US ARMY Research Institute of Environmental Medicine

CONSENT TO PARTICIPATE IN RESEARCH

Title of Protocol: 24-07-HC: Bioavailability of Ration Items Containing Tart Cherry

Principal Investigator: Tracey J. Smith, Ph.D., R.D.

Sponsor: N/A

Introduction: You are being asked to participate in this research study because you are a healthy adult age 18- 39. You do not have to take part in this research. It is your choice.

The table below summarizes some **key** points to think about. After reading this summary, if you think you might be interested in participating, read the rest of the consent form for more details about the study.

RESEARCH SUMMARY	
Informed Consent	It is important that you understand this research study so that you can make an informed decision. This process is called informed consent. • Please ask questions about anything you do not understand. • Feel free to talk with your family, friends, or others before you decide. • After your questions have been answered, you will be asked if you want to participate. If you agree, you will sign this consent form. • You will be given a copy of this form to keep.
Voluntary Participation	You do not have to take part in this research. It is your choice. You can also choose to stop participating at any time during the study.
Purpose	To determine how the shelf storage of tart cherry-containing food items impacts your body's ability to absorb and use the compounds within tart cherry.
Duration	You can expect to be in the study for a minimum of 25 days.
Procedures	If you agree to be in this study, you will be asked to: • Complete a questionnaire asking about your background. • Have your height and weight measured. • Provide a fecal sample once. • Record all the food you eat and beverages you drink during a 48-hour period on four separate occasions. • Have your blood drawn seven times (six times via an intravenous catheter and one time via a venipuncture) on four separate occasions.

	• Provide a urine sample seven times on four separate occasions. • Eat a food item, or drink a beverage, that may or may not contain tart cherry on four separate occasions.
Restrictions	Before each trial and the morning after, you should not: • Eat or drink (water allowed) for ≥12 hours • No tobacco and vigorous exercise for ≥24 hours • Follow a diet low in certain fruits, certain vegetables, and certain beverages during a 48-hour period. No food or beverages (besides water) during each trial No blood donation within 8 weeks of beginning the study.
Risks	The **main** risk from being in this study are: • ***Blood Draws.*** When the needle goes into a vein, it hurts for a short time. Also, there may be the minor discomfort of having the needle/plastic tube taped to your arm. • ***Diet Intervention (tart cherry food items).*** Bloating, gas, or other GI discomfort is possible.
Benefits	You will receive no direct benefits from participating in this study. This study is not being done to improve your physical condition or health. The information we gather may help improve ration components.
Payment	You will be paid for this study.

WHY IS THIS RESEARCH BEING DONE?

We are doing this study because tart cherry may have beneficial effects on military performance. However, before we test performance outcomes of ration items, we first need to determine how the shelf-storage of tart cherry-containing food items impacts your body's ability to absorb and use the compounds within tart cherry.

WHAT WILL HAPPEN DURING THIS RESEARCH?

<u>Medical Screening:</u>
You will meet with the staff of the Office of Medical Support and Oversight (OMSO) at USARIEM, or at your Unit's supporting medical facility in coordination with OMSO, for a health screening (~ 1 hour, ~2 visits) to ensure you may safely participate. The staff will draw less than a tablespoon of blood from your arm to see how quickly your blood clots and review your medical history. Information from the screening procedures will be used to determine if you are able to safely participate in this study.

<u>Study Procedures:</u>
There is a baseline testing session (~2 hours), four trials that each comprised of a 6.5-hours trial day and a morning after visit. Each trial is separated by at least 5 days.

<u>During the baseline testing, you will be asked to:</u>

- Complete a questionnaire asking about your background.
- Have your height and weight measured once.
- Provide a fecal sample once.

<u>In 48-hour period before and on each trial day, you will be asked to:</u>

- Record all the food you eat and beverages you drink during.
- Follow a diet low in certain fruits, certain vegetables, and certain beverages.

<u>During each trial, we will ask you to:</u>

- Have your blood drawn seven times (six times via an intravenous catheter on the trial day and one time via a venipuncture the day after the trial) on four separate occasions.
- Provide a urine sample seven times on four separation occasions.
- Eat a food item, or drink a beverage, that may or may not contain tart cherry on four separate occasions (the order of food assignment is randomly generated by the staff).

No genetic test will be performed on your stool, blood and urine samples and you do not have to answer any questions you do not want to answer. Your samples will not be used for commercial profit.

Baseline Questionnaire. We will ask you to fill out a questionnaire that asks you questions about your background (for example, your age, ethnic background, and prior education). This questionnaire takes ~5 minutes to complete. If at any time you are uncomfortable answering a specific question, you may skip that item and move on to the next.

Height and Weight. We will measure your height once at the beginning of the study and we will measure your weight on the morning of each trial (five times in total).

Stool sample collection. We will ask you to provide a stool sample during the baseline testing. We will provide you with materials (for example, disposable fecal catcher, gloves, sealable bag) to safely collect and transport your sample. We will ask you to store the sample at room temperature until delivering to study staff (as soon as possible, within 4 hours). If you do not provide a sample on the scheduled day, the collection period may be extended until you are able to provide a sample.

Pre-Trial Study Diet & Food Diary. In the 48 hours before each test session and on the day of each test session, we will ask you to follow a diet low in certain fruits, certain vegetables, and certain beverages (including tea and coffee). You will be asked to write down all the foods and beverages that you eat or drink. We will teach you how to do this, both by talking to you and giving you written instructions. You should record intake at the time the food or beverage is consumed and avoid waiting till at the end of the day. We will review these records with you on the morning of test site visits. If you do not follow the study diet, we will postpone your testing, if your schedule allows and if you still want to participate in the study. We will provide a list of food to avoid.

Study Trials. Each study trials composed of a trial day and a follow up day. We will ask you to avoid tobacco products and vigorous exercise 24 hours before each visit and arrive to the testing site after a 12-hour fast (no food or drink except water).

Within approximately 30 minutes of arriving to the testing facility for the trial, we will ask you to consume a food or beverage that may or may not contain tart cherry. All food items have passed food safety tests. You will not be allowed to consume any other food or drink (besides water, which we will provide) until the test session is complete (about six hours after you eat the snack items). We will provide you with lunch before you leave the testing site. You may eat and drink whatever you choose when you leave the testing site. You will return the next morning for the follow up sample collections.

Blood draws.
We will place a hollow needle/plastic tube (catheter) in your arm for taking blood samples. This catheter will be left in for about six hours and blood will be drawn six times. Sterile salt water is used to maintain the catheter opening while it's in your arm. If there is difficulty inserting the catheter, we may try again on another vein. If the tubing becomes clogged, making it impossible to get more blood from the vein, we may ask you if it is okay to start another catheter or if it is okay to take a one-time blood sample from an arm vein with a regular needle.

The morning after each day-long test session, we will take a blood sample from a vein in your arm. This is the standard type of blood draw you have likely experienced at a doctor's office.

There are 7 blood samples for each of the 4 trials, including the 6 blood samples from the catheter (the day of the trial) and the 1 blood sample (the day after the trial). This amounts to 81 ml (or about 5.5 tablespoons) of blood for each trial. In total, there are total 28 blood samples in this study (324 mL or about 22 tablespoons of blood).

Urine Collection: We will ask you to collect your urine at the timepoints below during each of the 4 trials. We will provide you with containers and private bathroom to do this. We will encourage you to drink water during to maintain hydration and encourage urine production. If you are unable to provide a sample, you will be provided another opportunity within 10 minutes of the sampling timepoint. If you are still unable to provide a sample, that time point will be skipped.

Timing of blood and urine collection

-30	-15	30-min	60-min	120-min	240-min	360-min*	24-hr
Review food records	▪Placement of IV catheter ▪Baseline blood sampling ▪Ingestion of food item	Blood Samping and urine collection					

**Lunch meal will be served after the 360 min blood draw.*

HOW LONG WILL I BE IN THE STUDY?

There will be one baseline testing day and four trials (each has two days) separated by at least 5 days. You can expect to be in the study for a minimum of 25 days.

WHAT PRECAUTIONS DO I NEED TO TAKE?

- You must not donate blood within 8 weeks of beginning the study.

- You must adhere to the study diet for two days prior to each trial and on the day of each trial.

- You must not eat or drink anything besides food or water in the 12 hours prior to each trial.

- You must not use tobacco products within 24 hours prior to each trial.

- You must not vigorously exercise within 24 hours prior to each trial. An easy way to tell if your exercise is “vigorous" is if you can’t say more than a few words without gasping for breath.

- You must not consume any food or beverages (besides water and the experimental foods/beverage) during each trial.

You should not participate in this study if any of the following applies to you:

- Unable to understand verbal or written instructions or testing materials in English.
- You are under the age of 18 (or 17 for military personnel) or over the age of 39.
- Have a bleeding disorder (e.g., von Willebrand Disease, hemophilia) or are being treated with medication that will impair blood clotting.
- History of GI-related conditions that may impact nutrient absorption (e.g., Crohn’s disease, ulcerative colitis, Celiac’s disease or gluten sensitivity, bariatric surgery or gastroparesis, short bowel, inflammatory bowel disease, etc.
- Have taken antibiotics or antimycotics, except topical antibiotics/antimycotics, in the past 3 months.
- Had a colonoscopy within the past 3 months.
- Regularly (i.e., weekly or more frequent) take over-the-counter medications (including antacids, laxatives, stool softeners, and anti-diarrheal) or nonsteroidal anti-inflammatory drugs (e.g., Advil), aspirin, corticosteroids or immunosuppressants (e.g., Humira).
- Have donated blood within the past 8 weeks of the first test session.
- Have an allergy or aversion to any of the test foods (tart cherry, corn syrup, milk, whey protein isolate, fructose, sugar, black cherry flavor, mixed berry flavor, oats, rice crisps).

HOW MANY PEOPLE WILL BE IN THE STUDY?

We will enroll approximately 30 men and women in the study.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Source of Risk or Discomfort:	Risk or Discomfort:	How We Minimize Risk or Discomfort:
Venipuncture, Intravenous (IV) Catheter Placement and Blood Draws	When the needle goes into a vein, it hurts for a short time.	• You will tell study staff if you have ever fainted during a blood draw • Trained staff will wash their hands, wear gloves, apply rubbing alcohol to the area and use a sterilized

	There may be the minor discomfort of having the needle/plastic tube taped to your arm. Local discomfort, swelling or bruising at the site or feeling faint or dizzy is possible. Blood clot, nerve damage or infections are possible, but extremely rare.	needle to place your IV or draw blood. • Trained staff will watch closely for any signs of infection. • Only qualified researchers will perform blood draw
Diet Intervention	Bloating, gas, or other GI discomfort is possible.	• Monitoring • You are not allowed to participate if allergic or sensitive to the study foods

WHAT ARE THE POSSIBLE BENEFITS FROM BEING IN THIS RESEARCH?

You will receive no direct benefits from participating in this study. This study is not being done to improve your physical condition or health. The information we gather may help improve ration components.

WHAT IF UNEXPECTED INFORMATION IS LEARNED ABOUT MY HEALTH?

If any unexpected health information is found during your participation, the findings will be documented and provided to you. You will be encouraged to make an appointment with your primary care provider (or OMSO for military) to follow-up. No diagnoses will be made by study personnel; therefore, the findings will not be reported to health providers.

WILL RESEARCH RESULTS BE SHARED WITH ME?

Yes, we will be able to share study findings once publications are available.

WHAT ARE MY OTHER OPTIONS IF I DO NOT PARTICIPATE IN THIS STUDY?

The only alternative is not to participate in the study.

WILL I HAVE TO PAY FOR ANYTHING IF I TAKE PART IN THIS RESEARCH?

If you do not live on the Natick Soldier Systems Center, you will be responsible for paying for your transportation to and from the center. You will not be reimbursed for any travel costs or other costs related to participation in this research.

WILL I BE PAID TO TAKE PART IN THIS RESEARCH?

Participants will receive $25 for each successful blood draw, for a total of up to $700 ($25 x 7 blood draws per trial x 4 trials) for each participant for study participation. You will not be paid for the blood draw during the medical screening.

Federal Government Civilians not on duty, and other civilians, will additionally be compensated for their time (~$10 per hour) as follows: $40 for completing baseline testing, $80 for completing the pre-trial low-polyphenol diet ($20 per session) and $280 for trials (7 hours/trial x $10/hour x 4 trials).

Therefore, if you are an Active-Duty military or federal employee on duty, you will receive up to $700; if you are a civilian or Federal Employees not on duty, you will receive up to $1100 for this study. Payment will be processed within approximately two weeks of study completion, and you will receive payment within approximately ten weeks of study completion. If you do not complete the study, you will be compensated for the activities completed before withdrawing from study participation.

Your social security number (SSN) will be needed to process your payment, as required by law. This information will be carefully protected. Total payments of $600 or more within one calendar year will be reported by the Defense Finance and Accounting Service to the Internal Revenue Service (IRS). This may require you to claim the compensation that you receive for participation in this study as taxable income.

WHAT HAPPENS IF I AM INJURED AS A RESULT OF TAKING PART IN THIS RESEARCH?

If at any time you believe you have suffered an injury or illness as a result of participating in this research, please contact Tracey J. Smith at 508-654-2295 (USARIEM, 10 General Greene Ave, Natick, MA 01760; emergency contact 508-561-0585.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active-duty military, dependent of active-duty military, retiree), you are entitled to medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are entitled to care for your injury at DoD hospitals or clinics, but care for your injury may be limited to a given time period, and your insurance may be billed. It cannot be determined in advance which DoD hospital or clinic will provide care. If you obtain care for research-related injuries outside of a DoD hospital or clinic, you or your insurance will be responsible for medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided. No reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights. If you believe you have sustained a research-related injury, please contact the Principal Investigator (PI). If you have any questions, please contact the PI.

HOW WILL YOU PROTECT MY PRIVACY AND THE CONFIDENTIALITY OF RECORDS ABOUT ME?

To protect your privacy, all of your research-related records and biological samples will be labeled with an assigned research participant number that will not include your name or any forms of identifiable information. The link between your participant number and your research records in a locked cabinet or on a password-protected computer file. Your consent form, which includes your name, but does not include a research participant number, will be kept separate from the rest of your research-related records in a locked cabinet by the principal investigator the study coordinator. The principal Investigator, a designated Associate investigator and the study coordinator are the only people that have access. The master link will be destroyed upon study closure.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity to others. No photographs, video or audiotape will be recorded without a signed photo/audio release form. In the event that it is discovered that you have been inadvertently photographed or visually recorded without your permission, the materials will be immediately destroyed. Permission through the Audio Visual Image Release form will be confirmed before any photographs or other visual recordings are used.

Authorized representatives of the following groups may need to review your research and/or medical records as part of their responsibilities to protect research participants:

- U.S. Army Medical Research & Development Command Institutional Review Board
- U.S. Army Human Research Protections Office and other DOD offices charged with oversight of human Research
- USARIEM Office of Research Quality and Compliance (ORQC)
- USARIEM, Office of Medical Support and Oversight (OMSO)

Once information that personally identifies you is removed from your data or specimens, then your data or specimens may be used for future research studies or given to other researchers for future research studies without your permission to do so.

Complete confidentiality cannot be promised for military personnel because information bearing on your health may be required to be reported to appropriate medical or command authorities.

WHAT IF I DECIDE NOT TO PARTICIPATE IN THIS RESEARCH?

It is your choice whether you want to participate in this research. You can choose not to be in the study now without any penalty or loss of benefits to which you are entitled.

If you decide to participate, you can stop taking part in this research at any time without any penalty or loss of benefits to which you are entitled. Deciding not to participate now or withdrawing at a later time does not harm, or in any way affect, your future relationships with USARIEM. You can withdraw by notifying the PI verbally or by writing (electronic or paper/pencil).

If you do not complete the entire study, you will be compensated for the number of activities completed. Any data and samples collected from you up until the point of withdrawal will be retained for future analysis and stored with all other study data. You will be asked to return any study food and/or wrappers that you had been provided.

WHAT COULD END MY PARTICIPATION IN THE RESEARCH?

The investigator may withdraw you from participating in this research if:

- If you are unable to follow the study restrictions such as study diets and exercise and not smoking before each trial.
- The researchers may have to withdraw you from the study if you become ill or injured during the research.

The investigator will make the decision and let you know if it is not possible for you to continue. Your taking part in the study may be stopped without your consent if it is determined by the investigator that remaining in the study might be dangerous or harmful to you.

WHAT IF ANY NEW INFORMATION IS FOUND OUT?

During the course of the research, the investigators will tell you of any new findings that might cause you to change your mind about continuing in the study. If you receive any new information, the investigators will obtain your consent to continue participating in this study.

WHO SHOULD I CALL IF I HAVE QUESTIONS OR CONCERNS ABOUT THIS RESEARCH?

If you have questions about the research at any time, you should contact Principal Investigator, Dr. Tracey Smith: 508-654-2295

If you have questions regarding your rights as a research participant, you may contact the HQ USAMRDC IRB Office at 301-619-2165 or by email to usarmy.detrick.medcom-usamrmc.other.irb-office@health.mil. Alternatively, you can also contact the USARIEM Office of Research Quality and Compliance at 508-206-2371 or by email to usarmy.natick.medcom-usariem.mbx.usariem-rqc-protocol@health.mil.

By signing below, I agree that I have been provided time to read the information describing the research study in this consent form. The content and meaning of this information have been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research participant.

SIGNATURE OF RESEARCH PARTICIPANT

____
Printed Name of Participant

____ _______________
Signature of Participant Date

SIGNATURE OF WITNESS

____
Printed Name of Witness

____ _______________
Signature of Witness Date