Informed Consent Form

Title: Measurements of Lipoproteins, Apolipoproteins, and Lipids in Three Separate Oral Challenges - Fat, Sugar, and Mixed Test Meals (The Mixed Meal Challenge Study)

NCT Number: NCT05087823

IRB Approval Date: November 22, 2021

You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 9 people who are being studied, at Emory.

Why is this study being done?

This study is being done to answer the question: What type of sample collection conditions are best (serum vs. plasma) for various dietary challenges (fat, sugar, and mixed), and what is the best fasting and post-meal sample collection time point for future studies on a larger group of individuals.

Do you have to be in the study?

It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?

If you are eligible and want to be part of the study, you will participate for 2 years (3 study visits). The researchers will ask you to do the following: drink a ~400 calorie supplement, one at each of 3 visits, blood draws, dual energy X-ray absorptiometry (DEXA) , and questionnaires. All these procedures will be paid for by the study.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question. This knowledge may be used to help others. This study is designed to learn more about lipid metabolism. Although you may not experience any benefits directly, the study results may be used to help others in the future.

What are the risks or discomforts I should know about before making a decision?

The study will take time. All studies have some risks. Some risks are relatively small, like being bored or losing time. Other risk includes possible discomfort from IV catheter placement, possible mild gastrointestinal symptoms after consuming meal challenge drinks, radiation exposure with DEXA, loss of privacy, and breach of confidentiality. A full list of expected risk, there frequency and severity are in “What are possible risk and discomforts?” section of this document.

Alternatives to Joining This Study
Since this is not a treatment study, the alternative is not to participate.

Costs
You WILL NOT have to pay for any of the study procedures, in particular those that are not covered by your medical insurance.

What Should I Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Take time to consider this and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: Measurements of Lipoproteins, Apolipoproteins, and Lipids in Three Separate Oral Challenges - Fat, Sugar, and Mixed Test Meals (The Mixed Meal Challenge Study)

Principal Investigator: Thomas R. Ziegler, Emory Hospital Clinical Research Center, Zsuzsanna (Susan) Kuklenyik, Clinical Chemistry Branch, Centers for Disease Control.

Sponsor: The Clinical Chemistry Branch in the Division of Laboratory Sciences at the Center for Disease Control and Prevention. CDC is authorized to conduct this research under Section 301 of the Public Health Service Act.

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form, you will not give up any legal rights.

What is the purpose of this study?
When you go to the doctor and get your blood drawn one of the tests that is done to find out if you might be at risk of a heart attack is the lipid panel test. This is where your total cholesterol (TC), high- and low-density lipoprotein cholesterol (HDL-C, LDL-C), and triglycerides (TG) are measured. If these measurements are too high, then you are at risk for a heart attack. These measurements have been used for several decades and have been the standard for determining if someone is at risk for cardiovascular disease (CVD).

However, CVD risk can still be tricky to estimate. Recent studies have found many people have heart attacks but still have lipid panel measurements that are normal. Also, it has been found that people who have high levels of total cholesterol and LDL cholesterol who have been taking statins still have heart attacks. To understand why this is happening, the Clinical Chemistry Branch (CCB) in the Division of Laboratory Sciences (DLS) at the Center for Disease Control and Prevention (CDC) is developing a new advanced lipid testing (ALT) method. The new method can measure a wider array of biomarkers that may do a better job of predictive cardiovascular events.

Before the CCB's new method can be used for predicting CVD risk, the CCB needs to find out how well the new method works on blood lipid test results when people consume food. The goal of this study is to see the relative effect

of consumption of different meals on people who have normal body weight or who are overweight. Blood will be drawn over the course of 7 hours and analyzed at the CDC for a wide panel of blood lipids.

What will I be asked to do?

If you agree to participate in the study, we will schedule three (3) study visit days for you at the Emory Clinical Research Center (CRC). Starting from 10pm the night before each study visit, we ask that you fast overnight. You may drink water during this time but avoid sugary drinks and any snacks.

When you arrive for your first visit at the Emory CRC, we will give you a paper consent form to sign to confirm your participation in the study and another consent form for you to sign, to let Emory store your samples. You will only have to sign these two forms once for you to enroll in the entire study. At the first visit you will be asked to fill out a Medical and Social History Form and a Demographics and Screening Form

At each of the three-study visit, you will receive a medical examination from a physician and have your vital signs, weight, and height measured. We will then ask you to provide a urine sample. This urine will be used to assess kidney function. If you are a woman of child-bearing potential, the urine will also be used to perform a pregnancy test for safety purposes. If you are pregnant, you cannot participate in the study. You will have your body fat composition measured one time for the entire study at the first visit.

Next, we will start the lipid challenge. Each of three challenges will take place over the course of six hours. Approximately 22.0 mL of blood will be drawn from a peripheral vein. This will be repeated at 0 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours from the first blood draw. Approximately 29.4 tablespoons of blood will be obtained during the entire study.

Specific Study Procedure Details:

Meal Challenge: During the first visit, you will be given a 100-gram high fat beverage called Calogen to drink. Calogen is a triglyceride emulsion. During the second visit, the meal challenge will be a sugar sweetened beverage (glucose challenge). During the third visit, the meal challenge will be a nutrition shake (mixed meal challenge). There will be a minimum of 2 weeks between challenges. Before each meal challenge, an intravenous peripherally inserted venous catheter will be placed into your arm and approximately 23-mL of blood will be withdrawn. After each meal challenge, your blood will be drawn again at 15 minutes, 30 minutes, 1 hour, 2 hour, 4 hour, and 6 hours. During each meal challenge, you may only drink water and you must avoid physical exertion.

Body composition: At each visit, we will measure how much bone, fat, and muscle are in your whole body with a special scanning machine called a DEXA. This is a painless and very safe exam. During the exam, you will lie flat on your back, breathe normally and rest comfortably. The scan will take about 10 minutes. DEXA will be for research purposes only. We will also measure your height and weight.

Urine collection: We will ask you to provide urine in a cup at each visit. We will measure markers of oxidative stress in your urine.

Pregnancy test: If you are a woman of child-bearing age and may become pregnant, a urine pregnancy test will be performed in the research unit at each visit.

Who owns my study information and samples?

If you join this study, you will be donating your samples and study information. The CDC will own the data that results from the study. You will not receive any compensation if your samples or information are used to make a new product. Your samples will not include analysis by whole genome sequencing. If you withdraw from the study, data and samples that were already collected from you will be destroyed.

What are the possible risks and discomforts?

Meal challenge drinks: As meal challenge you will be asked to drink 3-4 ounces of specific drinks.

For the fat challenge, the Calogen drink is a commercially available liquid high-energy long chain triglyceride fat emulsion which provides 50 grams of long chain triglycerides per 100 mL. It is used to fortify foods. If you happen to have a low tolerance for Calogen, you may experience gastrointestinal symptoms such as diarrhea.

For the sugar challenge, the Oral Glucose Tolerance Test drink contains 75 g if glucose in 200 mL water.

For the mixed meal challenge, the Ensure/Enlive nutrition drink contains 11 g of fat, 22 g of sugar and 20 g of protein. The meal challenges also require you to avoid physical activity for the 6 hours of the test.

Venipuncture: There is some minor discomfort and risk of mild bruising during venipuncture. Standard sterile techniques will be used during phlebotomy; thus, infection is unlikely. Disposable pre-sterilized needles and syringes will be used for all blood drawing in this study; needles and syringes will not be reused. Discomforts associated with venipuncture are rapidly reversible.

DEXA: DEXA involves exposure to small amounts of radiation. The radiation dose is equal to or less than the amount of background radiation received in a round-trip flight from New York to Los Angeles or the natural environmental radiation the average person receives in the United States annually. The risk from radiation exposure of this magnitude is considered to be negligible when compared to everyday risks. DEXA also involves specific positioning of the subject on the DEXA machine table for determination of VAT compartment measurements by the technician.

Other: The fixed timing of procedures or positioning on the DEXA table may be inconvenient to some subjects. Additional risks will be associated with confidentiality issues surrounding the collection/recording of data, but steps will be taken to minimize these risks.

Will I benefit directly from the study?

There may be no specific health benefit to your participation in the study. However, you will receive information on your body composition, which you can use to inform your own health decisions and activities. If we perform a pregnancy test, you will also be notified of the result. You will not receive the results of the blood tests; these tests will be performed for research purposes only.

This study is designed to learn more about lipid metabolism. Although you may not experience any benefits directly, the study results may be used to help others in the future.

Will I be compensated for my time and effort?

You will get $___100_ for first visit 1 if completed, $100 for visit 2 if completed, and $200 for visit 3 if completed, to compensate you for your time and effort. If you do not finish the study, we will compensate you for the visits you have completed. You will get $__400__ total, if you complete all study visits.

What are my other options?

Participation in this study is voluntary. You are free not to participate in this study, or to withdraw your participation at any time. Your decision to participate or not participate in this study will in no way affect your current or future medical treatment. Should you wish to withdraw once you have already donated samples, simply notify Dr. Thomas Ziegler at [redacted] or email [redacted]. Similarly, you do not have to agree to participate in any follow-up activities that may be asked of you at a later time.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results. All information and materials will be obtained for research purposes only, and the data will be kept in strict confidence for use in this proposed research only. All paper records related to you will be kept in locked file cabinets only accessible to the study team, while any electronic data will be encrypted in a protected database. The data will only be available to the PIs and the study team. No information will be given to anyone without your permission. We will ask you to sign an additional consent form if you agree to let us store your research samples from this study for use in future studies.

Storing and Sharing your Information

De-identified data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data and specimens from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

Optional Storage of Sample for Future Research

Blood and urine samples will be taken at the time of each study visit. There may be leftover samples after we've finished this study. These remaining samples will be stored in a freezer at Emory University for future analyses. These stored samples will be kept from samples that are already collected for the study. By keeping your samples in our freezer, we will be able to conduct more tests without asking you for more blood draws or urine. To protect your privacy all samples will be assigned a unique code that does not include any of your personal information. Your samples will be stored as long as it is useful unless you ask us to get rid of them sooner.

Storage of your extra samples is voluntary, and you have the right to refuse to participate. You may request that your stored samples be destroyed at any time by contacting (email or phone) the Dr. Tom Ziegler. Your data and specimens from this study may be useful for other research being done by the study investigators or other investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include:

- Blood values, such as insulin and glucose levels and urine tests for metabolites
- DEXA scan results
- Metabolomic data

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you believe you have become ill or injured from this research, you should contact Dr. Ziegler at telephone number ([redacted] You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory will help you to get medical treatment. Neither Emory nor the sponsor will pay for your medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

Emory and the sponsor have not, however, set aside any money to pay you if you are injured as a result of being in this study or to pay for this medical treatment. For Emory, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities. If the study procedures result in any medical complications that would not fall under "injury" as discussed above, the cost of treatment for those complications may be charged to you or your insurance.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.
The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy

Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

Main Study

PHI that will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form. If you do not sign this form, you may still receive non-research related treatment.

People who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- CDC is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.

- Other researchers and centers that are a part of this study.
- Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration
- Public health agencies.
- Research monitors and reviewer.
- Accreditation agencies.

- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Optional Study

Authorization for This Use of PHI is required to Participate in the Main Study, but not in the Optional study: You do not have to authorize the use and disclosure of your PHI for the optional study. If you do not authorize the use and disclosure of your PHI for the optional study, then you may not participate in the optional research study, but you can still be in the main research study.

People Who Will Use/Disclose Your PHI for Optional Study:

The following people and groups will use and disclose your PHI in connection with the optional research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- CDC is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
  - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
  - Other researchers and centers that are a part of this study.
  - Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration
  - Public health agencies.
  - Research monitors and reviewer.
  - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Thomas R. Ziegler, MD
Emory University Hospital
[redacted]

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly, and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information
Contact Dr. Thomas Ziegler at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the supplement or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

Consent and HIPAA Authorization for Optional Study/Studies:
Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional study/studies previously described:
_____Initials

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study, and any optional studies you initialed above. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____
Signature of Subject (18 or older and able to consent) **Date** **Time**

_____ _____
Signature of Legally Authorized Representative **Date** **Time**

_____
Authority of Legally Authorized Representative or Relationship to Subject

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion **Date** **Time**