Date: 24 August 2022

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

CONSENT TO PARTICIPATE IN RESEARCH

Title of Protocol: Erythropoietin induced hematological adaptations to enhance physical performance

Principal Investigator: Dr. Lee M. Margolis, PhD

Introduction: You are being asked to participate in a research study because you are between 18-39 years old with a body mass index of less than 30, are healthy, have been weight stable (±5 lbs) for at least two months, routinely participate in aerobic and/or resistance exercise at least two times a week and are representative of active duty male and female Soldiers. You do not have to take part in this research. It is your choice.

The table below summarizes some **key** things 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 decision. You can also choose to stop participating at any time during the study.
Purpose	This study will allow us to understand if injections of erythropoietin (EPO), a hormone that makes red blood cells, improves physical performance during periods of high physical activity. This study will allow us to understand if EPO injection improves iron status and changes how your body uses carbohydrate, fat, and protein for energy during exercise.
Duration	You will be in this study for about 42 days, but may be longer based on your schedule.

Procedures	While you are in the study, you will be asked to do the following:
	• Let us measure your height, body weight and composition
	• Complete 29 exercise sessions: 10 exercise testing sessions (3 practice sessions during the baseline phase, 2 load carriage exercise tests, 5 time trials), 3 aerobic fitness assessments, and 16 sessions of prescribed study exercise
	• Eat **only** food and drinks (except water) that we give you throughout the duration of the study
	• Participate **only** in supervised exercise training (endurance and resistance) that we prescribe you throughout the protocol/injection phase of the study (4 weeks; 16 sessions)
	• Keep a 3-day food record and 3-day activity log at the beginning of the study
	• Complete 12 injections of EPO (3 injections per week for 4 weeks)
	• Complete 6 biopsies (3 biopsies per day for 2 days) of your thigh muscle, midway between your knee and hip, while under a local anesthetic (numbing medication)
	• Complete metabolism/exercise study during the testing periods which includes **IV infusions, blood draws** (26 total), breath collections (12 total), and exercise
	• Complete 4 carbon monoxide (CO) rebreathing measures
	• Participate in medical monitoring
	  ○ During EPO injection phase of the study:
	  ▪ Vital signs and health questionnaire prior to each scheduled exercise session
	  ▪ Weekly safety blood draws (4 total)
	  ○ After final EPO injection (2 week follow up):
	  ▪ Weekly safety blood draws (2 total), daily health questionnaire and daily vital signs
	• **Avoid all non-study exercise, non-study foods, smoking, use of nicotine-containing products, drinking alcohol throughout the duration of the study, and refrain from taking any NSAIDS (i.e. aspirin, Advil®, Aleve®, Naprosyn®, or another other aspirin containing product) 10 days before and at least 5 days after each muscle biopsy.**

Risks	The **main** risks from being in this study are:
	• Minor discomfort and / or fainting associated with:
	  ○ Intravenous (IV) catheter placement & blood draws
	  ○ Subcutaneous injection
	  ○ Muscle biopsies
	  ○ Exercise
	  ○ CO rebreathing (blood draw, finger stick)
	• Chance of infection associated with:
	  ○ IV catheter placement & blood draws
	  ○ Muscle biopsies
	  ○ Place of injection site
	  ○ CO rebreathing (blood draw, finger stick)
	• Potential side effects with EPO injection
	  ○ Redness and pain at site of injection
	  ○ Increased blood pressure
	  ○ Blood clots
	  ○ Joint pain
	  ○ Nausea
	  ○ Dizziness
	  ○ Headaches
	  ○ Trouble sleeping
	  ○ Weight loss
	• Chance of headache associated with CO rebreathing
	Steps to lessen the risks are described later in this consent form.

Benefits	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.
Alternatives	The only alternative is to not participate.
Payment	You will be paid for your participation in this study.

WHY IS THIS RESEARCH BEING DONE?

The purpose of this research study is to determine if injection of EPO, a hormone that makes red blood cells, works to maintain iron status and physical performance during periods of high physical activity.. This research study also aims to determine the influence of EPO on how your body uses carbohydrate, fat, and protein for energy during exercise. If successful, this work will lead to advances in biomedical strategies and solutions that safely and ethically enhance Warfighter physical performance in training and operational environments.

WHAT WILL HAPPEN DURING THIS RESEARCH?

If you agree to participate in this research, you will be a study volunteer for about 42 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.

If you agree to participate in this research, you will also 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 face masks and use hand sanitizer 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 activities.

Study Phase	Duration/Activities
Pre-Testing Baseline Procedures	Up to 14 Days
	• Medical Screening (once for entire study, 1 hour) • Diet and Activity Records (1 record per day for 3 days) • Height measurement (1 time, 2 min) • Body weight measurement (fasted, 2 min/measurement) • Body Composition: DEXA Scan (≈10 min) • Resting Metabolic Rate (fasted, ≈1 hour) • VO_{2peak} Aerobic Fitness Test (fasted, ≈45 min) • 3 practice exercise testing sessions (fasted, 2 time trials, 1 load carriage, ≈1-2 hours/session)
Baseline Physical Performance Testing and CO Rebreathing (Controlled Feeding)	4 Days

	• 5km Time Trial (fasted, ≈1 hour)
	• Load Carriage Exercise & Carbohydrate Tracer Study (fasted, ≈6 hours)
	  ○ Muscle Biopsies (3 total, ≈10 min/each)
	  ○ Blood Sampling (8 total, ≈1 min/each)
	• CO rebreathing measures (2 total, ≈30 min/each)
	  ○ Blood Sampling (2 total, ≈5 min/each)
	  ○ Finger Sticks (2 total, ≈1 min/each)
	• Consume study diet

Injection Phase (Controlled Feeding)	26 Days
	• EPO Injection (3 times/week for 4 weeks, ≈ 5 min each) ○ The EPO being used for this protocol will be PROCRIT® (Janssen Products, LP, Titusville, NJ, USA), a man-made form of human EPO • Safety blood draws (1 time/week, 4 total, ≈5 min/each) • Prescribed study exercise (4 times per week for 4 weeks) • Three 5km Time Trials (fasted, ≈1 hour/session) • Two VO_{2peak} Aerobic Fitness Tests (fasted, about 45 min) • Blood pressure measurement (prior to each exercise session) • Health questionnaire (prior to each exercise session) • Body Composition: DEXA Scan (≈10 min) • Resting Metabolic Rate (fasted, ≈1 hour) • Three body weight measurements (fasted, 2 min/measurement) • Consume study diet
Post Injection Physical Performance Testing (Controlled Feeding) and CO Rebreathing	4 Days
	• One safety blood draw (≈5 min/each) • 5km Time Trial (fasted, ≈1 hour) • Load Carriage Exercise & Carbohydrate Tracer Study (fasted, ≈6 hours) ○ Muscle Biopsies (3 total, ≈10 min/each)

	○ Blood Sampling (8 total, ≈1 min/each) • Weight measurement (fasted, 2 min/measurement) • Consume study diet • Two CO rebreathing measures on the two subsequent days following performance testing (2 total, ≈30 min/each) ○ Blood Sampling (2 total, ≈5 min/each) ○ Finger Sticks (2 total, ≈1 min/each)
Post Injection Follow Up	14 Days
	• Two safety blood draws (1 time/week for two weeks, ≈ 5 min/each) • Daily vital sign screening (≈2 min/each) • Daily health questionnaire (≈5 min/each)

.

Study Timeline
Table 1: Study Timeline (Appendix A)

Refer to the timeline located at the end of the packet.

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

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 Office of Medical Support and Oversight (OMSO) to undergo a general medical clearance. In addition, OMSO will screen you for problems with blood clotting. The one-hour medical screening visit will be done at USARIEM or at your respective unit's medical oversite location. 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. Female volunteers will be asked to give a urine sample to test if you are pregnant prior to body composition scans. A female staff member will oversee the urine pregnancy test.

Height & Weight: A researcher will measure your height and weight at baseline. Additional weight measurements will be taken once a week during the injection phase of the study. All weight measurements will be taken following an overnight fast while wearing a t-shirt and shorts. This will take ~ 5 min.

3-Day Diet and Exercise Records: Study dietitians will provide you with forms you will use to write down your eating and exercising habits for three days during baseline. They will show you how to fill out and review the forms. It should take one hour, at most, to complete them daily.

Erythropoietin Injections: A sterilized needle will be used to insert a moderate dose of EPO into the abdominal skin 3 times per week for 4 weeks, for a total of 12 injections. Each dose will be about ½ teaspoon. You may notice redness and slight pain at the site of the injection, especially right after insertion. We will cover the injection site with a small bandaid after each injection. EPO injections take ~ 5 min.

VO_2peak (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. Measurements will be conducted at the beginning, middle and end of the study.

Resting Metabolic Rate: Following a 10 hr overnight fast, we will measure your energy needs using open circuit indirect calorimetry. For this, you will lie on your back for approximately 30-min before measurement in a quiet and dim, temperature regulated room. A hood will be placed over your head to collect your breath. You will be instructed to minimize movement. You will remain in this position with the hood on for another 20-30 minutes while measurements are being recorded. Measurements will be conducted at the beginning and end of the study. The procedure lasts a total of ~ 1 hr. This procedure can trigger claustrophobia. Individuals who experience claustrophobia may not wish to participate in this 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. You will be asked to return all wrappers to study dietitians. You will eat this diet throughout the duration of the study. No other food or beverage products (except water) can be consumed during this time. 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.

Study Exercise: During the injection phase of the study, you will participate in a supervised exercise training program four days a week. You will perform both weighted (treadmill; walking, running, and load carriage), unweighted (stationary bike) endurance type exercise, and resistance-type exercise throughout the injection phase of the protocol. Exercise sessions will range from 30-90 minutes. Exercise sessions may be broken up into a few (2-3) smaller sessions.

Load Carriage Exercise: On these testing days you will complete 90-min of exercise on a treadmill carrying a load that is 30% of your body mass. During exercise, you will breathe into a mouthpiece connected to a machine to collect breath samples. Blood and breath samples will allow us to measure how your body burns carbohydrate, fat and protein 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 six hours. Both tests will be conducted during the load carriage exercise protocol. Testing will start after a 10-h overnight fast. These studies will tell us how well your body uses carbohydrate as fuel during exercise when receiving EPO/PLA injections.

To measure how your body uses carbohydrate 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.

Muscle Biopsies: You will be awake during the muscle biopsies. A trained researcher will clean the skin with a medical cleaning solution (includes alcohol) and numb a small area of your thigh with a lidocaine shot (the same shots used when removing wisdom teeth), or similar product. The researcher will make a small cut (less than ½ inch) in the skin and use a needle to remove a small piece of muscle (about the size of an un-popped popcorn kernel). The researcher may need to use more than one needle to get a full sample. You may feel minor discomfort during a muscle biopsy, including some pressure (like a muscle cramp) or tugging. It should not be painful. You may feel a burn or sting where you get the lidocaine (or similar) shot. After the lidocaine (or similar) wears off, your leg may feel sore for about a week. The cuts will be covered with steri strips (a type of sticky bandaid), sterile gauze pad, clear sterile dressing, and an elastic bandage. The elastic bandage should be kept in place for 5 hours after the biopsy and then removed. The Principal Investigator or OMSO will remove the sterile dressing and gauze pad the following morning. You will be provided instructions on how to care for the biopsy wounds. To ensure proper healing, OMSO will follow-up with you within 72 hours after finishing the muscle biopsies. Biopsies will be performed on load carriage exercise days, which occur twice through the study. Biopsies will be taken immediately before, after, and 3-hrs post exercise. A total of 6 biopsies will be taken during the study. You will not exercise for 3 days after the biopsy. Each biopsy will take ~10 minutes.

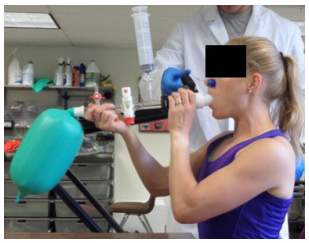
Blood Sampling: Blood samples will occur after an overnight (10 hr) fast. Blood will be collected using a catheter during the carbohydrate tracer studies or venipuncture for weekly safety blood draws and CO rebreathing. A finger stick will also be used to collect trace amounts of blood during CO rebreathing measures. A total of 26 (8 per carbohydrate tracer study days (16 total), 6 per safety checks, 4 per CO rebreathing measures) blood draws will be conducted. The total amount of blood taken during the study will be roughly 360 ml or 1 ½ cup. Blood collected on carbohydrate tracer study days will be about ~ ½ cup each and ~ ½ tsp per safety draw.

Breath Sampling: At various times during the load carriage exercise testing, you will wear a mouth piece and a nose clip, or a mask covering just your nose and mouth connected to a machine that measures the amount of oxygen you use and the amount of carbon dioxide you breathe out.

Time Trial: Following a 10-hr overnight fast, you will complete a self-paced 5km (~3 miles) time trail on a treadmill. The treadmill will be set at a constant 1% grade for the entire test. Following a warm-up period, you will blindly (you will not be able to see the display) set the speed of the treadmill in order to complete the distance as quickly as possible. You will be able to change the

speed as needed throughout the test. The only feedback you will be given will be distance covered every half mile. At each half mile, you will also be asked to rate how hard you're working based on a scale provided. You will also wear a strap around your chest to record your heart rate after every half mile. No motivation will be provided during the time trial. You may drink as much water as you want during the time trial. Following completion of the test, a self-selected cool-down will occur. You will perform this test five times throughout the protocol phase of the study. You will practice this exercise twice during the baseline phase to become familiar with it.

Carbon Monoxide Rebreathing: Carbon monoxide rebreathing measures the total amount of hemoglobin, a specific structure in your blood that carries oxygen. Before the rebreathing procedure, we will collect a small amount of blood from your arm vein and fingertip. Next, you will breathe into a portable CO detector. To begin the rebreathing procedure, you will place your mouth on a spirometer (breathing device), take in a deep, slow breath to be held for 10 seconds. While you are taking this breath, we will add a small amount of CO into the spirometer and open a valve allowing you to breathe oxygen from a small bag at the other end of the spirometer. You will continue to rebreathe the gases for another 1 minute and 50 seconds using your normal breathing pattern. After this time, you will breathe out as much air as you can, with the air collected into the small bag. After the rebreathing procedure, you will again breathe into the portable CO detector and we will collect blood from your fingertip. Female volunteers will be asked to give a urine sample to test if you are pregnant prior to each CO rebreathing measurement. A female staff member will oversee the urine pregnancy test.



HOW LONG WILL I BE IN THE STUDY?

The study will last a minimum of 42 days, but may last longer based on your availability. A two week follow up period will occur after completing the final injection. Study procedures will last between five minutes to six 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. In the event of a COVID-19 outbreak during the injection phase, participants will be dropped from the research study.

WHAT PRECAUTIONS DO I NEED TO TAKE?

You should not perform any additional exercise outside of what you have been told to do during the injection phase of the study (4 weeks). You should not consume any foods or beverages outside of those we provide you when you are on the study diet. You should not use any alcohol, dietary supplements, and nicotine while on the study diet. You should not participate in this study if you are pregnant or breastfeeding. You should not participate in this study if you have Anemia and/or Sickle Cell Anemia/Trait, or a history of blood clots. You should not participate in this study if you are taking oral contraceptives or hormone replacement therapy due to increased risk of blood clotting. You should not participate in this study if you have any allergies or intolerances to foods (including, but not limited to lactose intolerance/milk allergy) or medications (including, but not limited to, lidocaine or similar) or if you are a vegetarian or vegan.

HOW MANY PEOPLE WILL BE IN THE STUDY?

A total of 8 participants are needed to complete this study. We will enroll 60 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, you may not be tested.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Source of Risk or Discomfort:	Risk or Discomfort:	How We Minimize Risk or Discomfort:

EPO Injection	Redness and pain at the site of injection, increased blood pressure, blood clots, joint pain, nausea, dizziness, headaches, trouble sleeping, and weight loss.
	
	Rare but possible side effects include: heart attack and stroke
		• Moderate amount for your body weight will be used (pediatric dose)
		• Weekly safety blood draws to monitor red blood cells and minimize risk of blood clots
		  ○ If levels exceed study guidelines, EPO injections will be stopped.
		  ○ Levels will be checked again in 3 days. If values are normal you can return to regular study procedures.
		• Health questionnaire and vital signs (blood pressure, heart rate, oxygen saturation) conducted by study staff prior to exercise sessions. OMSO (licensed medics) will monitor and track copies of health records daily.
		• Continuation of vital signs (daily) and safety blood draws (1x/week) for two weeks following final injection

Muscle Biopsies	Rare risks included: feeling faint or fainting, pain, reddening of the skin, and bruising. Very rare risks include: infection, panic episode, bleeding, swelling, or long-term numbness. You may feel moderate stiffness and swelling around the cut after the biopsy.	• You will tell study staff if you have ever fainted during a blood draw • A qualified researcher will perform the biopsy under sterile conditions to prevent infection or pain and close the cut quickly to prevent scarring. • You will not take aspirin or other medications 10 days

	There might be minimal scarring as the cut heals and in rare cases permanent scars are possible.	before the first biopsy or 5 days after the last muscle biopsy, • You will receive biopsy care instructions and a qualified researcher will watch for any sign of infection, bleeding or bruising. • Any stiffness and/or swelling usually stops within days and does not interfere with walking and exercise.
Intravenous (IV) Catheter Placement and Blood Draws	Small risks include: feeling faint, irritation, bruising, swelling, infection, or allergic reaction	• 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 needle to place your IV. • Trained staff will watch closely for any signs of infection.
Lidocaine (or similar) Shot	Slight, brief pain and possible, rare side effects: You might feel a slight, brief pain when you get the lidocaine (or similar) shot. Rare, but possible side effects include: dizziness, confusion, shakiness, visual changes, nausea, unusually slow heartbeat and convulsions. Rare, but possible allergic reactions, include: swelling, itching, rash, and hives.	• You will be excluded if you have a known Lidocaine allergy. • Trained staff will watch closely for any signs of side effects or allergic reactions during the procedure. • If you have a bad reaction to lidocaine, medical staff will be called immediately.
Carbohydrate Tracer Study	No risk or side effects w/ administration of stable isotopes to humans Small risk with infusion: volume overload, infection, and allergic reaction	• Qualified pharmacists will prepare the injected tracers • Only qualified, credentialed study staff will administer the infusion • Infusions will be provided in small amounts to monitor the infusion
Fitness Assessment, Study Exercise, Load Carriage Exercise and Time Trial	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.	• Safety Spotters and CPR-certified Staff • You are healthy and fit and will be excluded if not.

Body Composition	Radiation, risk to fetus.	• Low dose of radiation, the 2 DEXA scans together equal the same amount of radiation received in a chest X-ray • Women who are pregnant or planning to become pregnant will be excluded from the study • Females will be pregnancy tested before
CO-rebreathing	Headache; see risks associated with blood draw	• Limit test to once a day • Built-in safe guards to prevent too much CO • Staff supervision

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 health problems identified during the screening process will be documented and a copy provided 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 and VO_2peak tests, if requested. 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.

WILL I BE PAID TO TAKE PART IN THIS RESEARCH?

You will receive $50 for each successful study blood draw. There are 26 blood draws during the entire study. This does not include the blood sample taken during your medical clearance, which you will not be compensated for. If you complete all 26 study draws, you will receive $1300. 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. 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

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 (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 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 or the study coordinator.

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 and retained at USARIEM indefinitely, for either re-analysis under this research effort or under approved, future research plans. 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.

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)

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.

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. If you do not complete the entire study, you will be compensated for the number of successful blood draws you did complete.

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

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 or USARIEM ORQC at phone (508-206-2371) or by email at 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

	Days																																							Weeks
	SV	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	≈ 2
Study Phase	<----Baseline Phase---->								<----Protocol Phase---->																															Post Injection Follow Up			
														<----Injection Period---->																												
Medical Screening	X																																										
Body Composition		X																																			X						
Height		X																																									
Weight		X																	X							X							X						X				
VO2peak		X																										X									X						
Resting Metabolic Rate		X																																			X						
3-d Exercise & Diet Record						X	X	X																																			
Practice Exercise			X	X	X																																						
Study Diet									X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Study Exercise															X	X	X	X				X	X	X	X				X	X	X	X				X	X	X	X					
Time Trial										X									X							X							X							X				
Load Carriage Exercise											X																													X				
Carbohydrate Tracer Study											X																													X				
Blood Sampling (IV Catheter)											X																													X				
Breath Sampling											X																													X				
Muscle Biopsy											X																													X				
CO Rebreathing												X	X																												X	X		
EPO Injection														X		X		X			X		X		X			X		X		X			X		X		X					
Blood Sampling (Sticks) hgb & Hct												X	X						X							X							X							X		X	X	X	X
Clinical Questionnaire															X	X	X	X	X			X	X	X	X	X	X		X	X	X	X	X			X	X	X	X	X	X	X	X	X	X
Vital Signs															X	X	X	X	X			X	X	X	X	X	X		X	X	X	X	X			X	X	X	X	X	X	X	X	X	X