TEXAS A&M UNIVERSITY HUMAN RESEARCH PROTECTION PROGRAM

INFORMED CONSENT DOCUMENT

Title of Research Study: **Anabolic response to beef vs plant protein in (pre)frail older adults using a novel stable isotope pulse method**

Investigator: Marielle P Engelen, PhD

Key Information:

The following table is a concise and focused presentation of key information to assist you in understanding why you might or might not want to participate in the research. More detailed information is listed later on in this form.

Why you are invited to take part in this study:	You are between the ages of 65-85 years old and in clinically stable condition without acute metabolic disorders (e.g., renal, liver failure, diabetes type 2).
Purpose of this study:	The purpose of this study is to learn how older adults' bodies use beef and plant proteins differently at various stages of frailty.
Voluntary Participation:	Your decision to be in this study is voluntary.
Right to Withdraw from Study:	If you decide to be in this study and then change your mind, you can leave the study at any time without penalty.
Length of Study Participation:	This study will include 1 screening visit (~3 hours) and 3 study visit (~6 hours). All visits will be scheduled at your convenience. We would like you to finish all study visits within 6 weeks.
Study Procedures:	The main procedures in the study include: Screening visit: Review the Informed Consent Form, conduct medical screening, cognitive and muscle function tests, and body composition measurements. Study visits: Arrive fasted in the morning, place an intravenous catheters in the hand, administration of a solution of amino acid tracers, followed by frequent blood draws. You will also be asked to complete several paper based and activity based tests. The study day will involve a bite feeding method: you will be given small, equal-sized bites of either beef, tofu, or water (used as a placebo). The bites are prepared to match in protein content. They will be consumed as small portions given every 20 minutes for 5 hours, along with a small sip of oral tracer.
Risks of Study Participation:	The most common risks from participation in the study will be from the following procedures. - Exposure to x-ray during body composition scan. - Bruise, infection, allergic reaction, lightheadedness, nausea and possibly vomiting during placement of catheter. - Responding to demographic and socioeconomic questions could cause you to feel uncomfortable or upset. Please tell the study staff if you feel uncomfortable or upset while answering the

	questions. - Gastrointestinal problems like nausea, bloating, diarrhea and vomiting associated with the intake of the study meals. - Minor irritation to your hand while placed in the warming box. - Fluid retention (edema, increased blood pressure) associated with stable tracer administration. Details are provided below in “Are there any risks to me?”
Benefit of Study Participation:	There is no direct benefit to you for participating, but your participation may help researchers learn more about metabolism.
Costs of Participation:	Aside from your time, there are no costs for taking part in the study.
Confidentiality of your information:	Information about you will be kept confidential to the extent permitted or required by law.

Detailed Information: The following is more detailed information about this study in addition to the information listed above.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team, Principal Investigator, Marielle P Engelen, PhD at 979-220-2282 or Research Staff at 979-422-1789 or email research@ctral.org.

This research has been reviewed and approved by the Texas A&M Institutional Review Board (IRB). You may talk to them at at 1-979-458-4067, toll free at 1-855-795-8636, or by email at irb@tamu.edu., if

- You cannot reach the research team.
- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in the research?

We expect about 60 people to participate in this research at our site.

What happens if I say yes, I want to be in this research?

Your participation in this study will include 1 screening visit and 3 study visits. All visits will be scheduled at your convenience. You are anticipated to finish all study visits within 6 weeks. All procedures performed are for research purposes only and are not considered medical treatment or standard medical care. All personnel have received training for performing the research procedures but may not have a medical license. The procedures you will be asked to perform are described below.

<u>The screening visit</u>

This visit will last about 3 hours and takes place before the first study visit. Before any study-related tests and procedures are performed, researchers will discuss the study,

its risks, benefits, and compensation with you. If you agree to participate, you will need to sign this consent form.

A. You will be asked questions about your health history and use of medication to determine eligibility.

B. We will assess body weight, height, and vital signs.

C. Body composition and bone density will be assessed by Dual energy X-ray Absorptiometry (DXA) and bioelectrical impedance analysis (BIA).

D. Basic demographic information and daily life questionnaires will be administered.

E. A handgrip test will be done to measure muscle strength and endurance. You will be required to squeeze a hand-held instrument 3 times for your strength test, and repeat for 60 seconds to test endurance.

F. Your leg muscle strength will be measured. You will have some practice time before beginning. You will be asked to extend your leg as hard and as fast as possible and immediately flex your leg as hard and as fast as possible. Several measurements, under different conditions will be collected.

G. You will be fitted with the Kinesis which will be worn only during a walking test and will give us information about your gait. You will walk on a path around the clinical area for six minutes at your desired pace. We will measure the continuous oxygen saturation during and after your walk for a total of 15 minutes.

H. We will assess your hand dexterity by asking you to take the pegs from a container, one by one, and place them into the holes on the board. We will record the time you complete this measurement using both your left and right hand, separately.

Once the screening test results have been reviewed by the study personnel, we will contact you about participating in the study.

<u>The study visit(s):</u>

On the evenings before all study visits, from 10pm on, you will refrain from any food and drink intake. Drinking water is allowed. You may take your prescription medication in the evening and the morning with water only (not with any food). At the end of the study visits, you are allowed to eat and drink again. During the visits there will be the opportunity to watch television, and listen to music etc., as long as you remain in a lying or elevated position on the bed. We will also provide you with a meal at the end of the visit. This visit will last about 6 hours.

A. During each visit, we will also measure your body weight. We will ask you to fill out questionnaires about your overall health and well-being.

B. The research nurse will place a catheter (small, flexible, plastic tube) in a vein of the arm or hand. We will use this catheter to provide you with a small dose of stable tracers of amino acids and collect blood for analysis. Amino acids are parts of protein typically found in food. These are labeled to make them a little heavier than normal so we can recognize them afterwards in the blood. Stable means NOT radioactive. Your body already has some of these; we provide a small amount so that our lab machines can count them.

C. The hand will be placed in a warmed box to increase blood flow. If the hand feels too warm, remove your hand from the box and notify study personnel. A cloth or gauze can be placed over the hand. The hand may be removed from the box between blood draws, but must be kept in the box for 10 minutes prior to the next blood draw. The total volume of blood drawn during the visit will be 4 tablespoons, or 65 ml.

D. Before administration of the tracer solution, a baseline blood will be collected once for measurement of the natural enrichment of metabolites and acute clinical chemistry biomarkers. This blood will be analyzed by Quest Diagnostics.
    a. Hemoglobin A1C
    b. Insulin
    c. Renal function panel (Alb/BUN/Calcium/CO2/Cl/Creat/Glucose/Phosp/Potassium/Sodium)
    d. Hepatic function panel (ALT, AST, Alb, Alk Phos, Direct bili, Total Bili, Total protein)
    e. Lipid panel (Total Cholesterol, HDL Cholesterol, LDL Cholesterol, Triglycerides, VLDL Cholesterol)
    f. CBC (DIFF/PLT) (Hematocrit, Hemoglobin, MCV, MCH, MCHC, RBC, WBC, Platelet count, and percentage and absolute differential counts)
    g. hsCRP
    h. Cytokines (These are analyzed by CTRAL at a later date).

E. On each study visit, you will eat either a bite of either beef, tofu, or water every 20 minutes for 5 hours. The intervention you receive each day will be chosen by chance, like flipping a coin. You will have a one in three chance of being given each treatment. Along with every bite, you will also receive a sip of water that contains a tracer. You will complete this study visit 3 times so that you will eventually receive all types of bites.

All the above-mentioned procedures are experimental. Results of the body composition scan and clinical chemistry (markers measured by Quest) can be shared upon your request.

What are my responsibilities if I take part in this research?

If you take part in the research, it is important for your safety that you:

- Follow the directions of the study doctor and research staff.
- Tell your other health care providers that you are in a research study.

- Tell your study doctor and staff about all medications you are taking (prescription and over the counter) and all of your health issues.
- Call the study doctor or research staff at 979-422-1789 if you have any questions.

What happens if I say yes, but I change my mind later?

You are free to leave the study at any time. There are no penalties and you do not lose any benefits to which you are otherwise entitled. Data that we have already used will stay in the study database and cannot be removed in order to maintain the integrity of the research.

Can I be removed from the research without my OK?

The doctor, research nurse or investigator in charge of the research study or the sponsor can take you out of the study even if you do not ask to leave. This may happen if:

- A condition develops that would interfere with the research methods, and which was not applicable at screening (e.g., illness, drugs).
- Signs and symptoms not seen at baseline or that worsen in severity during/ after intervention .
- Catheters needed for research methods are removed before completion of the study day.
- You are not willing or unable to comply with the guidelines and procedures explained to you and mentioned in this Informed Consent form.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What are the risks of being in this study? (Detailed Risks)

The things that you will be doing or undergoing have significantly more risk than you would come across in everyday life. The discomforts and risks include the following:

A. Amino acid tracers: The amino acid tracers are mixed under supervision of a licensed pharmacist in a certified clean room in the Human Clinical Research Building. On the study days, the tracers are filtered as they go directly into the blood. The risks associated with administration include allergic reaction and infection, such as a change in body temperature, blood pressure and/or heart rate, flushing, itching, nausea, vomiting, fatigue, body ache, headache, sweating and chills. We will monitor for these side effects during the infusion and stop the study if needed.

B. Blood draws / catheterization: Blood will be drawn multiple times during the study visits. You will receive saline after each blood sample is taken; you should experience no noticeable effects of the blood draws. A risk associated with having blood drawn is a low concentration of red blood cells. This might increase the need for blood transfusions. This is unlikely for you due to the low volume of blood samples needed for this study. Furthermore, there is a risk of infection due to having blood drawn. This risk is small because we use strict procedures to prevent infections.

In some instances, there might be a hematoma or bruise at the site of the catheters, or you might experience some pain as the vessel wall is pierced. Some people have a sudden drop in blood pressure during placement of the catheter. This may cause lightheadedness, nausea, vomiting, and fainting. There are no long-term problems associated with this response. Skin rash is associated with an allergic reaction to tape or other medical disposables used for the study. There may also be bleeding when the needles are inserted and when the catheters are removed. If you have this response, you will be examined by the study nurse or physician and given the option of discontinuing the experiment. If they find no reason to stop the study and you want to continue, you will be able to finish the study.

C. Use of temperature controlled box: The box is used to collect "arterialized" blood by heating the air inside the box and around your hand to 50-55°C. In the event that you have discomfort to the heat, a wash cloth or gauze will be placed over the back of your hand and knuckles to minimize heating of the thin skin over the knuckles. Additionally, your hand may be removed from the box between samples to improve comfort, but must be placed inside the box 10 minutes before each blood collection.

D. Assessment of body composition and bone mineral density by dual energy X-ray absorptiometry (DXA): This procedure is used to estimate the amount of fat and muscle mass in your body and to measure bone mineral density in your spine and hip. For the scan you will be required to lie flat on a table for approximately 10 minutes. The scan expose you to minimal radiation (2.5 mRem), equal to the natural atmospheric background radiation during 2 days in College Station. It is not harmful to you. All radiation doses carry a finite risk of inducing cancer or genetic disorders in a fetus. The scan doses are such that these risks are small by comparison with the natural incidence of these conditions. All forms of birth control are acceptable for this scan.

E. Demographic and Socioeconomic Questions: Responding to demographic and socioeconomic questions could cause you to feel uncomfortable or upset. Please tell the study staff if you feel uncomfortable or upset while answering the questions.

F. Nutrition: Gastrointestinal problems like nausea, bloating, diarrhea and vomiting may be associated with the intake of the study meals.

Although the researchers have tried to avoid risks, you may feel that some questions/procedures that are asked of you will be stressful or upsetting. You do not have to answer anything or undergo any procedures you do not want to.

If you become pregnant during the study, you should tell the study team. You will discontinue the study as this is an exclusion criteria.

What are the costs of being in the research?

Taking part in this research study will not lead to any costs to you.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information include the TAMU HRPP/IRB and other representatives of this organization.

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

If direct identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

The sponsor, monitors, auditors, the TAMU HRPP, the US Office for the Protection of Human Research Protections (OHRP) and the Food and Drug Administration (FDA) may be granted direct access to your records to conduct and oversee the research. By signing this document you are authorizing this access.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Federal law provides additional protections of your health-related records and information. These are described in the HIPAA Authorization.

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What else do I need to know?

If you become ill or get injured as a result of this study (medications, devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

Texas A&M University has no program to pay for medical care for research-related injury. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research, we will pay you for each visit you complete:

- $50 for the screening visit.
- $125 for each study visits.

If all visits are completed, you will be compensated a total of $425 for your time and effort. If the study must be stopped at any time, due to personal reasons or facility-

related circumstances, you will be compensated for your time up to the point of discontinuation.

The financial office at Texas A&M University may be given your name, address, and Social Security Number in order to issue a check for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

Texas A&M University has no program to pay for medical care for research-related injury. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you have an injury or illness from the procedures required for this study, the reasonable medical expenses required to treat such injury or illness may be paid for by the study sponsor.

The coverage for such injury or illness is only available if the injury/illness is directly related to the research and is not the result of a pre-existing condition or the normal progression of your disease, or because you have not followed the directions of the study doctor. If your insurance is billed, you may be required to pay deductibles and co-payments that apply. You should check with your insurance company about any such payments.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	