V. 1-2019

#PBRC 2019-017 NCT04120363

CONSENT TO PARTICIPATE IN A RESEARCH STUDY FOR AN ADULT
INFORMED CONSENT - PART I

Title of Study: A randomized, double-blind, placebo controlled trial of testosterone undecanoate for optimizing physical and cognitive performance during military operations (OPS II)

Study Sponsor: Department of Defense

Key Information:

- **Why am I being asked to review this form?**
  - You are being asked to take part in a research study. This form is provided so that you may read and understand the reasons why you might or might not want to participate in the research. Your participation is voluntary.
- **What is the purpose, duration, and procedures of this study?**
  - The purpose of this research study is to determine the effects of maintaining normal levels of testosterone during simulated military stress (calorie and sleep restriction, and high physical activity levels) and recovery in healthy men
  - Your expected time in this study will be approximately 2 months after screening and consist of 4 parts:
    - Screening: 2 screening visits
    - Phase 1: 7 outpatient days
    - Phase 2: 20 days with 24 hour stays, and
    - Phase 3: 22 outpatient days
  - The procedures involved in this study include
    - Height, weight, blood pressure, pulse
    - Medical history, physical exam, and ECG
    - Blood collection, urine collection, and urine drug screen
    - Questionnaires and cognitive testing
    - Food and activity logs
    - Wearing of activity monitors on the wrist and waist
    - DXA, BIA, and circumference measurements (body composition measures)
    - In house and take home meals for 49 days
    - In-patient live-in period for 20 days
    - Aerobic fitness and exercise performance tests
    - Testosterone or placebo injection
    - Muscle sampling
    - Exercise intervention and calorie and sleep restriction
    - Protein balance assessments

- **What are the possible risks and discomforts?**
  - Infection and/or pain and bruising at the vein on your arm where the needle or IV is inserted.
  - Potential side effects of testosterone treatment include acne, oiliness of skin, increased growth of body hair, breast tenderness, a reversible increase in hemoglobin, sleep apnea, leg edema and weight gain.
  - Mild to severe pain, soreness, bruising, and a small scar are common risks related to muscle biopsies.
  - Mild pain, soreness, or bruising at the site for the placebo or testosterone injection
  - Redness or irritation at the site of ECG electrodes or activity device placements
  - Lethargy, listlessness, or irritability related to sleep and calorie restriction
  - Foot pain, joint pain, muscle fatigue, weakness, soreness and/or muscle pulls or tears related to the exercise tests and intervention.
  - A more comprehensive and detailed description of reasonably foreseeable risks to subjects are included later in Section 6 of the informed consent.
- **What are the possible benefits?**
  - We cannot promise any benefits from your being in the study. However, possible benefits include the following: You will receive health and medical screening examinations and the results will be discussed with you.
- **If you choose not to participate in the study, are there other choices?**
  - You have the choice at any time not to participate in this research study.
  - If you decide not to participate in this study, your other choices may include:
    - Increasing your physical activity on your own or through another program or study
    - Ask your health care professionals to complete medical evaluations

Detailed Information:

1- Who is doing the study?

Investigator Information:

Principal Investigator: Jennifer Rood, PhD
(225) 763-2524

Medical Investigator: Frank Greenway, MD
(225) 763-2578
24-hr. Emergency Phone Nos.:
(225) 763-2578 (Weekdays 7:00 a.m.-4:30 p.m.)
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Sub Investigators: Stefan Pasiakos, PhD
Lee Margolis, PhD
Alyssa Varanoske, PhD
Arny Ferrando, PhD

Dr. Jennifer Rood directs this study, which is under the medical supervision of Dr. Frank Greenway. We expect about 38 people from 1 site will be enrolled in this study. The study will take place over a period of 2 years. Your expected time in this study will be approximately 2months after screening. This study is a collaborative effort between Pennington Biomedical Research Center (PBRC) and the US Army Research Institute of Environmental Medicine (USARIEM), and funded by the US Army Medical Research and Materiel Command.

2- Where is the study being conducted?

This study takes place at the PBRC campus. A small muscle tissue sample, a urine sample, and a blood sample will be shipped to University of Arkansas for Medical Sciences (UAMS) and USARIEM, and other study collaborators for protein, muscle profiling, and other analysis.

3- What is the purpose of this study?

The goal of this study is to determine the effects of maintaining normal levels of testosterone during simulated military stress (calorie and sleep restriction, and high physical activity levels) and recovery in healthy men.

4- Who is eligible to participate in the study?

- Are a male 18-35 years old
- Are physically active
- Meet age-specific U.S. Army body composition standards according to Army Regulation 600-9, which includes estimates of body fat based on height, weight, and circumference measures (neck and waist)
- Have normal ranges for total testosterone concentration (300-1,000 ng/dL)
- Are willing to give informed consent, willing to be randomized to either testosterone or placebo, and willing to follow the protocol for the group to which you have been assigned
- Are willing to live on the PBRC inpatient unit for 20 consecutive days
- Are not taking any prescription medications and/or willing to refrain from all medication use prior to and throughout the entire study period, unless prescribed or approved by the study physician
- Are willing to refrain from alcohol, smoking, e-cigarettes, or use of any nicotine product, caffeine, and dietary supplement use throughout the entire study period
- Are willing to have your data, blood, urine and muscle samples stored for future use at PBRC, UAMS, USARIEM and with other study collaborators
- Are willing to have a urine drug screening test completed

You may not qualify for this study based on other eligibility criteria not listed. The study coordinator will go over this information in detail.

5- What will happen to you if you take part in the study?

This study will be divided into 4 parts: screening, phase 1, phase 2, and phase 3. If you successfully pass the screening eligibility requirements, you will then participate in phase 1. Phase 1 is a 7-day period of diet acclimation (adjustment). You will visit the center daily for meal pickups and additional testing on some of the days. After you complete phase 1, you will then begin phase 2. Phase 2 occurs from day 8 to day 27. During this period, you will live at the center and be on a calorie-restricted diet, participate in daily exercise sessions, receive a one-time injection of testosterone or placebo, and have tests performed throughout the period, ending on day 28, after completing 20 full days of simulated military stress. During this time you will lose body weight. After completing post-phase 2 measures on day 28, you will begin phase 3, which starts on day 29 and ends on day 48 (20 full days). During phase 3, you will return to the center daily for meal pick-ups and additional testing like you did in Phase 1. Final study measures will take place on day 50, after completing the 20 days of recovery. Your participation in the study is complete after testing is done on day 50.

Description of Study Visits:

The list below describes each visit and procedure that will be done during the course of the study. The tests and procedures will occur when you come to PBRC. The following tables show what will happen at each phase of the study and study visits:

Screening and Phase 1: Diet Acclimation (Adjustment)

	Screening		Phase 1 (Days)						
	SV1	SV2	1	2	3	4	5	6	7
Informed Consent	X								
Blood Pressure, Pulse	X	X							
Height	X								
Weight	X	X	X	X	X	X	X	X	X
Neck/Waist Circumference	X								
Medication Use	X	X							
ECG (Electrocardiogram)		X							
3 Day Food Record		X							
Medical History	X								
Physical Exam		X							
Blood Draw including Archives		X	X						
Total Body Water (TBW)									X
Urine Collection		X							X
Food and Activity Log	X	X	X	X	X	X	X	X	X
Questionnaires	X	X	X	X	X	X	X	X	X
Lifestyle Consultation		X							
Resting Metabolic Rate (RMR)		X							

	Screening		Phase 1 (Days)						
	SV1	SV2	1	2	3	4	5	6	7
Accelerometry	X	X	X	X	X	X	X	X	X
Body Composition									X
Cognitive Testing				X		X		X+	
Exercise Familiarizations*		X	X						
Aerobic Fitness Test ($V0_2$ Max Test)						X			
Exercise Performance Tests						X	X		
Adverse Event Assessment		X							X
In-House Meal & Pick-Up			X	X	X	X	X	X	X
Protein Balance Test with blood draws									X
Muscle Biopsy									X

+Cognitive testing includes electrical stimulation task. This test may be moved to another visit day within the same phase.
*Exercise Familiarizations may be moved to another visit day within the same phase.

Screening Visit 1. SV1: About 2-3 hours (non-fasting)
At this visit, the main study informed consent form will be explained to you by our study staff before any study procedures are performed. If you agree to participate and sign the consent, the following tests and procedures will be performed to determine if you qualify to participate in this research study:

- Height and weight
  - If you do not meet the height/weight criteria, a neck and waist circumference will also be measured to determine your eligibility
- Blood pressure and heart rate
- You will be asked questions about your:
  - Physical activity and risk factors
  - Medication and supplement use
  - Medical history, lifestyle, socioeconomic status, and other demographic questions
- Meet with study staff to discuss current eating habits and dietary requirements for each phase of the study
- An accelerometer (a small device to count your steps, body positions and activity for approximately 7 days which is worn on your waist) will be given to you with instructions for use. You will be asked to log your physical activity.
- Meet with study staff to review eligibility criteria

Screening Visit 2. SV2: 3.5-4.5 hours *(fasting visit: Please do not eat any food or drink anything but water for 12 hours before this appointment and no alcohol or exercise for 24 hours beforehand)*
You will need to return to the clinic approximately 7-10 days after your SV1. At this visit the following tests and procedures will be performed:

- Weight, blood pressure, pulse
- Physical exam

- ECG – graphical tracking of your heart's activity
- You will be asked questions about your:
  - Eating and physical activity habits
  - Medication use and adverse events update
  - Medical history
- Your blood will be drawn. We will collect approximately 2 tablespoons of blood from your vein in your arm
- Urine will be collected for a urinalysis and urine drug screening
- You will rest for a 30 minute period in a lying position. You will lie for 30-45 minutes with a clear plastic hood over your head and shoulders in order to measure your resting metabolic rate (RMR)
- You will be instructed on how to record your daily food and activity. You will be asked to complete a 3-day food record (2 weekdays, 1 weekend day) before returning to your next visit.
- An accelerometer will be given to you with instructions for use.
- You will be asked to wear a weighted pack and go on a practice hike.
- Meet with study staff to discuss your lifestyle and the study requirements
- Meet with study staff to review eligibility criteria

Once you have completed all of the screening procedures and your test results have been received and reviewed, your eligibility will be reviewed by the study staff. If you are eligible to continue in the study, the study coordinator will contact you to schedule the start of Phase 1. If more than 45 days lapse between your screening measures and the scheduled start date of Phase 1, you may be asked to repeat eligibility testing in an abbreviated visit.

Phase 1: Diet Acclimation (free-living). Day 1 – Day 7: 1-5 hours *(fasting visits: Please do not eat any food or drink anything but water for 12 hours before these appointments and no alcohol beforehand.)*

You will return to clinic daily for 7 consecutive days. The following tests and procedures will be performed during this phase of the study.

- You will return to PBRC once a day to be weighed, eat one meal on site, and receive additional meals for the day to take to go.
- You will be asked to wear 2 accelerometers for the 1-week period.
- You will be asked to record your food and activity daily throughout Phase 1.
- Your blood will be drawn on day 1. We will collect approximately 2 tablespoons of blood from your vein in your arm.
- Your body composition (fat, muscle, and bone density) will be measured on day 7 via DXA Whole Body Scan (Dual energy x-ray absorptiometry), Bioelectrical Impedance Analysis (BIA), and circumference measures.
- To measure your total body water on day 7, you will be asked to provide a urine sample prior to consuming deuterium water. Approximately 4 hours after you drink the water, you will collect a second urine sample.
- You will be asked questions about your:
  - Memory, thinking skills, sleep, mood, exercise, medication use update, and adverse events
- Cognitive testing will be performed on days 2, 4, and 6 over a 1.5-2 hour period

each day. These tests will be either computer based or pen and paper tests to assess different aspects of your cognitive function. Testing on day 6 will include an electrical stimulation task.

- You will be asked to complete exercise familiarizations on day 1. The familiarization will be used to establish appropriate settings and exercise workloads for aerobic fitness and performance tests.
- You will be asked to complete an aerobic fitness test and exercise performance tests on days 4 and 5.
- You will have an IV inserted on day 7 for a 60 minute protein balance test. Two amino acid stable isotope solutions will go through the IV line. Approximately every 5 to 10 minutes, you will have blood drawn from an IV line in your arm. Approximately 6 tablespoons of blood will be collected throughout the procedure. During the test, you will have 2 muscle biopsies on the same leg (outside of your thigh). You will also consume an amino acid stable isotope beverage and your urine will be collected for the next 24 hours.

Randomization

Once phase 1 testing is completed, you will be randomly assigned to either receive a testosterone or placebo injection. Random assignment means that your treatment assignment is determined by chance, like flipping a coin. You will not be able to choose which treatment you receive. Neither study staff nor you will know which treatment that you will be receiving. Once you are randomized on day 7, you will be admitted the next morning (day 8) to the inpatient unit to begin phase 2 of the study.

Below is a table that shows what will occur for phase 2:

Phase 2: Energy Deficit

	Phase 2 (Days)																				
	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Blood Pressure, Pulse	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Injection	X																				
Blood Draw	X	X	X		X		X		X		X		X		X		X		X		X
Urine Collection																					X
Accelerometry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body Composition & TBW																					X
Cognitive Testing					X		X			X					X					X+	
Exercise Familiarizations*																X					
Aerobic Fitness Test: $V0_2$ Max																		X			
Exercise Performance Tests																		X	X		
Adverse Event Assessment	X					X					X					X					X
In-House Meal	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
24 Hour Stay	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Questionnaires	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Low Sleep (4 Hours/Day)			X	X	X			X	X	X			X	X	X			X	X	X	
High Sleep (8 hours/Day)	X	X				X	X				X	X				X	X				
High Exercise			X	X	X			X	X	X			X	X	X			X	X	X	
Low Exercise	X	X				X	X				X	X				X	X				
Protein Balance Test																					X
Muscle Biopsy																					X

+Cognitive testing includes an electrical stimulation task. This test may be moved to another visit day within the same phase.
*Exercise familiarizations may be moved to another visit day within the same phase.

Phase 2: Energy Deficit (live-in diet & activity control): Day 8—Day 28 (24 hour days)

- During the energy deficit phase, you will live on PBRC inpatient unit in a 24-hour-a-day controlled setting. Once a day, you will have your vitals (blood pressure, pulse) measured. All meals during Phase 2 will be derived from US military combat rations, including the Meal, Read-to-Eat (MREs) and will be provided to you, eaten on the unit (or PBRC grounds) and monitored. You will be required to eat all of the food that is provided to you. You will be weighed each day. Additionally, a wrist-worn accelerometer will be used throughout phase 2. The accelerometer will measure your activity and sleep.
- An injection (placebo or testosterone) will be given on day 8.
- To measure your total body water on day 28, you will be asked to provide a urine

sample prior to consuming deuterium water. Approximately 4 hours after you drink the water, you will collect a second urine sample.

- Throughout phase 2, you will complete supervised exercise sessions throughout the day that include both indoor and outdoor activities.
- You will have high and low stress days related to amount of exercise and sleep. On high days, you will perform longer and more challenging exercise bouts as well as have your sleep limited to 4 hours per day. High days include days 10, 11, 12, 15, 16, 17, 20, 21, 22, 25, 26, and 27. On low days, you will perform shorter and less challenging exercise bouts as well as have your sleep limited to 8 hours per day. Low days include days 8, 9, 13, 14, 18, 19, 23, and 24.
- Blood draws will occur on days 8, 9, 10, 12, 14, 16, 18, 20, 22, 24, and 26. We will draw approximately 1 tablespoon of blood from a vein in your arm on each of these days.
- Cognitive testing will be performed on days 12, 14, 17, 22, and 27. Testing on day 27 will include an electrical stimulation task.
- You will be asked to complete exercise familiarizations on day 23.
- You will be asked to complete the exercise performance tests on day 25 and 26.
- Your body composition (fat, muscle, and bone density) will be measured on day 28 via the DXA, BIA, and circumference measures.
    - You will have an IV inserted on day 28 for a 60 minute protein balance test. Two amino acid stable isotope solutions will go through the IV line. Approximately every 5 to 10 minutes, you will have blood drawn from an IV line in your arm. Approximately 6 tablespoons of blood will be collected throughout the procedure. During the test, you will have 2 muscle biopsies on the same leg (outside of your thigh). You will also consume an amino acid stable isotope beverage and your urine will be collected for the next 24 hours.
- You will be asked questions about your:
    - Memory, thinking skills, sleep, mood, medication use update, and adverse events
- You will reside in the inpatient unit at PBRC during phase 2, thus the time commitment for this phase is 24 hours per day.
- You will be released from the in-patient unit after completing all tests on day 28.

Below is a table that shows what will occur for the final phase of your participation in the study:

Phase 3: Out-Patient Recovery (Free-Living)

	Phase 3 (Days)																					
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49+	50*
Blood Pressure, Pulse				X						X						X					X	
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Blood Draw+	X			X						X						X					X	X
Urine Collection																					X	X
Accelerometry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Total Body Water																					X	
Food & Activity Log	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Body Composition																					X	
Cognitive Testing				X+						X+												
Exercise Familiarizations*																X						
Aerobic Fitness Test ($V0_2$ Max Test)																		X				
Exercise Performance Tests																		X	X			
Adverse Event Assessment	X					X					X					X					X	
In-House Meal & Pick-Up	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Questionnaires	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Protein Balance Test																					X	
Muscle Biopsy																					X	

+PRN Visits: After the completion of D50, you may be asked to return to Pennington for additional blood draws to measure your testosterone or other blood levels. +Cognitive testing includes an electrical stimulation task. This test may be moved to another visit day within the same phase.
*Exercise familiarizations may be moved to another visit day within the same phase.

Phase 3: Out-Patient Recovery (Free-Living). Day 29 – Day 50: 1-5 hours ***(fasting visits: Please do not eat any food or drink anything but water for 12 hours before these appointments and no alcohol beforehand)***

- You will return to PBRC once a day to be weighed, eat one meal on site, and receive additional meals for the day to take to go. You will be provided the same foods as given in Phase 1. Additionally, a wrist-worn and waist-worn accelerometer will be used throughout phase 3. The accelerometer will measure your activity and sleep.
- You will be asked to record your food and activity daily throughout Phase 3.
- Blood draws will occur on days 29, 32, 38, 44, and 50. We will draw approximately 1 tablespoon of blood from a vein in your arm on each of these days.
- Cognitive testing will be performed on days 32 and 38. Testing will include an electrical stimulation task.

- To measure your total body water on day 49, you will be asked to provide a urine sample prior to consuming deuterium water. Approximately 4 hours after you drink the water, you will collect a second urine sample.
- You will be asked to complete exercise familiarizations on day 44.
- You will be asked to complete the exercise performance tests on day 46 and 47.
- Your body composition (fat, muscle, and bone density) will be measured on day 49 via the DXA, BIA, and circumference measures.
- You will have an IV inserted on day 49 for a 60 minute protein balance test. Two amino acid stable isotope solutions will go through the IV line. Approximately every 5 to 10 minutes, you will have blood drawn from an IV line in your arm. Approximately 6 tablespoons of blood will be collected throughout the procedure. During the test, you will have 2 muscle biopsies on the same leg (outside of your thigh). You will also consume an amino acid stable isotope beverage and your urine will be collected for the next 24 hours.
- You will be asked questions about your:
    - Memory, thinking skills, sleep, mood, medication use update, and adverse events
- You will be asked to return on day 50 to have a blood draw and to return your collected urine.

PRN: As Needed Follow-up Visit

- After the completion of your Day 50 visit, you may be asked to return to PBRC for an additional blood draw (approximately 1 teaspoon) to measure your testosterone level.

Description of Tests and Procedures:

The list below describes each test and procedure that will be done during the course of the study. The tests and procedures will occur when you come to the Pennington Biomedical Research Center.

Accelerometer:
You will be asked to use a small device, similar to a pedometer, to count your steps, body positions and activity for a certain period of time. You will be asked to wear this wristband and waist worn device on your arm throughout the study.

Biospecimens (archives)

Blood, urine, and muscle tissue will be collected during the study. These bodily materials are called biospecimens. Some biospecimen samples will be stored and used for the study and other biospecimen samples will be stored for future studies. The samples will be stored indefinitely. The future research may take place at PBRC, UAMS, USARIEM, and other study collaborators and may involve these researchers in this study. The future research may not take place at PBRC and may not be reviewed by PBRC Institutional Review Board. For privacy and confidentiality, your biospecimens will be labeled with a unique series of letters and numbers. PBRC, UAMS, and USARIEM will store your biospecimens with this unique identifier and the

minimum number of personal identifiers to meet laboratory standards. The research done with your specimens may help to develop new products in the future, or may be used to establish a cell line or test that could be patented or licensed. You will not receive any financial compensation for any patents, inventions or licenses developed from this research.

Exercise Performance Test: About 3 hours
You will be asked to complete an exercise performance test to assess your muscular strength, power, speed, and endurance. This test includes a vertical jump test, a deadlift, a bike sprinting test, treadmill running test and a weighted pack ruck march (walking) for 2.5 miles.

Exercise Sessions:
Exercise will be performed multiple times per day during phase 2. A variety of exercise modalities will be used including aerobic and resistance exercise activities, hiking with and without a pack, jogging, completing obstacle courses, field test training, and other field-based military activities.

IV Procedure (Intravenous Procedure):
An IV line will be placed in your arm vein for blood draw purposes and will remain there throughout the testing. Blood will be drawn at specific times. **During your IV procedure, a small amount of your own blood (less than 1 teaspoon) will immediately be returned into your vein through the IV after each specimen is collected.**

Medication Inventory
You will be asked to bring in all your prescription and non-prescription medications you are currently taking.

Muscle Biopsy:
This procedure is used to sample muscle cells from underneath the skin of the leg. After cleaning the skin with iodine and using a local anesthetic, medical staff will make a small incision in the skin and introduce a needle under the skin to remove muscle cells. About 250-300 milligrams (less than a teaspoon size) of muscle will be removed. After the biopsy is completed, the skin will be held closed with a sterile adhesive bandage and an antibiotic ointment will be applied.

Physical Measurements: about 30 minutes
You will have your blood pressure, pulse, height, weight, and body circumference measured. A complete physical exam will be done during screening.

Protein Balance Test
You will have an IV inserted in your arm where you will receive 2 stable isotopes (non-radioactive labeled amino acids). Your blood will be drawn from the IV during the 1 hour test. You will also be asked to drink another stable isotope (non-radioactive

labeled amino acid) and collect your urine over a 24 hour period. You will be given a plastic bottle and instructions on collecting all of your urine for a 24 hour period. The urine should should be kept in a cool area prior to returning to PBRC. These isotopes and sample collections will measure if your body is building more muscle than its breaking down.

Questionnaires

You will be asked to complete different questionnaires throughout the study.

Resting Metabolic Rate:
After you rest for 30 minutes, a clear plastic hood will be placed over your head and chest area. The hood id ventilated with fresh air. Your oxygen intake and carbon dioxide out-put will be measured for 30-45 minutes to determine how many calories you burn during the time that you are being tested.

Total Body Water (TBW):
You will be asked to drink 100-150 mL of water containing the stable isotope (non-radioactive) deuterium. Measurement of the deuterium will be used to determine total body water.

Electrical Stimulation:
You will be asked to wear a device attached to one of your limbs that gives you little electrical shocks. The purpose of these shocks is to understand how you respond to painful events. These electrical shocks are carefully controlled so that they make you feel uncomfortable but not in severe pain. The device is also designed so that the electricity only travels through your limb, not throughout your body. Before we start the test on you, we will adjust the settings on the device so that it makes you feel discomfort but not extreme pain. But, if the discomfort caused by these electrical shocks is too difficult for you, we will discontinue the test.

Whole Body Scan GE iDXA **(**Dual energy x-ray absorptiometry): ~10 minutes
This scan measures the amount of bone, muscle, and fat in your body. The scan will be performed using a whole-body scanner. You will be required to wear a hospital gown, to remove all metal-containing objects from your body, and to lie down on the table. You will be carefully positioned on the table, and your legs will be placed together using two Velcro straps. A scanner emitting low energy X-rays and a detector will pass along your body. You will be asked to remain completely still while the scan is in progress. The scan takes approximately ten minutes. This scan is for research purposes only and not for diagnostic treatment.

Bioelectrical Impedance Analysis **(BIA) Measurements (about 10 minutes):**
You will be asked to change into a gown and to remove all footwear and socks/stockings. Once changed and barefoot, you will be asked to stand on a scale (similar to a large gym scale), and you may be asked to hold on to hand electrodes on

each side of the scale. You will be asked to step off of the scale once the measurement is complete (less than one minute).

6- What are the possible risks and discomforts?

There are some potential (possible) discomforts and risks associated with participating in this study.

Blood Draws**:** There is the possibility of infection and/or pain and bruising at the vein on your arm where the needle is inserted. Aseptic (sterile) technique and trained personnel minimize these risks.

Blood Pressure Testing. You may experience temporary discomfort during blood pressure recordings due to the pressure of the cuff on their arm.

ECG. There are minimal risks associated with this test. There is a small possibility there may be some redness or irritation while cleaning the skin prior to applying the electrodes or if you happen to be allergic to the adhesive.

Exercise performance tests: All Core standard operating procedures are in accordance with the American College of Sports Medicine's Guidelines for Exercise Testing and Prescription as well as the American Heart Association. There is minimal risk of injury or a cardiovascular event during exercise testing protocols. We believe the risk of an event during exercise testing is minimized with a pretest review of the medical history, physical examination by a physician or mid-level health care professional, use of a highly trained staff, participant familiarization, and well-defined emergency procedures. Participants may experience temporary discomfort during blood pressure recordings due to the pressure of the blood pressure cuff on the arm and may experience muscle fatigue, weakness, soreness and/or muscle pulls or tears. All tests are conducted in the presence of Core personnel with extensive experience in conducting exercise testing. All laboratory staff are trained in BLS (basic life support – CPR) and/or ACLS (advanced cardiac life support). In the event of a life threatening emergency, the participant would be treated with BLS/ACLS by trained individuals and subsequently be transported to the nearest acute care medical-surgical facility via Emergency Medical Services which is a parish wide paramedic response unit.

Exercise Sessions: The proposed exercise intervention is unlikely to cause major problems. There is the possibility of adverse events ranging from musculoskeletal problems to, in very rare cases, cardiovascular events. Occasionally study participants experience minor orthopedic problems, but most are self-correcting with rest and standard first aid. These orthopedic injuries will be minimized by gradually progressing participants to their prescribed dose at the start of the study and alternating exercise sessions between various modes of exercise. In rare instances, an injury may occur which would prevent participants from exercising via a specific mode of training like treadmill running. Exercise supervisors are trained in first aid and basic CPR. Each

staff member is trained in either advanced or basic life support, and an automated external defibrillator and fully-stocked crash cart are kept on site. Although some study participants will be at moderately elevated risk for CVD, they will receive a thorough health screen including a physical examination by a study physician or mid-level health care professional and a maximal exercise test. According to the available data on adverse events resulting from the types of exercise proposed here, risk should be low in this study. Fatal events during exercise are extremely rare.

Food Allergies and Gastrointestinal (GI) Discomfort
Because of the way our meals are prepared for research, and the possibility that the ingredients in the foods we get from commercial vendors could change at any time without our knowledge, it cannot be guaranteed that allergens will be identified and removed from the foods used in our research studies. If you have a food allergy, and you are participating in a study where foods are provided, there is a risk that you could have an allergic reaction. All participants with known life-threatening food allergies must inform staff of their allergies. Additionally, consumption of our meals and MREs may cause GI discomfort including excess gas, constipation, and diarrhea.

Interviews/Questionnaires
Fatigue and anxiety may occur due to the number and length of the questionnaires. You do not have to answer any questions you do not want to answer.

IV Procedure: There is a possibility of pain, bruising, or infection at the site of the needle insertion for the IV line. Aseptic (sterile) technique and trained personnel minimize these risks.

Loss of Confidentiality: Taking part in this research may involve providing information that you consider confidential or private. Efforts such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe. We will label your stored samples with a unique series of letters and numbers. PBRC will store your blood and samples with this unique identifier and the minimum number of personal identifiers to meet laboratory standards. If your samples will be transmitted outside PBRC (i.e., those sent to UAMS, USARIEM, and other study collaborators), all identifying information about you will be removed from the samples before they are released to any other investigators. Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally.

Muscle Biopsy**:** Mild to severe pain, soreness, bruising, and a small scar are common risks. A hematoma (collection of blood in the tissue) may occur. There is a slight risk that a superficial nerve may be cut; the nerve may heal, or it may result in a permanent loss of sensation in the skin at the biopsy site. Although infrequent, there is risk of infection at the biopsy site, which may need treatment with antibiotics.

Protein Balance Test: There are no known risks related to exposure or consumption of the non-radioactive amino acid isotopes for this study procedure.

Resting Metabolic Rate (RMR): There is no known risk in having a RMR (resting metabolic rate). If you are claustrophobic, it may be uncomfortable to have the plastic hood over your upper body.

Electrical Stimulation: The electrical stimulation will be uncomfortable. Before the test, we will adjust the device so that it is not too painful. But the discomfort during the test could still be upsetting to you. We will stop the test if the electrical stimulation upsets you too much. Also, we may rub some gel on your skin before attaching the stimulator device to it. There is a small chance that this gel could irritate your skin. If so, we will wipe the gel off and not use the electrical stimulator. If your skin is irritated, it will soon clear up.

Testosterone: Potential side effects of testosterone treatment include acne, oiliness of skin, increased growth of body hair, breast tenderness, a reversible increase in hemoglobin, sleep apnea, leg edema, weight gain, aggressiveness, oil embolism, and emotional lability. Emotional lability is when an individual experiences rapid or exaggerated changes in mood. An oil embolism is when droplets of oil could travel to your lungs and cause coughing, trouble breathing, chest pain or other symptoms.

Total Body Water: The extra neutron in the water is not radioactive and has no risk.

Urine Collection: There are no known risks of collecting urine into a container

DXA Whole Body Scan (Dual energy x-ray absorptiometry)**:** We are exposed to radiation in the environment on a daily basis; however, some scientists have suggested that humans have a lifetime maximum exposure limit. Exposure to radiation is not without risk, but it is difficult to quantify the exact amount someone is exposed to. By participating in this study you will be exposed to radiation that will add to this lifetime maximum exposure limit. If you believe you have been exposed to a significant amount of radiation as part of your occupation or due to treatment for a specific medical condition, you should notify the study team to discuss whether or not this study would be appropriate for you.

Bioelectrical Impedance Analysis (BIA) Measurements:

There is no known risk associated the BIA measurement.

Will I be notified if my data or samples results in an incidental finding?
During a research study, a researcher may notice something that he or she was not looking for. This is called an “incidental” or “unexpected” finding. These incidental findings are not directly related to the research. However, they may show important information about the health of a research volunteer.

Researchers may share some or all of their findings with you. However, you may not learn about any findings for a very long time. If such findings occur, you will be notified by the medical investigator or trained study personnel and referred to a treatment facility for further testing and/or treatment.

Risks: It can be very upsetting to learn unexpected information about your health. This is especially true if you learn that you have or will develop a condition that has no treatment or cure. There is a chance that unexpected findings could affect your family or social relationships, change your family planning decisions, or affect you financially. You might need more tests and procedures to find out what the information really means. It's also possible that the information might be incorrect, so you would worry without cause.

Unknown Risks: In addition to the risks listed above, you may experience a previously unknown risk or side effect.

A committee of health experts called the Data Safety Monitoring Board will be reviewing all study activities at regular intervals to assure that the risks and benefits being described to you are accurate.

7- What are the possible benefits?

We cannot promise any benefits from your being in the study. However, possible benefits include the following: You will receive health and medical screening examinations and the results will be discussed with you.

8- If you do not want to take part in the study, are there other choices?

You have the choice at any time not to participate in this research study. If you choose not to participate, any health benefits to which you are entitled will not be affected in any way. You have the right to take part now and change your mind later on. You may choose to increase your activity level on your own without enrolling in this study.

9- If you have any questions or problems, whom can you call?

If you have any questions about your rights as a research volunteer, you should call the Institutional Review Board Office at 225-763-2693 or the Executive Director of PBRC at 225-763-2513. If you have any questions about the research study, contact Dr. Jennifer Rood at 225-763-2524. If you think you have a research-related injury or medical illness, you should call Dr. Frank Greenway at 225-763-2578 during regular working hours. After working hours and on weekends you should call the answering service at 225-765-4644. The on-call physician will respond to your call.

10- What information will be kept private?

Every effort will be made to maintain the confidentiality of your study records. However, someone from the Food and Drug Administration, the PBRC, USARIEM, and UAMS

may inspect and/or copy the medical records related to the study. The study is supported by the US Army Medical Research and Materiel Command and their representatives have access to study records as part of oversight activities. Results of the study will be published; however, we will keep your name and other identifying information private. Other than as set forth above, your identity will remain confidential unless disclosure is required by law.

De-identified Information and/or Biospecimens for Future Research
Any personal information that could identify you will be removed from your data and/or biospecimens. Your data and/or biospecimens may be used for future research studies or given to another investigator for future research without asking for your additional permission.

ClinicalTrials.gov
A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by US Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

Biospecimens and Commercial Profit
Your urine, blood, and muscle samples may be used to develop new drugs or other products that may result in commercial profit that will not be shared with you.

Volunteer Registry Database
It is the policy of the US Army Medical Research and Development Command that data sheets are to be completed on all volunteers participating in research for entry into this Command's Volunteer Registry Database. The information entered into this confidential database includes your name, address, Social Security Number, study name, and dates. The intent of the database is two-fold: first, to readily answer questions concerning an individual's participation on research sponsored or funded by the USAMRDC; and secondly, to ensure that the USAMRDC can exercise its obligation to ensure research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The information with the stored at the USAMRCC for a minimum of 75 years.

11- Can your taking part in the study end early?
Dr. Jennifer Rood, Dr. Frank Greenway, or the study sponsor can withdraw you from the study for any reason or for no reason. Possible reasons for withdrawal include failure to follow study instructions, the investigator decides that continuation could be harmful to you, you need treatment not allowed in the study, the study is cancelled, or other administrative reasons. The sponsor of the study may also end the study early.

You may withdraw from the study at any time without penalty; however, all data PBRC has previously collected cannot be removed from the study.

If your participation in the research ends early because of the investigator or by your choice, termination procedures may need to be completed or follow-up data may need to be obtained to ensure your safety. The study staff will go over the details with you.

12- What if information becomes available that might affect your decision to stay in the study?

Significant New Findings
During the course of this study there may be new findings from this or other research, which may affect your willingness to continue participation. Information concerning any such new findings will be provided to you.

Clinically Relevant Research Results
In this study, you will be informed of any clinically relevant research results, including your individual results that may be discovered.

13- What charges will you have to pay?
None

14- What payment will you receive?
If you agree to take part, we will compensate you up to $7,500 *for completion of the study.* You will be compensated $500 after the completion of phase 1 (Day 7), $5,000 after the completion of phase 2, and $2,000 after the completion of Phase 3. *If you do not complete the entire study, you will be only be compensated for the study visits completed.* For Phase 2, you must complete the entire live-in period and testing on day 28 to obtain the full $5,000. If you fail to meet this requirement, your payment will be prorated based upon the number of days that you have completed. Your check will be requested from the LSU payroll department when you complete the study or at the appropriate milestone if you are compensated during the course of the study. It usually takes about 3-4 weeks for it to arrive at PBRC.

US citizens, legal resident aliens, and those who have a work eligible visa will need to provide their social security number to receive payment.

You are subject to a 1099 for receiving compensation. Payments in excess of $600 per calendar year are considered taxable income. If you will be paid more than $600, PBRC/LSU will report this income to the IRS. Non-US citizens are subject to having taxes withheld from payment and will need a passport, visa and I-94 for payment to be processed.

I authorize that all information provided on this Informed Consent form and HIPAA Authorization form, including any and all personal and financial data may be shared with the Internal Revenue Service (IRS) for tax reporting. This data will be securely retained indefinitely.

15- Will you be compensated for a study-related injury or medical illness?

No form of compensation for medical treatment or for other damages (i.e., lost wages, time lost from work, etc.) is available from the Pennington Biomedical Research Center. In the event of injury or medical illness resulting from the research procedures in which you participate, you will be referred to a treatment facility. Medical treatment may be provided at your expense or at the expense of your health care insurer (e.g., Medicare, Medicaid, Blue Cross-Blue Shield, Dental Insurer, etc.) which may or may not provide coverage. The PBRC is a research facility and provides medical treatment only as part of research protocols. Should you require ongoing medical treatments, they must be provided by community physicians and hospitals.

16- Signatures

By signing this consent form, I agree to participate in the study as it is described. The study has been discussed with me and all my questions have been answered. I understand that additional questions regarding the study should be directed to the study investigators. I agree with the terms above and acknowledge that I will be given a copy of this signed consent form.

With my signature, I also acknowledge that I have been given either today or in the past a copy of the Notice of Privacy Practices for Protected Health Information.

_____
Printed Name of Volunteer

_____ _____
Signature of Volunteer Date

_____
Printed Name of Person Administering Informed Consent

_____ _____
Signature of Person Administering Informed Consent Date

Dr. Jennifer Rood
Principal Investigator

Dr. Frank Greenway
Medical Investigator

With this additional signature, I agree to be re-contacted for follow-up information related to this study.

_____
Printed Name of Volunteer

_____ _____
Signature of Volunteer Date

17- What you need to know about future research with your data, biospecimens or imaging.

Some of your blood, urine, and muscle samples will be sent to UAMS, USARIEM, and other study collaborators. Any personal information that could identify you will be removed before the blood, urine, and muscle samples are shared.

What you should know about your biospecimens:

- The samples will be stored indefinitely.
- If you agree to have your samples stored, you can change your mind later.
- For privacy and confidentiality, your samples will be labeled with a unique series of letters and numbers. PBRC, UAMS, and USARIEM will store your samples with this unique identifier and the minimum number of personal identifiers to meet laboratory standards.
- The future research may or may not take place at PBRC, UAMS, and USARIEM and may or may not involve their researchers.
- You will not be compensated for any research studies that might be conducted in the future.
- You will not be informed of the details of any specific research studies that might be conducted in the future.
- The collection of samples may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases.
- The research done with your specimens may also help to develop new products in the future, or may be used to establish a cell line or test that could be patented or licensed. You will not receive any financial compensation for any patents, inventions, or licenses developed from this research.

Withdrawal of Consent

If you decide you would like to withdraw your consent to use your data, biospecimens or imaging, you must provide a written request to have your samples destroyed. In the event you withdraw your consent, it will not be possible to destroy the data, samples or imaging that have already been given to researchers.

For destruction of your data, biospecimens or imaging, you can send a request to the Principal Investigator at:

Dr. Jennifer Rood
Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808

Pennington Biomedical IRB FWA 00006218
Approved August 24, 2020

PENNINGTON BIOMEDICAL RESEARCH CENTER (PBRC)
INSTITUTIONAL REVIEW BOARD

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AUTHORIZATION FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION FOR RESEARCH PURPOSES

INFORMED CONSENT – PART II

(Instructions for Investigators: This form must be reviewed and signed by subjects participating in research/clinical trials that require a signed Informed Consent. These documents should be kept together. A copy of this Authorization and the Informed Consent must be given to the subject and/or his/her representative.)

Title of Research Project: **A randomized, double-blind, placebo controlled trial of testosterone undecanoate for optimizing physical and cognitive performance during military operations (OPS II)**

Principal Investigator: **Dr. Jennifer Rood** IRB Number: **2019-017 OPS II**

I hereby request and authorize the PBRC to use and disclose protected health information from the record(s) of:

Subject's Name/Address: _____

Birth Date: _____/_____/_____

Social Security Number: _____ *(This section only needs to be completed if you are receiving a participant stipend)*

Specifically, I request and authorize any part of my health information relevant to the research project, identified above and in the Informed Consent document, to be used and/or disclosed to the Principal Investigator identified above or his/her designee, in connection with the research project. I understand that this may include information relating to: Human Immunodeficiency Virus ("HIV") infection or Acquired Immunodeficiency Syndrome ("AIDS"); treatment for or history of drug or alcohol abuse; and/or mental or behavioral health or psychiatric care.

I understand that copies of the records indicated above will be:

- Used by employees of PBRC including researchers and treatment providers, and/or other members of its workforce.
- Disclosed to government officials or government agencies, study sponsors, study monitors, or others responsible for oversight of the research project.
- Sent to collaborating researchers outside PBRC if and to the extent indicated in the attached Informed Consent document(s).

I understand that by signing this form, I will allow PBRC and its researchers to use or disclose my health information in connection with the attached Informed Consent and for the purpose of the

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research that is described in the Informed Consent. For example, the researchers may need the information to verify that I am eligible to participate in the study, or to monitor the results, including expected or unexpected side effects or outcomes. Other University and government officials, safety monitors, and study sponsors may need the information to ensure that the study is conducted properly. I understand that any privacy rights not specifically mentioned in this Authorization are contained in the Notice of Privacy Practices that I received or will receive from the Principal Investigator or at the facility that I attend.

I understand that I may revoke this authorization at any time, except to the extent that PBRC has already relied on the authorization, by sending or transmitting of a facsimile, a written notice to the contact person listed in the attached Informed Consent document(s).

I understand that if my information already has been included in a research database or registry as described in the attached Informed Consent document(s), PBRC considers itself to have relied on it, and therefore my information will not be removed from those repositories. Unless otherwise revoked, I understand that this authorization will not expire. I understand that if I do not sign this form, I will not be able to participate in the above research study or receive the study-related interventions, but that PBRC cannot otherwise condition treatment on my signing this form.

While the research study is in progress, my right to access any research records or results that are maintained by the facility may be suspended until the research study is over. If my access is denied, I understand that it will be reinstated at the end of the research study.

I understand the information disclosed by this authorization may be subject to re-disclosure by the recipient and no longer be protected by the Health Insurance Portability and Accountability Act. The PBRC facility, its employees, officers, and physicians are hereby released from any legal responsibility or liability for disclosure of the above information to the extent indicated and authorized herein.

I UNDERSTAND THAT THIS AUTHORIZATION SUPERSEDES ANY CONTRARY INFORMATION IN ANY OTHER DOCUMENTS I HAVE SIGNED RELATED TO THE ATTACHED STUDY.

_____ _____
Signature of Subject or Subject's Legal Representative Date

Printed Name of Legal Representative (if any): _____

Representative's Authority to Act for Subject (e.g., relationship to subject): _____

Verification of Representative's Authority: ( ) viewed driver's license ( ) viewed Power of Attorney

( ) viewed other_____ (specify)