UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study (this "Research Study")?

Nicotinamide riboside as an Enhancer of Exercise Therapy in hypertensive older adults – The NEET Trial

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator: Robert Mankowski, PhD 352-294-5055

Other research staff: Study Coordinator 352-273-9212

4. Who is paying for this Research Study?

The sponsor of this study is the National Institute on Aging. ChromaDex is providing medication (nicotinamide riboside and placebo) for this research study.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved? The purpose of this study is to test if nicotinamide riboside improves an

effect of walking exercise training on cardiovascular function among older adults with elevated blood pressure. Participation from initial screening to closeout visit will consist of 22 visits (including four study visits and 18 exercise visits) and could take up to ten weeks.

b) **What is involved with your participation, and what are the procedures to be followed in the research?** There will be four in-person visits. The visits will vary in length and will include monitoring of overall health, blood draws, questionnaires, ambulatory blood pressure recording, arterial stiffness testing, group assignment, and pill dispensing. You also may be randomly assigned to an exercise group, which meets three times per week.

c) **What are the likely risks or discomforts to you?** Potential risks are those associated with health information privacy, blood pressure measurement, venipuncture, product supplementation, and participation in exercise training and testing.

d) **What are the likely benefits to you or to others from the research?** Benefits may include information about your health and assessments of your cardiovascular status.

e) **What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?** If you do not wish to be in this study, please tell a study team member and do not sign this form.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

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

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

No procedures in this study will be part of your normal clinical care.

7. What will be done only because you are in this Research Study?

An initial telephone screening indicated that you may be eligible to participate in the study. The first study visit (“Screening visit”) will further determine if you are eligible to participate. Should you be eligible to participate in the study, you may be asked (by random assignment) to participate in a structured physical activity program three days a week for 6 weeks. You will be asked to consume the nutritional supplements provided to you for 6 weeks and to return to the clinic for additional assessment visits to monitor your safety and measure study results.

This exercise program includes: center-based walking exercise intervention for 6 weeks. Following a brief warm-up, you will be instructed to walk for 30 minutes at a moderate intensity (able to speak freely during exercise) with encouragement for 10 minutes to be vigorous (unable to speak easily during exercise). Sessions will also include balance training to promote cool-down. You will be introduced to exercises in such a way that they begin with lighter intensity and gradually increase. The progressive nature of the intervention is designed to minimize discomfort and prevent injury.

You will be randomly assigned (like flipping a coin) into one of three groups: exercise and 1,000 mg/day of encapsulated NR (Niagen®), or 1,000 mg/day of NR alone, or exercise and placebo (an identically appearing pill containing no NR). The placebo is a sugar pill with cellulose coating. NR is an alternative form of Vitamin B3 (also known as niacin) and is converted into an enzyme with reported beneficial health effects. You will be asked to consume your provided supplement daily. You will not know if the supplement contains NR or if it is a placebo.

If you wish to participate, your first visit will be to determine your eligibility for the study. Details regarding the tests to be conducted during this screening visit and other study visits (if you are eligible) are described below. Visits will take place at the University of Florida Clinical and Translational Research Building (CTRB), and the physical activity program will take place at the IOA Health Promotion Center.

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

Screening Visit: The screening visit is expected to take 1 to 2 hours. Details of study procedures that will be conducted during this visit are below. The order of these procedures may vary based on the schedules of study staff.

Pregnancy test

Women participants aged 55-62 will be asked to complete a urine pregnancy test.

Questionnaires

You will be asked questions about your medical history and medication use. You will also be asked to complete a short test of memory and reasoning.

Physical Measurements and Exam

We will take measurements of your height, body weight, BMI (calculated in database only), pulse, and blood pressure at the clinic. A medical professional will also give you a physical exam/nursing assessment to determine if it is safe for you to participate in the study. This may also be done at the baseline visit prior to randomization, depending on doctor/nurse availability.

24-hour Blood Pressure Recording

You will receive a blood pressure monitor to wear on your arm for 24 hours. This monitor will measure your blood pressure every 20 minutes during the day (from 7:00 AM until 10:00 PM) and every 60 minutes overnight (10:00 PM until 7:00 AM). We will give you a pre-paid envelope to return this monitor to us after the 24-hour collection has completed; this measure will be used to determine eligibility.

Medical records release authorization

The study team will ask you to sign the Medical Records Release Authorization. We would like to have this form signed by you if we need to request your health records if you are hospitalized or any health problems worsen and the study team has to report details of these events to regulatory authorities (Institutional Review Board, the study sponsor, etc.) to ensure your safety during participation in this research study. This form will be signed only once – during the Screening Visit. Health information collected using this release will be used only for any health events that occur during your participation in this research.

At the end of this visit, the study team will determine if you can participate in this study. If you are not eligible, this will be your only study visit.

Demographics form

We will collect your background information such as your gender, ethnicity, race, date of birth, age, education level, contact information, and emergency contact.

Baseline Visit: Should you be eligible for the study; you will be asked to return to the clinic for the baseline study visit. This visit is expected to take 2 to 3 hours and will include:

Blood Draw

You will be asked to fast before your appointment because blood will be collected during this visit. We will provide a snack for you before you continue with your visit procedures, after we draw your blood. We will collect approximately 2 tablespoons of blood from a small vein in your arm or hand. The purpose of this blood draw is to determine levels of certain compounds in your blood that will help us determine some details of your health and study eligibility.

We will also collect urine samples at this visit, to be analyzed after data collection is complete. The first urine sample will be collected between 8 am to 11 am when you come in the morning to participate in the in-person visit. Then, the study coordinator will provide you with the urine sample collection cup to collect the second urine sample between 5 pm to 8 pm. The study coordinators can help transport the second urine sample from your location to the research building or, if you prefer, you could bring the second urine sample back to the research building and hand it to the study coordinator.

Physical measurements

We will take measurements of your body weight, pulse, and blood pressure at the clinic. If not already completed at the Screening Visit, a medical professional will also perform a physical exam/nursing assessment prior to randomization to determine if it is safe for you to participate in the study.

Questionnaires

You will be asked questions about your perception of your physical abilities. We will also ask you if you have had any changes in your health since your last visit.

Physical Performance Tests

You will be asked to complete tests of your physical ability. You will be asked to walk as far as you can for a duration of 6 minutes

24-hour Blood Pressure Recording

You will receive a blood pressure monitor to wear on your arm for 24 hours. This monitor will measure your blood pressure every 20 minutes during the day (from 7:00 AM until 10:00 PM) and every 60 minutes overnight (10:00 PM until 7:00 AM). We will give you a pre-paid envelope to return this monitor to us after the 24-hour collection has completed.

Arterial Stiffness Measurement

We will measure the flexibility of your arteries by measuring the pulse in your neck and the pulse in your thigh at the same time. We will measure the distance between these two points to calculate the flexibility of your arteries.

Randomization and Study Supplement Distribution

You will be randomized to one of three groups at the end of the Baseline Visit (Exercise plus NR study supplement; Exercise plus Placebo; NR study supplement alone). You will be provided with your nutritional supplement (NR or placebo) to be taken orally until your next appointment. You will be sent home with a 1-month supply of study capsules. You will be asked to take a dose of the capsules twice a day (2 pills in the morning and 2 pills in the evening). The instructions will be clearly marked on the pill container. If you forget to take a dose, you will be instructed to skip that dose and take your next regularly schedule dose.

Additionally, you will receive a Supplement Intake Diary as well as instructions for completing it. We will ask you to return this at future visits.

Collection of AEs and update medication changes

3 Week Visit: This visit is expected to take 1 to 2 hours and will include:

- Measurement of pulse, blood pressure and body weight at the clinic
- Collection of another blood sample after you have fasted the evening before
- Collection of urine samples (same as the procedure at the baseline visit)

- Questions about any adverse experiences or changes in your health since last visit
- Return any unused study supplement (including empty bottles).
- You will be provided with your nutritional supplement (NR or placebo) to take until your next appointment
- We will collect the diary you completed after the last visit and dispense a new one to complete.
- 24-Hour BP recording: As in previous visits, you will receive a blood pressure monitor to wear on your arm for 24 hours. This monitor will measure your blood pressure every 20 minutes during the day (from 7:00 AM until 10:00 PM) and every 60 minutes overnight (10:00 PM until 7:00 AM). We will give you a pre-paid envelope to return this monitor to us after the 24-hour collection has completed.
- We will collect adverse events and update medication changes.

6 Week (close-out) Visit: This will be the final study visit. It is expected to take 2 to 3 hours and will include:

- Measurement of pulse, blood pressure and body weight at the clinic
- Collection of another blood sample after you have fasted the evening before
- Collection of another urine samples (same as the procedure at the baseline visit)
- Questions about any adverse experiences or changes in your health since last visit
- Questions about your perception of your physical abilities (as during Baseline Visit)
- Perform tests of physical performance (as during Baseline Visit)
- 24-hour BP recording: As in previous visits, you will receive a blood pressure monitor to wear on your arm for 24 hours. This monitor will measure your blood pressure every 20 minutes during the day (from 7:00 AM until 10:00 PM) and every 60 minutes overnight (10:00 PM until 7:00 AM). We will give you a pre-paid envelope to return this monitor to us after the 24-hour collection has completed.
- Arterial Stiffness Measurement (as done at Baseline Visit)
- Return any unused study supplement (including empty bottles).
- We will collect the diary you completed after your previous visit.
- We will collect adverse events and update medication changes.

If you have any questions now or at any time during the study, please contact one of the research team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect

- Name

- Social Security Number for compensation purposes
- Contact Information
- Date of Birth
- Emergency Contact Information
- Laboratory results
- Information about your health and medical history
- Information about medication you are taking
- Information about your vital signs and body measurements
- Information about your physical abilities
- Information about your mental abilities

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (listed in Question 4 of this form).
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections.
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state, and local health departments.
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

You may be in this study for up to 10 weeks.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

We expect to screen about 315 participants in order to reach a goal of 54 participants to complete the study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

Risks of NR Supplementation

Previous clinical trials on NR supplementation have shown side effects among older adults to include nausea, tiredness, headaches, diarrhea and stomach discomfort. We expect these side effects to be mild and the chance of experiencing these side effects is low.

Risks of Testing Mobility Performance, walking exercise sessions and Other Walking Tasks

There is a risk of falling during walking and balance tests. Falls can lead to injuries ranging from minor to serious, such as damage to joints and muscles (for example, spraining an ankle). It is also possible that you could experience fatigue, soreness, and/or discomfort due to physical activity during this study. These are unlikely to be worse than what you would experience due to increased physical activity outside of the study. Some types of discomfort are normal responses to exercise and most discomfort will generally disappear within a matter of days.

Having high blood pressure increases the risk of a cardiac event, like a heart attack or stroke. While acute exercise does further increase blood pressure temporarily, it is considered a treatment that over time can lower resting blood pressure. We will monitor your blood pressure closely and ask how you're feeling at the exercise sessions for your safety. We will measure your resting blood pressure prior to each exercise session and prior to physical function tasks at clinic visits; if your blood pressure on the day of the exercise session or clinic visit is >200/110, we will not complete the exercise session or physical function tasks that day and we will ask you to follow-up with your primary care physician.

Risks of blood pressure testing

The risks of placing a blood pressure cuff on a participant are that it may cause pinching, slight bruising, discomfort, or skin irritation from the cuff.

Risks of a blood draw

The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure.

Questionnaires about your health and lifestyle

Some participants may feel uncomfortable with the number or detail of questions we ask about your health and lifestyle. You are not required to answer any question. However, if we are unable to obtain sufficient information to assess enrollment criteria and satisfy our primary study objectives, then you might not be able to continue in the study.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

Benefits include information about your health and assessments of your cardiovascular status. You will be encouraged to communicate the results from the study to your primary care provider. Moreover, if you are randomly assigned to one of the exercise groups, you will receive supervised exercise training and instruction about how to maintain exercise habits at home. If you are randomly assigned to the NR alone group, you may experience potential benefits of the supplementation.

Potential benefits of NR alone may be lowering systolic blood pressure and improving the flexibility of your arteries. The combination of NR and exercise may have better effects than exercise or NR alone on systolic blood pressure reduction and improving the flexibility of your arteries.

13b. How could others possibly benefit from this Research Study?

Information gained from participation in this study may help to provide doctors with new information for recommending exercise treatments. The study may also provide scientists and physicians with new knowledge about the use of nicotinamide riboside and potential beneficial effects when combined with exercise.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

14. What other choices do you have if you do not want to be in this study?

If you do not want to be in this study do not sign this form. If you have already signed this form, please notify the Principal Investigator listed in question 3 above. If you do not want to be in this study, the alternative choice is simply to not participate.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- If the Principal Investigator or study physician decide that your participation in
- the study could be harmful to you
- If you develop a medical condition or need treatment not allowed in the study
- If you do not follow study instructions
- If the study is cancelled
- Other various administrative reasons

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

Study Services

The Sponsor will pay for or provide all study services/activities required as part of your participation in this study. There will be no cost to you other than incidental costs associated with traveling to the study site (e.g., cost of gas) or purchasing food before or after your visit. If you receive a medical bill related to this study, please contact Robert Mankowski, PhD 352-294-5055 or Study Coordinator 352-273-9212.

Items/Services Not Paid for by the Sponsor

Any medical services you receive would have been provided to you even if you were not in this study. These services will be billed to you or your insurance company in the usual manner. You will be responsible for paying any deductible, co-insurance, co-payments, for those services, and for any non-covered or out-of-network services.

17. Will you be paid for taking part in this Research Study?

Yes, you will be compensated up to $380 in the form of gift cards. A gift card in the amount of $75 will be given at the completion of the baseline assessment visit and the 6-week closeout visit. You will be given a $50 gift card at the completion of the 3-week follow-up visit. You will be compensated at a rate of $10 per class attended for attending the study exercise classes. You will receive compensation for attending the study exercise classes at the 3-week and 6-week closeout visit. You will not be compensated for the screening visit.

If you are paid more than $199 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to nonresident aliens must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payment contact the study coordinator.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the

Professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact the study physician at (412) 607-3914 if you experience an injury or have questions about any discomforts that you experience while participating in this study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization | Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing | Date