CONSENT FOR RESEARCH

The Pennsylvania State University

Title of Project: Peanut consumption, blood sugar control, and gut health

Principal Investigator:

Name: Dr. Kristina Petersen
Address: 320 Chandlee Lab
Telephone: 814-863-8622

Subject's Printed Name: _____

We are asking you to be in a research study. This form gives you information about the research.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

Please ask questions about anything that is unclear to you and take your time to make your choice.

1. Why is this research study being done?

We are asking you to participate in this research to evaluate the effects of nighttime peanut consumption (i.e., after dinner and before sleep) on fasting blood sugar levels, longer-term blood sugar control, and risk factors for cardiovascular disease. We will also be investigating how peanut consumption affects gut health and how this relates to blood sugar control.

This research is being done because elevated fasting blood sugar levels (or prediabetes) affects approximately 84 million adults in the US and therefore strategies are required to improve blood sugar control. Based on previous evidence, nighttime peanut consumption may improve fasting blood sugar levels, although no study has directly tested this. This study will be the first to examine the effect of evening peanut consumption on fasting blood sugar levels, risk factors for cardiovascular disease, and gut health.

Approximately 45 people will take part in this research study conducted at the Pennsylvania State University, University Park Campus, PA.

2. What will happen in this research study?

General overview of the study

If you agree to participate in this study, your participation will last approximately 16 weeks in total. There are two treatment phases each lasting 6 weeks and separated by an approximate 4-week break. The two treatment periods will include: 1) evening (i.e., after dinner and before sleep) consumption of one-ounce of peanuts; 2) evening (i.e., after dinner and before sleep) consumption of a calorie matched snack. The calorie matched snack will be whole wheat crackers and spread (e.g. margarine, cream cheese). These foods will be provided to you biweekly. You will follow your normal self-selected diet, although the treatment foods

provided must be consumed as an evening snack and no other foods/beverages (except water) can be consumed after your evening meal.

Over the course of the study you will receive both study foods; the order you receive the foods will be randomly assigned and your treatment order may be different from that of other participants. This assignment is done in a way similar to flipping a coin – we use a computer program to assign the order of treatments that you will receive.

During each treatment period, you will be required to avoid peanut or tree nut consumption other than what is provided to you. You will be required to pick-up your study foods from the metabolic kitchen on the Penn State University campus biweekly. In addition, you will be required to complete a log of your daily treatment intake. This is not a weight loss study, so you must try to keep your body weight and physical activity level constant throughout the entire study.

Procedures to be followed

Screening:

If you decide to participate in the study and are considered eligible after the telephone screening, you will be further screened for eligibility during a visit to the Clinical Research Center (CRC) at Penn State. The screening clinic visit will consist of filling out forms (informed consent, medical history, personal information); measuring height and weight so that body mass index (BMI) can be calculated; and measuring blood pressure to determine eligibility. If your blood pressure is >140/90 at screening you will require written approval from your Primary Care Physician to enroll in the study. If, after these measurements, it is determined you are still eligible to continue in the research, a blood sample will be taken from a forearm or hand vein and a complete blood count, including liver and kidney function and a blood fat panel will be performed (approximately 19 ml of blood or 1.25 tablespoons will be taken). You will feel a small pinch or discomfort when the needle is inserted. If the initial blood draw is unsuccessful it may need to be repeated, with your permission. If you take thyroid medicine, and do not have a current lab test (within 6 months), we will draw 3.5 ml (0.2 Tbsp) more blood to conduct a thyroid test. If you are female of child bearing potential, you will be given a urine pregnancy test. You will be contacted within 3-5 days with the results of the screening blood sample. A clinician at the CRC will review all of the screening data and based on this the research team will determine your eligibility. If you are eligible for the study, you will be contacted to schedule your start date and baseline data collection appointments. There will be no charge for the screening blood work or measurements and you will get these results. If you agree to continue your participation in this study, you will agree to check with the study staff before participating in any other research studies; the study coordinator will determine if it is alright for you to participate.

Baseline and endpoint testing

At the beginning and end of each treatment period you will have your weight measured. If you are female of child bearing potential, you will be given a urine pregnancy test.

Blood sampling:

You cannot consume any food or drinks except for water for 12 hours, and cannot drink alcohol during the 48 hours prior to having your blood taken.

In addition to the blood taken at screening, blood samples will also be taken on two consecutive days at the beginning and end of each treatment period for a total of 8 times. After a 12 hour fast (consumption of no food or drink except water), a blood sample will be taken from your arm. If the initial blood draw is unsuccessful it may need to be repeated, with your permission. Approximately 60 ml (about 4 tablespoons) of blood will be collected at each endpoint over the two days (30 ml or 2 tablespoons each day). Therefore, over the ~16 week study, blood will be taken 8 times with a total amount of approximately 240 ml. A typical American Red Cross blood donation is 1 pint (473 ml). Blood samples will be frozen and analyzed at the end of the study (when all subjects have completed). The results of the study will only be available at the end of the study (which may take up to 3 years). Your blood may be tested for the following: blood fats (total cholesterol, LDL- cholesterol, HDL-cholesterol, triglycerides), blood sugar (glucose and fructosamine), and insulin. No personal information will be kept with any sample – only ID# assignments and only the Primary Investigators and the Study Coordinator will have access to the ID# assignments with the study files.

Measures of vascular health:

Pulse wave analysis (PWA) and Pulse Wave Velocity (PWV):

You will undergo a test that measures your blood pressure and pulse wave forms at the beginning and end of each treatment period. The PWA measurement is very similar to a routine blood pressure measurement. Prior to the measurement, you will be asked to sit quietly with your feet flat on the floor for at least 5 minutes. A blood pressure cuff will be placed on your upper arm. The cuff will inflate, then deflate for 5 seconds, and then partially re-inflate. It is important that you remain still during this measurement. The procedure will be repeated twice, for a total of 3 measurements. Repeated measurements are used to increase accuracy. For the PWV measurement, we will ask you to lay flat on a hospital bed without a pillow. A blood pressure cuff will be placed on your upper leg. We will gently place a hand-held sensor against an artery in your neck. This will measure the pressure waves of the blood in your artery. Once a good waveform is obtained, the blood pressure cuff on your leg will inflate to measure the pressure waveforms in that artery. Having these simultaneous measurements allows the device to calculate the speed at which blood is traveling through your arteries. The PWV test will also be performed three times.

Fecal collection:

At the beginning and end of each treatment period you will be asked to collect a fecal sample (~50 g). You will be provided with a stool sample kit and detailed instructions for collection of a clean sample. The amount and number of different bacteria will be measured in your stool samples as a measure of your gut microbiome.

Dietary intake:
You will be asked to complete a 24-hour dietary recall at the beginning and end of each diet period; a total of 4 recalls. You will complete these recalls using an online system (Automated Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool). Study staff will provide you with a login code and you will be asked to provide information about the foods, beverages, and supplements you consumed during the previous day. You will have the option of completing this dietary recall at home or at your visit.

3. What are the risks and possible discomforts from being in this research study?

Study Treatments
You will be asked to report any food allergies during the telephone screening, however it is possible that an unknown food allergy may manifest during the study. This is most likely to occur within the first week of a treatment phase since the same foods will be repeated daily. It is unlikely that you will experience any discomfort with the addition of peanuts or the calorie matched snack to your diet. However, you may have an unknown sensitivity to this amount of peanuts or the calorie matched snack that may cause you to experience GI (stomach) upset such as bloating, diarrhea, or gas. You should report any adverse reactions to study personnel.

Food preparation
All foods will be prepared according to accepted standards of sanitation and provisions are made to ensure the safety of foods provided for off-site consumption. However, it is possible that incorrect food handling during shipping, storage or preparation, if not detected, could result in food-borne illness. Every effort will be made to safeguard against this possibility. To date, no food related contamination or illnesses have occurred.

Blood Sampling
Blood draws often cause mild pain, swelling or bleeding. There may be some bruising (blood under the surface of the skin), which will be minimized by pressing on the site after the needle is removed. There is also a slight chance of infection, dizziness or fainting. These risks will be minimized and most likely eliminated by having trained medical staff draw the blood in a clinical setting using sterile supplies. If dizziness or fainting occurs, the symptoms will be alleviated by having you lie flat with your feet raised. The medical staff will ask that you remain at the clinic until your blood pressure has been checked and you are cleared from any further risk.

Pulse Wave Analysis (PWA) and Pulse Wave Velocity
There are no known risks associated with these measurements. The sensation of pressure from the blood pressure cuff or hand-held probe may be uncomfortable. There is a possibility for red blotching or mild bruising (petechiae) appearing on the skin above and below the location of the blood pressure cuff. Studies indicate that petechiae are rare (occurring in less than ½ of 1% of patients) and it is typically not uncomfortable and does not require treatment.

Loss of Confidentiality
Your participation in this research is confidential. However, there is always a potential for loss of confidentiality despite our best efforts. To prevent this from occurring all records are coded with a unique ID number and no names are used. Records containing names or other identifying information are kept under lock at the PI's research office. All records associated with your participation in the study will be subject to the usual confidentiality standards applicable to medical records. In the event of publication of this research, no personal identifying information will be disclosed.

Stool collection
You may experience some level of embarrassment or discomfort from being asked to collect stool samples. However, you will be provided with detailed instructions on how to collect the samples within the comfort of your own home, and at your convenience, to help reduce any concerns you may have.

4. What are the possible benefits from being in this research study?
4a. What are the possible benefits to you?

Participants will receive their screening laboratory results, including a complete blood count, interpretation of liver and kidney function, and blood lipid values, at no cost.

4b. What are the possible benefits to others?

The proposed study will investigate whether evening consumption of peanuts improves blood sugar control and risk factors for cardiovascular disease. It will also explore how peanut change gut health and how this relates to blood sugar control. This study will provide evidence for a strategy that could be used to improve blood sugar control in people with elevated blood sugar levels.

5. What other options are available instead of being in this research study?

You may decide not to participate in this research.

6. How long will you take part in this research study?

If you agree to take part, it will take you about 16 weeks to complete this research study. There are two treatment periods each lasting 6 weeks, separated by a ≥ 4 week break. You will be expected to pick up the test foods biweekly at the diet center on campus. At the beginning and end of each treatment period, endpoint data collection will occur (8 visits total).

Total time for study visits, after the initial screening is approximately 6 hours. Times may vary and females will require an additional 5 minutes for a urine pregnancy test at baseline and the end of each diet period. The following is an estimate of the amount of time you will spend in study activities:

Screening appointment: Forms, blood pressure, weight, height, blood draw – 45-60 minutes
(pregnancy testing: females only – 5 minutes)

Beginning of treatment period 1 and 2

- Day 1: blood draw, weight, PWA, PWV – 60 minutes
  (pregnancy testing: females only – 5 minutes)
- Day 2: blood draw – 30 minutes

End of treatment period 1 and 2:

- Day 1: blood draw, weight, PWA, PWV – 60 minutes
  (pregnancy testing: females only – 5 minutes)
- Day 2: blood draw – 30 minutes

Picking up food, completing stool sample collections, and 24-hour dietary recalls: ~ 5 hours

Total time for clinic and diet center visits from baseline to the end of the study ~11 hours

7. How will your privacy and confidentiality be protected if you decide to take part in this research study?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information.

- A list that matches your name with your code number will be kept in a locked file or password protected file in the PI's research office.
- Your research records will be labeled with a unique ID number and will be kept locked at the PI's research office. All records associated with your participation in the study will be subject to the usual confidentiality standards applicable to medical records.
- Your research samples will be labeled with your unique ID number and will be stored in locked freezers at the CRC and in 318 Chandlee Lab. They will be maintained until three years after the date from when the study is published, and then destroyed unless you give permission for us to keep your blood samples for future use (see end of document).

  For research specimens sent to other laboratories or facilities for analysis, no personal identifiable information will be used. Samples will be labelled only with ID numbers. Blood samples will be sent to Quest diagnostics, Pittsburgh, PA. Fecal samples will be sent to Wright Labs LLC, Huntingdon PA.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

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.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may find out about your participation in this research study. For example, the following people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- U.S. Food and Drug Administration
- The research study sponsor, The Peanut Institute
- The Institutional Review Board (a committee that reviews and approves research studies) and
- The Office for Research Protections.

Some of these records could contain information that personally identifies you. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed.

8. What happens if you are injured as a result of taking part in this research study?

In the unlikely event you become injured as a result of your participation in this study, medical care is available. It is the policy of this institution to provide neither financial compensation nor free medical treatment for research-related injury. By signing this document, you are not waiving any rights that you have against The Pennsylvania State University for injury resulting from negligence of the University or its investigators.

9. Will you be paid or receive credit to take part in this research study?

For your participation in this study you will receive monetary compensation of $400.00, prorated as follows and paid at the completion of your participation in the study. If you drop out of the study for any reason before its completion, the following compensation will be provided:

Completion of first treatment period and endpoint testing= $100
Completion of second treatment period and endpoint testing= $300
Total for completion of the study = $400
If you are a Penn State employee, you will be asked to provide you name and Penn State ID number and payment will be provided by direct deposit via the payroll system. If you are not a Penn State employee, you will be paid by check and your Social Security Number must be collected for tax reporting purposes. The compensation that you receive for participation in this study is taxable income.

Total payments within one calendar year that exceed $600 will require the University to report these payments to the IRS annually. This may require you to claim the compensation that you receive for participation in this study as taxable income.

If determined that specific work or visa laws conflict, participants may not be eligible for compensation. Participants can discuss this with the research team for more information.

10. Who is paying for this research study?

The funding for this study is provided by The Peanut Institute. However, the funding source will not be involved in data analysis. They will have the right to review all publications before submission, however there are no contractual agreements that allow them to have influence on, or restrict, the publication of results.

11. What are your rights if you take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.
- If you stop being in the research, already collected data may not be removed from the study database.

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include non-compliance with the study protocol (consuming treatment foods) or study visits (attending clinic visits).

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If you have questions or concerns about this research study, whom should you call?

Please call the head of the research study (principal investigator), Dr. Kristina Petersen, at 814-863-8622 if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the Office for Research Protections at (814) 865-1775, ORProtections@psu.edu if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns or general questions about the research.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

INFORMED CONSENT TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____
Signature of person who explained this research	Date	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and agree to allow your information to be used and shared as described above.

_____	_____	_____
Signature of Subject	Date	Printed Name

Optional part(s) of the study

In addition to the main part of the research study, there is another part of the research. You can be in the main part of the research without agreeing to be in this optional part.

Optional Storage of Tissue for Future Research

In the main part of this study, we are collecting blood samples and fecal samples from you. If you agree, the researchers would like to store leftover sample(s) for future research.

- These future studies may be helpful in understanding cardiovascular disease and diabetes.
- It is unlikely that these studies will have a direct benefit to you.
- Neither your doctor nor you will receive results of these future research tests, nor will the results be put in your health record.

- Sometimes tissue is used for genetic research about diseases that are passed on in families. Even if your samples are used for this kind of research, the results will not be put in your health record.

Your leftover samples will be labeled with a code number that will be linked to a master list accessible only to the PI and research coordinator. This list will be destroyed 3 years after publication of the study results. These samples will be stored in a locked freezer in a locked office of the PI's.

- The length of time they will be used is unknown.
- You will be free to change your mind at any time before the master list is destroyed (approximately 3 years after publication of the study results) at which point we will no longer be able to identify your samples.
- You should contact the principal investigator if you wish to withdraw your permission for your blood samples or fecal samples to be used for future research. If it is still possible to identify your samples, any unused samples will be destroyed and not used for future research studies.

You should initial below to indicate what you want regarding the storage of your leftover blood samples and fecal samples for future research studies.

a. Your samples may be stored and used for future research studies to learn about diabetes and cardiovascular disease prevention.
_____ Yes _____ No

c. Your samples may be shared with other investigators/groups without any identifying information.
_____ Yes _____ No

Do we have permission to keep your personal information and contact you about your interest in participating in future studies for Dr. Kris-Etherton, Dr. Petersen and their collaborators?

_____ Yes _____ No

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the optional part(s) of the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____
Signature of person who explained this research	Date	Printed Name

Signature of Person Giving Informed Consent

Signature of Subject

By signing below, you indicate that you have read the information written above and have indicated your choices for the optional part(s) of the research study.

_____	_____	_____
Signature of Subject	Date	Printed Name