INFORMED CONSENT DOCUMENT
Older group

Project Title: **Blood pressure responsiveness in older adults following dietary nitrate supplementation**

Principal Investigator: Darren Casey

Research Team Contact: **Darren P. Casey, PhD**
(319) 384-1009

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you are a healthy person between the ages of 60 and 85.

The purpose of this research study is to examine the effects of dietary nitrate supplementation (beetroot juice) on blood pressure responsiveness in older adults.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 3 months. You will be asked to complete a total of 4 separate visits. Each visit will have the same tests and will last up to 3.5 hours.

WHAT WILL HAPPEN DURING THIS STUDY?

You will arrive at Dr. Casey's laboratory after fasting overnight (not eating or drinking fluids other than water). Prior to arrival at the laboratory for each study day, you will be emailed an SF-36 Questionnaire and asked to have this filled out before arriving.

You will have 8 small adhesive patches placed on your chest and abdominal areas to measure your heart rate using an electrocardiogram throughout the study. Your blood pressure will also be monitored throughout the study by a temporary device attached on the end of your finger (Nexfin). Your oxygen saturation levels will be monitored throughout a portion of the study by a temporary device clipped on the end of your finger. You will then be asked to lie down on your back on an exam table and rest. During this study, you will take part in the experimental procedures outlined below.

- Venous blood draw in a vein at the elbow: About 15-20 cc (3-4 teaspoons) of blood will be drawn at the start of the study through a vein at the elbow. The skin will be cleaned before the needle is inserted.

- Arterial stiffness measurement: A small, pen-like device that measures blood vessel pressure will be placed on the skin over an artery in your wrist, neck, and groin.

- Breathing through a special face mask: You will breathe normal air through a mask while measurements of heart rate, respiratory rate, and tidal volume are taken.

- Breathing air with a low oxygen content: For two separate periods of up to 6 minutes each, you will be asked to breathe air that has a low oxygen content (roughly half that of normal air) through a special face mask. This will increase your rate of breathing and heart rate and is similar to what happens when you travel to higher altitude (15,000 feet elevation).

- Isometric forearm muscle contraction: You will be asked to squeeze a handgrip device for 2 minutes. With 3 seconds remaining you will feel an occlusion cuff (placed on the upper arm) inflate to a high pressure (240 mmHg) and remain inflated for 2 minutes and 15 seconds during which time you will lie relaxed face up.

- Rhythmic forearm muscle contractions: You will be asked to repeatedly squeeze a handgrip device at a mild and moderate weight (approximately 9 and 18 pounds). Each exercise trial will last 4 minutes.

- Cold pressor test: Heart rate and blood pressure will be measured during a 2-minute period of cold exposure by placing your hand in ice water.

- Doppler ultrasound: Will be used to measure blood flow in the elbow artery.

Nitrate consumption: You will be asked to consume a nitrate rich supplement (BeetElite, Neogenis) or placebo for 4 weeks. Both drinks will taste the same. You will have the opportunity to have both

drinks during the study, and the order that you receive the drink will be randomized. That means that whichever study drink you receive will be determined purely by chance, like flipping a coin. You will have a 50/50 chance of receiving the nitrate rich supplement first. You will be asked to consume one packet (10g) of beetroot powder mixed with 4 ounces of water once a day. Consumption of each beetroot juice will last for 4 weeks with a 4 week washout period (no juice) in between. All subjects will consume both beetroot juice with nitrate and placebo during the course of the study. You will not know which juice you are receiving in each 4 week period. The following is a timeline of the study protocol.

Visit	**Time**
Experimental Day #1	3.5 hours
Consumption of juice (either nitrate rich or placebo; once a day)	4 weeks
Experimental Day #2	3.5 hours
Washout period	4 weeks
Experimental Day #3	3.5 hours
Consumption of juice (either nitrate rich or placebo; once a day)	4 weeks
Experimental Day #4	3.5 hours

Visits 2, 3, and 4 will consist of the same testing performed on visit 1 and last up to 3.5 hours each. The procedures outlined above are commonly used in the lab.

We plan to keep your initial screening form to possibly contact you for future studies. Agreeing to be in the current study does not obligate you to participate in one of your future studies. A separate Consent Document would be signed for any future studies.

At the end of each study day, you will be provided the option to receive a snack, juice/water, or a meal voucher at the UIHC cafeteria.

Blood/Data Storage for Future Use

As part of this study, we are obtaining blood samples from you. We would like to study your blood samples in the future, after this study is over.

The tests we might want to use to study your blood samples may not even exist at this time. Therefore, we are asking for your permission to store your blood samples so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding blood vessel function, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your blood samples might be used to develop products or tests that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

If you agree now to future use of your blood samples, but decide in the future that you would like to have it removed from future research, you should contact **Darren P. Casey at (319) 384-1009**. However, if some research with your blood samples has already been completed, the information from that research may still be used.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

1. Insertion of a small needle into the ante-cubital vein at the elbow: The most common complications of inserting a small needle in the arm is a small bruise and pain at the site of needle insertion which may last several days.

2. Blood withdrawal: Risks associated with withdrawal of 3-4 teaspoons of blood from healthy people may include feeling light headed or nauseous and/or fainting.

3. Forearm muscle contractions: Handgrip exercise is a commonly used experimental test. There are no major risks associated with this procedure. However, isometric and rhythmic handgrip exercise can lead to minor fatigue in the forearm and soreness for a day or two.

4. Breathing air with a low oxygen content: During breathing of air with a low oxygen content, it is possible you will feel distress, anxiety, hyperventilate (breathe very quickly), or feel lightheaded. These symptoms resolve rapidly when you return to breathing room air.

5. Doppler Ultrasound: There are no risks or harmful effects from Doppler Ultrasound.

6. Applanation tonometry and blood pressure measurements. There are no risks or harmful effects from applanation tonometry or blood pressure measurements. However, inflation of the cuff might cause discomfort for longer time than what is experienced when a doctor or nurse takes your blood pressure.

7. Cold pressor testing: The cold pressor test may cause some discomfort in your hand, but you can discontinue the trial if you feel unusual or extreme discomfort. This discomfort lasts only as long as your hand remains immersed in the ice water.

8. ECG (Electrocardiogram): There is the possibility of an allergic reaction to the ECG electrodes.

9. Consumption of beetroot juice: There is no risk associated with consumption of beetroot juice. However, red urine or stools for 1-2 days following consumption have been reported.

10. A loss of confidentiality of data is also a risk associated with the study.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because of the potential information gained related to how blood pressure responsiveness is controlled after dietary nitrate supplementation.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study. You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

If you finish the study, you will receive $300.00. This money is for the time you spend in this study. If you start but stop before finishing the study, you will receive $15.00 for each hour of participation.

WHO IS FUNDING THIS STUDY?

Neogenis is funding this research study. This means that the University of Iowa is receiving payments from Neogenis to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from Neogenis for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves

research studies)

To help protect your confidentiality, we will keep all hard copy documents in the principal investigator's laboratory in locked cabinets. Your confidentiality will be assured by coding of all subjects' identities, with that coding only accessible to the investigators. To accomplish this we will use study ID numbers to de-identify study documents and data. All electronic files will be stored in a secure database which is password protected under a secure server space allocated for only the study team. All blood samples will be coded with study ID numbers and stored in a secured freezer. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

"A description of this clinical trial 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 search this website at any time."

The University of Iowa Hospitals and Clinics generally requires that we document in your medical record chart that you are participating in this study. The information included in the chart will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you decide to leave the study early, we will ask you to notify the principal investigator Darren Casey at (319) 384-1009.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we will promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because

- in our judgment it is in your best clinical interest not to continue,
- you do not follow the study procedures.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Darren P. Casey at (319) 384-1009. If you experience a research-related injury, please contact: Darren P. Casey at (319) 384-1009.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

Do not sign this form if today's date is on or after EXPIRATION DATE: 07/21/17.

_____ _____
(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)