INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**United States Department of Agriculture / "Health Impacts of Different Meat Types Incorporated into Different American Diet Patterns"**
Protocol Number:	**HS68**
Principal Investigator: (Study Investigator)	**David Baer, Ph.D.**
Telephone:	**(301) 504-8719** **(240) 565-5509 (24 Hours)**
Address:	**US Department of Agriculture** **10300 Baltimore Ave.** **BARC-East, Building 307B** **Beltsville, MD 20705**

KEY INFORMATION
You are invited to take part in a research study. The goal of the study is to better understand health effects of different types of meat consumed with different diet patterns. Meat provides important essential nutrients, such as protein, iron, and vitamin B12. But the health effects of meat on cardiovascular health and cancer have been controversial in the nutrition research community. Therefore, the U.S. Department of Agriculture (USDA) and the National Cattlemen's Beef Association are co-sponsoring this research study to investigate the effects of different types of meat consumed with different dietary patterns.

For this study, subjects will eat a diet of only foods we provide for four sessions, and each session will last 4 weeks (4 months total on the study diet). The foods will be typical American foods, and we will provide you with the right amount of food to neither gain nor lose weight. At the beginning of the study and during the last week of each session, subjects will provide 2 blood samples separated by 1-2 days and will collect two fecal samples using collection kits we provide. We will analyze the blood for markers of heart disease and diabetes, and we will analyze the fecal samples for gut bacteria and their metabolic products that affect health.

The main reasons a volunteer might want to join this study would be to enjoy the chef-prepared food provided and to receive the payment associated with completing the procedures. The main reason a volunteer might choose not to participate would be because it will require multiple visits to the USDA Nutrition Center (to pick up food and collection supplies and to drop off the samples), the discomfort of blood collection, the inconvenience of collecting

fecal samples, and the requirement to eat only the foods we provide and all the foods we provide for 4 months.

Please read this form carefully. Take your time to ask the study investigator or study staff as many questions about the study as you would like. The study investigator or study staff can explain words or information that you do not understand.

Reading this form and talking to the study investigator or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

BACKGROUND AND PURPOSE
You are being asked to participate in this research study because you are a healthy adult.

The purpose of this study is to learn about the health effects of different types of meat when eaten with two different dietary patterns. One dietary pattern will be the typical America diet, and the other dietary pattern will be the Dietary Guidelines diet.

About 60 subjects will participate in this study.

WHAT WILL HAPPEN DURING THE STUDY?
Your participation in this study will last approximately five months (four months following the study plan, with breaks between each study session) and will include approximately 60 visits to the study center.

Screening:
Before any study-related tests and procedures are performed, you will be asked to read, sign, and date this consent document. The following screening tests and procedures will then be performed to determine if you qualify to take part in this study:

- You will complete a study application and health history form.
- You will fast for 12 hours (no food or drink except water for 12 hours) then you will arrive at the USDA Nutrition Research Center on your scheduled morning to provide a blood and urine sample and have your height, weight, waist circumference, and blood pressure measured.
- You will need to wear a mask when you are in the building for the health screening (as well as other visits).
- Review the study schedule and a list of study foods to confirm that you can eat all of the foods on the menu and participate in all the study procedures.

Once we have received your application, health history form, blood & urine analyses, blood pressure measurement, and height and weight measurements, we will evaluate whether you are eligible for the study. The list below is a list of exclusion criteria; if any of the following apply to you, you cannot participate in the study:

Exclusion Criteria (who cannot participate in the study)

- Younger than 25 years old and older than 80 years old at the beginning of the intervention.
- Body mass index less than 18 or greater than 40 kg/m^2.
- Blood pressure greater than 160/100 mm Hg or use of medication to treat hypertension for less than 6 months.
- Use of medications that will affect the study outcomes, including cholesterol lowering medications.
- Pregnant women, lactating women, women who plan to become pregnant during the study, or women who have given birth during the previous 12 months.
- Fasting blood glucose over 125 mg/dL or type 2 diabetes requiring medication.
- Body weight change of 10% in the past 3 months.
- History of bariatric or other gastrointestinal surgery that would affect digestion.
- History or presence of diabetes, kidney disease, liver disease, certain cancers, gout, hyperthyroidism, untreated or unstable hypothyroidism, gastrointestinal disease, pancreatic disease, other metabolic diseases, or malabsorption syndromes.
- Smokers, vapers, or other tobacco users (within 6 months prior to the start of the study).
- Use of an antibiotic within 1 month of the start of the study or during the study.
- Plans to have a colonoscopy during the study.
- Allergy to any food included in the study menus.
- Unable or unwilling to give informed consent or communicate with study staff.
- Self-report of alcohol or substance abuse within the past 12 months and/or current acute treatment or rehabilitation program for these problems (long-term participation in Alcoholics Anonymous is not an exclusion).
- Other medical, psychiatric, or behavioral factors that in the judgment of the study Investigator may interfere with study participation or the ability to follow the intervention protocol.

This study will use competitive enrollment. This means that when a target number of subjects begins the study, all further enrollment will be closed. Therefore, it is possible that you could be in the screening phase, ready to begin the study, and be discontinued without your consent if the target number of subjects has already begun the study.

If you qualify to take part in this study and are selected as a subject, then the following will happen:

Washout Period: You will be asked to stop taking most vitamin, mineral, fiber, protein, oil, and herbal or botanical supplements because they may affect the study results. This is called the washout period, during which the effects of these supplements leave your body. You may continue calcium supplements and vitamin D.

Study Treatment: The study treatment will be 4 different versions of a diet of typical American foods prepared by chefs at the USDA Nutrition Research Center. During the study, you will visit the USDA Nutrition Research Center 3 times each week (between 8 & 10AM or between 4 & 6PM) to pick up a cooler filled with your food for the next 2-3 days. You will eat the foods on their designated day (eating Monday's food on Monday, Tuesday's food on Tuesday, etc.). You will eat all of the foods we provide and only the foods we provide during each of the 4-week study sessions. We will provide the right amount of food so that you will not gain or lose weight during the study periods. The food will be fully cooked and provided cold in coolers. You should put your food into a refrigerator as soon as possible. You will heat the food to your liking in a microwave when you are ready to eat.

During the study sessions, coffee, tea, and diet soda will be restricted to 2 servings per day (2 cups for tea/coffee and 2 12-ounce cans for diet soda). Water will be unlimited. You will record your daily beverage consumption on a form we will provide. Alcohol consumption will not be allowed during the study sessions, but will be allowed during the breaks.

You will be randomly assigned by chance (like the flip of a coin) to the order of the different diets you will receive. There will be 24 different sequences of the 4 different diets. Everyone will receive all 4 diets, but it will be chance for the order of the diets. This is an open-label study. This means that you, the study investigator, study staff, and the sponsor will know the foods that you are given.

You will have the following study visits and undergo the following procedures:

- You will visit the USDA Nutrition Research Center 3 times per week to pick up your study food and to return your previous food cooler. Pick up times will be between 8 & 10AM or 4 & 6PM on Mondays, Wednesdays, and Fridays.
- You will wear a mask at all times while inside the building.
- Every day of the study, you will complete a one page questionnaire to record consumption of coffee or tea (2 cups are allowed daily), diet soda (2 12-ounce cans are allowed daily), medication, and any health-related symptoms you may be experiencing. The forms will be included in your food cooler.
- Before the intervention starts, complete a questionnaire about your diet. This questionnaire will be given on a computer (if you do not have access to a computer, we will provide access). The questionnaire will ask about what foods you have eaten and how much you have eaten.
- At the beginning and end of each of the four diet periods, answer questions (on your phone) about your diet. These questions will be asked throughout the day (11 times total).
- At the end of each of the four diet periods, you will answer questions (on your phone) about the diet.
- You will weigh yourself 3 times per week at the USDA Nutrition Research Center and record your body weight at each visit.

- You will report to the USDA Nutrition Research Center 10 times during the study to have a blood sample collected. These blood collections will occur in the morning, before 10AM. You will not eat or drink anything (except water) for 12 hours prior to your blood sample collection time. We will also measure your blood pressure at these visits. Over the course of the 5 month study, we will collect less than a pint of blood (the standard donation amount).
- You will collect a fecal sample 10 times during the study. We will provide collection kits to make the process as easy as possible. You will record the time that the sample was produced, store it in the cooler we provide, then bring it to the USDA Nutrition Research Center at your next visit.
- You will meet with a study staff member once per week for about 10 minutes to discuss any concerns or problems you may be having on the study.

<u>After Study Treatment</u>:
Between the study treatment periods, there will be a break, which is expected to be between 5 days to about 2 weeks, depending on when holidays or USDA Nutrition Research Center conflicts fall. The break may be extended up to 4 weeks if necessary.

After you have completed all four study sessions, the study will be over, you will return to your normal, self-selected diet, with no further sample collections.

EXPECTATIONS
If you participate in this study, you will be expected to do the following:

- Read, sign, and date this informed consent form and return it to the study staff.
- Complete the study application and health history form.
- Wear a mask at all times when you are in the USDA Nutrition Research Center building.
- Have your height, weight, and blood pressure measured when you deliver your application and health history form.
- Provide a blood sample and a urine sample, after eating no food nor drink for 12 hours (except water), during your study screening visit.
- Discontinue vitamin, mineral, protein, fiber, oil, and herbal or botanical supplements except calcium and vitamin D.
- Not take antibiotics for one month prior to the study nor during the study.
- Refrain from having a colonoscopy for one month prior to the study and during the study.
- Complete a 30-minute questionnaire about your diet, three times, before the start of the controlled-diet. This questionnaire is completed online – if you do not have access to a computer, we will provide access.
- Consume a diet provided by the USDA Nutrition Center for 4 sessions lasting 4 weeks each (16 weeks total of eating the USDA diet) and eat all the foods and only the foods provided to you.

- Visit the USDA Nutrition Research Center 3 times per week (between 8 & 10AM or 4 & 6 PM on Monday, Wednesday, and Friday) during each study session to collect food and to return your empty food coolers.
- Meet with a study staff member once per week, for about 10 minutes, during a food pick-up visit, to discuss any problems you are having with the study or diet.
- Weigh yourself and record your weight each time you visit the USDA Nutrition Research Center to collect food.
- Right before and at the end of each of the 4 diet periods, complete questions about the diet. These questions will be asked 11 times throughout the day, and will take about 1 to 2 minutes to complete each time. You can use your phone to complete these questions.
- At the end of each diet period, answer questions about the diet. You can use your phone to complete these questions.
- Provide a blood sample 10 times during the study: twice at the beginning of the study and twice at the end of each study period.
- Collect a fecal sample 10 times during the study using the collection kits we provide: twice at the beginning of the study and twice at the end of each study period.

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

For the Study Diets:

It is common to feel a bit bloated or full when you change your diet pattern. This risk affects about 1/20 subjects and usually resolves within a week.

Risks of Study Procedures:

- Blood samples: Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
- USDA Prescribed Diet: You may want to eat foods of your choosing, but you will need to eat only our study foods during the study sessions.
- Fecal Collection: If hands are not washed after fecal collection, illness may occur. Please wash hands after the fecal collection.

UNFORESEEN RISKS

Additionally, there may be other risks that are unknown.

BIRTH CONTROL RESTRICTIONS

There are no birth control restrictions, and this study poses no risk to pregnancy, pregnant women, fetuses, or lactating women. However, subjects on the study will be maintained at a constant body weight, and pregnancy requires weight gain, therefore, if you become pregnant during the study, you will be dismissed from the study.

ALTERNATIVES TO PARTICIPATION
You do not have to be in this study. You may talk to the study investigator, family, or friends about your options before you decide whether or not you will take part in this study. This research study is for research purposes only. The only alternative is to not participate in this study.

If you are an employee, your participation or your family member's participation will not place you in good favor with the study investigators, your supervisor, or the study sponsor (for example, increase in salary, promotion, extra vacation, or the like). Not participating will not adversely affect your employment, in particular the position that you currently hold.

NEW FINDINGS
Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

BENEFITS
Your health is not expected to benefit or be affected as a result of your participation in this study. Information learned from the study may help other people in the future.

COMPENSATION FOR PARTICIPATION
You will receive a total of up to $2800 after completion of the entire study. You will be paid for the visits you complete according to the following schedule:

- $650 for completion of all procedures for Month 1.
- $1300 for completion of all procedures for Month 1 and 2.
- $1950 for completion of all procedures for Month 1, 2, and 3.
- $2800 for completion of all procedures for Month 1, 2, 3, and 4.

For each month, completion of all procedures means arriving on time for meal pick up every scheduled day (3 times per week), completion of all questionnaires, weighing and recording body weight at every visit to the USDA Nutrition Center, meeting with a study staff member every week to discuss study issues, participation in all scheduled blood collection, and collection of all scheduled fecal samples including delivery to the USDA Human Nutrition Research Center.

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

Payments will be made at the end of the study with no exceptions. Payment will only be made by direct deposit. If there is evidence that you have not complied with the study plan, it is possible that we will remove you from the study with no monetary compensation. If there is a lien against you or your property that involves the government, then the National Finance Center will use your compensation to off-set the lien. Compensation for research subjects is considered taxable income. Amounts of $600.00 or more will be reported to the Internal Revenue Service (IRS).

There will be no additional compensation for travel to and from the USDA Nutrition Center. If you have any questions regarding your compensation for participation, please contact the study staff.

CONFIDENTIALITY AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study investigator, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

Medical and other personal information given in participation of this research is confidential. A law passed by the U.S. Congress, known as the Privacy Act, places strict limits on how federal agencies may use such information, and requires that subjects be informed as to why the information is requested and how it will be used. All information will be kept in strictest confidence. You will be assigned a code number for the study. This number will be assigned at the initial visit and will be used to identify samples and data. Names or other identifiers will only be used for procedures where person-to-person communication is required. You will not be personally identified in any of the reports of research.

Your study records including confidential information about you collected during the study will be kept at a secure location. Data and samples from this study will be disposed of after all publications concerning the study are completed. As required by the U. S. Department of Agriculture, consent forms and medical screening data will be kept for 25 years, and then destroyed. All other data, records, and samples will be kept until manuscripts have been published, and then they will be destroyed. Samples collected at screening will be destroyed immediately after analysis. Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner. You may revoke your permission at any time by writing to the study investigator at the address listed on the first page of the form.

While every effort will be made to protect the privacy of your information, absolute confidentiality cannot be guaranteed. This does not limit the duty of the researchers and others to protect your privacy.

By signing and dating this informed consent and authorization form, you authorize to the collection, access, use, and disclosure of your information as described above.

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.

To make sure that the health information collected in this study is accurate, it will need to be checked from time to time against your medical records. This information may include your name, address, phone number, date of birth, medical history, and information from your study visits, including test results. Some persons may need to see these records in order to monitor the research and verify the accuracy of the study data, including:

- A limited number of representatives from the study sponsoring company (namely its monitors and auditors),
- The research ethics review board – *Advarra* IRB (an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study subjects),
- Government regulatory authorities including Health Canada, the US Food and Drug Administration (FDA) and other foreign regulatory agencies.

Your health data will be used to conduct and oversee the research, including comparing the study to other similar studies.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your study records including confidential information about you collected during the study will be kept at a secure location. Your right to access your health data will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

While every effort will be made to protect the privacy of your information, absolute confidentiality cannot be guaranteed. This does not limit the duty of the researchers and others to protect your privacy.

If you decide not to sign and date this form, you will not be able to take part in the study.

By signing and dating this informed consent and authorization form, you authorize to the collection, access, use, and disclosure of your information as described above.

COMPENSATION FOR INJURY

We will make every effort to prevent injuries or illness from occurring while you are in the study. In the case of an injury, illness, or other harm occurring to you during, or resulting from, the study, you should seek medical treatment. You should also contact the study investigator as soon as possible. You or your insurance company will be charged for any continuing medical care and/or hospitalization that are not a part of the study.

If you suffer an injury related to the study procedures, the reasonable costs of necessary medical treatment of the injury will not be reimbursed by USDA. If you have an injury or illnesses occurring during, or resulting from the study, you, your medical insurance, a third-

party payer, or a government program you've enrolled in will be expected to provide coverage for your medical care.

The Federal government does not have any program to provide compensation to you if you experience injury or other bad effects that are not the fault of the study investigators. If you are injured while participating in this research project as a result of the negligence of a United States Government employee who is involved in this research project, you may be able to be compensated for your injury in accordance with the requirements of the Federal Tort Claims Act. Compensation from individuals or organizations other than the United States might also be available to you. If you are a federal employee acting within the scope of your employment, you may be entitled to benefits in accordance with the Federal Employees Compensation Act. You still have the right to seek compensation for injury related to malpractice, negligence, fault, guilt, or blame of those involved in the research. In no way does signing this consent form waive your legal rights nor does it relieve the study investigators, sponsor, or involved institutions from their legal and professional responsibilities.

No funds have been set aside, by the USDA, Advarra IRB, or its affiliated entities to repay you in case of injury, illness, or other harm occurring during, or resulting from the study, and their current policies do not provide for payments for lost wages, cost of pain and suffering, or additional expenses. By agreeing to this you do not give up your rights to seek compensation in the courts.

COSTS
There will be no charge to you for your participation in this study. The study diets, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

FUTURE RESEARCH STUDIES
Identifiers might be removed from your identifiable private information or identifiable biospecimens collected during this study and **could then be used for future research studies or distributed to another investigator for future research studies** without additional informed consent.

COMMERCIAL PROFIT
Your biospecimens collected during this study will not be used for commercial profit.

CLINICALLY RELEVANT RESULTS
Research results that are clinically relevant, including individual research results, will not be disclosed to you. If you contact us after the study is complete and the results have been published, we will provide you with the publication of the results for the study group as a whole.

GENOME SEQUENCING
Researchers can look closely at large amounts of your genetic information by sequencing, or "reading," every letter in your DNA (your genome). Reading a person's entire genetic code is

called whole genome sequencing. The research **will not include** whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

WHOM TO CONTACT ABOUT THIS STUDY
During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research subject;
- Eligibility to participate in the study;
- The study investigator's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study investigator at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00066801.

VOLUNTARY PARTICIPATION / WITHDRAWAL
Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

The study investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date