Partners HealthCare System
Research Consent Form

Subject Identification

General Template
Version Date: August 2016

Protocol Title: Biomarkers in Individuals At-Risk for Prion Disease

Principal Investigator: Steven E Arnold, M.D.

Site Principal Investigator:

Description of Subject Population: Carriers of PRNP Mutation and Subjects with a History of Prion Disease

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.

Why is this research study being done?

We are doing this research to identify biomarkers for individuals who are at-risk for familial prion disease. We hope to use these biomarkers in order to predict timing of disease onset in pre-symptomatic individuals and to guide the direction of future clinical trials.

We are asking you to take part in this study because you either had genetic testing to indicate that you are a carrier of a *PRNP* mutation or have a family history that indicates you potentially carry a *PRNP* mutation.

At MGH, we plan to enroll 60 subjects, including 30 prion protein gene (*PRNP*) mutation carriers and 30 *PRNP* non-carrier controls (familial or unrelated).

You can still enroll in this study if you do not know whether or not you have a *PRNP* mutation. It is possible that you may desire to learn your genotype. Such testing will not be performed within the scope of the study, but subjects who express interest can be referred to a qualified neurologist or genetic counselor at MGH to discuss the option to pursue testing in a clinical context, outside of this research study.

All predictive testing for genetic prion disease in the U.S. is handled by the CLIA-certified prion lab at the National Prion Disease Pathology Surveillance Center in Cleveland, OH. Costs of predictive testing are waived by the Surveillance Center for individuals with a known family history of prion disease. Any clinical consultation you choose to pursue will be outside the scope of this research study.

This study will also be testing the effectiveness of the DCTclock test in detecting cognitive change.

This study is being funded by Prion Alliance and the MGH department of Neurology.

How long will I take part in this research study?

It will take you about approximately 1 year to complete this research study.
We will ask you to complete a 1-day visit and return 8-16 weeks later for a follow-up visit.

We may invite you to return for additional annual follow-up visits. The first annual visit would occur within one year of your initial visit. We may invite you to participate annually up to 5 more times.

We will also call you the day after each study visit to review how you are feeling and to check for any side effects.

What will happen in this research study?

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

Lumbar Puncture ("LP" or "spinal tap"): you will be asked to undergo a lumbar puncture performed by a neurologist or trained nurse practitioner. They will carefully insert a needle into your lower back area in order to collect and look at the fluid that bathes the spinal cord. They will monitor you for as long as needed to ensure that you feel fine and are safe to return home or to your hotel. After the LP, a member of the study staff will ask you to fill out a short form about your experience.

Cognitive Testing: You will be asked to complete a series of cognitive tests. Some tests will be administered using pencil and paper and others will be administered on an iPad. You will also be asked to draw some clocks using the DCTclock pen. The DCTclock pen uses a camera to record slight hand motions while you write. It will take you approximately 1 hour to complete all of the cognitive tests.

Initial Visit

The morning of your initial visit will involve the following tasks:

- Medical history review
- Physical Exam
- Cognitive Exam
- Measure height, weight, vital signs
- Blood Draw and finger stick (including pregnancy test if necessary)
- Cognitive Testing

After these tasks have been completed, we will take a break for lunch and wait for the blood results (if necessary). After confirming that you are eligible to continue, Dr. Steven Arnold or another qualified practitioner will perform the lumbar puncture.

Visit 2

You will be asked to return for a repeat visit approximately 8-16 weeks after your initial visit. The tasks included in this repeat visit are the same as those performed during the first visit, including the lumbar puncture.

Annual Visits

You will be asked to return for a repeat visit every 9-12 months. Visit 3 will ideally occur 9-12 months after your first visit. Subsequent follow-up visits will take place 9-12 months following Visit 3. The tasks included in this repeat visit are the same as those performed during the first visit, including the lumbar puncture.

Post-Visit Phone Check

A review of symptoms will be performed over the phone by a member of the study team. The phone call will be reviewed by a study doctor.

Reasons for Withdrawal

You will be taken out of the study if:

- Any adverse event (AE), concurrent illness, or other medical condition or situation occurs that would make the research pose a risk to your health.
- You meet any exclusion criteria.

You are free to withdraw from the study at any time.

Sending data/specimens to research collaborators outside of Partners
We will remove identifying factors such as your name and medical record number from the spinal fluid and blood samples we collect before sending them to our research collaborators, including Sonia Vallabh and Eric Minikel, at the Broad Institute. Sonia and Eric and other collaborators will measure biomarkers including the quantity of PrP protein and analyze the samples to confirm the presence or absence of a PrP mutation if reported or determine the genotype if not known or reported. De-identified CSF and blood will also be shared with qualified investigators for additional molecular characterization and research purposes, including but not limited to studies of prion disease. Samples may also be sent to the National Cell Repository for Alzheimer's Disease (NCRAD) for biobanking, storage, and further distribution to researchers.

Digital Cognition Technologies, Inc, (DCT) will analyze and evaluate information it receives and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the DCT. DCTclock data that is collected from you for this study may have commercial value. Digital Cognition Technologies, Inc. does not intend to provide any benefits, financial or otherwise, to you from any of these developments.

Storing Samples & Health Information at MGH for Future Use
We would like to store some of your samples and health information for future research related to prion disease. We will label your samples and health information with a code instead of your name. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password protected computer.

Do you agree to let us store your samples and health information for future research related to prion disease?

☐ Yes ☐ No Initials_____

If later you change your mind and want your samples destroyed, contact the study doctor.

Future Contact
We may wish to collect more information from you in the future or for other studies.
Is it okay to contact you for additional information or for other studies in the future?

☐ Yes ☐ No Initials_____

If later you change your mind and would listed to be removed from our list, contact the study doctor.

Study information that will be included in the electronic medical record
A notation that you are taking part in this research study may be made in your electronic medical record. **For this study, only a study number, and NOT the title of the study, will be in your record: for example Study #123.** 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.

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

Lumbar puncture ("LP" or "spinal tap"): 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 out of 3 people 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 this happens, there are no plans to pay you for time missed from work or school or for other costs, such as paying for a babysitter.

If you get a headache, you should contact Dr. Steven Arnold, who is in charge of this study. Pain medication will be given to you, 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.

Genetic Information: Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies or employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record. We have also masked the title of this study in your medical record for your privacy.

Taking part in a genetic study may also have a negative impact on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk.

Blood Draws: The risks associated with having blood drawn include bruising and local discomfort. Rarely an infection may occur at this site, and if an infection does occur it will be treated by the study physician. Approximately 20cc (about 1.5 tablespoons) of blood will be drawn from your vein and a few drops of blood will be collected from a finger stick at both visits.

Neurocognitive testing: The neurocognitive tests that will be administered to assess mental performance may be stressful and may cause anxiety, fatigue, and frustration. In our prior experience, similar risks have rarely occurred and very few subjects have ended testing. However, testing will be stopped immediately upon your request to do so.

Questionnaires: Questionnaires may cause you to feel sad or upset about your hereditary risk or neurocognitive functioning. Study staff is experienced with these concerns and will be sensitive to these issues. Any question can be omitted per your request.

Other Risks: Reviewing health-related information might be stressful or make you feel uncomfortable. You do not have to answer any questions that you do not want to.
There may be other risks that are currently unknown.

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

You will not benefit from taking part in this study.

We hope that what we learn from this study will help us better understand the symptoms of Prion Disease and how the disease progresses in humans. Patients with Prion Disease may benefit from what we learn from this study in the future.

What other treatments or procedures are available for my condition?

No effective treatments have been identified for human prion diseases. This study will not offer a treatment for Prion disease, but we hope to identify biomarkers that may help direct future clinical trials and therapies.

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?

Participants will receive:

- Parking fees paid for all in-person visits.
- Lunch voucher provided for you and a companion (if present) at each study visit, which can be used at the cafeteria at MGH CNY 149.
- $250 for completing a study visit.
- If for any reason we need to stop a visit, you will be compensated $50 for that visit.

If you are coming from outside the region appropriate travel expenses will be reimbursed as follows:

- Transportation: up to $500 per visit.
- Lodging: up to $250 per night (limited to the night before and the night of scheduled visits).

Note that these limits also apply to international participants.

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

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.
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.

Dr. Steven Arnold, M.D. is the person in charge of this research study. You can call him at (617) 643-5607 available M-F 9-5.

If you have questions about the scheduling of appointments or study visits, call the clinical research coordinator, Anna Bolling, at (617) 726-1259.

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?

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.

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:

- Partners research staff involved in this study
- 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 study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- 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)
- Other: Co-investigators, Eric Minikel and Sonia Vallabh, and their research team at the Broad Institute will be responsible for storage and preparation of your samples for analysis.

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.

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:

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.

Subject	Date	Time (optional)

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)

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