

The U.S. Army Research Institute of Environmental Medicine (USARIEM)

**CONSENT TO PARTICIPATE IN RESEARCH**

**Title of Protocol:** Effects of Pioglitazone on Exogenous Carbohydrate Oxidation and Physical Performance during Steady-State Exercise at High Altitude

**Principal Investigator:** Dr. Lee M. Margolis, PhD

**Introduction:** You are being asked to participate in a research study because you are a male between 18-39 years old, healthy, routinely participate in physical activity (i.e., running, cycling, body weight workouts, resistance training) at least two times per week and are representative of active duty male Soldiers.

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.

<b>RESEARCH SUMMARY</b>	
<b>Informed Consent</b>	<p>It is important that you understand this research study so that you can make an informed decision. This process is called informed consent.</p> <ul style="list-style-type: none"><li>• Please ask questions about anything you do not understand.</li><li>• Feel free to talk with your family, friends, or others before you decide.</li><li>• After your questions have been answered, you will be asked if you want to participate. If you agree, you will sign this consent form.</li><li>• You will be given a copy of this form to keep.</li></ul>
<b>Voluntary Participation</b>	You do not have to take part in this research. It is your decision. You can also choose to stop participating at any time during the study.
<b>Purpose</b>	This study will help us determine if a medication, Pioglitazone (PIO), which is used to improve blood sugar in patients with diabetes, will improve how your body uses sugar as a fuel source when you exercise at high altitude (HA) compared to when you exercise at HA when taking a placebo (sugar pill). Additionally, it will evaluate PIOs effect on the body's inflammatory response and iron status.
<b>Duration</b>	You will be in this study for 24 days total, but may be longer based on your schedule.

<b>Procedures</b>	<p>While you are in the study, you will be asked to do the following:</p> <ul style="list-style-type: none"><li>Let us measure your height, body weight and composition</li><li>Complete 8 exercise sessions:<ul style="list-style-type: none"><li>2 aerobic fitness assessments (1 at sea level (SL) and 1 at HA)</li><li>2 practice sessions during the baseline phase (1 on the stationary bike, and 1 on the treadmill; both at SL)</li><li>2 exercise sessions on a stationary bike (1 per each 5-day trial period; both at SL)</li><li>2 exercise sessions on a treadmill at HA (1 per each 5-day trial period)</li></ul></li><li>Take a pill by mouth while under supervision of the Office of Medical Support and Oversight (OMSO) 10 times (1 dose each day for both 5-day trial periods)</li><li>Ascend to HA (4300 m, approximately 14,000 feet) in an altitude chamber for about 7 h twice (1 per each 5-day trial period)</li><li>Eat <b>only</b> food and drinks (except water) that we give you throughout each 5-day trial phase of the study</li><li>Complete <b>IV infusions, blood draws</b> (18 total; 9 per each testing day), breath collections (24 total; 12 per each testing day), and exercise</li></ul>
<b>Study Restrictions</b>	<ul style="list-style-type: none"><li>During the controlled feeding and 5-day trial periods (2 trial periods; 10 days total):<ul style="list-style-type: none"><li>You <b>will not</b> be allowed to smoke, use nicotine-containing products, or drink alcohol</li><li>You <b>will not</b> be allowed to consume any non-study foods or beverages (other than water)<ul style="list-style-type: none"><li>Caffeine will be restricted to one calorie-free caffeinated beverage per day (must be provided by study staff) and may not be consumed prior to participating in bike or treadmill exercise sessions and/or during any fasting requirements</li></ul></li><li>You <b>will not</b> be allowed to participate in non-study exercise or physical activities (i.e., rec sports, personal work outs, army PT work outs)</li></ul></li></ul>

<b>Risks</b>	<p>The <b>main</b> risks from being in this study are:</p> <ul style="list-style-type: none"><li>• Minor discomfort and / or fainting associated with:<ul style="list-style-type: none"><li>◦ Intravenous (IV) catheter placement &amp; blood draws</li><li>◦ Exercise</li></ul></li><li>• Chance of infection associated with:<ul style="list-style-type: none"><li>◦ IV catheter placement &amp; blood draws</li></ul></li><li>• Potential side effects from PIO<ul style="list-style-type: none"><li>◦ Cold-like symptoms</li><li>◦ Headache</li><li>◦ Sinus infection</li><li>◦ Muscle pain</li><li>◦ Sore throat</li><li>◦ Rare but possible: low blood sugar, excess fluid retention, weight gain</li></ul></li><li>• Potential side effects from HA exposure<ul style="list-style-type: none"><li>◦ Low blood-oxygen level</li><li>◦ Lightheadedness</li><li>◦ Acute Mountain Sickness (AMS) which can present as one or more of the following symptoms:<ul style="list-style-type: none"><li>▪ Headache, nausea, loss of appetite, lethargy, dizziness, tiredness, weakness, insomnia, vomiting</li></ul></li><li>◦ Ear pain/discomfort</li><li>◦ Swelling of the legs, hands, and/or face</li><li>◦ High altitude cerebral edema (HACE) – swelling of the brain</li><li>◦ High altitude pulmonary edema (HAPE) – swelling of the lungs</li></ul></li></ul> <p>Steps to lessen the risks are described later in this consent form.</p>
<b>Benefits</b>	There is no direct health or other benefits related to participating in this study. Information gathered from this research may benefit other people in the future.
<b>Alternatives</b>	The only alternative is to not participate.
<b>Payment</b>	You will be paid for your participation in this study.
<b>Covid-19 Risk Mitigation</b>	If you agree to participate, you will be asked to follow all COVID-19 risk mitigation procedures in place at USARIEM during the time of data collection. You may be asked to wear facemasks and use hand sanitizer or wash your hands during data collection activities (in accord with prevailing recommendations at the time of data collection) and may be asked to wear gloves (i.e., nitrile gloves) during data collection. You also may be asked to undergo COVID-19 testing (via nose swab performed at USARIEM) prior to study activities.

## WHY IS THIS RESEARCH BEING DONE?

Service members who deploy and quickly ascend to areas of HA (mountainous regions) for military operations have declines in physical performance. Decreases in physical performance is, in part, the result of changes in how the body uses carbohydrate for fuel during exercise. As carbohydrate is an important fuel source to support physical performance, especially during HA exposure, finding a way for the body to better use consumed carbohydrate during exercise is important.

The purpose of this research study is to determine if PIO, a medication that is approved for use in managing blood sugar in patients with diabetes, improves how the body uses carbohydrate as an energy source for exercise at HA compared to exercising at HA when taking a placebo (sugar pill) in healthy individuals. The use of PIO in healthy individuals in this research effort is experimental.

## WHAT WILL HAPPEN DURING THIS RESEARCH?

If you agree to participate in this research, you will be a study volunteer for about 24 days (depending on your schedule). You will be asked to do the activities in the table below. This is an example schedule and the order you complete each task may vary.

Throughout the study, you will wear PT attire or appropriate athletic attire (t-shirt, athletic shorts, socks, and running shoes) and wear a heart rate monitor during exercises.

Study Phase	Duration/Activities
Pre-Testing Baseline Procedures	<p>Up to 14 Days</p> <ul style="list-style-type: none"><li>• Medical Screening (<i>once for entire study, 1 hour</i>)</li><li>• Height measurement (<i>1 time, 1 min</i>)</li><li>• Body weight measurement (<i>fasted, 1 min/measurement</i>)</li><li>• Body Composition: DEXA Scan (<i>fasted, approximately 10 min</i>)</li><li>• 2 VO<sub>2peak</sub> Aerobic Fitness Test (<i>fasted, 1 at SL, 1 at HA, approximately 45 min</i>)</li><li>• 2 practice exercise testing sessions (<i>fasted, 1 treadmill, 1 stationary bike, approximately 1-2 hours/session</i>)</li></ul>
Trial 1 (Controlled Feeding)	<p>5 Days</p> <ul style="list-style-type: none"><li>• Stationary Bike Exercise, medium to hard difficulty (<i>fasted, approximately 60 min</i>)</li><li>• PIO/placebo pill by mouth (<i>once per day, daily for 5 days, approximately 5 min</i>)</li><li>• Consume study diet for 4 days</li><li>• Follow all study restrictions</li><li>• Steady-state treadmill exercise at HA &amp; Carbohydrate Tracer Study (<i>fasted, approximately 7 hours total, 80 min treadmill exercise</i>)<ul style="list-style-type: none"><li>○ Blood sampling (<i>9 total, approximately 1 min/each</i>)</li><li>○ Breath sampling (<i>12 total, approximately 1 min/each</i>)</li><li>○ Drink carbohydrate (sugar) beverage while exercising on treadmill (<i>4 drinks, approximately 1 1/4 cup to 2 1/4 cup each</i>)</li></ul></li></ul>

Washout Period	Minimum 10 Days
	<ul style="list-style-type: none"><li>• No study restrictions</li></ul>
Trial 2 (Controlled Feeding)	<p>5 Days</p> <ul style="list-style-type: none"><li>• Stationary Bike Exercise, medium to hard difficulty (<i>fasted, approximately 60 min</i>)</li><li>• PIO/placebo medication by mouth (<i>once per day, daily for 5 days, approximately 5 min</i>)</li><li>• Consume study diet for 4 days</li><li>• Follow all study restrictions</li><li>• Steady-state treadmill exercise at HA &amp; Carbohydrate Tracer Study (<i>fasted, approximately 7 hours total, 80 min treadmill exercise</i>)<ul style="list-style-type: none"><li>◦ Blood sampling (<i>9 total, approximately 1 min/each</i>)</li><li>◦ Breath sampling (<i>12 total, approximately 1 min/each</i>)</li><li>◦ Drink carbohydrate (sugar) beverage while exercising on treadmill (<i>4 drinks, approximately 1 ¼ cup to 2 ¼ cup each</i>)</li></ul></li></ul>

### **Screening Procedures:**

After signing the consent form, if you still wish to be in the study, you will be asked to answer questions about your medical history and make an appointment for a medical screening visit.

*Medical Screening:* You will meet with the staff of the OMSO to undergo a general medical clearance. The one-hour medical screening visit will be done at USARIEM or at your respective unit's medical oversite location. The screening visit will include a blood draw. You will be told about any possible medical concerns found from the screening by the medical staff.

Health problems found during the screening process will be documented by the medical staff, and you will be provided a copy. You are encouraged to make an appointment with your doctor to follow up with a full evaluation of the identified health concerns. If you have any evidence of existing physical, mental and/or medical conditions that would make the proposed study more hazardous, you will be excluded.

### **Study Procedures:**

Body Composition: We will use dual energy x-ray absorptiometry (DEXA) scan to measure your total body, muscle, and fat mass twice during the study. For this, you will lie on your back and remain still for about 8-10 min while the x-ray scanner moves over your body. The DEXA will not cause pain or discomfort.

Height & Weight: A researcher will measure your height and weight at baseline. Additional weight measurements will be taken the day you exercise at HA. All weight measurements will be taken following an overnight fast while wearing a t-shirt and shorts. This will take approximately 5 min.

**VO<sub>2</sub>peak (Fitness Assessment):** You will perform this test on a treadmill after a 10 hr overnight fast to determine how well your body can use oxygen to produce energy. Following a warm-up you will begin running for 4-min at a comfortable pace, determined before testing starts, at a 0% grade. At 4-min, the grade will be increased to 4% followed by an additional 2% every 2 min thereafter until you cannot run anymore.

During the fitness assessment test you will wear a nose clip and breathe into a mouthpiece connected to a machine that measures the amount of oxygen you use and the amount of carbon dioxide you breathe out. You will also wear a strap around your chest to record your heart rate during the test. The procedure takes about 15 minutes. Two measurements will be conducted at the beginning of the study, one at SL and one at HA.

**PIO/placebo Medication by Mouth:** A pill containing 15 mg of Pioglitazone (PIO) or a placebo (sugar pill) will be taken in the morning by mouth daily for 5 days. OMSO will administer and observe you when you take the pill to ensure compliance. OMSO will conduct medical oversight throughout your participation in the study. This is a randomized, double-blind trial, so you will not know if you are taking PIO or placebo. The order in which you take PIO/placebo will be random. Study staff will also not know if you are taking PIO/placebo. The OMSO will be unblinded so they can provide the correct study treatment (PIO/placebo) and ensure appropriate medical oversight throughout the study.

**Study Diet:** During the protocol phase of the study, all food and drinks (except water) will be prepared and given to you by study dietitians and will be largely from military combat ration and supplemental food items (ex. Frozen prepared dinners, breakfast sandwiches, commercial granola bars, etc.). You will be asked to return all wrappers to study dietitians. You will eat this diet for 8 days total (first 4 days of each 5-day trial period). No other food or beverage products (except water) can be consumed during this time. You will be allowed one calorie-free caffeinated beverage per day if you choose, but it must be supplied by study staff and not consumed during fasting periods or prior to exercise. The different amounts of nutrients in this diet are similar to amounts military personnel within your age range normally eat, and will be individualized by study dietitians to maintain body weight.

**Glycogen Normalization:** To make sure the only difference between testing periods is the PIO+HA or placebo+HA, we control your exercise and diet during each trial period. Specifically, following an overnight (10 hour) fast, you will complete a bout of exercise on a stationary bike to reduce the amount of carbohydrate stored in your body. To do so you will ride the stationary bike at different exercise intensities based on your fitness assessment. After warming-up for 5 min, we will increase the intensity to about  $80 \pm 5\%$  of your peak fitness level. You will pedal at this intensity for 2 min followed by a 2 min recovery period at about  $50 \pm 5\%$  of your peak fitness. You will complete this 2 min exercise to recovery interval 12 total times in about 50 min. If you cannot complete 2 min of pedaling at  $80 \pm 5\%$  of your peak fitness level, we will decrease the exercise intensity to make sure you can finish the cycling exercise. After the bike ride, we will refeed you a carbohydrate-rich diet for 4 days to ensure carbohydrate storage is similar between testing periods. You will do one practice bout during the baseline phase to become familiar with the exercise.

**High Altitude Exposure:** On testing days you will ascend to HA (4,300 m, approximately 14,000 feet) in a simulated altitude chamber for approximately 7 hours. The first 5 hours in the altitude chamber will be used to ensure that you exercise in a state of lower oxygen levels. After these 5 hours, you will begin steady-state exercise on a treadmill (80 min) and will descend back down to SL shortly after that. You will always be in the presence of study staff members when in the

altitude chamber. Additional staff will be on the outside of the chamber for close monitoring and communication with those in the chamber.

**Steady-State Exercise:** On testing days you will ascend to HA in a simulated altitude chamber to complete 80-min of exercise on a treadmill at a medium intensity ( $55 \pm 5\%$  of your peak fitness level at HA). During exercise, you will breathe into a mouthpiece connected to a machine to collect breath samples. Periodic blood and breath samples will be collected to allow us to measure how your body uses carbohydrate for fuel during exercise. This test will happen twice during the study. You will practice this exercise once during the baseline phase to become familiar with it.

**Carbohydrate Tracer Studies:** This test will happen twice during the study and will last for approximately three and a half hours. Both tests will be conducted during the steady-state treadmill exercise at HA. Testing will start after a 10-h overnight fast. These studies will tell us how well your body uses carbohydrate as fuel during exercise with PIO+HA and placebo+HA.

During exercise, you will consume a beverage containing 145 g (approximately  $11 \frac{1}{2}$  Tbsp) of sugar that will be divided into four separate beverages. The first beverage will be approximately 2.5 cups and consumed at the start of exercise. The next three beverages will be approximately  $1 \frac{1}{4}$  cup and consumed during exercise at 20, 40, and 60 min. To measure how your body uses carbohydrate (sugar) we will inject a carbohydrate tracer into your bloodstream by an intravenous (IV) catheter placed in your arm. A second catheter will be placed in your other arm to collect blood samples. Blood sampling will occur eight times throughout the duration of this test. The tracers are a carbohydrate that is labeled with a stable non-radioactive isotope. These isotopes are naturally occurring in your body and are considered safe.

**Blood Sampling:** Blood samples will occur after an overnight (10 hr) fast. Blood will be collected using a catheter during the carbohydrate tracer studies. A catheter is similar to a regular blood draw, only a soft, flexible plastic tube will remain in your arm and the needle will be retracted to reduce pain and allow you to move your arm. Once in your arm, study staff are able to take blood draws without having to restick you with a needle every time. For the two testing periods of the study a total of 18 blood draws (9 per trial period) will be taken. IV catheters will be placed upon arrival to the altitude chamber to complete testing, and removed after your final blood draw one hour after exercise is completed. Total amount of blood taken during the study will be roughly 340 ml or approximately  $1 \frac{1}{2}$  cup.

**Breath Sampling:** At various times during the steady-state treadmill exercise, you will wear a mouth piece and a nose clip connected to a machine that measures the amount of oxygen you use and the amount of carbon dioxide you breathe out. These breathe collections will be 5 minutes each and will occur at the 5, 20, 40, 50, 60, and 75 minute mark. You will also breath into single use breath collection bags. These collections take approximately 10 seconds each and will occur at the approximately -300, 0, 20, 40, 45, 50, 55, 60, 65, 70, 75, and 80 min mark.

## **HOW LONG WILL I BE IN THE STUDY?**

The study will last a minimum of 24 days, but may last longer based on your availability. Study procedures will last between five minutes to seven hours per visit.

**COVID-19 related events and study duration:** In the event that research processes must be halted in response to a potential or confirmed COVID-19 exposure or case involving study

participants or staff members, the study duration may be extended to accommodate the halt by repeating baseline measures, trial 1, or trial 2.

## WHAT PRECAUTIONS DO I NEED TO TAKE?

You must not drink alcohol, smoke (including e-cigarettes), vape, chew tobacco and/or use any nicotine containing products, or take dietary supplements during the controlled feeding and testing periods of the study.

You must adhere to study physical restrictions. You will be asked not to participate in outside/personal exercise or recreational activities (i.e., pick-up basketball) during the baseline period and each trial period.

You must only eat the foods and drink the beverages provided to you, except water, during the controlled feeding period.

You are advised to refrain from whole body blood donations for 8 weeks following your final day of study participation.

## HOW MANY PEOPLE WILL BE IN THE STUDY?

A total of 8 participants are needed to complete this study. We will enroll 24 individuals to account for dropouts. All screening will stop once complete data has been collected on 8 participants. Though you may be eligible and want to participate, if we are able to finish data collection on 8 participants before you are scheduled to begin testing, your participation in the study may be terminated.

## WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Source of Risk or Discomfort:	Risk or Discomfort:	How We Minimize Risk or Discomfort:
PIO Medication	<p>Most common risks include: cold-like symptoms, headache, sinus infection, muscle pain, sore throat</p> <p>Rare but possible side effects include: low blood sugar, excess fluid retention, weight gain</p> <p>Unlikely side effects: bladder cancer</p>	<ul style="list-style-type: none"><li>• A low-dose (starting dose) of 15 mg will be administered</li><li>• PIO will only be administered for short-term use (5 days), which is far less time associated with development of side effects, particularly rare side effects need years to develop</li><li>• No other medications that can lower blood sugar will be provided and if you are already take a medication to improve blood sugar will be excluded from participating</li><li>• Diet and exercise will be controlled while taking the medication</li><li>• You will be recruited to participate in the study if you are healthy and have no known health problems that could increase the risk of side effects</li></ul>
HA exposure	Lightheadedness increasing risk of fall	<ul style="list-style-type: none"><li>• Risk of fall from lightheadedness will be reduced by having at least one staff member near you during exercise</li></ul>

		<ul style="list-style-type: none"> <li>If you become lightheaded while exercising you will be assisted off the treadmill and instructed to lay down with feet up until you feel better</li> </ul>
	<p>Low blood oxygen levels without side effects or present a range of risks from mild discomfort, to potentially lethal (very rare) conditions</p>	<ul style="list-style-type: none"> <li>Probability of experiencing symptoms and severity of symptoms vary greatly among different people</li> <li>You will be monitored by study staff the whole time you are in the altitude chamber</li> <li>If you become uncomfortable at any time or a staff member feels you have become too ill to participate you may exit the altitude chamber</li> <li>Individuals taking medications that interfere with oxygen delivery and transport will be excluded from participating in this research study</li> </ul>
	<p>Acute Mountain sickness (AMS)</p> <p>Symptoms of AMS include: headache, nausea, anorexia, lethargy, dizziness, tiredness, weakness, insomnia, and vomiting</p>	<ul style="list-style-type: none"> <li>AMS is common when unacclimatized lowlanders are exposed to altitude with symptoms usually appearing within 4-6 hours. Symptoms reach severity between 18-24 hours of exposure. Due to the duration (approximately 7 h) of altitude exposure in the study, AMS may occur but should not reach its most severe symptoms</li> <li>You will be monitored by study staff the whole time you are in the altitude chamber</li> <li>If you become uncomfortable at any time or a staff member feels you have become too ill to participate you may exit the altitude chamber</li> </ul>
	<p>Unlikely side effects: High Altitude Pulmonary Edema (HAPE; swelling of the lungs) &amp; High Altitude Cerebral Edema (HACE; swelling of the brain)</p>	<ul style="list-style-type: none"> <li>Incidence of HAPE in unacclimatized lowlanders exposed to HA for at least a few days is less than 1%, and the incidence of HACE is even lower</li> <li>If either or both are recognized early and treated by descent, they are completely reversible</li> <li>Risk of developing HAPE/HACE in this study is extremely low. But if you do show symptoms you will be removed from the altitude chamber</li> <li>Individuals with prior diagnosis of HAPE/HACE will be excluded from participating in this research study</li> </ul>
	<p>Ear pain/discomfort</p>	<ul style="list-style-type: none"> <li>Ear pain/discomfort may occur due to changes in air gas pressure while going to or returning from altitude as gas can get trapped in the body</li> <li>Swallowing, yawning, or tensing your throat may help reduce this discomfort, as well as forced exhale against a closed nose and mouth can help with pain</li> <li>Descent may be stopped and the chamber pressure may change until the pain goes away; descent will then be restarted at a slower rate</li> <li>Damage to eardrums is likely only under the unusual situation where deliberately rapid descent is needed due to an emergency</li> </ul>

	Swelling of the legs, hands, and/or face	<ul style="list-style-type: none"> <li>Though uncomfortable, these conditions are not a risk and will resolve with descent</li> </ul>
Intravenous (IV) Catheter Placement and Blood Draws	Less likely risks include: feeling faint, irritation, bruising, swelling, infection, or allergic reaction	<ul style="list-style-type: none"> <li>You will tell study staff if you have ever fainted during a blood draw</li> <li>Trained staff will wash their hands, wear gloves, apply rubbing alcohol to the area and use a sterilized needle to place your IV.</li> <li>Trained staff will watch closely for any signs of infection.</li> <li>You should not donate blood for eight weeks before or after this study</li> </ul>
Carbohydrate Tracer Study	No risk or side effects w/ administration of stable isotopes to humans  Unlikely risk with infusion: volume overload, infection, and allergic reaction	<ul style="list-style-type: none"> <li>Qualified pharmacists will prepare the injected tracers at Johnson Pharmacy</li> <li>Infusions will be provided in small amounts to monitor the infusion</li> </ul>
Fitness Assessment, Steady-State Treadmill Exercise and Stationary Bike Exercise	Lightheadedness, Fatigue, Cardiovascular Risk, Musculoskeletal Strains or Soreness  You may feel discomfort and fatigue in your muscles during and shortly after exercise.  Mild to severe muscle soreness may continue for one to seven days.	<ul style="list-style-type: none"> <li>Safety Spotters and CPR-certified Staff</li> <li>You are healthy and fit and will be excluded if not.</li> </ul>
Body Composition	Radiation, risk to fetus.	<ul style="list-style-type: none"> <li>Low dose of radiation, a DEXA scan is about the same amount of radiation received in a chest X-ray</li> </ul>

## WHAT ARE THE POSSIBLE BENEFITS FROM BEING IN THIS RESEARCH?

There is no direct health or other benefits related to participating in this study. Information gathered from this research may benefit other people in the future.

## WHAT IF UNEXPECTED INFORMATION IS LEARNED ABOUT MY HEALTH?

Any incidental or unexpected health findings identified by OMSO during the screening process or throughout the research process will be documented and disclosed to you. You will be encouraged to make an appointment with your primary care physician.

## WILL RESEARCH RESULTS BE SHARED WITH ME?

Yes, we will be able to share results of your body composition, VO<sub>2</sub>peak tests, and baseline dietary intake if requested once you have completed all study procedures. No other information will be shared.

### **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.

If you are an active duty Soldier coming to Natick to participate in research on temporary duty station (TDY) permissions, your transportation and lodging will be paid for by the study and compensation for meals will be provided at the local per diem rate for days you are not following the controlled study diet.

### **WILL I BE PAID TO TAKE PART IN THIS RESEARCH?**

You will receive \$50 for each successful study blood draw. There are 18 blood draws during the entire study. This does not include the blood sample taken during your study screening/medical clearance, which you will not be compensated for. If you complete all 18 study draws, you will receive \$900. If you do not complete the entire study, you will receive money for every successful blood draw you do complete. If a blood draw fails, but you complete the study, you will be paid in full. You will not be eligible for any other form of compensation during this study.

Your Social Security Number (SSN) will be needed to process your payment, as required by law. This information will be carefully protected. Study payments will be provided by direct deposit. Payments will be processed when you conclude the study (end of study period or voluntary withdrawal), as a total lump-sum payment. The Defense Finance and Accounting Service will report total payments of \$600 or more within 12 months to the Internal Revenue Service

(IRS). This may require you to claim the compensation that you receive for participating 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:

Lee M. Margolis, PhD  
U.S. Army Research Institute of Environmental Medicine  
Building 42, Room 203A  
10 General Greene Ave  
Natick, MA 01760  
Phone Number: 508-206-2335  
Email: [lee.m.margolis.civ@health.mil](mailto:lee.m.margolis.civ@health.mil)

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.

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 (Lee Margolis and 508-206-2335).

### **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 Social Security Number. The link between your participant number and your research records will be kept in a locked cabinet or on a password-protected computer file and Dr. Lee Margolis and the study coordinator are the only people who have access. The master link will be destroyed upon study closure.

Your de-identified biological samples will be stored in a designated laboratory freezer and will either remain at USARIEM until analysis or will be shipped to another laboratory (Metabolic Solutions) for later analysis. There will be no serum or plasma remaining from samples we send to Metabolic Solutions. A portion of some or all of the biological samples you provide during this study will be frozen, de-identified and retained at USARIEM indefinitely, for either re-analysis under this research effort or under other approved, future research plans. 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 or future consent to do so. If you do not wish your samples to be retained for future use by any organization that is not listed, you should not participate in this study. De-identified electronic data records will be maintained for a period of at least ten years after the study has been completed.

When the results of the research are published, no information will be included that would reveal your identity to others. Specific permission to use photographs or video recordings of you and the manner in which they may be used will be requested and documented in an Audio/Visual Image Release form. If you do not sign the photo release form, no photos of you will be taken.

If any photographs or video recordings are taken of you inadvertently, they will be destroyed immediately. You do not have to sign a photo release to participate in this study

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:

- US Army Medical Research & Development Command Institutional Review Board responsible for review and oversight of human research
- DoD and other Federal offices charged with regulatory oversight of human research
- USARIEM Office of Research Quality and Compliance (ORQC)

- The Food and Drug Administration (FDA)

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

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 results. You can search this Web site at any time.

## **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 or 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. At the time of study withdrawal, you can voluntarily disclose to the PI your reason for withdrawing from study participation, however this is not required. If you do not complete the entire study, you will be compensated for the number of successful blood draws you did complete. Withdrawal from the study will result in you being sent back to respected unit/duty station if you are non-HRV military at or around the time of withdrawal. If you choose to withdraw when in the altitude chamber, you will descend to SL and be allowed to leave the altitude chamber.

## **WHAT COULD END MY PARTICIPATION IN THE RESEARCH?**

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

- You are not willing to follow study diets and exercise prescriptions
- You become ill or injured, or to protect your health and safety

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.

If you are withdrawn or decide to withdraw during the study, no further data will be collected from you. You will be asked to return any study food and/or wrappers that you had been provided. The data that has been collected from you up to that point may still be used for analysis.

## **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 new information is provided to you, 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 Lee M. Margolis, PhD (the Principal investigator); Office phone: 508-206-2335; Email: [lee.m.margolis.civ@health.mil](mailto:lee.m.margolis.civ@health.mil)

If you have questions regarding your rights as a research participant, you may contact the HQ USAMRDC IRB Office at 301-619-6240 or by email to [usarmy.detrick.medcom-usamrmc.other.irb-office@mail.mil](mailto:usarmy.detrick.medcom-usamrmc.other.irb-office@mail.mil) or USARIEM ORQC at phone (508-206-2371) or by email at [usarmy.natick.medcom-usariem.mbx.usariem-rqc@health.mil](mailto:usarmy.natick.medcom-usariem.mbx.usariem-rqc@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 has 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

Appendix A: Study Timeline

Study Day	Baseline					Trial 1					Washout	Trial 2					
	SV	1	2	3	4	5	6	7	8	9		10-19	20	21	22	23	24
Medical Screening	X																
Body Composition		X															
Height		X															
Weight		X								X							X
VO <sub>2</sub> peak		X	X														
High Altitude Exposure			X							X							X
Practice Exercise				X	X												
Glycogen Normalization						X							X				
PIO/PLA						X	X	X	X	X			X	X	X	X	X
Study Diet						X	X	X	X				X	X	X	X	
Steady-State Exercise										X							X
Carbohydrate Tracer Study										X							X
Blood Sampling										X							X
Breath Sampling										X							X

Timeline may shift based on participant availability, weekend, and holiday schedules.