Attachment 8— IDEAL Consent Booklet and Form

Changes have been made to the consent form in response to direction from the **NIEHS IRB**, the new IRB overseeing the IDEAL protocol. The greatest of these changes is the decision to combine the content of the consent forms for the BLSA/IDEAL Screening Visit, Routine BLSA Visit, and BLSA Home Visit, and to present this information in the form of a consent booklet and consent form. Both the booklet and form contain content that is general to all three visit types, but also content that is exclusive to the visit type in question. In Attachment 8 the content specific to the BLSA/IDEAL Screening Visit is highlighted in yellow.

The **BLSA Informed Consent Booklet** is 35 pages long and covers all Screening and Routine Exam content. The content of the first 6 pages provide the participant presenting for a screening visit with a brief BLSA overview and Screening Exam-specific content as described below:

- Cover, Introduction, and Table of Contents (pp 1-4)
- Description of Screening Visit Tests, Procedures, Risks and Discomforts (pp 5-6):
  A. Blood and Urine Samples
  B. Echocardiogram
  C. Electrocardiogram
  D. History and Physical
- BLSA Contact Information (p35).

The balance of the booklet provides enrolled participants with information about routine and other exams and testing that may be conducted as a BLSA participant.

Similarly, the **BLSA Informed Consent for Research with Human Subjects** is 14 pages long, and includes both general and Screening Exam-specific content.

Looking just at the general and Screening Exam-specific content (i.e., excluding the Routine BLSA Visit, and BLSA Home Visit content), the new Informed Consent Booklet and the Informed Consent cover all the same content as the original Screening Informed Consent for Clinical Research. The new consent form does have a few additions and changes, as follows:

- **Who Can Participate?** The original Screening Consent form only had a section about who cannot participate – the new documentation includes both "Who Can?" and "Who Cannot?"
- **What Will I Be Asked To Do In This Study?** This content was included in the original Screening Consent form, whereas in the current documentation, the reader is referred to the Consent Booklet for details.
- **What Will Happen If I Take Part In This Study**? This content was included in the original Screening Consent form, whereas in the current documentation, the reader is referred to the Consent Booklet for details.
- **HIV, Hepatitis B and C, and Syphilis Testing**: Although HIV testing was referenced in the original Screening Consent, there was a separate informed consent form for this testing. Now, it is part of the main documentation.
- **What Are The Possible Risks**? This content was included in the original Screening Consent form, whereas in the current documentation, the reader is referred to the Consent Booklet for details.
- **Will I Be Given Results From This Study?** In the original Screening Consent, this information was part of the discussion of benefits of taking part in the study. Now, it is a stand-alone topic.
- **What If I Want To Stop Participating In This Study?** In the original Screening Consent, this information was included under the heading "How Long Will I Be in the Study?"
- **Conflict Of Interest:** This content is new.

IDEAL – Informed Consent

OMB No.: 0925-0631
Expiration Date: xx/xx/20xx

BLSA BALTIMORE LONGITUDINAL STUDY OF AGING

03-AG-0325

THE BALTIMORE LONGITUDINAL STUDY OF AGING

BLSA

INFORMED CONSENT BOOKLET

March 21, 2014

INTRODUCTION

The Baltimore Longitudinal Study of Aging (BLSA) is aimed at understanding human aging and discovering information that will help people age better.

The BLSA follows federal regulations for research with human subjects. These regulations require us to make sure that you understand the tests and procedures performed in the BLSA and the risks associated with them. This information is reported in this booklet. Please read this booklet before you agree to participate and any time you want more information about the study. We welcome any questions that you might have.

Please, **do not** sign the consent form(s) until the research staff has had the opportunity to review the consent(s) and study procedures with you.

If you are participating in a BLSA Screening Visit, please see pages 5-6 for a description of your visit tests and procedures.

If you are participating in your routine BLSA Visit, please see pages 7-30 for a description of your visit tests and procedures.

If you are participating in a BLSA Home Visit, please see pages 31-34 for a description of your visit tests and procedures.

Thank you for your participation and support of the BLSA.

TABLE OF CONTENTS

I. BLSA SCREENING VISIT TESTS, PROCEDURES and RISKS and DISCOMFORTS

The following tests and procedures will be performed unless otherwise noted to determine your eligibility to participate in the BLSA study. This visit should take 2-3 hours. A meal ticket will be provided so that you may eat after the visit. The BLSA medical staff will review your results and a letter will be sent to you to inform you of your eligibility.

A. Clinical Laboratory

Blood Collection: We will draw fasting (nothing to eat or drink except plain water for 10 hours) blood samples to measure your blood count, liver and kidney function, serum chemistries, HIV, Hepatitis B antigen and Hepatitis C antibodies, syphilis and other tests to determine whether you meet the requirements for participation in the BLSA.

HIV, Hepatitis and Syphilis Testing: As part of this study, we may test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS, Hepatitis B and C, and Syphilis. If your laboratory results indicate that you have any of these diseases, you will not be able to participate. If positive, we will tell you what the results mean, how to find care, how to avoid infecting others, how we report the results, and the importance of informing your partners at possible risk because of your infection. A positive result will be reported to the Maryland Department of Health by the testing Laboratory and by the Research Physician or Nurse Practitioner at the Clinical Unit at the NIA.

You will be asked to report if you have any problems giving blood samples, including whether you are a hemophiliac (bleeding problems), are taking blood thinning medications, or have experienced a large volume of blood loss (blood donation, surgical procedure etc.) within the past 3 months. The results will be reported to you so you can share them with your doctor.

Risks and Discomforts: You may experience some pain or discomfort at the site of needle entry when taking blood from your veins. There is a risk of bleeding and bruising at the site. There is also a remote chance of fainting or infection.

Urine Collection: We will collect a fasting (nothing to eat or drink except plain water for 10 hours) urine sample. Women under the age of 56 years will be considered of childbearing age (except if your uterus was surgically removed-hysterectomy) and a urine pregnancy test will be performed. We will notify you if you are pregnant. If you are found to be pregnant, you will not be able to participate in the BLSA until you are no longer breastfeeding.

Risks and Discomforts: There is no risk associated with this test.

B. Electrocardiogram (EKG)

A recording of the electrical activity of the heart will be done by placing electrodes (sticky pads) on the skin of the chest, arms and legs.
Risks and Discomforts: The only risk may be skin irritation at the electrode sites.

C. History and Physical

You will have a physical examination, including multiple measures of blood pressure, an extremities exam and an assessment of balance, walking and function. You will be asked information about your social demographics, medical history, general health status and physical symptoms, physical function and disability, psychological health, and medications. Sensory function will be evaluated using vision, hearing, touch, and orientation tests. You will be given tests to assess cognitive performance.
Risks and Discomforts: Occasionally, psychological tests may be tiring, stressful, disturbing, or anxiety producing.

D. Echocardiogram

This test will only be performed if during the screening process the medical staff determines that an echocardiogram is needed to determine your eligibility to participate in the BLSA. We will place a transducer (a device that looks like a microphone) on the skin of the chest which will allow us to see the various heart chambers and valves.
Risks and Discomforts: There are no risks associated with this test.

END OF BLSA SCREENING VISIT PROCEDURES AND TESTS

II. BLSA ROUTINE VISIT TESTS, PROCEDURES and RISKS and DISCOMFORTS

As a participant in the BLSA, you will be scheduled for most, but not necessarily all of the tests described in this booklet during your visit. The visits are scheduled for 3 days. However, there may be circumstances where a shorter or longer visit is indicated. If you are unable to complete your tests, you may be asked to return within 6 months of your visit to complete them. Some information collected during the visit is central to the purpose of the BLSA. Therefore, participation in the BLSA implies that you agree to perform the following CORE tests unless the Principal Investigator waives your participation or you do not meet the eligibility criteria for those tests:

- Collection of blood samples for laboratory testing
- Measures of muscle strength
- Measures of gait, balance and physical performance
- Basic tests of cognitive function
- Standardized physical examination
- Health-related interview

Not all of the tests described in this booklet will be scheduled during a visit. It is your option to decline any non-core tests.

A. BLSA CORE PROCEDURES

1. Clinical and Research Laboratory

Blood Collection: We will draw fasting (nothing to eat or drink except plain water for 10 hours) blood samples (clinical and research) to help us understand the aging process. You will be asked to report if you have any problems giving blood samples, including whether you are a hemophiliac (bleeding problems), are taking blood thinning medications, or have had a large amount of blood loss (blood donation, surgical procedure etc.) within the past 3 months. Based on this information, the amount of blood taken may be limited. The total amount of blood taken during a BLSA visit ranges from 150 ml (10 tablespoons) to 450 ml (30 tablespoons). The amount of blood usually taken during a blood donation (Red Cross, for example) is 450 ml. Because the exact amount of blood taken may vary, we ask that you do not plan to give blood for 56 days after your visit and that if you need to have blood drawn for medical reasons that you inform your provider.
Risks and Discomforts: You may experience some pain or discomfort at the site of needle entry when taking blood and when starting an intravenous (IV) line. There is a risk of bleeding and bruising at the site. There is also a remote chance of fainting or infection.

Genetic Testing: A portion of the blood that you donate may be used to measure DNA and RNA, which are used for specific types of genetic testing. These are molecules that hold your unique genetic information that you inherited from your

parents. For example, different genes are responsible for hair and eye color. Recent research suggests that genes may be associated with a higher or lower risk of you developing some diseases. The samples will be used for research purposes to understand the genetic aspects of the aging process and the mechanisms of chronic diseases that frequently occur in older individuals. Most results of these studies contain new, unverified information of unclear significance and, therefore, will not be given to you or your doctor. Your decision to consent, or not to consent, to DNA/ RNA sample collection, analysis and storage has no impact on your eligibility to participate in the BLSA.

Below **is an example** of the choice you will be asked to make on the informed consent concerning DNA/RNA collection

_____*I consent to the DNA collection*

_____*I do NOT consent to the DNA collection*

Your genetic information will be kept confidential to the maximum extent possible. The results of your genetic testing will be kept in a locked and secured manner at the NIH. Genetic information about you will not be revealed to others, including your relatives, without your written permission. Similarly, you will not receive information about other family members. NIA researchers do not plan to provide you with the results of any laboratory investigations involving the use of your samples for genetic testing. These results will, in general, be preliminary. In many cases, additional research may be necessary to determine whether these results are meaningful in terms of health and disease.

A Federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. According to this law, health insurance companies or group health plans cannot request your genetic information or use it to make decisions about your eligibility or premiums; and employers cannot use it in deciding to hire, promote, or fire you or in setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The following link contains details on this policy: http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf . You may ask your research team for additional information or a copy of The Genetic Information Nondiscrimination Act of 2008 informational document.

Urine Collection: We will collect a fasting (nothing to eat or drink except plain water for 10 hours before) urine sample. Women under the age of 56 years will be considered of childbearing age (except if your uterus was surgically removed-

hysterectomy) and a urine pregnancy test will be performed on the first morning of the visit. We will notify you if you are pregnant. Tests that may be harmful to your unborn baby will be avoided.
Risks and Discomforts: There is no risk to providing a urine sample.

Stored Samples and Future Studies: We would like to store samples of your blood and urine in a deep freeze. We may also ask that you provide skin swabs, saliva, stool, and toenail clippings. All samples collected will create a "bank" of samples, which can then be used in current or future NIA studies concerning the aging process and the causes of diseases. Your samples will be stored in secured freezers at a NIA facility. The stored samples will be kept indefinitely, controlled and managed by the Principal Investigator (PI) and the NIA. We will keep the study information private to the extent possible by the law. Strict privacy about the samples will be maintained and your name and identifying information will be removed and we will assign the samples a code. The key to the code will be kept in a separate, secure area. Your samples will be used only for the studies that are in the scope of the BLSA, as explained in this consent form unless you give us permission to use them for other studies. If a future research project arises where your samples could be useful, we ask you to designate as to whether or not your sample can be used. Any future research use will require approval by the Institutional Review Board.

Below **is an example** of the choice you will be asked to make on the informed consent concerning the collection of samples.

Please initial by the line indicating your wishes.

_____***YES**, I give permission to use my (blood or other fluids, tissues) samples in future research studies under the following conditions:*
_____*These samples may be used for other research projects without contacting me only if the identification code is removed so that the sample can no longer be identified as mine*

_____*These samples may be used for other research projects without contacting me even if the code is left on the samples. I understand that if the samples are coded, they may be able to be traced back to my personally identifiable information and my medical records.*

_____***MAYBE**, I wish to be re-contacted if further studies with my samples are considered. After the study has been explained, I will then decide if I want my samples to be included.*

_____ ***NO**, under no circumstances shall my samples be used for any future studies. My samples should be discarded once the present study is complete.*

If you allow future research on your sample and the research provides information important for your health, we will try to contact you. If you wish to be contacted, please keep the principal investigator for this study, the BLSA Clinical Coordinator or the NIA Administrative staff updated about changes in your address or phone number.

2. Gait

You will be asked to do a number of balance and walking tests to measure your walking-related movement. These tests are performed in a room equipped with a computerized system of 3-dimensional (3D) video cameras. You will wear lightweight clothing with markers attached to your skin.
Risks and Discomforts: There may be slight skin irritation from the glue from the markers. During the test, there is some risk of falling, which is similar to the risk of falling while performing many activities of daily living.

3. Physical Performance Measures (PPM)

These tests include timed walks, rising and sitting from a chair, standing and balance tests, and walking 400 meters (1/4 mile). During some of these tests you may be asked to breath in a mask connected to a portable machine that estimates your energy use during these activities.
Risks and Discomforts: During the tests that involve walking, there is some risk of falling, which is similar to the risk of falling while performing many activities of daily living.

4. Leg Strength

While in a seated position, you will be asked to perform a series of strength tests with your right and left leg. You will be asked to report any pain or discomfort.
Risks and Discomforts: Maximal exertions on strength testing are associated with fatigue, muscle and joint pain and muscle strains and sprains. Most of these symptoms are promptly resolved when exercise ceases.

5. Grip Strength

While in a seated position, we will position your arm on a table and you will be asked to squeeze a device (dynamometer). You will be asked to report any pain or discomfort.
Risks and Discomforts: Maximal exertions on strength testing are associated with fatigue, muscle and joint pain and muscle strains and sprains. Most of these symptoms are promptly resolved when exercise ceases.

6. Interview

You will be interviewed to obtain information on your social background, general health status and physical symptoms, how much time you spend in ordinary day-to-day and recreational activities, physical function and disability, psychological health and social functioning, lifestyle and health habits.
Risks and Discomforts: There are no risks associated with this interview.
Fatigue Questionnaire: How you feel performing routine activities may provide insight into the aging process. You will be asked to answer questions about the degree of tiredness you feel or would expect to feel after doing several different types of activities.

7. History & Physical

We will ask a series of questions about your current health and medical history (including information on reproductive history, urinary symptoms and sexual function). You will have a standardized physical examination. The discomfort to you will be minimal. You should not consider the examination as a substitute for a regular medical exam done by your private physician. The physical examination includes multiple measures of blood pressure, a joint exam and an assessment of balance and function.

Risks and Discomforts: There are no risk factors associated with the medical examination.

Body Measurements: We will weigh you and measure various body dimensions, using a tape measure and other similar techniques.

Risks and Discomforts: There are no risks associated with these measurements.

Manual Dexterity Testing: How quickly and accurately you can work with your hands will be tested using a "Perdue Pegboard" and "finger tapping" exercises. During the Perdue Pegboard test, you will be asked to pick up and place objects or to assemble items. During the finger tapping test, you will be given two sequences of keys to tap on a standard computer keyboard for 10 seconds on each hand. The computer records the number of key taps and time between key taps.

Risks and Discomforts: There are no risks associated with performing these tests.

8. Electrocardiogram (EKG)

A recording of the electrical activity of the heart will be done by placing electrodes (sticky pads) on the skin of the chest, arms and legs.

Risks and Discomforts: The only risk may be skin irritation at the electrode sites.

9. Cognition Testing (BVRCORE)

You will be given some tests to assess memory, problem solving, learning, language, attention, emotions, feelings, ability to manage finances, take care of household chores and other items relevant to your daily life. These tests take about 90 minutes. You may also be scheduled for an additional 90 minutes of testing depending on your age and other characteristics. You will be asked to provide the name and contact information of a family member or close friend who can provide information regarding your daily activities. With your approval, a series of questionnaires will be given to both you and your designated family member or close friend in order to assess your ability to perform routine daily activities. You also may be contacted by phone between regularly scheduled visits to answer questions relating to medical conditions, medications, or any treatment received in the past year. You will also be asked to answer 11 short, simple questions that provide information about your memory. The staff may ask to videotape you while taking the tests. We will use the videotape only for research and only research staff will see it. If we note significant memory problems or symptoms of depression, we will contact you and suggest that you may need to have a comprehensive clinical evaluation.

Risks and Discomforts: Psychological testing may be tiring, stressful, disturbing, or anxiety producing.

B. ADDITIONAL BLSA STUDY PROCEDURES

1. Hearing

We will evaluate your hearing function to help us determine how the hearing (auditory) portion of the inner ear changes with age. A machine called an audiometer will be used to determine your hearing ability at different sound (tones) and talking levels. The test will be performed in a sound proof hearing booth. A set of headphones or small foam earphones will be used. You will be asked to repeat words and sentences and also to press a button when sounds are heard. The staff will record the results. You will not be eligible for this test if you have too much wax build-up in your ears.
Risks and Discomforts: There are no risks associated with this procedure.

2. HIV, Hepatitis and Syphilis Testing

As part of this study, we may test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS, Hepatitis B and C, and Syphilis. If you are already enrolled in the BLSA and you become infected with any of these diseases, you will still be able to participate. If your laboratory results indicate that you have any of these diseases, we will tell you what the results mean, how to find care, how to avoid infecting others, how we report the results, and the importance of informing your partners at possible risk because of your infection. A positive result will be reported to the Maryland Department of Health by the testing Laboratory and by the Research Physician or Nurse Practitioner at the Clinical Unit at the NIA. If you agree to undergo the cytapheresis procedure (described on page 27-29), your blood will be tested each time you agree to undergo that procedure.

3. 2-Hour Oral Glucose Tolerance Test (OGTT)

We will perform a test used to diagnose diabetes. After fasting (nothing to eat or drink except water) for at least 10 hours, you will be asked to drink a 10-ounce sweet orange-flavored drink. A blood sample will be taken before taking the drink and at different time points over the following 120 minutes (2 hours). At the end of the OGTT test you will receive a meal. An intravenous (IV) line may be placed in an arm vein. The maximum amount of blood taken in the glucose tolerance test is 60 ml (4 tablespoons).
Risks and Discomforts: Drinking the sugar solution may lead to a temporary sense of stomach fullness and discomfort, nausea, vomiting, or diarrhea, but it is a rare occurrence. You may experience some pain or discomfort at the site of needle entry. There is a risk of bleeding and bruising at the site. There is also a remote chance of fainting or infection.

4. Microbiome Collection

In order to help us better understand how our bodies and microorganisms, such as bacteria, fungus or algae, interact to affect health and disease, we may ask to collect toenail clippings, saliva samples, stool samples and swabs of your skin.
Risks and Discomforts: There is no risk from providing stool, saliva or skin swab samples. There may be a very slight risk of bleeding from obtaining toenail samples.

5. 24-Hour Urine Collection

You will be asked to collect and save all of your urine over a 24-hour period. We will test your urine for substances that will help us estimate your body composition (amount of fat, muscle and bone) and how well your kidneys work.
Risks and Discomforts: There is no risk to providing urine samples.

6. Resting Metabolic Rate (RMR)

In the morning, before eating or drinking, you will be asked to breath into a mask, hood, or single-use mouthpiece connected to an air analyzer for approximately 10-15 minutes.
Risks and Discomforts: There are no risks associated with this procedure.

7. 24-Hour Holter Monitoring

You may be asked to wear a small monitor that will record your EKG (heart rate and rhythm) continuously for approximately 24 hours.
Risks and Discomforts: The only risk may be skin irritation at the electrode (sticky pad) sites.

8. Pulse Wave Velocity and Reflected Waves

These are measurements taken that record blood vessel stiffness.
Pulse Wave Velocity: We will place Doppler probes (like small microphones) on your neck, arms and legs to record the pressure and flow in the carotid (neck), radial (wrist), and femoral (groin area) arteries and other vessels.
Risks and Discomforts: There are no risks associated with this test.
Ankle-Brachial Index (ABI): We will place blood pressure cuffs on your arms and legs to measure your Ankle-Brachial Index (ABI), which is a test that screens for lower extremity peripheral vascular disease (diseases of the blood vessels in your legs).
Risks and Discomforts: There are no risks associated with this test.

9. Echocardiogram and Carotid Sonogram

We will place a probe or sensor on your chest using a gel to guide its movement. This will allow us to see the various heart chambers and valves. We will also place a probe or sensor on the skin of the neck and/or leg which will allow us to see blood vessels such as the carotid (neck) or femoral (groin) arteries. This will allow us to measure the thickness and stiffness of the blood vessels.
Risks and Discomforts: There are no risks associated with these tests.

10. Treadmill Exercise Test

We may ask you to walk on a treadmill. During the test the speed and incline are increased to make your heart work harder (make your pulse go up). Your EKG, blood pressure, breathing, and in some instances, blood samples are taken periodically throughout the exercise and after the test. The staff may stop the test at any time due to your level of fatigue or unsteadiness, heart rate, EKG or blood pressure changes and/or other complaints you may indicate to the tester. In addition, you are instructed to inform the staff if you have chest pain, shortness of breath, dizziness or other symptoms. You may also stop the test if you request. Your heart rate, rhythm and blood pressure will continue to be monitored for at least 5 minutes after the test. The treadmill test determines your physical fitness level and may find heart problems that you may have or may not have been aware of. The test is monitored by a physician or trained technician but will not be performed if you have health problems, such as orthopedic problems limiting your ability to walk, certain heart- valve problems, history of heart attack in the last three months, current chest pain, high heart rate, poorly controlled congestive heart failure, uncontrolled high blood pressure (>200/110 mmHg) or severe pulmonary (lung) hypertension.

Risks and Discomforts: In rare cases this activity can lead to chest pain, shortness of breath, irregular heartbeats, and dizziness. In most cases, these symptoms disappear after a few minutes of rest. In people that have risk factors for heart disease and where the treadmill testing is indicated for the diagnosis of coronary heart disease, the percentage of patients who develop a heart attack is lower than 2/10,000 and the risk of death is very rare, approximately 5/100,000. In the BLSA population, the risk of major complications is expected to be much lower. There may be a slight, temporary irritation of the skin from the breathing mask.

11. Pulmonary Function Test (PFT)

We will test your lung function by having you take deep breaths in and out of a device that you hold in your mouth. The results will allow us to see how well your lungs are working.

Risks and Discomforts: You may feel slightly dizzy from the deep breathing. This will go away shortly after finishing the test.

12. Nerve Conduction and Surface Electromyography (EMG)

Nerve conduction studies measure how fast nerves conduct electrical activity between nerves and muscles. We will tape small metal disk electrodes attached to wires onto the skin of your foot to record the activity. We will place a metal probe on the skin of your leg to deliver a small electrical shock. The shock will tingle or sting (feel like static electricity) and may make the muscle in your leg/foot twitch.

Risks and Discomforts: You might experience some discomfort during the nerve stimulation. You may experience some discomfort at the site of electrical stimulation and rarely mild pain in the contracting muscle. Both symptoms disappear after a few minutes.

13. Peripheral Sensitivity

You will be asked to put your foot on a box that will vibrate. You will press a button when you feel the vibration.

Risks and Discomforts: There are no risks associated with performing the test.

14. Proprioception

You will receive tests for the assessment of proprioception, which is the ability to sense body position, even when your eyes are closed. During the test, you will be seated with your feet strapped to two pedals and you will be blindfolded. The equipment moves your right ankle and you will be asked to perform with your left ankle the same movement that you feel on the right ankle.

Risks and Discomforts: There are no risks associated with performing this test.

15. Taste Bud Photograph

We will take a picture of your tongue to study taste buds. After rinsing your mouth with water you will rest your chin on a chin rest. Then, two small pieces of clear plastic will be placed on the tip of your tongue and images will be taken of your tongue. Next, blue food coloring will be applied to the tongue and pictures will be taken again.

Risks and Discomforts: Your tongue may be stained blue for a brief period of time but the food coloring will come off easily over time.

16. Vestibular Testing

Eye Movement: To assess vestibular function (balance as it relates to your inner ear and eyes), we will ask you to perform head movements within your comfort range. This test will measure the function of your semicircular canals, structures located in your inner ear. For this procedure, you will be asked to wear light-weight video goggles. We will track your eye movements while your head is moved in different directions.

Risks and Discomforts: It is possible that the head movements could cause some discomfort. You may experience some dizziness with the test.

Vestibular-Evoked Myogenic Potentials (VEMP): This test will be performed to assess the function of structures located in your inner ear. For this procedure, small foam inserts will be placed in your ears and/or you may be asked to wear headphones. Small electrodes will be placed on the skin of your neck and face. Sound (clicks) will be played in your ear and we will present vibrations with gentle taps to your forehead or through a bone conductor (device that allows you to hear sound through the bones in your head). The electrodes will record your muscle response.

Risks and Discomforts: It is possible that the head movements could cause some discomfort. You may experience some dizziness with the test. The electrodes applied to your skin may cause minor skin irritation.

17. Visual Acuity and Depth Perception

We may test your visual acuity and contrast sensitivity while you are sitting in front of an eye chart with and without glaring lights.

Risks and Discomforts: There are no risks associated with this test.

18. Visual Fields

We will also test your peripheral vision. You will be asked to look into a machine that will display lights that blink on and off and we will ask you to press a button when you see the lights.

Risks and Discomforts: There are no risks associated with this test.

19. Strip Meniscometry

Dry eyes are a common age-associated condition. We will measure the amount of water in your eyes using a sterile strip that will be placed near the surface of your eyes for 5 seconds.

Risks and Discomforts: In rare instances, you may have brief irritation or additional tearing if the strip comes in contact with your eye.

20. Food Frequency Questionnaire (FFQ)

You will be asked to complete a dietary intake questionnaire.

Risks and Discomforts: There are no risks involved.

21. Accelerometry (Actiheart/Watch)

During your clinic visit, you may be asked to wear a device(s) (accelerometer) that records your activity and/or heart rate. In addition, you may be asked to wear the device for 5-14 days when you return home. If you agree to wear the device at home, you will be provided with instructions including how to return the device to the BLSA using a pre-addressed and pre-stamped envelope that will be provided before you leave.

Risks and Discomforts: The electrodes applied to your skin may cause minor skin irritation.

22. Dual X-ray Absorptiometry (DEXA)

You will be asked to complete a dual energy x-ray absorptiometry (DEXA) scan. The test provides information on joint and bone quality and fat and muscle location in the body. This study involves the use of radiation.

Risks and Discomforts: The NIH Radiation Safety Committee has reviewed the use of radiation in this research study. Using the standard way of describing radiation dose, from participating in this study, you will receive no greater than a total of 1.74 rem to your skin, muscle and bone. All other organs will receive smaller amounts of radiation. Although each organ will receive a different dose, the amount of radiation exposure received from this study is equal to a uniform whole-body exposure of 0.52 rem. For comparison, the average person in the United States receives a radiation exposure of 0.3

rem per year from background sources such as the sun, earth's atmosphere, and radioactive materials found naturally in the earth's air and soil. The dose you may receive from this research study will be less than or equal to the amount you would normally receive in 1.7 years from these natural sources. One possible effect that could occur at these doses is a slight increase in the risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4, (or 25 percent). The increase in your chance of getting a fatal cancer as a result of the radiation exposure may increase from 25 percent to 25.02 percent. This change in risk is small and cannot be measured directly. The amount of radiation from this study is below the dose guidelines established by NIH Radiation Safety Committee for research subjects. The current guideline is a total of 5 rem (or 5,000 mrem), effective dose, per 12 consecutive calendar months. If you have received radiation exposure in the 12 months prior to your visit, you could theoretically exceed the NIH 5 rem safety limit. If you are pregnant, you will not participate in this part of the research study.

Please advise your doctor if you have participated in research studies at the NIH or other institutions that involved the use of radiation so it may be determined whether the total radiation dose from all studies is too much. Examples of such studies include x-ray studies, such as dental x-rays and mammograms, and other x-ray studies conducted in radiology departments, cardiac catheterization and fluoroscopy, as well as nuclear medicine studies, e.g., technetium and PET scans.

23. Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS)

The structure and function of the central nervous system (brain and spinal cord) will be studied with MRI and MRS. Information collected will help us understand the cause of changes in mental function that often occur in aging individuals. A technique called "functional magnetic resonance imaging" (fMRI) will be used to explore what parts of the brain are used to perform specific tasks. FMRI and MRS studies will be done at rest, during tests of memory, language and decision-making, and during tests of motor function such as (but not limited to) finger and foot presses. In addition to images of the brain, we will also use MRI techniques to obtain images of the abdomen, liver and muscles of the legs. Images may be obtained while you are at rest and during and after exercise. The MRI assessments may be divided in multiple sessions, with total scan time not to exceed 3 hours. Prior to your exam, you will be asked to complete a standard questionnaire to ensure that you are able to safely enter the MRI area. Some questions refer to possible exposure of metal in your eyes and face. MRI and MRS do not involve the use of radiation. However, in order to ensure your safety, a clinical x-ray may be performed prior to the MRI if there is a suspicion of metal in your body. If you have metal fragments in your body which are subject to magnetic pull, you will not be allowed to have an MRI for this research study. You will be told the approximate amount of radiation you will be exposed to compared to normal background radiation for a year. All radiation exposure carries some risk.

To start your MRI test, you will lie on a padded table. The table on which you are lying will be moved into the machine, which looks like a long narrow tube. Some people feel

confined (claustrophobic) in small places, if this bothers you, please notify the MRI staff. You may end your participation in this study at any time by telling the MRI staff. When MRI images are taken, it is normal for the MRI machine to make loud, banging and clicking noises. You will be asked to wear earplugs or headphones for your comfort during the exam. During the exam, the MRI staff is able to see and hear you. You will be able to hear the MRI staff. The MRI staff will be talking to you throughout your MRI exam and may issue simple instructions regarding holding your breath, maintaining position, etc. Generally, you will be requested to lie still throughout the exam.

Risks and Discomforts: The effects of magnetic fields in an MRI scanner have been extensively studied and the risks associated with an MRI exam are low, particularly if you qualify for the testing based upon the screening questions. You may experience some discomfort while lying still for a while. You may also be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the test. You will be asked to wear earplugs or earphones while in the magnet. You may not participate in this study if you have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to advise the MRI staff if you have had brain surgery for a cerebral aneurysm, implanted medical or metallic devices, or may have metal in your body from an injury or accident such as shrapnel or metal flecks in your eye from welding occupations and the like.

C. OPTIONAL BLSA PROCEDURES OR STUDIES

As a participant in the BLSA, you may decide that you want to participate in additional studies or procedures that are listed in this section. Please discuss your interest with the research staff member consenting you or with the Clinical Coordinator for the BLSA.

1. Accelerometry and Doubly-Labeled Water

You may be asked to participate in a study on energy expenditure. The purpose of this study is to understand how aging affects energy and movement. This research project is not designed to provide any direct benefit to you.

Purpose:

Total energy expenditure is the amount of energy that you use in a 24-hour period and includes energy use at rest, for the breakdown of food and for physical activity. Two methods will be used to determine your 24-hour energy expenditure: doubly labeled water (DLW) and accelerometry.

Exclusion Criteria:

You cannot be in this study if any of the following apply to you:

- You have completed this study before
- You have mild cognitive impairment or dementia diagnosis
- You are less than 60 years old

- You have allergies to the adhesive used on the electrodes
- You have or are found to have kidney disease
- You tend to have urine leakage or have difficulty urinating
- You are unable to complete the BLSA physical performance measures with or without a walking aid
- You are unable to provide urine samples 7-days, but no later than 14 days after the BSLA visit.
- You are not willing or able to follow the protocol procedures as explained to you by the physician or staff member

Procedures:

The following procedures will start on the last day (Day 3) of your BLSA visit

Urine Collection:

- In the morning, you will be asked to provide a fasting (nothing to eat or drink except plain water for 8 hrs) urine sample
- Approximately an hour later, another fasting urine sample will be collected
- After the doubly labeled water is given, you will be asked to provide a non-fasting urine sample every 1.5 hours for the next 6 hours (4 additional samples)

Doubly Labeled Water Administration:

- Following the second urine collection, you will be asked to drink water that has been labeled with a known concentration of a naturally occurring non-radioactive substance
- You will be asked to drink 2-4 8oz glasses of water over the next 4-5 hours

Accelerometry:

- The actiheart (device worn around your chest to record your heart rate and activity) and the actigraph (a device worn on your hip and your right and left wrist for a total of 3 devices) will be placed after the doubly labeled water is given
- You will be asked to wear these devices for the next 7 days. Instruction will be provided and you will be asked to log any problems during this time

Physical Performance Measures:

- You will be asked to breath in a mask connected to a portable air analyzer that estimates oxygen and energy consumption during the following activities:
    - Chair stands (2 sets of 10)
    - 400 meter walk at your "usual" pace (about a quarter mile)
    - Fast walking for 3 minutes
    - Sitting for 3 minutes
    - Standing for 3 minutes
    - Lying for 3 minutes

Basal Metabolic Rate after Exercise:

- Following the physical performance measures, you will be asked to sit or lie down with the mask and the portable analyzer for 15-20 minutes to record your energy

Return Visit or Sample Pickup:

- You may choose to either return to the NIA Clinical Research Unit after 7-14 days or you may choose to have your samples picked up from your home

- If you choose to return to the Clinical Unit, your visit will last 2-3 hours. We will collect 2 non-fasting (you will eat and drink before collecting the samples) urine samples 1- hour apart.
- If you choose to have your samples picked up at home, you will collect 2 non-fasting (you will eat and drink before collecting the samples) urine samples 1- hour apart. Instructions for the collection and storage of the samples will be given to you. A courier will pick up the samples from your home on that day
- You will return the actiheart and the 3 actigraph devices and the log when you return to the clinic or you may give them to the courier

Risk and Discomforts:

Actiheart: There may be slight skin irritation from the electrodes (sticky pads).
Doubly Labeled Water: There are no known risks from drinking non-radioactive doubly labeled water.
Physical Performance Measures: In rare cases the exercise can lead to chest pain, shortness of breath, irregular heartbeats, and dizziness. In most cases, these symptoms disappear after a few minutes of rest. During the tests that involve walking there is some risk of falling, which is similar to the risk of falling while performing many activities of daily living.
Mask: There may be a slight, temporary irritation from wearing the breathing mask.

END OF ACCELEROMETRY SECTION

2. Core Body Temperature

You may be asked to participate in a study on core (internal) body temperature. Change in internal body temperature may occur with aging and may affect the health of older persons. This study is not designed to provide any direct benefit to the participant.

Purpose:

A lower internal body temperature may be lead to a longer life span, but few human studies have been done. Core body temperature appears to follow a 24-hour rhythm, lowest in the second half of the sleep cycle then rising during active periods and falling during rest.

Exclusion Criteria:

You will not be eligible if you:
- Weigh less than 80 pounds
- You have mild cognitive impairment or dementia diagnosis

- Have known or suspected disorders of the gastrointestinal tract including but not limited to diverticulitis and inflammatory bowel disease
- Have an impaired gag reflex
- Have had previous gastrointestinal surgery
- Have problems swallowing or have esophageal problems
- Have a history of hypo-mobility or obstruction of the gastrointestinal tract
- Have a pacemaker or other implanted electro medical device
- Have an MRI scheduled 5 days after your BLSA visit

Procedures:

You will be asked to swallow a pill, about the size of a large multivitamin, containing the sensor with 8oz of room temperature water and to wear a 24 hour monitor that will record the temperature. In most cases, the pill with the sensor will be excreted through your normal bowel elimination in 24-36 hours.

Risk and Discomforts:

There are no known risks associated with ingestible temperature sensors in persons who have no contraindications to using the device. You will be screened on admission and if you meet the exclusionary criteria, you will be excluded from this procedure.

END OF CORE TEMPERATURE SECTION

3. <u>Creatine-Skeletal Muscle Mass</u>

You may be asked to participate in a study to understand the effects of aging on muscle quantity. Low muscle quantity in older people is a strong risk factor for illness and death. This study is not designed to provide any direct benefit to you.

Rationale:

Creatine is a substance that is normally found in muscles and is lost from muscle and excreted in the urine. We intend to measure how your body uses the creatine in order to study muscle breakdown.

Exclusion Criteria:

You cannot participate in this study if:

- You are pregnant, lactating, or trying to become pregnant
- You have mild cognitive impairment or dementia diagnosis
- You are a woman <56 years old and you: have not been surgically sterilized, are not using an approved form of birth control such as a pill, patch or injection, you are not using an intrauterine device or you have not been post-menopausal for at least 2 years.

- You cannot swallow pills

Procedures:
The following events will take place:
- You will be called prior to your BLSA visit and asked whether you want to participate in this study
- You will be sent a copy of the informed consent with a letter of instruction
- If you agree to participate (or not), you will be asked to sign the informed consent indicating your response (yes or no) and to send it back to us in the prepaid envelope
- If you agree to participate and upon receipt of your consent, we will send you either by mail or express mail, a 30mg creatine capsule with further instructions
- You will be asked to take the capsule 72-96 hours prior to the first testing day of your visit and to record the time and date on the instruction sheet
- You will be instructed not to exercise 2 days prior to your visit
- We will ask you to bring with you the instruction sheet that you recorded the time and date that you took the creatine capsule
- During your visit, and in the morning 96 hours after you took the capsule, we will obtain a fasting urine sample and we will take a small sample of blood (approximately 5ml, or 1 teaspoon)
- You will then be allowed to resume your regular exercise habits as per the guidelines of your BLSA visit

Risk and Discomforts:
Blood Draw: You may experience some pain or discomfort at the site of needle entry when taking blood from your vein. There is a risk of bleeding and bruising at the site. There is also a remote chance of fainting or infection.
Creatine Capsule: There are no known side effects from taking creatine at this dose level.

(For Women): Because the risk to an embryo, fetus or nursing mother is unknown, if you are pregnant, lactating or trying to become pregnant, you cannot participate in this study. You may be eligible if you are not trying to become pregnant and you are <56 years old, you have been surgically sterilized, you are on an approved form of birth control such as pills, patches or injections, you are using an intrauterine device, or you are post-menopausal for at least 2 years.

Only you can take the study drug. Do not share it with anyone else. It must be kept out of reach of children and persons who may not be able to read or understand the label. There may also be risks and side effects, other than those listed above that we cannot predict.

END OF CREATINE SECTION

D. MORE THAN MINIMAL RISK PROCEDURES

1. Computerized Tomography (CT)

You will be asked to complete a computerized tomography (CT) scan. The test provides information on joint and bone quality and fat and muscle location in the body. The study involves the use of radiation.

Risks and Discomforts: The NIH Radiation Safety Committee has reviewed the use of radiation in this research study and has approved this use as involving **slightly greater than minimal risk** necessary to obtain the research information desired. Using the standard way of describing radiation dose, from participating in this study, you will receive no greater than a total of 1.74 rem to your skin, muscle and bone. All other organs will receive smaller amounts of radiation. Although each organ will receive a different dose, the amount of radiation exposure received from this study is equal to a uniform whole-body exposure of 0.52 rem. For comparison, the average person in the United States receives a radiation exposure of 0.3 rem per year from background sources such as the sun, earth's atmosphere, and radioactive materials found naturally in the earth's air and soil. The dose you may receive from this research study will be less than or equal to the amount you would normally receive in 1.7 years from these natural sources. One possible effect that could occur at these doses is a slight increase in the risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4, (or 25 percent). The increase in your chance of getting a fatal cancer as a result of the radiation exposure may increase from 25 percent to 25.02 percent. This change in risk is small and cannot be measured directly. The amount of radiation from this study is below the dose guidelines established by NIH Radiation Safety Committee for research subjects. The current guideline is a total of 5 rem (or 5,000 mrem), effective dose, per 12 consecutive calendar months. If you have received radiation exposure in the 12 months prior to your visit, you could theoretically exceed the NIH 5 rem safety limit. To ensure your safety, you will not be eligible for the BLSA CT scan if your total radiation exposure estimate is greater than 3.0 rem. If you are pregnant, you will not participate in this part of the research study.

Please advise your doctor if you have participated in research studies at the NIH or other institutions that involved the use of radiation so it may be determined whether the total radiation dose from all studies is too much. Examples of such studies include x-ray studies, such as dental x-rays and mammograms, and other x-ray studies conducted in radiology departments, cardiac catheterization and fluoroscopy, as well as nuclear medicine studies, e.g., technetium and PET scans.

2. Cytapheresis

You may be asked to participate in a study to collect white blood cells through a process called cytapheresis. NIA scientists use these cells to perform a number of studies mostly related to change in immune function with aging. This study is not designed to provide any direct benefit to you.

This procedure involves more risk than is the usual every-day risk that healthy people face with preventative health care. Side effects can be serious, long lasting and/or life threatening.

Purpose:

Cytapheresis is a process of white blood cell removal. The procedure allows blood components that are not collected (such as red blood cells) to be continuously returned to the donor. The white blood cells collected will be used to study age-associated changes in the immune system and gene and protein expression.

Exclusion Criteria:

You will not be able to participate if:

- You are pregnant or a nursing mother
- You have mild cognitive impairment or dementia diagnosis
- Your veins are not adequate for the procedure
- You have a current illness (active infections, allergies, etc.) that as judged by the study physician will substantially increase the risks associated with cytapheresis.
- You have significant abnormalities on your physical exam, cognitive evaluation, health history questionnaire or in your blood tests that, as judged by the principal investigator or the BLSA medical staff make you not eligible
- You weigh less than 110 lbs.
- You are affected by a mental health condition that contraindicates the procedure
- You have congestive heart failure (CHF) that your doctor classified as moderate to severe (have shortness of breath or get tired easily with little or no physical movement) or have had a heart attack, severe chest pain, called angina, or a stroke in the last 6 months
- You are taking chronic blood thinning medications (examples are coumadin, heparin or antiplatelet agents other than low dose aspirin)
- You have a pulse rate less than 45 beats per minute (BPM), unless you are an otherwise healthy athlete.
- You have a pacemaker with a heart rate < 50 (unless the participant is a healthy athlete) or >100 beats per minute or are affected by a severe cardiac arrhythmia
- You have a pulse over 100 BPM

- Your blood pressure is too high (over 180 systolic or 100 diastolic), or pathologically too low (low blood pressure is not an exclusion as long as blood pressure normally runs low and is not associated with symptoms)
- Your temperature is higher than 37.5 C (99.5 F)
- You have a history of allergy to acid- citrate- dextrose (ACD) anticoagulant (a type of blood thinner used during the procedure)
- You have a history of an active bleeding disorder;
- You have a hemoglobin less than 10 g/dL and/or hematocrit less than 30%
- Your platelet count is less than 100,000/ul
- You have made a blood donation in the past 56 days
- You have a white blood count (WBC) less than 3.0/ul
- You have an active migraine headache
- You are taking a medication that, in the opinion of the investigator, would confound the science in a way that would make use of collected cells very unlikely
- You have started a treatment with insulin or drugs active on the cardiovascular system less than 4 weeks before or has had any change in treatment regimen in last two weeks
- You have received treatment for cancer in the past six weeks or longer if, in the judgment of the physician, a full recovery from the treatment has not occurred. Some low risk cancers including squamous or basal cell carcinomas of the skin are not cause for exclusion
- You are affected by Chronic Obstructive Pulmonary Disease (COPD), also known as emphysema or chronic bronchitis, and are having serious difficulty breathing at the time of donation. Medications for asthma do not disqualify you
- You are within eight weeks of planned major surgery;
- You have a history of seizures within the last 3 months
- You have sickle cell disease or sickle cell trait
- You are currently being treated for Tuberculosis
- You have any of the following infections: Lyme disease (unless six weeks after treatment has been completed and no new symptoms), Chagas disease, Babesiosis, or leishmanias
- You have been treated for syphilis or gonorrhea less than one year prior to the procedure
- You have a history of HIV, Hepatitis B or Hepatitis C. If newly diagnosed with Hepatitis B or C at the time of the first cytapheresis procedure, will be excluded from future procedures. However, if you become positive for one of these conditions and you have already participated in the procedure in the past, you are still eligible.
- You have participated less than 6 weeks prior to the procedure in another research study that is felt by the principal investigator to be incompatible with this study

Procedures:

As part of your BLSA blood laboratory tests, tests to screen for HIV and Hepatitis B and C will be drawn. You will be asked to complete a health history screening questionnaire. In addition, your blood test results and the results of your physical exam will be reviewed by

the medical staff. If you are found eligible and you agree to participate, the procedure will be performed as per your BLSA schedule.
The following procedures will be followed:

- Your blood pressure, pulse, respirations and temperature will be taken.
- A finger or ear stick will be done to check your red blood cell levels (only occurs if you have not had BLSA blood work in the last 2 days).
- A needle will be placed into a vein in each arm usually at the bend of the elbow. Blood from one arm via sterile tubing, enters the machine and mixes with a blood thinner solution that prevents the blood from clotting while outside of your body. The blood spins and is separated. A portion of your white blood cells and plasma (liquid part of your blood) is pumped into a collection bag. The remaining blood is returned to you through the needle in the other arm. The procedure lasts about 90 to 120 minutes. Approximately 240ml (1 cup) is donated.
- At the end of the procedure, the needles will be removed and pressure bandages will be applied for about 4 hours. You will be instructed to avoid heavy lifting for 24 hours. A snack will then be provided.
- The number of white blood cells collected is a small fraction of the total number of white cells in your body. Removal of these cells, which are quickly replaced by your body, has no impact on your health

Risk and Discomforts:

Donations are generally very safe.

- Discomfort from this procedure are mainly due to the needle sticks and limited movements of your arms during the procedure
- Pain, bruising, infection, bleeding, or swelling that may occur at the needle site
- Feeling lightheaded, dizzy, or faint from the blood draw
- Very rarely, temporary or permanent nerve damage may occur at the needle placement site
- In rare cases of machine failure, losing more blood (usually less than a pint)
- If blood flow is blocked in the tubing, hemolysis (destruction of red cells) may occur and the procedure will be stopped
- Feeling cooler as your blood is returned to you
- Tingling or numbness around the mouth or fingers, muscle cramps, chills, stomach upset or pain, and diarrhea from the blood thinner. These are seen in about 30-50% of procedures. Using less blood thinner, stopping the procedure for a short time, or taking milk or a calcium supplement (example Tums) easily treats these symptoms
- Seizures which are rare
- Uneven pulse, nervousness, skin rashes, hives, and flushing
- It is possible that research testing of your blood samples could reveal an unexpected medical condition, such as an increased susceptibility to an inherited or other disease that may affect you and your family. The NIA physician may decide it is in your best interest to inform you of them. It is possible that knowledge of these results will affect your social or psychological wellbeing. It might even lead to discrimination (unfairness), stigmatization (shame), or difficulties with health/life insurance

- Reproductive risks: You will be excluded if you are pregnant. This procedure may involve risks to an embryo or fetus (unborn child) that are currently unknown

There may also be risks and side effects other than those listed above that we cannot predict. If you have any unwanted side effects, please let the staff or the investigator know. Medication or other things may be done to make the side effects less uncomfortable. Many side effects go away shortly after the procedure is stopped, but in some cases side effects can be serious, long lasting and/or life threatening.

END OF CYTAPHERESIS SECTION

3. Muscle Biopsy

Researchers frequently need biological (living) samples for their studies on aging. You may be asked to donate a small amount of muscle tissue. This study is not designed to provide any direct benefit to you.

This procedure involves more risk than is the usual every-day risk that healthy people face with preventative health care.

Purpose:

Analysis performed on muscle specimens may help researchers better understand the effects of aging on muscle. A muscle biopsy will be done to obtain small pieces of muscle tissue.

Exclusion Criteria:

You cannot be in this study if any of the following apply to you:

- You have a history of increased bleeding due to either a known medical condition or an undiagnosed cause
- You have mild cognitive impairment or dementia diagnosis
- You are taking medicines that may increase the risk of bleeding such as Coumadin, Plavix, or Heparin (blood thinning medications)
- You are taking non-steroidal anti-inflammatory agents (NSAIDs) such as Motrin (Ibuprofen), Advil (Ibuprofen) or Naprosyn (Naproxen) and you are unable to stop taking them 4 days before and 3 days after the procedure
- You are taking more than 81 mg of aspirin a day and you are unable to stop taking it for 4 days before and 3 days after the procedure
- You are allergic to Lidocaine (Xylocaine) or any other local anesthetic or you have had in the past a severe allergic reaction to similar drugs
- You have active infections or chronic skin conditions that would prevent access to the biopsy area and/or any condition that would impair wound healing, such as uncontrolled diabetes or chronic oral steroid use

- You are unable to sign an informed consent and/or are not willing or able to follow the protocol procedures as explained to you by the physician or staff member
- You are pregnant

Procedures:

The biopsy will be performed in most cases on the outer part of the thigh muscle, about 6 inches above the knee or in rare instances on the upper arm. The skin area will be cleaned with anti-bacterial soap and protected with a sterile surgical drape.

- Local anesthesia will be injected to numb the area. After the biopsy site is numb, a small incision will be made in the skin (about a 1/4 of an inch long). This should not hurt, since the area should be numb.
- There are two different size needles that may be used. One needle is a little larger and longer than the intravenous (IV) needle used to draw your blood during your oral glucose tolerance test (OGTT) and the other needle is about the size and diameter of a pencil. The needle will be inserted through the skin access site 1 to 6 times. The amount of muscle tissue collected is very small and removing it has no practical consequences. You should not feel any pain during this procedure, but you may feel slight pressure.
- At the end of the procedure a pressure dressing will be applied at the biopsy site. If the larger needle is used (pencil size), we may also use a self-absorbing suture or steri-strip (sterile tape strip) to close the incision. The pressure dressing can be removed 4 hours after the procedure.
- Prior to discharge from the Clinical Research Unit your incision will be checked by medical personnel and you will be given discharge instructions.

Risk and Discomforts:

Potential risks and side effects related to muscle biopsies include:

- An allergic reaction to the soap (betadine) used to clean your leg/arm or the anesthetic Lidocaine (Xylocaine) (numbing medicine). Please inform the staff if you have any allergies
- Burning and pain at the site of the injection from the anesthetic for a few seconds
- Feeling pressure or pain when the needle is inserted into the muscle. There is also the possibility of a small scar at the site
- Some pain in the muscle and area of the incision site after the anesthetic wears off. You can take Tylenol for this, but not aspirin, ibuprofen (Motrin, Advil), naproxen (Naprosyn) or any other non-steroidal anti-inflammatory drugs as these may increase the risk of bleeding. If you have any question about the use of a medicine, please speak with the BLSA Clinical Research Coordinator – Linda Zukley, Ph.D., RN.
- An infection at the biopsy site. If redness, worsening pain, discharge from the wound, or fever occurs, please speak with the BLSA Clinical Research Coordinator – Linda Zukley, Ph.D., RN.
- A small chance of bleeding or bruising

END OF MUSCLE BIOPSY SECTION

4. Skin Biopsy

Researchers frequently need biological (living) samples for their studies on aging. You may be asked to donate a small amount of skin. This study is not designed to provide any direct benefit to you.

This procedure involves more risk than is the usual every-day risk that healthy people face with preventative health care.

Purpose:

Analysis performed on skin specimens may help researchers better understand the affects of aging on the skin. A skin biopsy will be done to obtain small pieces of skin tissue.

Exclusion Criteria:

You cannot be in this study if any of the following apply to you:

- You have a history of increased bleeding due to either a known medical condition or an undiagnosed cause
- You have mild cognitive impairment or dementia diagnosis
- You are taking medicines that may increase the risk of bleeding such as Coumadin, Plavix, or Heparin (blood thinning medications)
- You are taking non-steroidal anti-inflammatory agents (NSAIDs) such as Motrin (Ibuprofen), Advil (Ibuprofen) or Naprosyn (Naproxen) and you are unable to stop taking them 4 days before and 3 days after the procedure
- You are taking more than 81 mg of aspirin a day and you are unable to stop taking it for 4 days before and 3 days after the procedure
- You are allergic to Lidocaine (Xylocaine) or any other local anesthetic or you have had in the past a severe allergic reaction to similar drugs
- You have active infections or chronic skin conditions that would prevent access to the biopsy area and/or any condition that would impair wound healing, such as uncontrolled diabetes or chronic oral steroid use
- You are unable to sign an informed consent and/or are not willing or able to follow the protocol procedures as explained to you by the physician or staff member
- You are pregnant

Procedures:

A skin biopsy involves removing a piece of skin measuring 3-4mm (about the size of a pencil eraser), usually from your inner arm using a small instrument. The skin area will be cleaned with anti-bacterial soap. Local anesthetic (numbing medicine) will either be injected or applied to the skin. After the biopsy site is numb, the tissue will be collected using a biopsy tool (small round blade) and a small dressing will be applied. You will be instructed to keep the area covered for 24 hours.

Risk and Discomforts:

Potential risks and side effects related to skin biopsies include:

- An allergic reaction to the soap (betadine) used to clean your arm or the anesthetic Lidocaine (Xylocaine) (numbing medicine). Please inform the staff if you have any allergies
- Burning and pain at the site of the injection from the anesthetic for a few seconds
- Feeling pressure or pain when the needle is inserted into the skin. There is also the possibility of a small scar at the site
- Some pain at the incision site after the anesthetic wears off. You can take Tylenol for this, but not aspirin, ibuprofen (Motrin, Advil), naproxen (Naprosyn) or any other non-steroidal anti-inflammatory drugs as these may increase the risk of bleeding. If you have any question about the use of a medicine, please speak with the BLSA Clinical Research Coordinator – Linda Zukley, Ph.D., R.N.
- An infection at the biopsy site. If redness, worsening pain, discharge from the wound, or fever occurs, please speak with the BLSA Clinical Research Coordinator – Linda Zukley, Ph.D., R.N.
- A small chance of bleeding or bruising.

END OF SKIN BIOPSY SECTION

END OF BLSA ROUTINE VISIT PROCEDURES AND TESTS

III. BLSA HOME VISIT TESTS, PROCEDURES and RISKS and DISCOMFORTS

To be eligible for a BLSA home visit, you must already be a BLSA participant. The decision to include you in the BLSA home visit cohort is based on your current health and functional status or other reasons that interfere with your participation in the normal routine visit performed at the NIA Clinical Research Unit. This decision is made by the BLSA Principal Investigator. During your home visit, you will be scheduled for all of the tests described unless you are not eligible. It is your option to decline any test. This will not affect your continual participation in the BLSA.

A. History and Physical

You will have a physical examination, including multiple measures of blood pressure, a joint exam and an assessment of balance. You will be asked information about your social demographics, medical history, general health status and physical symptoms, physical function and disability, psychological health and social functioning, lifestyle and health habits and medications. We will also ask a series of questions about your current health, how well you can perform certain activities, and how much time you spend in ordinary day-to-day and recreational activities. Together the general and medical history interviews take about 45 minutes. Sensory function will be evaluated using vision, hearing, touch and orientation tests. We will weigh you and measure various body dimensions, using a tape measure.

Risks and Discomforts: There are no risks associated with these measurements.

B. Clinical and Research Laboratory

You will be contacted to schedule a separate visit for your blood tests. A trained and certified phlebotomist will draw fasting (nothing to eat or drink except plain water for 10 hours) blood samples. About 58 ml (about 4 tablespoons) of blood will be taken from a vein in your arm. The samples will be taken to measure basic clinical blood tests and we will store the remaining samples. The basic clinical blood tests will be reported to you so you can share them with your doctor. The stored samples will be used to measure levels of substances in your blood that may be found particularly in the elderly. Because the clinical relevance of these tests is unknown or not proven, these results will not be given to you.

You will be asked to report if you have any problems giving blood samples, including whether you are a hemophiliac (bleeding problems), are taking blood thinning medications, or have experienced a large volume of blood loss (blood donation, surgical procedure etc.) within the past 3 months.

Risks and Discomforts: You may experience some pain or discomfort at the site of needle entry when taking blood from your veins. There is a risk of bleeding and bruising at the site. There is also a remote chance of fainting or infection.

***Genetic Testing**:* A portion of the blood that you donate may be used to extract DNA and RNA, which are used for specific types of genetic testing. These are molecules that hold your unique genetic information that you inherited from your parents. For example, different genes are responsible for hair and eye color. Recent research suggests that genetics may be associated with a higher or lower risk of developing some diseases. The samples will be used for research purposes to understand the genetic aspects of the aging process and the mechanisms of chronic diseases that frequently occur in older individuals. Most results of these studies contain new, unverified information of unclear significance and, therefore, will not be given to you or your doctor. Your decision to consent, or not to consent, to DNA/ RNA sample collection, analysis and storage has no impact on your eligibility to participate in the BLSA.

Below **is an example** of the choice you will be asked to make on the informed consent concerning DNA/RNA collection

_____*I consent to the DNA collection*

_____*I do NOT consent to the DNA collection*

Your genetic information will be kept confidential to the maximum extent possible. The results of your genetic testing will be kept in a locked and secured manner at the NIH. Genetic information about you will not be revealed to others, including your relatives, without your written permission. Similarly, you will not receive information about other family members. NIA researchers do not plan to provide you with the results of any laboratory investigations involving the use of your samples for genetic testing. These results will, in general, be preliminary. In many cases, additional research may be necessary to determine whether these results are meaningful in terms of health and disease.

A Federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. According to this law, health insurance companies or group health plans cannot request your genetic information or use it to make decisions about your eligibility or premiums; and employers cannot use it in deciding to hire, promote, or fire you or in setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The following link contains details on this policy:
http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf .
You may ask your research team for additional information or a copy of The Genetic Information Nondiscrimination Act of 2008 informational document.

***Stored Samples and Future Studies*:** We would like to store samples of your blood in a deep freeze. All samples collected will create a "bank" of samples, which can then be used in current or future NIA studies concerning the aging process and the causes of diseases. We will study the stored samples to gain a better understanding of the aging process and the major diseases that occur in older people. Future research is likely to include a more focused effort to study genes and the effects on the aging process. Your samples will be stored in secured freezers at a NIA facility. The stored samples will be kept indefinitely, controlled and managed by the Principal Investigator (PI) and the NIA. We will keep the study information private to the extent possible by the law. Strict privacy about the samples will be maintained and your name and identifying information will be removed and we will assign the samples a code. The key to the code will be kept in a separate, secure area. Your samples will be used only for the studies that are in the scope of the BLSA, as explained in this consent form unless you give us permission to use them for other studies. If a future research project arises where your samples could be useful, we ask you to designate as to whether or not your sample can be used. Any future research use will require approval by the institutional review committees.
Below **is an example** of the choice you will be asked to make on the informed consent concerning the collection of samples.

Please initial by the line indicating your wishes.

_____***YES**, I give permission to use my (blood or other fluids, tissues) samples in future research studies under the following conditions:*

_____*These samples may be used for other research projects without contacting me only if the identification code is removed so that the sample can no longer be identified as mine*

_____*These samples may be used for other research projects without contacting me even if the code is left on the samples. I understand that if the samples are coded, they may be able to be traced back to my personally identifiable information and my medical records.*

_____***MAYBE**, I wish to be re-contacted if further studies with my samples are considered. After the study has been explained, I will then decide if I want my samples to be included.*

_____ ***NO**, under no circumstances shall my samples be used for any future studies. My samples should be discarded once the present study is complete.*

If you allow future research on your sample and the research provides information important for your health, we will try to contact you. If you wish to be contacted, please keep the principal investigator for this study, the BLSA Clinical Coordinator or the NIA Administrative staff updated about changes in your address or phone number.

C. Grip Strength

We will measure your grip strength when you squeeze a hand-held device (dynamometer).
Risks and Discomforts: Strength testing may cause muscle fatigue and/or joint pain. These discomforts usually go away when the activity is stopped.

D. Gait and Physical Performance Measures

We will ask you to perform tests of physical function, which include timed walks, rising from a chair, maintaining balance and hand, arm and leg movement.
Risks and Discomforts: During the tests that involve walking there is some risk of falling, which is similar to the risk of falling while performing many activities of daily living.

E. Cognition

You will be given some tests to assess memory, problem solving, learning, language, attention, emotions, feelings, ability to manage finances, take care of household chores and other items relevant to your daily life.
These tests take about 90 minutes. You will be asked to provide the name and contact information of a family member or close friend who can provide information regarding your daily activities. With your approval, we will administer a series of questionnaires both to you and to your designated family member or close friend in order to assess your ability to perform routine daily activities. You may also be contacted by phone between regularly scheduled visits to answer questions relating to medical conditions, medications, or any treatment received for the past year. You will also be asked to answer 11 short, simple questions that will provide information about your memory. If we note significant memory problems or symptoms of depression, we will contact you and suggest that you may need to have a comprehensive clinical evaluation.
Risks and Discomforts: Psychological testing may be tiring, stressful, disturbing, or anxiety producing.

END OF BLSA HOME VISIT PROCEDURES AND TESTS

IV. ADDITIONAL STUDIES

You may be asked to participate in other studies. Some of these studies are conducted in collaboration and co-sponsored by the NIA and the Johns Hopkins Medical Institutions and require a separate consent form. You are free to withdraw from any or all research studies at any time without penalty or loss of any benefit to which they are otherwise entitled.

V. BLSA CONTACT INFORMATION

Principal Investigator: Stephanie Studenski, M.D., MPH	410-350-3964
Medical Officer: Chee Chia, M.D.	410-350-7376
Clinical Research Coordinator: Linda Zukley, Ph.D., RN	410-350-3983
Clinical Research Unit: Monday-Thursday: Anytime Anytime before 4:00pm on Fridays Anytime after 3:00pm on Sundays	410-350-3950 or 410-350-3955

TRANSLATIONAL GERONTOLOGY BRANCH
NATIONAL INSTITUTE ON AGING
NATIONAL INSTITUTES OF HEALTH
DEPARTMENT OF HEALTH AND HUMAN SERVICES

INFORMED CONSENT FOR RESEARCH WITH HUMAN SUBJECTS

Study: THE BALTIMORE LONGITUDINAL STUDY OF AGING - BLSA

Principal Investigator: Stephanie Studenski, M.D., MPH
Associate Investigators: Yuri Agrawal, M.D., Josephine M. Egan, M.D., Luigi Ferrucci, M.D., Ph.D., Gary Gerstenblith, M.D., Edward G. Lakatta, M.D., Richard O'Brien, M.D., Susan Resnick, Ph.D., Eleanor M. Simonsick, Ph.D., Adam Spira, Ph.D., Robert Weiss, M.D.
Medical Advisory Investigator: Chee W. Chia, M.D.

Study Number: 03-AG-0325

INTRODUCTION

We invite you to take part in a research study at the National Institute on Aging (NIA).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled.

You may receive no direct benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIA, or with family, friends or your personal physician or other health professional.

What is the purpose of this study?

The Baltimore Longitudinal Study of Aging (BLSA) is an observational study of the physiological and psychological aspects of human aging and diseases and conditions that increase with age. This study does not provide any treatment. It follows what happens to individual participants as they age. Information from the BLSA may help to define strategies to improve quality of life in old age and prevent and delay loss of independence. By participating in this study you may help us learn why some people tend to develop health problems when they get older. The scientific value of the data collected in the BLSA will be substantially improved by doing analyses comparing the data with that collected in other clinical and epidemiological studies (the study of the incidence, distribution, and risk factors for disease in a population).

Study population

About 10,000 people will take part in this study, currently, participants are recruited and evaluated at the NIA Clinical Research Unit located in Baltimore.

Who can participate in this study?

You may be eligible for this research study if you:

- Are > 20 years of age
- Weigh ≤ 300lbs and/or your body mass index (BMI) is ≤40
- Do not have established genetic diseases
- Are able to perform daily self-care without assistance
- Are able to walk independently for at least 400 meters without assistance and without developing symptoms
- Are able to perform normal activities of daily living (walking or climbing stairs) without shortness of breath
- Do not have substantial cognitive impairment based on mental status screening tests
- Do not have a history of cardiovascular disease (including angina, heart attack, congestive heart failure, cerebro-vascular diseases, uncontrolled hypertension)
- Do not have a history of diabetes (requiring any medical treatment other than diet and exercise)
- Do not have active (any activity in the last 10 years) cancer, except for locally limited basal cell cancer
- Do not have a history of metabolic disease
- Do not have severe hormonal dysfunction (requiring supplementation or chronic drug treatment)
- Do not have a history of neurological diseases or birth defects (other than minor anatomical abnormalities, which do not affect physical and/or cognitive function)
- Do not have a history of kidney or liver disease (associated with reduced kidney or liver function)

- Do not have a history of severe gastrointestinal (G.I.) diseases
- Do not have muscle-skeletal conditions due to diseases or traumas (that cause pathological weakness and/or chronic pain)
- Do not have a history of severe psychiatric conditions (associated with behavioral problems or requiring chronic medical treatment)
- Do not have any medical condition that requires absolute and continuous need for long term treatment with antibiotics, corticosteroids, immunosuppressors, H2 blockers and/or proton pump inhibitors, or pain medications
- Do not have important sensory deficits (legally blind and/or any condition that precludes you from being tested with standard neuropsychological tests or providing informed consent)

If any of these conditions develop while you are on the study, you will remain in the study and participate in the tests that you are able to complete.

Who may not be in this study?

You will not be eligible for this research study if on your **Screening Visit** you have any of the conditions listed above.

What will I be asked to do in this study?

The ***BLSA Informed Consent Booklet*** includes the full description of the study. After reading the booklet, you can ask as many questions as you may have and we will address them before you sign this informed consent.

What will happen if I take part in this study?

The ***BLSA Informed Consent Booklet*** will provide the study procedures in detail and will help you understand your participation in this study. After reading the booklet, the Principal Investigator or approved designee will go over this consent with you and answer any questions you may have. If now or in the future you have or develop a condition that prevents you from fully understanding the study protocol and your role as a participant, we will ask a legal representative or (if a legal representative is not available) a close relative or friend to assist you in the decision. An overall description of a BLSA study visit is also provided in the BLSA DVD video that was sent to you before your arrival on the unit.

SCREENING VISIT

☐ This is a **Screening Visit**

If you are scheduled for a Screening Visit to determine if you are eligible to be a participant in the BLSA, you will receive an abbreviated version of some of the testing listed in this consent. The tests and procedures that you will be involved in will be outlined in the BLSA

Informed Consent Booklet under the heading of **Screening Visit**. The Screening Visit will take 2-3 hours to complete.

For each test, please initial to indicate that you understand the risks involved in each procedure and that you consent or do not consent to performing that test if you are eligible.

Screening Visit Procedures

TEST/PROCEDURE	**ESTIMATED TIME**	**PARTICIPATION STATUS-*YES***	**PARTICIPATION STATUS-*NO***
Clinical Laboratory: Blood and Urine	10 minutes	☐ *I consent to participate _____*	☐ *I do NOT consent to participate _____*
Human Immunodeficiency Virus (HIV) ***Refer to HIV Testing Section of this Informed Consent***	5 minutes	☐ *I consent to HIV testing _____*	☐ *I do NOT consent to HIV testing _____*
Electrocardiogram (EKG)	15 minutes	☐ *I consent to participate _____*	☐ *I do NOT consent to participate _____*
History and Physical	60 minutes	☐ *I consent to participate _____*	☐ *I do NOT consent to participate _____*
Echocardiogram-Optional as determined by Research Staff	30 minutes	☐ *I consent to participate _____*	☐ *I do NOT consent to participate _____*

ROUTINE BLSA VISIT

☐ This is a **Routine BLSA Visit**

If you are already enrolled in the BLSA, you will be scheduled for most, but not necessarily all of the tests described in the booklet during your visit. The visits are scheduled for 3 days. However, there may be circumstances where a shorter or longer visit is indicated. If you are unable to complete your tests, you may be asked to return within 6 months of your visit to complete them. Some information collected during the visit is central to the purpose of the BLSA. Therefore, participation in a Routine BLSA Visit implies that you agree to perform the following CORE tests unless the Principal Investigator waives your participation or you do not meet the eligibility criteria for these tests:

1) Collection of blood samples for laboratory testing
2) Measures of muscle strength
3) Measures of gait, balance and physical performance
4) Basic tests of cognitive function
5) Standardized physical examination
6) Health-related interview

Not all of the tests described will be scheduled during a visit. It is your option to decline any non-core tests.

BLSA CORE Study Procedures

*The details on these procedures are included in the **BLSA Informed Consent Booklet**.*

For each test, please initial to indicate that you understand the risks involved in each procedure and that you consent or do not consent to performing that test if you are eligible.

TABLE 1: BLSA CORE Procedures

TEST/PROCEDURE	ESTIMATED TIME	PARTICIPATION STATUS-*YES*	PARTICIPATION STATUS-*NO*
Clinical Laboratory: Blood and Urine	10 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Research Laboratory: Blood Samples ****Refer to Stored Samples and Future Studies Section of this Informed Consent***	5 minutes	☐ *I consent to participate* ____ ☐ ***I consent to DNA Collection*** _____	☐ *I do NOT consent to participate* _____ ☐ ***I do NOT consent to DNA collection*** _____
Research Laboratory: Urine Samples ****Refer to Stored Samples and Future Studies Section of this Informed Consent***	5 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Gait	60 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Physical Performance Measures (PPM)	10 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Strength-Leg	65 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Strength-Grip	10 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Interview	60 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
History and Physical	2 hours	☐ *I consent to participate* _____	☐ *I do NOT consent to participate* _____
Electrocardiogram (EKG)	10 minutes	☐ *I consent to participate* _____	☐ *I do NOT consent to participate* _____
Cognition Testing (BVRCORE)	1.5 - 3 hours	☐ *I consent to participate* _____	☐ *I do NOT consent to participate* _____

Additional BLSA Study Procedures

Items below are tests/procedures that you may be asked to participate in. Deciding not to participate in these tests/procedures will not impact your participation in the BLSA. The details on these procedures are included in the ***BLSA Informed Consent Booklet****.*

For each test, please initial to indicate that you understand the risks involved in each procedure and that you consent or do not consent to performing that test if you are eligible.

TABLE 2: Additional BLSA Study Procedures

TEST/PROCEDURE	**ESTIMATED TIME**	**PARTICIPATION STATUS-*YES***	**PARTICIPATION STATUS-*NO***
Hearing	30 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Human Immunodeficiency Virus (HIV). ****Refer to HIV Testing Section of this Informed Consent***	5 minutes	☐ ***I consent to HIV testing if indicated***_____	☐ ***I do NOT consent to HIV testing*** _____
2-Hour Oral Glucose Tolerance Test (OGTT)	2 hours	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Microbiome Collection: Saliva, Toenail Clippings, Stool and Skin swabs.	5 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
24 hour urine collection	24 hours	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Resting Metabolic Rate (RMR)	20 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
24-hour Holter	24 hours	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Pulse Wave Velocity Ankle-Brachial Index (ABI)	75 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Echocardiogram & Carotid Sonogram	60 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Treadmill Exercise Test	60 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Pulmonary Function Test (PFT)	10 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____

TABLE 2: Additional BLSA Study Procedures (continued)

TEST/PROCEDURE	**ESTIMATED TIME**	**PARTICIPATION STATUS-*YES***	**PARTICIPATION STATUS-*NO***
Nerve Conduction and Surface Electromyography (EMG)	30 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate ____*
Peripheral Sensitivity	15 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate ____*
Proprioception	15 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate ____*
Taste Bud Photograph	15 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Vestibular Testing	15 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Visual Acuity & Depth Perception	15 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Visual Fields	30 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Strip Meniscometry	5 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Food Frequency Questionnaire (FFQ)	60 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Accelerometry (Actiheart/Watch)	Home-7 days	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Dual-Energy X-ray Absorptiometry (DEXA)	30 minutes	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*
Magnetic Resonance Imaging (MRI) Magnetic Resonance Spectroscopy(MRS) and/or Functional Magnetic Resonance Imaging (fMRI)	2-hours	☐ *I consent to participate ____*	☐ *I do NOT consent to participate _____*

TABLE 3: Optional BLSA Procedures or Studies

TEST/PROCEDURE	ESTIMATED TIME	PARTICIPATION STATUS-*YES*	PARTICIPATION STATUS-*NO*
Accelerometry Doubly Labeled Water (DLW) ***Refer to page 17 of the BLSA Informed Consent Booklet for description and risks***	1.5 hours	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Core Body Temperature ***Refer to page 19 of the BLSA Informed Consent Booklet for description and risks***	24 hours	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Creatine-Muscle Mass ***Refer to page 20 of the BLSA Informed Consent Booklet for description and risks***	72-96 hours	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____

BLSA More Than Minimal Risk Procedures

For each test, please initial to indicate that you understand the risks involved in each procedure and that you consent or do not consent to performing that test if you are eligible.

TABLE 4: BLSA More Than Minimal Risk Procedures

TEST/PROCEDURE	ESTIMATED TIME	PARTICIPATION STATUS-*YES*	PARTICIPATION STATUS-*NO*
Computerized Tomography (CT) ***Refer to page 23 of the BLSA Informed Consent Booklet for description and risks***	60 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Cytapheresis ***Refer to page 24 of the BLSA Informed Consent Booklet for description and risks***	2 hours	☐ *I consent to participate* _____	☐ *I do NOT consent to participate* _____
Muscle Biopsy ***Refer to page 27 of the BLSA Informed Consent Booklet for description and risks***	30 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Skin Biopsy ***Refer to page 29 of the BLSA Informed Consent Booklet for description and risks***	15 minutes	☐ *I consent to participate* _____	☐ *I do NOT consent to participate* _____

HOME VISIT

☐ This is a **Home Visit**

If at any time you become unable to come to the study clinic for a regular follow-up visit you may be offered a Home Visit or a telephone interview aimed at collecting a subset of the information obtained during a regular BLSA visit. The information collected during the Home Visit is also central to the purpose of the BLSA.

The tests and procedures performed in a Home Visit are outlined in the BLSA Informed Consent Booklet under the heading of **Home Visit**.

Items below are tests/procedures that you may be asked to participate in. Deciding not to participate in these tests/procedures will not impact your participation in the BLSA. The details on these procedures are included in the ***BLSA Informed Consent Booklet****.*

For each test, please initial to indicate that you understand the risks involved in each procedure and that you consent or do not consent to performing that test if you are eligible.

Home Visit Procedures

TEST/PROCEDURE	**ESTIMATED TIME**	**PARTICIPATION STATUS-*YES***	**PARTICIPATION STATUS-*NO***
History and Physical	45 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Clinical Laboratory: Blood Samples	5 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Research Laboratory: Blood Samples *****Refer to Stored Samples and Future Studies Section of this Informed Consent***	5 minutes	☐ *I consent to participate* _____ ☐ ***I consent to DNA Collection*** _____	☐ *I do NOT consent to participate* _____ ☐ ***I do NOT consent to DNA collection*** _____
Grip Strength	5 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Gait and Physical Performance Measures (PPM)	10 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____
Cognition	90 -120 minutes	☐ *I consent to participate* ____	☐ *I do NOT consent to participate* _____

HIV, Hepatitis B and C, and SyphilisTesting: As part of this study, we may test you for Hepatitis B and C, syphilis, and human immunodeficiency virus (HIV), the virus that causes AIDS. If you are already enrolled in the BLSA and you become infected with these diseases, you will still be able to participate. If you are on a Screening Visit and your laboratory results indicate that you are HIV positive or that you have Hepatitis B or C and/or syphilis, you will not be able to participate in this research study. If positive, we will tell you what the results mean, how to find care, how to avoid infecting others, how we report newly diagnosed infection, and the importance of informing your partners at possible risk because of your infection. A positive result will be reported to the Maryland Department of Health by the testing Laboratory and by the Research Physician or Nurse Practitioner at the NIA Clinical Research Unit.

*****Stored Samples and Future Studies*:** We would like to store samples of your blood and urine in a deep freeze. We may also ask that you donate samples of skin swabs, saliva, stool, and toenail clippings. All biological samples collected will create a "bank" of samples, which can then be used in current or future NIA studies concerning the aging process and the causal pathways leading to diseases that are highly prevalent and frequent causes of disability in older persons and the development of frailty. We will study the stored biological samples to gain a better understanding of the aging process and the major diseases that occur in older people. Future research is likely to include efforts to identify and characterize genes and gene regulation important for the aging process, and new genes, variations of known genes, or gene regulatory mechanisms affecting the risk of age-related diseases.

Your samples will be stored in secured freezers at a NIA facility. The stored samples will be kept indefinitely, controlled and managed by the Principal Investigator (PI) and the NIA. We will keep the study information private to the extent possible by the law. Strict privacy about the samples will be maintained and your name and identifying information will be removed and we will assign the samples a code. The key to the code will be kept in a separate, secure area. Your samples will be used only for the studies that are in the scope of the BLSA, as explained in this consent form unless you give us permission to use them for other studies.

If a future research project arises where your samples could be useful, we ask you to designate as to whether or not your sample can be used. Any future research use will require approval by the institutional review committees.

Please initial by the line indicating your wishes.

_____YES, I give permission to use my (blood or other fluids, tissues) samples in future research studies under the following conditions:

_____These samples may be used for other research projects without contacting me only if the identification code is removed so that the sample can no longer be identified as mine

_____These samples may be used for other research projects without contacting me even if the code is left on the samples. I understand that if the samples are coded, they may be able to be traced back to my personally identifiable information and my medical records.

_____MAYBE, I wish to be re-contacted if further studies with my samples are considered. After the study has been explained, I will then decide if I want my samples to be included.

_____ NO, under no circumstances shall my samples be used for any future studies. My samples should be discarded once the present study is complete.

If you allow future research on your sample and the research provides information important for your health, we will try to contact you. If you wish to be contacted, please keep the Principal Investigator for this study, the BLSA Clinical Coordinator or the NIA Administrative staff updated about changes in your address or phone number.

What are the possible risks?

If you decide to participate in this study, you should know there may be risks. You should discuss these with the investigator or their designee and/or your regular doctor and you are encouraged to speak with your family and friends about any potential risks before making a decision. The list of potential risks and side effects are described following the description of each test or procedure in the ***BLSA Informed Consent Booklet***.

There may be risks and side effects, other than those listed, that we cannot predict. Many side effects go away shortly after the procedure is stopped, but in some cases side effects can be serious, long lasting and/or life threatening. If you have any unwanted side effects, you should ask the research staff whether there are any medications or other things that may be done to diminish the side effect. For more information about risks and side effects, ask the examiner administering the test or contact the BLSA Coordinator at 410-350-3983.

☐ _____ I have read and received a copy of the ***BLSA Informed Consent Booklet*** and I understand the risks involved in each of the study procedures.

What are the possible benefits?

The study is not designed to provide direct benefits to any participants. We hope the information learned from this study will benefit others in the future.

Do I have an alternative to participating?

The alternative to participating in this study is not to participate. This study does not provide treatment and does not replace any therapy that your own doctor is giving you.

Will I be given results from this study?

We will discuss the results of your clinical laboratory values with you. In addition, as applicable, you will receive copies of your clinical tests such as the blood tests, EKG, DEXA and treadmill. However, these tests do not replace tests prescribed by your primary care physician. A copy of these tests may be provided to your doctor but only after you have provided written release to us. If we find any abnormal results from your tests, you will be notified to seek attention from your primary care physician. The study doctor may recommend that a test be repeated if in their opinion the test result is inconclusive. Because this is a research study only, we cannot provide more in depth testing for diagnostic purposes nor prescribe treatments for you.

Some results from the research-oriented tests may be provided to you but you need to be aware that the results of these tests have limited diagnostic value. Your doctor should decide whether based on the results of these tests you need further medical testing.

Will it cost me anything to participate?

There are no costs to you other than your time and travel. However, if taking part in this study leads to procedures or care not included in the study, it may lead to added costs for you or your insurance company. You will not be charged for the tests and procedures that are part of this research study.

What if I want to stop participating in this study?

Every effort is made to follow all participants through their lifetimes. If you remain interested, we would like to schedule visits at several-year intervals. We are very interested in following you for the rest of your life to observe the changes that occur throughout the aging process. In the event that you are unable or unwilling to return to the study site, we ask permission to contact you at home for follow-up information, including a possible home visit and a telephone interview.

The investigator may decide to take you off this study if it is believed to be in your best interest, you fail to follow instructions, new information becomes known about the safety of the study, or for other reasons the investigator or NIA believes are important. Your participation in the BLSA study may be stopped at any time by the Principal Investigator without your consent if you do not complete the essential core BLSA tests for which you were eligible.

You may stop participating at any time. We ask that you notify the investigator by email or mailed letter of your wishes. The NIA will retain custody of your samples for studies as outlined. You will retain the right to have the sample material made unavailable for future genetic testing and other specific testing at any time by contacting the Principal Investigator of the study. The NIA is the exclusive owner of any data, discoveries or derivative materials from the sample materials and is responsible for the restriction of sample use at your request. If a potential

commercial product is developed from this research project, the NIA will develop patents and promote commercialization of the product as required by law. You will not profit financially from such a product. The data and samples collected in the BLSA can be used by NIA investigators and their collaborators. Part of the data can be published in the public domain but always de-identified so that the data cannot be linked to any specific participant.

OTHER PERTINENT INFORMATION

1. **Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named or identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

   The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. **Policy Regarding Research-Related Injuries.** The BLSA will provide short-term medical care for any injury resulting from your participation in this research study. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the BLSA, NIH, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.
3. **Payments.** The amount of payment to research volunteers is guided by the NIH policies. In general, participants are not paid for taking part in research studies at the NIH. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

   You will not be paid for participating in this study. However, a room on the unit and meals will be provided. If a room is unavailable on the unit, hotel accommodations will be provided at no cost to you.

4. **Conflict of Interest.** The NIH reviews staff researchers at least yearly for conflicts of interest. The following link contains details on this process http://sourcebook.od.nih.gov/ethic-conduct/COI_Guide_121209.pdf You may ask your research team for additional information or a copy of the Protocol Review Guide.

5. **Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Stephanie Studenski, M.D., MPH (410) 350-3964 or Chee W. Chia, M.D. (410) 350-7376. For medical assistance during the evening or on weekends,

call the NIA Security Office at (410) 558-8119 and request that they contact the NIA Physician-on-Call.

If you have any questions about your rights as a research participant, please contact the NIA Protocol Office at (410) 350-3947, NIA Clinical Director at (410) 350-3922, or the NIEHS Office of Human Research Compliance (OHRC) at (919) 541-3852.

6. Consent Document. Please keep a copy of this document in case you want to read it again.

A description of this research study will be available on http://www.clinicaltrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can reach this website at any time.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

_____ _____

Signature of Adult Patient/Legal Representative Date

_____

Print Name

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JANUARY 2, 2014 THROUGH JANUARY 1, 2015.

_____ _____ _____ _____

Signature of Investigator Date Signature of Witness Date

_____ _____

Print Name Print Name