared with or copied by authorized representatives from the following organizations for the purposes of managing, monitoring and overseeing this study:

- The study Sponsor, representatives of the sponsor and other collaborating organizations
- Representatives of VCU and the VCU Health System
- Officials of the Department of Health and Human Services

In general, we will not give you any individual results from the study. If we find something of medical importance to you, we will inform you, although we expect that this will be a very rare occurrence. There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value. The information and samples collected as part of this study will not be used or distributed for future research studies, even if identifiers are removed.

HOW WILL MY HEALTH INFORMATION BE USED AND SHARED DURING THIS STUDY?

As part of this research study, we will ask you to share identifiable health information with us and/or permit us to access existing information from your healthcare records. New health information may also be created from study-related tests, procedures, visits, and/or questionnaires. This type of information is considered "Protected Health Information" that is protected by federal law.

Authority to Request Protected Health Information
The following people and/or groups may request my Protected Health Information:

- Principal Investigator and Research Staff
- Research Collaborators
- Government/Health Agencies
- Others as Required by Law
- Institutional Review Boards
- Data Safety Monitoring Boards

Authority to Release Protected Health Information
The VCU Health System (VCUHS) may release the information identified in this authorization from my medical records and provide this information to:

- Health Care Providers at the VCUHS
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards
- Others as Required by Law
- Principal Investigator and Research Staff
- Research Collaborators
- Institutional Review Boards
- Government/Health Agencies

Type of Information that may be used or shared with others during this research: complete health record.

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Right to Revoke Authorization and Re-disclosure
You may change your mind and revoke (take back) the right to use your protected health information at any time. If you revoke this authorization, you may ask also to have your health information removed from the study database. If you revoke this authorization you will no longer be allowed to participate in the research study. To revoke this authorization, you must write to the Principal Investigator (Salvatore Carbone, PhD, FHFSA) at the address listed in the sections below.

Expiration of This Authorization: This authorization will expire when the research study is closed, or there is no need to review data generated by the research project, whichever is later.

Statement of Privacy Rights
You may change your mind and revoke (take back) the right to use your protected health information at any time. However, even if you revoke this authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization, you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator (Salvatore Carbone, PhD, FHFSA) at the address listed in the next paragraphs.

WHOM SHOULD I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY?
If you have any questions, complaints, or concerns about this research, contact:

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roshanak.markley@vcuhealth.org

The researchers above are the best persons to call for questions about this study.
If you have general questions about your rights as a participant in this or any other research, you may contact:

Office of Research,
Virginia Commonwealth University
800 East Leigh Street, Suite 3000,
Box 980568 - Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at https://research.vcu.edu/human-research/hrppirb/research-participants/.
Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

STATEMENT OF CONSENT
I have been provided with an opportunity to carefully read this consent form. All of the questions that I wish to raise concerning this study have been answered.

By signing this consent form, I have not waived any of the legal rights or benefits to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form once I have agreed to participate.

_____
Participant Name, printed

_____ _____ _____
Participant Signature Date Time

_____
Name of Person Conducting Informed Consent, printed

_____ _____ _____
Signature of Person Conducting Informed Consent Date Time

_____ _____
Principal Investigator Signature (if different from above) Date