

Protocol Title: Study of Urate Elevation in ALS – Phase II (SURE-ALS2)

Principal Investigator: Sabrina Paganoni, MD, PhD

Site Investigator:

NEALS study site:

Description of Subject Population: Amyotrophic Lateral Sclerosis (ALS)

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called “subjects.” This term will be used throughout this consent form.

[Name of site] is **[description of site]**. This research is being conducted at academic centers that are part of the Northeast ALS (NEALS) Consortium.

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

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.

Why is this research study being done?

We are doing this research study to find out if inosine is safe to take without causing too many side effects in people with amyotrophic lateral sclerosis (ALS).

Amyotrophic lateral sclerosis (ALS) is a degenerative disorder of the nerves controlling movement (“motor neurons”). ALS causes muscles to become weak and thin, which leads to paralysis (the loss of the ability to move). Oxidative damage to the motor neurons, similar to rust destroying the molecular machinery that runs them, is one of the proposed mechanisms (ways) that causes their degeneration (worsening) and resulting paralysis in ALS. It is possible that drugs that reduce oxidative stress may be beneficial in ALS.

Inosine is as an over-the-counter supplement. Taking inosine causes an increase in the blood levels of urate (uric acid). Urate is a natural antioxidant present in the body that may help counteract (cancel out) oxidative stress. The U.S. Food and Drug Administration (FDA) has not approved inosine to treat ALS.

We are asking you to take part in this research study because you have ALS. About 60 subjects with ALS will take part in this research study at 3 Northeast ALS Centers in the United States. About **[INSERT NUMBER]** subjects with ALS will take part in the study at **[INSERT SITE NAME]**.

The study is being paid for by the Salah Foundation and the MGH cure ALS Fund.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example, list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

How long will I take part in this research study?

It will take you about 27 weeks to complete this research study.

During this time, we will ask you to make at least 4 in-person study visits. We will call you approximately 15 times during the study to remind you of your schedule and to let you know what your urate (uric acid) levels are. We may adjust the dose of inosine/placebo based on the urate (uric acid) levels. Each phone call will last about 15 minutes.

What will happen in this research study?

This is a double-blind, placebo controlled study where the subjects are selected by chance (like tossing a coin) to be in 1 of 2 groups – this is called ‘randomization’. “Double-blind” means that neither you, the study doctor, nor any of the study staff will know which drug you are receiving, although your study doctor can find out in case of an emergency. The placebo looks and tastes exactly like the study drug, but contains no study drug.

You have a 2 in 3 chance of being assigned to the treatment group and a 1 in 3 chance of being assigned to the placebo group.

- Group 1- Inosine (study drug)
- Group 2 – Placebo

You will take your study drug (capsule) orally (by mouth) twice a day, once in the morning and once at night for the first 2 weeks. Your study drug dose will then be adjusted based on your urate (uric acid levels) during the rest of the study.

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

MOBILE APPLICATION

This study will utilize a mobile application to collect information on tasks that you perform while using your smartphone. You will be required to have and use a smartphone to participate in this study.

The mobile application will primarily collect two different types of data - active data and background data. Active data is information that will be collected when you complete certain tasks using the smartphone app like answering surveys, recording your voice, and completing exercises using your finger. Background data is information that is collected from your smartphone when you are not using the app like how often and with what speed do you type, how long and frequent are phone calls made, when your phone is off or on, etc. We will not be collecting data about the actual content of your phone call conversations, multimedia messages, text messages, contacts, web activity or emails.

Data that is collected is automatically secured and encrypted before it is transmitted to an online HIPAA-compliant Amazon Data Storage account. Once your data reaches the online storage account, it is further secured by another layer of security. The Amazon S3 Data Storage is where encrypted information relayed from your smartphone will be stored and accessed by research teams. Your encrypted information will only be accessed after your participation in the study has ended. The data is sent only through a Wi-Fi connection and not through your smartphone's data plan.

Passive Data Collection – refers to data that is collected when you are not using the app.

Accelerometer - The app records information about your phone's movement when the phone is on. This information can be used to estimate how long you sat still, when you were walking, how many steps you took while walking, and other general activity levels.

GPS – The app records information regarding your smartphone's location and the accuracy of such information. The GPS data will be used to calculate movement based on the relative

differences between coordinates. GPS coordinates are recorded, but not on a map. It cannot identify how you travelled. This data will only be transmitted when you are connected to Wi-Fi. We will not track your location in real time. It is not possible to completely remove information about where and when you have travelled. The app does not record GPS continuously, only intermittently.

Phone/Screen Usage – The app records when you turn on or off your smartphone’s screen, when you turn off or reboot your smartphone, and when you plug in or unplug your smartphone. Tracking when the screen is on provides some information for when you are using your smartphone.

Nearby Wi-Fi Routers – The app records a list of all Wi-Fi routers with which your smartphone can communicate, and the signal strength of each of those routers. This serves to provide information regarding your relative location. When your smartphone has a very strong, clear signal from a Wi-Fi router, it is probably in the same room as that router.

Phone Call Log – The app records specific data on all incoming, outgoing, and missed calls to and from your smartphone. It does not record the audio or content of the calls. It also does not record the identity or actual phone number of the person called. It records the time of each call and the length of the call.

Text Message Log – The app records specific information on the text messages sent from and received by your phone. It does not record the content of text messages, and does not record the phone number of the person called. It records the time each message was sent or received and the length of the message (in number of characters).

Active Data Collection – refers to data that is collected when you are using the app.

The app will remind you to take a questionnaire, voice recording, or virtual slider exercise by making a notification appear on your smartphone’s screen. The app will record how long it takes to answer questions and how long it takes to complete each of the following items:

Survey Data – the app will ask you to fill out weekly surveys. Each survey appears with a notification on your smartphone.

ALSFRS-R Questionnaire – the app asks you to fill out a weekly 12-question questionnaire. Each questionnaire appears with a notification.

Voice Recordings –Once a week, the app may ask you to make voice recordings. Your voice will be saved as an audio file so that researchers can analyze it.

SCREENING VISIT

At this visit, we will do some tests and procedures to see if you qualify to take part in this research study. The study doctor will review the results of these tests and procedures. If you don't qualify, the study doctor will tell you why.

Length of time = about 1 hour

At this visit, we will:

- Obtain written informed consent
- Review eligibility criteria
- Review your medical history and demographic information (for example, your race and gender)
- Review your ALS diagnosis history
- Perform the Slow Vital Capacity (SVC)
- Perform physical examination, including height, weight and vital signs
- Perform neurological examination
- Collect blood for screening labs and check the level of urate (uric acid) in your body (approximately 3 tablespoons)
- Ask about medications and supplements you are currently taking and/or any therapies you are receiving
- Review side effects and changes in your health after signing the consent form

NOTE: The study doctor or study coordinator will call you about 1-5 days after this visit to tell you if you are eligible for this study. If you are eligible, you will be asked to return for a Baseline Visit within 21 days of the Screening Visit.

BASELINE VISIT

Length of time = about 2 hours

At this visit, we will:

- Review eligibility criteria
- Review the medications and supplements you are currently taking and/or any new therapies you are receiving
- Ask you to complete the ALSFRS-R questionnaire
- Complete the suicide questionnaire (a questionnaire about suicidal thinking and behavior)

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- Collect a urine sample for urinalysis
 - Draw blood samples for routine safety lab test and to check the level of urate (uric acid) in your body
 - Ask you about changes in your health condition since your last visit
 - Give you the first dose of study drug/placebo in the office. We will observe you for 10 minutes after you take the drug to monitor for immediate drug reaction.
 - Download, install and briefly orient you to the mobile application

NOTE: You may receive a phone call within 5 days of this visit and you may be asked to take alkalization therapy (with Potassium Citrate) if the results of the urinalysis test show that you have acidic urine. The alkalization therapy will help to make your urine less acidic, reducing your risk of kidney stones. If your urinalysis test comes back normal, you will not be asked to take alkalization therapy.

Taking the Study Drug

We will give you a supply of study drug/placebo to take home with you at the Baseline Visit to last until Week 12. We will make sure you know how to take the study drug.

You will take the study drug/placebo by mouth with or without food for the entire study. Study staff will give you specific instructions on how many capsules of study drug/placebo to take from the time of your screening visit to your next visit.

From Week 3 to Week 20, the dose of study drug/placebo will be adjusted based on the results of the blood tests that will be performed at Week 3, Week 6, Week 9, Week 12 and Week 16. You will receive a phone call within 5 business days of your appointment and may be instructed to increase (take more), decrease (take less) or maintain (keep the same) the dose of study drug/placebo.

It is important for you to follow our instructions about how to take the study drug. Bring any unused study drug and empty bottles with you to the Week 12 and Week 20 study visits.

Your Study Drug Diary

We will give you a study diary to fill out at home each day. You will write down the date and time you take the study drug/placebo and how much study drug/placebo you take. Bring this diary with you to the Week 12 and Week 20 visits.

WEEK 3, 6, 9 AND 16 VISITS

Length of time = about 15 minutes

In between the study visits, we will ask you to go to a local Quest Diagnostics Laboratory for blood draws. You will receive a written schedule that will tell you exactly when to go to the lab

for blood draws. These blood draws will allow us to monitor the levels of urate (uric acid) in your blood. We need to do so because taking inosine results in elevated urate (uric acid) levels and we want to make sure that the dose of inosine is the right one for you and results in the right levels of urate (uric acid). We will give you the exact address and phone number of the closest Quest facility where your blood draw will be performed.

TELEPHONE CALLS

Length of time = 15 minutes

We will call you within 5 days of your blood draw to discuss the following:

- Review results of the urate (uric acid) level test
- Tell you to increase (take more), decrease (take less) or maintain (keep the same) your dose of study drug/placebo
- Review the medications and supplements you are currently taking and/or any new therapies you are receiving
- Ask you about changes in your health condition since your last visit
- Discuss initiation of alkalization therapy (if applicable)
- Review your study diary

WEEK 12 Visit

Length of time = about 2 hours

At this visit, we will:

- Ask you about changes in your health condition since your last visit
- Review the medications you are currently taking and/or any new therapies you are receiving
- Ask you to complete the ALSFRS-R questionnaire
- Complete the suicide questionnaire (a questionnaire about suicidal thinking and behavior)
- Collect weight and vital signs
- Perform the Slow Vital Capacity (SVC)
- Collect a urine sample for urinalysis
- Draw blood samples for routine safety lab test and to check the level of urate (uric acid) in your body (about 3 tablespoons)
- Review your study diary
- Perform study drug accountability and collect all unused study drug and empty containers
- Dispense enough study drug/placebo to last until Week 20

NOTE: You will receive a phone call within 5 days of this visit with instructions to increase (take more), decrease (take less) or maintain (keep the same) your study drug/placebo dose. In addition, you may be asked to take alkalization therapy (with Potassium Citrate) if the results of the urinalysis test show that you have acidic urine. The alkalization therapy will help to

make your urine less acidic, reducing your risk of kidney stones. If your urinalysis test comes back normal, you will not be asked to take alkalization therapy.

WEEK 20 VISIT

Length of time = about 2 hours

At this visit, we will:

- Ask you about changes in your health condition since your last visit
- Review the medications you are currently taking and/or any new therapies you are receiving
- Ask you to complete the ALSFRS-R questionnaire
- Complete the suicide questionnaire (a questionnaire about suicidal thinking and behavior)
- Perform a physical exam, including weight and vital signs
- Perform a neurological examination
- Perform the Slow Vital Capacity (SVC)
- Collect a urine sample for urinalysis
- Draw blood samples for routine safety lab test and to check the level of urate (uric acid) in your body (about 3 tablespoons)
- Review your study diary
- Perform study drug accountability and collect all unused study drug and empty containers
- Assist you with the uninstallation and removal of the mobile application

TELEPHONE CALL AT WEEK 24

Length of time = about 15 minutes

During this call we will:

- Ask you about changes in your health condition since your last visit
- Review the medications you are currently taking and/or any new therapies you are receiving
- Ask you to complete the ALSFRS-R questionnaire

After You Complete the Study

After you complete the study, we will refer you back to your own doctor for your ongoing medical care.

IF YOU WANT TO STOP STUDY DRUG

If you wish to stop the study drug, you should tell Dr. [INSERT SITE INVESTIGATOR NAME] so that [he/she] may plan for your continued medical care. [INSERT SITE INVESTIGATOR NAME] may decide to stop your study drug or participation in the study,

without your permission if [he/she] feels that you cannot follow the study plan or if your health is in question. Side effects from the study drug are an example of a reason for the study doctor to stop the study drug.

Also, the study doctor may take you out of the study without your permission. This may happen because:

- The study doctor thinks it is best for you to stop taking the study drug
- You can't make the required study visits
- The Sponsor decides to stop the study
- We stop doing the study for other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to come in for a final study visit as described above.

IF YOU STOP THE STUDY EARLY

If you stop study drug early or stop participating in the study before the end of the study, you will be asked to come in for a final safety visit and receive a phone call about 28 days after your last dose of study drug. If you stop using the mobile application, we will ask you that you follow certain procedures to un-install it.

FINAL SAFETY VISIT

Length of time = 2 hours

At this visit, we will:

- Ask you about changes in your health condition since your last visit
- Review the medications you are currently taking and/or any new therapies you are receiving
- Ask you to complete the ALSFRS-R questionnaire
- Complete the suicide questionnaire (a questionnaire about suicidal thinking and behavior)
- Perform a physical exam, including weight and vital signs
- Perform a neurological examination
- Perform the Slow Vital Capacity (SVC)
- Collect a urine sample for urinalysis
- Draw blood samples for routine safety lab test and to check the level of urate (uric acid) in your body (about 3 tablespoons)
- Review your study diary
- Perform study drug accountability and collect all unused study drug and empty containers
- Assist you with the un-installation of the mobile application

FINAL TELEPHONE CALL

Length of time = 15 minutes

We will discuss the following:

- Ask you about changes in your health condition since your last visit
- Review the medications you are currently taking and/or any new therapies you are receiving
- Ask you to complete the ALSFRS-R questionnaire

What are the risks and possible discomforts from being in this research study?

Risks of Taking Inosine

Taking inosine may cause you to have one or more of the side effects listed below. These side effects are due to high urate (uric acid) levels that occur as a result of taking inosine.

Serious side effects:

- Gout (pain and swelling in some joints)
- Kidney stones (pain in the back or belly, pain on urination, red or brown urine)

Acidic urine can increase the risk of uric acid kidney stone formation. For this reason, we will check the acidity of your urine prior to taking initial dose of study drug at Baseline and at Week 12. If urine tests show that you have acidic urine, we will encourage you to drink lots of water and will prescribe the medication potassium citrate, which has an antacid effect.

High urate (uric acid) levels have also been found in people with high blood pressure and history of heart attack and stroke. However, we don't know if high urate (uric acid) caused these problems. There may be other risks that are currently unknown.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risk of Potassium Citrate [Alkalinization Therapy]

Potassium citrate will only be prescribed if you have acid urine. It may help to reduce your risk of developing uric acid kidney stone. If you do not have acidic urine, you will not be asked to take potassium citrate.

Possible side effects of potassium citrate include nausea, vomiting, diarrhea, stomach pain or upset and rarely gastrointestinal bleeding. Call a doctor at once if tarry (black colored) stools or other signs of gastrointestinal bleeding are noticed.

Potassium citrate is available over-the-counter and works by raising urinary pH. In the unlikely event that you are allergic to or unable to take potassium citrate, another alkalinizing medication will be prescribed based on your individual needs. The risks of this medication would be discussed with you in detail if it were prescribed.

If you are started on potassium citrate you will have extra blood and urine tests. These blood tests will help us check for too much potassium in your blood, for any signs of kidney disease, and for too few red blood cells (anemia). The urine tests will tell us how acidic your urine is, and we may ask you to perform some of these extra urine tests at your own home.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of inosine on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study drug.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 3 months after your last dose of study drug.

Acceptable birth control methods for use in this study are:

- hormonal methods, such as birth control pills, patches, injections, vaginal rings, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)
- abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

If you are sexually active and able to father a child, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 3 months after your last dose of study drug.

Acceptable birth control methods that you can use in this study are:

- condoms with spermicide (a foam, cream, or gel that kills sperm)
- abstinence (no sex)

Acceptable birth control methods that your partner(s) should use are:

- hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)

If your female partner becomes pregnant, the study doctor would like to follow the outcome of the pregnancy. You should notify us immediately if your partner becomes pregnant. She may be asked to sign a release of medical information form that gives her doctors permission to provide information to the study doctor. You will not have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Risks of Taking Inosine with Other Medications

Do not take inosine from other sources, allopurinol, probenecid while you are in the study. Do not take more than 300mg vitamin C daily (you may take a standard multivitamin containing vitamin C up to one tablet or capsule daily). Taking these drugs and inosine together may cause serious side effects.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting.

Acute Kidney Damage as a result of Dehydration

If you become dehydrated for any reason, there is a possibility you will be at risk of kidney damage. It is possible that elevating uric acid levels could contribute to kidney damage due to dehydration. To avoid the risk of dehydration you should drink lots of water when taking study drug and if you have initiated the alkalization therapy. If you are restricted to a limited water intake due to reasons such as a medical precaution or due to religious fasting, please let the study staff know immediately.

Study Questionnaires and Health Questions

The daily activity questionnaire (ALSFRS-R) and reviewing health information may cause you to feel sad or upset about how ALS has changed how well you can perform daily activities, and how it has affected your quality of life, or may make you uncomfortable. Although we would like you to answer all the questions, you may skip over any questions that you do not wish to answer. You may stop a health interview at any time.

Mobile Application

The mobile application questionnaires may cause you to feel sad or upset about how ALS has changed how well you can perform daily activities, and how it has affected your quality of life. You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Slow Vital Capacity

The risks and discomforts associated with the Slow Vital Capacity testing include feeling tired, light-headed or short of breath. These symptoms will disappear with rest.

Confidentiality Risks

Every possible effort will be made to keep the research information strictly confidential, but we cannot provide an absolute guarantee that unintentional disclosure may not occur.

For this research project, some identifiable information may be collected and stored in the data repository, which is collect via the mobile application. This might include information like your date of birth or the date your symptoms began. At the end of this project, all data will be de-identified (all identifying information including dates will be removed). The de-identified dataset combined with information from other projects will then become available for sharing with other researchers.

Other Risks

Reviewing health related information might be stressful or make you feel uncomfortable. You do not have to answer any questions you do not want to, and you may stop the interview at any time if it is too uncomfortable. There may be other risks to taking the drug used in this study

that are not known yet. It is possible that the study drug may make your symptoms of ALS worse, or make your ALS progress faster, although this is not expected.

Unknown Risks

There may be additional risks that we don't know about at this time.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this research study. If you receive inosine, it is possible that your ALS symptoms will improve while you are taking it. Others with ALS may benefit in the future from what we learn in this study.

What other treatments or procedures are available for my condition?

You do not have to participate in this study to receive care for ALS. There may be other clinical research studies available to you. The study doctor can discuss with you other studies open for enrollment at this time.

Riluzole (Rilutek®) and Edaravone (Radicava®) are two drugs that are FDA approved for the treatment of ALS. You are allowed to take Riluzole and/or Edaravone during this study if you wish to do so.

Please be sure to let the study doctor know if you are taking either of these drugs, and/or if you change the dose you are taking during the study.

Will I be paid to take part in this research study?

You will not be paid to take part in this research study. We will pay for parking in the hospital garage during study visits.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

What will I have to pay for if I take part in this research study?

Subject Identification

Study funds will pay for the study drug (inosine), study-related procedures, study visits that are done only for research and the mobile application. You/your health insurer will be responsible for the costs of other treatments, including care for your ALS, because this would be needed for your care even if you are not in the study.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

Can I still get medical care within [SITE NAME] if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within [Site Name] now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

The decision to withdraw from the study will not affect in any way your current or future medical care or any other benefits to which you are otherwise entitled.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

[Insert name and academic degrees] is the person in charge of this research study. You can call him/her at [Insert phone number] [insert when person is available M-F 9-5 or 24/7]. You can also call [Insert name(s)] at [Insert phone number(s)] [insert when each person is available M-F 9-5 or 24/7] with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call [Insert name(s)] at [Insert phone number(s)].

If you want to speak with someone **not** directly involved in this research study, please contact the [Insert name of local IRB]. You can call them at [Insert phone number of local IRB].

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as “health information.” In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

INSTRUCTIONS: Below in RED is Partners Approved IRB HIPAA authorization language. Sites can use this language, or use their own language, or use a separate authorization form.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Research staff involved in this study
- Non-research staff within the institution who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this NEALS clinical study and their ethics boards
- Other researchers and medical centers that are not part of this NEALS clinical study but are part of the NEALS Consortium
- MGH NCRI (the NEALS Coordinating Center and Data Coordinating Center)
- A group that oversees the data (study information) and safety of this research
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Representatives of the MGH Biostatistics Department (the academic group responsible for the data analysis for the study)
- Individuals at the local lab where your blood is processed will have access to limited identifiable information, specifically your gender and date of birth, in order to properly run their tests
- Individuals working with the mobile applications, including Dr. Jukka-Pekka Onnela and Dr. Jordan Green and their research teams

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information

is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Subject Identification

Consent of Non-English Speaking Subjects Using the “Short Form” in the Subject’s Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter

Date

Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject’s own language, and that the subject was given the opportunity to ask questions.

Name

Date

Time (optional)

Subject Identification

Witness to Consent of Subjects Who Cannot Read or Write or are Physically Unable to Talk or Write

Statement of Witness

I represent that the consent form was presented orally to the subject in the subject's own language, that the subject was given the opportunity to ask questions, and that the subject has indicated his/her consent and authorization for participation by (check one box as applicable):

- Making his/her mark above
- Other means _____
(Fill in above)

Witness

Date

Time (optional)

Consent Form Version/Date: v2.0 / 01 July2019