Protocol Title: A Phase 1b Multi-Center, Double-Blind, Randomized, Placebo-Controlled Dose Escalation Study of the Safety, Tolerability, and Immunogenicity of ACI-24 in Adults with Down Syndrome

Principal Investigator: Dr. Brian Skotko

Site Principal Investigator:

Description of Subject Population: Adults with Down syndrome age 25-45

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.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as “Partners.”

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.

Some of the people who are eligible to take part in this study may not be able to give consent to take part because of their medical condition. Instead we will ask the person’s authorized representative to give consent. Throughout the consent form, “you” always refers to the person who takes part in the 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.

Your Study Partner

For this study, you will need a study partner. It is important that you and your caregiver understand the description of the research study before you agree to take part. If for some reason
your caregiver cannot continue in the study, you will need to find a caregiver for the study or stop the study. This form will also be given to your caregiver to review and sign.

We will ask a caregiver to come to some of the visits with you. Your caregiver is someone who knows you well and will help provide information about you at your visits.

**Why is this research study being done?**

We are doing this research study to find out if a vaccine, ACI-24, can help people with Down syndrome. We also want to find out if ACI-24 is safe to take without causing too many side effects. ACI-24 is administered by an injection into the skin (either to the upper arm or thigh).

ACI-24 is not approved by the U.S. Food and Drug Administration (FDA). This means that ACI-24 can only be used in research studies.

About 40 subjects with Alzheimer’s disease taking part in research studies have received ACI-24 so far. This is the first use of ACI-24 in adults with Down syndrome.

This research study will compare ACI-24 to placebo. The placebo looks similar to ACI-24, but contains no ACI-24. During this study you may get a placebo instead of ACI-24. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons. There is a chance that you may get the low dose, high dose, or placebo. You will have 3 chances out of 4 to be assigned to one of the active drug groups:

- Group 1 (ACI-24): 300 µg of ACI-24
- Group 2 (ACI-24): 1,000 µg of ACI-24
- Group 3 (Placebo): No active study drug

We are asking you to take part in this research study because you have Down syndrome. ACI-24 is a vaccine being developed for the treatment of protein β –Amyloid (Aβ) which is related to cognitive decline in Down syndrome and for the treatment of Alzheimer’s disease. Too much Aβ in the brain is believed to play an important role in cognitive decline in subjects with Down syndrome. We want to find out if ACI-24 has a positive effect on cognitive decline by reducing the amount of Aβ in the brain.

About 16 subjects will take part in this research study with an optional increase of 8 people totaling 24 people. The optional dose is determined by the drug group that is optimal based on data received. About 5 subjects will take part at Massachusetts General Hospital (MGH).

AC Immune S.A., the LuMind Foundation, and the National Institutes of Health are paying for this research to be done.
How long will I take part in this research study?

It will take you about 2 years to complete this research study. During this time, we will ask you to make about 22 study visits to MGH.

What will happen in this research study?

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

Screening Visit (up to 4 weeks before Visit 1) – About 3 – 5 hours

The Screening Visit will take about 3-5 hours and may be completed over several visits during a 2-4 week period. 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.

At this visit, we will:

- Collect information about your medical history, current medications, and vitamins and review your medical records.
- Do a physical and neurological exam
- Perform a Kaufman Brief Intelligence Test (KBIT-2)
- Take your vital signs: blood pressure in sitting and standing positions, heart rate, respiratory rate, and temperature
- Ask questions to measure personal and social skills such as communication, daily living skills, and socialization
- Ask questions to make sure that you are not becoming depressed. Depression is not a known side-effect of the study drug; however, it is a routine measure for all drugs which affect the brain. If the answer to any of these questions is yes, we will do further evaluation with a questionnaire named the Columbian-Suicide Severity Rating Scale (C-SSRS).
- Do an ECG (electrocardiogram).
- Ask you for a urine sample. The urine sample is for routine laboratory tests.
- Draw a blood sample. This sample will be tested to confirm that you do not have diseases such as human immunodeficiency virus (HIV), Hepatitis B, Hepatitis C or Syphilis. About 3 tablespoons of blood will be drawn from a vein in your arm. The blood sample is for routine laboratory tests.
  - The blood and urine samples will help ensure that there are no medical
conditions that might interfere with your participation in the study, or that could be responsible for changes in your condition throughout the study period.

- A serum blood test at screening will be done to ensure you are not pregnant, if you are a female able to become pregnant. Pregnant women cannot take part in this research study.
- Do an MRI
- Ask you to fill out some questionnaires about your general health and well-being, quality of life, mental health, emotional health, mood, and memory

**ECG (electrocardiogram)**
This test checks the electrical activity of your heart. We will place several small, sticky pads on your chest, arms, and legs. Each pad has a wire attached. The wires connect to a machine that makes a recording of your heart rhythm. This painless test takes about 15 minutes.

**MRI (Magnetic Resonance Imaging)**
This test takes pictures of your brain while you lie still in a large machine. This painless test will takes about 45 minutes.

We will take detailed pictures of your brain using an MRI scan. An MRI uses a strong magnet and radio waves to make these pictures. Before you have the MRI, we will ask you to complete a screening form. The form asks you questions to make sure that it is safe for you to have an MRI. Since the MRI uses a large magnet, people with pacemakers and certain metal implants in their bodies should not have an MRI scan.

We will ask you to change into a gown and keep your belongings outside of the MRI room. You will be asked to remove all metal items before the scan. During the MRI scan, you will lie quietly on a narrow table that slides you into a large, tunnel-like tube. The top and the sides of the tunnel will be very close to your face and body. The narrow tunnel may cause you to have a feeling of claustrophobia (discomfort in confined spaces).

It is important to lie very still during the scan so that we can get a clear picture of your brain. As it creates pictures, the MRI makes loud banging noises, as if it were being pounded on the outside with a hammer. We will offer you earplugs to help reduce this noise. If you have difficulty lying still, or feel very nervous, one of the study staff will stay with you to try to make you comfortable. If you continue to be uncomfortable, the study staff will immediately remove you from the MRI machine. You will be able to hear and speak to the research staff at all times during the scan. You can ask us to stop the MRI at any time. The MRI scan will take about 45 minutes.
If you are anxious about the MRI, you may be given a medication to help you relax during the MRI scan. If the doctor decides you would benefit from this medication, you may be asked to test it first at home to be sure there are no side effects. Sometimes people feel upset to their stomach or dizzy after having this medication.

**Treatment Period (Visit 1 to Visit 18) – About 2–10 hours each**

During the treatment period of 12 months, you will be asked to come in for regular visits about every 2-8 weeks. These study visits will take about 2-10 hours. At the end of each visit, we will remind you of what will happen at your next visit. The study visit may also be conducted over two consecutive days.

Visit 1 will confirm if you are eligible for the study or not.

If you are eligible for the study, we will assign you by chance (like a coin toss) to one of 3 groups: the 300 µg ACI-24 group, the 1,000 µg ACI-24 group, or the placebo group. You and the study doctor cannot choose your study group. You and the study doctor won’t know which study group you are in, but s/he can find out if necessary.

You will have 3 chances out of 4 to be assigned to one of the ACI-24 groups.

You will have a 1 in 3 chance of being assigned to the placebo group.

One or two injections are necessary to give the study drug or placebo. The study drug or placebo will be given a total of 7 times. The injections are given under the skin in the same area, either in your arm or in your thigh. You will be requested to stay at the clinic for 8 hours for monitoring of safety after you receive the first injection and for 4 hours after the subsequent injections. There will be a visit 2 weeks after each injection.

At Visit 1 through Visit 18, we will:

- Record your vital signs
- Ask about any side effects or adverse events since your last study visit
- Collect a list of medications and vitamins you are currently taking
- Do a physical and neurological exam
- Give you a questionnaire about your functioning in daily life
- Give you tests of your memory and thinking skills
- Assess suicidal ideation/behavior at Visits 1 and 17
- Do an MRI at Visit 8, 11, and 17
- Do an ECG at Visit 11 and 17
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Version Date: August 2016

- Ask you for a urine sample to test for pregnancy, if you are female who can become pregnant at Visits 1, 3, 5, 7, 10, 13, and 16
- Take a blood sample of about 50mL (3 tablespoons). Laboratory tests will be conducted on Day 1 should the visit be conducted over two days.

At Visit 1, your blood will be analyzed for information on your genetic material (called “DNA”). Every person carries in his/her blood genetic material that may indicate whether he/she is likely to develop certain diseases. In this study, this will help to see if there is a link between your DNA and cognitive decline. All the blood samples will be coded with an identification number that will not allow you to be identified.

In addition, the following procedures will be performed:

- Assess your condition. The study doctor will report if your condition has improved or worsened at each study visit
- Do a Global Assessment of Tolerability. The study doctor will assess how well you tolerate the study drug at Visits 2-18
- Perform Neuropsychological tests to measure your memory and other areas of brain function at Visits 1, 8, 11, 14, and 17
- Do a Lumbar Puncture (optional, only if you agree to take part)

**Lumbar Puncture**
We will also ask you to take part in a lumbar puncture (LP) – also known as a “spinal tap” – at the beginning and at the end of the treatment period, (Visit 1 and Visit 17). You do not have to take part in the lumbar puncture if you don’t want to. If you decide you do not want to have a lumbar puncture, you can still take part in the rest of this study.

A lumbar puncture is a procedure that involves inserting a needle in the lower back in order to collect a small amount of the spinal fluid that surrounds the brain and spinal cord. During the procedure you will lay on your side curled up into a ball, or you will sit on the edge of a chair or bed and lean forward, whichever is easier. The lower part of your back will be cleaned with antiseptic. A local anesthetic (lidocaine, 1%) will be injected into the skin of your lower back at the area of the lumbar puncture. When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back, well below the level where the spinal cord ends.

Approximately 15-20mL (about 4 teaspoons) of spinal fluid will be removed for analysis and optional sample storage. Your body replaces this spinal fluid within 1-2 hours.

After the lumbar puncture is complete, you will remain at the site for about 30 minutes. You will be given something to eat and drink before you leave. You should avoid any strenuous physical activity for the next 24 hours. This includes lifting, bending, doing housework and gardening, or doing exercise such as jogging or bicycle riding.
Study staff will call you the day following your lumbar puncture to discuss how you are feeling.

If you agree to let us perform a lumbar puncture, we will ask you to sign your name after reading the risks of this procedure (below).

**Follow-up Period (Visit 19 to 21) – About 2 hours each**

After you stop taking the study drug you will come in for 3 follow-up visits. Between these visits, you will be contacted by phone at least 2 times to make sure that you have not experienced any side effects or adverse events. These visits will take place at Month 15, Month 18, and Month 24.

At Visit 19 through Visit 21, we will:
- Record your vital signs
- Ask about any side effects or adverse events since your last study visit
- Collect a list of medications and vitamins you are currently taking
- Do a physical and neurological exam
- Give you a questionnaire about your functioning in daily life
- Give you tests of your memory and thinking skills
- Assess suicidal ideation/behavior at Visit 21
- Do an MRI at Visit 21
- Do an ECG at Visit 21
- Take a blood sample of about 15 mls (3 teaspoons)
- Ask you for a urine sample to test for pregnancy, if you are female who can become pregnant

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

**Stopping the Study Early**

If you decide to stop taking part in the study for any reason, we will ask you and your caregiver to make a final study visit to have the final procedures completed as in Visit 21 above.

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.

Review of Medical Records from Hospital Admissions or Emergency Department Visits

Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study.

Study Information Included in Your Electronic Medical Record

We will try to keep sensitive information related to the study out of your hospital electronic health record. However, information about serious side effects, serious allergic reactions, or important, unexpected results in imaging studies might become part of your records at MGH. The pharmacy keeps copies of all drug dispensing information as required by law.

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

Genetic & Biomarker Research

During this study, blood and CSF (“cerebral spinal fluid” or “spinal fluid”) samples will be collected from you for genetic and biomarker research. The samples will be sent to the study Sponsor, the study Sponsor’s contracted laboratories and/or the Alzheimer’s Disease Cooperative Study (ADCS) Biomarker Core at the University of California, San Diego (UCSD).

Earlier studies have shown that a gene called apolipoprotein E (“ApoE”) may influence the rate of disease progression or a subject’s response to treatment. We will test some of your blood to see what form of the ApoE gene you have. This genetic testing is not optional.

The results of these tests will be maintained in scientific databases for this research study. These results are important only for research - not for helping to care for you. For this reason, the results will not be released to you or your family.
No information regarding your genetic or biomarker research will be entered into your regular medical record. If you are concerned about a potential genetic disorder, you should discuss this with your primary care doctor. You and your doctor may choose to test specifically for it, but this would require additional blood samples and would not be part of this research project.

Data from your tests will not be revealed to other sites that are participating in the clinical study, family members, insurance companies, employers, or other individuals or organizations.

Although the study researchers and the study Sponsor will have access to coded individual data, any information gained from this research will be reported in publications in anonymous summary form. Data will be stored in a locked file, and in a computer with restricted access. Any information that could be used to potentially identify you in the computer will be stored in a separate file and encrypted. Only the researchers and their research assistants will have access to the original research data.

**Sample Storage & Future Use**

With your consent, we would like to store your leftover samples (genetic, blood, and CSF) for future research studies related to Alzheimer’s disease and other neurodegenerative disorders in adults with Down syndrome. The samples will be sent to the laboratory at the Alzheimer’s Disease Cooperative Study (ADCS) at UCSD. This will only be done if you have signed a separate section of this informed consent form. If you decide you do not want to have your leftover samples stored for future research studies, you can still participate in this study.

Dr. Skotko and the Sponsor will be responsible for deciding how the samples will be used. The specimens collected from you and the DNA that they contain may also be used in additional research to be conducted by the University of California personnel collaborating in this research. These specimens, DNA, and their derivatives may have significant therapeutic value or commercial value. By agreeing to be in this study you consent to such uses.

Samples will be stored indefinitely at the ADCS Laboratory and may be shared with other researchers studying Alzheimer’s disease or aging. If your samples are sent to other researchers, they will be identified only by a code number and descriptive data (such as your age and gender). No other personal identifying information will be attached to your samples, so it will not be possible to identify you from any of the samples.

There will be no direct benefit to you from this study since you will not be provided with any results or information regarding your DNA test. The investigator, however, may learn more about Alzheimer’s disease in adults with Down syndrome.
Do you allow us to store your de-identified leftover samples (genetic, blood, and CSF) for future research studies related to Alzheimer’s disease and other neurodegenerative disorders in adults with Down syndrome?

☐ Yes  ☐ No  INITIALS: _____________  DATE: ______________

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

**Risks of Taking ACI-24**

Taking ACI-24 may involve risks that are currently not known. Strict monitoring for signs and unwanted side effects will be closely followed during this study. It is very important for your safety to carefully follow the study protocol and to attend all planned study visits. It is also essential that you report to the study team as early as possible any unusual event or side effect that worries you.

To date, ACI-24 has shown no drug-related serious adverse effects. The non-serious events have been mild to moderate in severity and not known to be in relation to the study drug.

You will be told of any new risks or significant findings that develop during the course of this study.

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.

The following potential safety issues will be specifically monitored during the trial:

- **Reaction at the injection site.** It is possible that some redness, itching, or swelling might be observed at the site of the injection.

- **Meningoencephalitis (brain inflammation).** There is a risk that ACI-24 might lead to inflammation in the brain, which is also called meningoencephalitis. The study physician will look for any signs of this by examining you at the study visits. In addition, the MRI scans, and optional examinations of the CSF, will help to identify early if there are any signs of inflammation. No signs of
meningoencephalitis have been observed to date in the ongoing study in Europe or in animal studies with ACI-24

- **Amyloid-related imaging abnormalities (ARIAs).** There is a risk that, by removing the amyloid protein from blood cells, ACI-24 might cause small areas of bleeding (so-called “microhemorrhages”) and leakage of water into the brain (“vasogenic edema”). These are usually not noticeable to you but could cause symptoms such as headache, confusion, or dizziness. MRI scans and clinical examination are done to detect any brain abnormalities early. Such reactions have not been observed to date in the ongoing study in Europe or in animal studies with ACI-24.

Participating in this study may involve additional risks or discomforts, outlined below.

**Risks of Taking ACI-24 with Other Medications**

Only a small number of people have taken ACI-24. Therefore, we don’t know about all the side effects that can happen when taking ACI-24 with other drugs. Certain medications are not permitted throughout the study. Therefore, any changes in medication must be discussed first with the study doctor.

**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.

**Risks of Radiation Exposure**

There is no extra risk of radiation exposure as part of participating in this study.

**Risks of MRI Scans**

MRIs use powerful magnets to make images. There are no known radiation risks associated with MRI. However, persons with metal implants, such as surgical clips, or pacemakers should not have an MRI. All credit cards and other items with magnetic strips should also be kept out of the MRI room. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow tube. The MRI makes loud banging noises as it takes images. Earplugs can be used to reduce the noises. The MRI can be stopped at any time at your request. If you are or suspect you are pregnant, you should not participate in this study. The MRI has the potential, during normal routine use, to cause localized warming of your skin and the underlying tissues. You should immediately inform us if you experience discomfort due to warming and the procedure will be stopped.
We are doing the MRI scan in this study which may answer research questions, not as part of your medical care. The MRI scan results will not be part of your hospital record. The scan is not the same as one that your own doctor would order. It may or may not show problems that would be found on a standard MRI scan. If we do see something that looks like a medical problem, we will tell you and help you get follow up care. If the results show that there is not a medical problem, we may have caused you to worry needlessly about your health.

**Risks of Lumbar Punctures (optional)**

In total, up to 40mL (less than 3 tablespoons) of cerebrospinal fluid (CSF) may be taken during this entire study and your body will make up for this loss.

Lumbar puncture is a standard procedure used in medical practice. When spinal fluid is removed during a lumbar puncture, the risks include headache, bleeding and pain at the site where the needle was put in, and infection. Pain during the lumbar puncture procedure will be prevented or minimized by using local anesthesia (lidocaine). Infection after a lumbar puncture is very rare, but serious, and would be treated with antibiotics.

About 1 in 3 patients who have a lumbar puncture develop a post-lumbar puncture headache. Headache can occur if the lining around the spinal fluid (dura) is torn and some of the fluid leaks out. Post-lumbar headaches are more common in females and in people less than 30 years old. This headache can be mild to severe. You may also have nausea, dizziness, and ringing in the ears.

If you develop a headache, you will need to lie down to reduce the headache pain and symptoms. Post-lumbar puncture headaches get worse when you are sitting or standing. Occasionally, the headache may be severe enough to interfere with your normal daily activities, such as going to work or school.

If you get a headache, you should contact Dr. Skotko, who is in charge of this study. We will give you medicine to treat the pain, if needed. If the headache lasts more than three days, a procedure called a blood patch may be performed. This procedure involves taking blood from your arm and injecting it in the same place where the spinal needle was put in during the lumbar puncture. The clotting of the blood in this space should stop further fluid leaking and stop the headache.

Do you agree to participate in the **optional** CSF sub-study, which involves a lumbar puncture?

☐ Yes ☐ No  
INITIALS: __________________ DATE: ________________
Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of ACI-24 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 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.

Risks of Taking ACI-24 with Other Medications

Only a small number of people have taken ACI-24. Therefore, we don’t know about all the side effects that can happen when taking ACI-24 with other drugs. Certain medications are not permitted throughout the study. Therefore, any changes in medication must be discussed first with the study doctor.

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

You may not benefit from taking part in this research study. If there is a benefit, it is uncertain when the effect may occur and how long it may last.

Others with Down syndrome 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 take part in this research study. Another alternative is not to participate in this study and to continue under standard medical care.
Can I still get medical care within Partners 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 Partners 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.

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.

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

We will pay you and a caregiver $1650 each if you complete the study. If you do not complete the study, we will pay you and a caregiver $75 each for each visit you complete. It may take a few weeks for study staff to process these payments.

You will be given a parking voucher for each visit to cover fully the cost of your parking in approved MGH parking lots.

We will also provide the participating caregiver, an additional $25 per visit to offset the costs of transportation. We will provide one gift card totaling $30 for each visit to be used between you and your caregiver for the purposes of lunch and snack expenses.

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?
AC Immune S.A. is providing the study drug at no cost.

Study funds will pay for study-related procedures that are done only for research.

**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.

Brian Skotko, MD, MPP, is the person in charge of this research study. You can call him at 617-726-2000 and ask for pager number 18597. Dr. Skotko is available 24 hours a day, 7 days a week. You can also call Amy Torres at 617-726-7927 Monday-Friday 9am-5pm with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call Amy Torres at 617-726-7927.

If you want to speak with someone not directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.
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?**

Federal law requires Partners to protect the privacy of health information that identifies you. In the rest of this section, we refer to this information simply as “health information.”

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

**Certificate of Confidentiality for Health Information and Other Identifying Information from the Research**

In this research study, we have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). By granting the Certificate, DHHS is not approving the research itself, but is helping us strengthen the privacy protections for your health information and other identifying information from the research. With the Certificate, we cannot be forced (for example by court order or subpoena) to disclose your health information or other identifying information from the research in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings. (Note that information that is not from the research, such as existing hospital or office health records, is protected by general privacy law but does not receive the Certificate’s stronger protection. The Certificate also does not prevent you or a member of your family from voluntarily releasing any information about yourself or your involvement in this research study.)

**Why Health Information and Other Identifying Information from the Research Might Be Used or Shared, and By/With Whom**

Even with these privacy protections, your health information and other identifying information from the research may still be used within Partners by the researchers and the staff involved in
this research study, by the Partners ethics board that oversees the research, and by other staff within Partners who need the information to do their jobs (such as for treatment, payment (billing) or health care operations such as overseeing the quality of care or research). Your information may also be shared by these groups with others outside of Partners for certain purposes as follows.

We may use and share your information with:

- The sponsor(s) of the research study, and people or groups it hires to help perform this research study
- Other researchers and medical centers that are part of this research study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- People or groups that we hire to do certain work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as DHHS and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), with other U.S. or foreign government bodies, and with organizations that provide independent accreditation and oversight of hospitals and research. For example, disclosure may be necessary upon request of DHHS for an audit, program evaluation, or investigation. Disclosure may also be necessary if required by the federal Food, Drug, and Cosmetic Act or its regulations.
- A public health or public safety authority, or with specific individuals who may be at risk of harm, if we learn information that could mean harm to you or others. When state mandatory reporting statutes would require us to disclose information, including about child or elder abuse, we will voluntarily disclose that information.

What Study Information May Become Part of Your Electronic Medical Record?

As described above, we have obtained a Certificate of Confidentiality for this research study. With the Certificate, we cannot be forced (for example, by court order or subpoena) to disclose identifying information from the research. 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). Any information from this research study that is placed in your medical record may not be protected by the Certificate. This information may be accessible by court order or subpoena, or by your health insurer, by your doctors or hospitals, or by others for treatment, payment, health care operations or other purposes.
Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

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 protections of the Certificate of Confidentiality and other Partners privacy protections will continue to apply to your health information and other identifying information from the research for as long as our researchers keep the information.

The results of this research 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. The Certificate of Confidentiality and other Partners privacy protections will continue to apply to your health information and other identifying information from the research that our researchers keep.
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.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject (if they are their own legal guardian):

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Signature of Subject (if they have a legal guardian):

Signature will be recorded on the separate Assent Form.

Signature of Guardian or Authorized Representative for Adult:

I give my consent for the person I am authorized to represent to take part in this research study and agree to allow his/her health information to be used and shared as described above.

Print Name (check applicable box below)

☐ Court-appointed Guardian
☐ Health Care Proxy

Page 19 of 20
Partners HealthCare System
Research Consent Form

Certificate of Confidentiality Template
Version Date: August 2016

☐ Durable Power of Attorney
☐ Family Member/Next-of-Kin

______________________________  _______________  __________________
Signature                      Date                  Time (optional)

Relationship to Subject: ________________________________  _______________  __________________

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

□ I have explained the research to the study subject.
□ I have answered all questions about this research study to the best of my ability.

______________________________  _______________  __________________
Study Doctor or Person Obtaining Consent                      Date                  Time (optional)

Consent Form Version: 23-MAY-2017