Participant Informed Consent for Exploratory Study of Entire-body PET Scans for Multiple Sclerosis (EPSMS)

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You are being invited to participate as a volunteer in a clinical research trial. This study will be conducted based on rules set by the US Federal and California State governments. Under these rules, a researcher will first explain the study and what is expected of you, and then he or she will ask you if you would like to volunteer. You will be asked to sign this consent form, which states that the study has been explained, that your questions have been answered, and that you agree to participate. This process is called *informed consent*. Then, if you decide to participate in the study, you will sign and date this form in the presence of the person who explained the study to you. You will be given a copy of this form to keep.

California Experimental Subjects Bill of Rights

- Someone will explain this research study to you, including: a) the nature and purpose of the research study, b) the procedures to be followed, and c) any drug or device to be used.
- Any common or important discomforts and risks.
- Any benefits you might expect.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.

What is the purpose of this study?

The purpose of this clinical research trial, called the Exploratory Study of Entire-body PET Scans for Multiple Sclerosis (EPSMS), will be to examine whether recent state-of-the-art PET-CT scanners, such as the United Imaging uEXPLORER and the Siemens Biograph Vision, with their much greater sensitivity and resolution, can serve as improved imaging devices to monitor better the demyelination and remyelination that may occur in the white matter of the nervous system of persons with multiple sclerosis when compared to normal healthy subjects. This demyelination and remyelination may correlate with the relapses and remissions of multiple sclerosis.

These new PET-CT scanners are now able to scan most if not all of the human body at the same time. They are also much more efficient than previous PET-CT scanners and have the potential to make a big impact in clinical care and medical research. All participants in the EPSMS pilot study will receive the same kind of PET-CT scan with the same imaging dye, an FDA-approved radiopharmaceutical called Amyvid. This single scan will be performed at one of possibly several collaborating medical imaging centers and may take several hours of your time. All participants may accept or decline to be informed of the results from this PET-CT scan. If you do wish to be informed of the scan results, then you must also agree to participate in educational counseling sessions with questionnaires (ie, psychological screening tests), before and after the PET scan. Each of these sessions may also take several hours of your time. If you do not wish to be informed of the PET scan results, then you will not be required to attend the educational counseling sessions with the questionnaires before and after the PET scan.

The study will be managed by experienced researchers at Brain Health Alliance (BHA), and the PET scans will be performed by experienced physicians and technologists at collaborating medical imaging centers. The questions addressed in the study will ask whether PET imaging with an entire-body PET scanner and the Amyvid imaging dye to monitor demyelination and remyelination in multiple sclerosis will ultimately help your doctor to treat you, manage your illness, and benefit your health. However, the PET scanner only takes a picture and provides information. It does not constitute a treatment by itself. And the Amyvid imaging dye is neither known nor presumed to be a treatment of any kind.

PET scans with the radiopharmaceutical Amyvid for detecting amyloid in the grey matter of the brain were approved by the FDA in 2012 for “adult patients with cognitive impairment who are being evaluated for Alzheimer’s Disease (AD) and other causes of cognitive decline” (Amyvid Prescribing Information, 2012, Eli Lilly and Company). PET scans with the radiopharmaceutical Amyvid for monitoring myelin in the white matter of the nervous system have *not* yet been approved by the FDA, and are *not* yet considered a standard procedure as part of the routine clinical care of multiple sclerosis. Thus, at present, the PET imaging with the radiopharmaceutical Amyvid and entire-body PET scanners will be used for research purposes only in the EPSMS clinical trial.

Why am I being asked to join this study?

You are being asked to join this study because you are between the ages 25 and 55 inclusive, have been diagnosed with multiple sclerosis by a credentialed neurologist experienced in the clinical care of multiple sclerosis. Alternatively, you are between the ages 25 and 55 inclusive, and have volunteered to participate as a normal healthy research subject. In either case, you must be able to provide a recent medical report from your neurologist if you are a multiple sclerosis patient, or from your internist or family physician if you are a normal healthy subject, documenting

your current medical condition with a current lab report of blood tests. If your blood tests indicate that your kidneys are not healthy and not working well, then you will be excluded from the study. If you are a woman of child-bearing age, you must also be willing to take a pregnancy test at the time of the PET-CT scan, and you will be excluded from the study if you are pregnant. In addition, you must be able to lie on your back in a long PET-CT scanner for the duration of the scan, which will be approximately 10 to 20 minutes. Finally, you have advised us that a friend, relative or family member has agreed to assist and accompany you throughout the study, especially to the imaging center on the day of the PET scan. If you do agree to participate, you may discontinue participation at any time. If you withdraw from the study, no new data will be collected from you for research purposes. If you agree to participate, researchers will use the information about you and your health care that you provide to BHA for research purposes only with the EPSMS clinical trial.

What am I being asked to do for the project?

For this study, you are being asked to consent to the following: a) Allow information about you, your health, and your PET scan imaging to be collected for up to one year. b) Give BHA researchers your name, phone number, street address, social security number, and date of birth so the researchers can match your informed consent and participation in the clinical trial with the medical records that you request be shared and sent by your health care providers. Sign the release of information requests to your health care providers so that your medical records can be transmitted to the BHA researchers. Only trained research staff at BHA and the collaborating medical imaging center that performs your PET scan will have access to your personal information. c) Optionally, if you have a past record of medical imaging scans with PET, MRI or CT, and wish to opt-in to a retrospective analysis and comparison of your past scans with any new scans done for the EPSMS Study, then request that digital copies of your past scans be shared and sent via mail on a DVD disk or USB stick to the BHA researchers. d) Participate in a single scan with an entire-body PET-CT scanner and Amyvid radiopharmaceutical. e) If you wish to be informed of the PET scan imaging results, then you must also participate in the educational counseling sessions with questionnaires before and after the PET scan. f) Allow your PET scan and any other data collected from the questionnaires, which will be stripped of all personal identifying information, to be analyzed for the current EPSMS research and also archived at BHA for future research.

What happens to any biospecimens collected?

Any biospecimens (such as blood or urine) collected from you at your local imaging center (eg, UC San Diego Health Imaging and Radiology) for this imaging study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them in this EPSMS Study conducted by not-for-profit education and research organizations.

Are there any other forms I must sign?

You will be asked to sign and date a separate form for at your local medical imaging center (eg, UC San Diego Health) authorizing access, use, creation, or disclosure of health information about you. Members of the research team and other staff or representatives of your local medical imaging center (eg, UC San Diego Health) whose work is related to the research or to protecting your rights and safety. This consent form and some details of your study participation will be noted in your medical record at your local medical imaging center. People involved with your medical care and insurance at your local medical imaging center and affiliated healthcare organizations may become aware of these details.

How long will I be in the study? What will happen during the study?

An anticipated 20 participants will join the study over approximately one year in this initial pilot phase of the EPSMS clinical trial. During this time, you will have a single PET scan with an entire-body PET scanner at a collaborating medical imaging center. You will also speak with a doctor at BHA and complete some questionnaires both before and after the PET scan. If the exploratory study is extended to a multi-year clinical trial and enlarged to a much greater number of participants, and if you are already participating in the pilot phase of the research as a multiple sclerosis patient, then you may choose to continue your participation in the EPSMS clinical trial with serial PET scans over the future years of the trial, which may help monitor and measure the relapses and remissions of your illness.

What are the risks?

During your participation in this research study, you will be exposed to radiation from a molecular imaging scan with a PET-CT scanner. The total exposure resulting from these imaging studies is calculated to be approximately 7

mSv. This amount is more than you would receive from one year of natural exposure in the San Diego area, which is approximately 1.6 mSv. Cumulative exposure from radiation may increase your risk of developing certain types of cancer in the future. If you are especially concerned with radiation exposure, or you have had a lot of x-rays or imaging scans already in the past, you should discuss this concern with a study doctor or your regular doctor.

The PET imaging test performed with the radiopharmaceutical Amyvid (F18-florbetapir) as described in this consent form is *not* experimental and has been safely used in clinical practice ever since the imaging agent was first approved by the FDA in 2012. However, there are risks associated with this imaging test that will be discussed with you and also addressed again in a separate consent form at the collaborating medical center where the imaging test will be performed with the entire-body PET scanner. These risks include exposure to very low doses of radiation, which is much lower than the amount for a regular diagnostic CT scan. During the scan, you will be in an enclosed space and this may cause some people to experience discomfort or claustrophobia (fear or anxiety when in a small confined space). The injection of the radiotracer may cause pain at the injection site, and rarely, may cause an allergic reaction. The most common adverse side effect has been headache affecting less than 2% of persons who are injected with Amyvid and imaged with a PET scanner. You will be carefully monitored to minimize these effects in the event that you experience any of them.

Also, the PET scan may reveal incidental findings and/or suspicious findings of unclear cause which may need further follow-up procedures. Medical follow-up may include doctor's visits, more scans or surgery and may expose you to additional risks from the follow-up procedures. Your participation in this study is voluntary. You do not have to participate in this study if you do not wish to do so. There may be other choices available to you. You will not lose any services, benefits, or rights you would normally have if you choose not to participate in this clinical trial.

Another known risk of participating in this type of research study is the possibility of unintentional release of your personal health information. The research team takes extra precautions to lessen and minimize this risk. For the research study database, you will be identified only by a unique number. Your name and other identifying personal information will not be included in the research study database. Any identifying personal information will be accessed only by trained research staff personnel who need it to make requests for health care information obtained from your health care providers for which you must sign permission for them to release any records to the research study. An example of such information would be your multiple sclerosis disability scores and clinic notes from your neurologist who is caring for your illness. This information will be recorded in the research study database with only your unique code number, and will have your name and identifying information removed from the information prior to entry in the research database. Any new important information that is discovered during the research study and which may influence your willingness to continue participation in the study will be made available to you.

What if I am hurt or injured in the study?

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the medical imaging center where your PET-CT scan is performed (eg, UC San Diego Health) will provide the necessary medical treatment. If your scan is completed at UC San Diego Health, the costs of any necessary medical treatment may be covered by the University of California or billed to you or your insurer just like other medical costs depending on a number of factors. The University and the sponsor BHA do not normally provide any other form of compensation for injury. For more information about this, you may contact the UC San Diego Office of IRB Administration at 858-246-4777 or irb@health.ucsd.edu.

How will I benefit from the study?

The benefit to you from joining the research study is that, subject to your agreement to participate in the disclosure of imaging results to you and your treating physician, your direct care provider may receive the results of your PET scan and may use that information in supporting your future care. Additionally, you may benefit from increased knowledge about the PET scan's influence on clinical decision making and medical outcomes when the study results become available. In the future, the knowledge learned during this study could help guide the appropriate use of PET scan imaging in patients whose conditions are difficult to diagnose and monitor.

Will it cost me anything to participate?

There will be no cost to you for participating in this study. Your research PET scan and interactions with research staff conducting the pilot study will be paid for by the sponsor BHA. You will not be asked to pay for any other expenses related to the costs of the PET scan such as the Amyvid imaging agent which will be provided by Avid Radiopharmaceuticals. However, if you do not reside near the medical imaging center that has agreed to perform your PET-CT scan, and nevertheless, you still wish to participate in the EPSMS clinical trial, then you should expect to pay for your own travel expenses to and from the medical imaging center including any lodging before and after

the day of your PET scan. You and/or your health plan/insurance company will need to pay for all other costs of treating your condition with multiple sclerosis while in this study under the care of your clinical neurologist, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no cost. Before you decide to be in the study, you should check with your health plan/insurance company to find out exactly what they will reimburse.

Who is funding the study?

Brain Health Alliance sponsors and manages the EPSMS clinical trial. Avid Radiopharmaceuticals has agreed to fund the first 20 doses of Amyvid for the pilot phase of the clinical trial. Research study doctors and staff do not receive any direct income from the study sponsor or supporters. The sponsor and supporters of the study may be changed or additional sponsors and supporters may be added, especially if the initial pilot study is extended to a multi-year clinical trial with a much greater number of study participants.

What happens if I decide to volunteer for the amyloid PET-CT scan?

There is no special preparation required for an amyloid PET-CT scan. On the day of your scan, you will go to the medical imaging center assigned to you for your entire-body PET-CT scan. A technologist will ask you some questions and/or may give you some tests to make sure everything is OK for the PET scan. If you are a woman of child-bearing potential, a urine pregnancy test will be performed. Your height and weight will be measured. You will be asked to remove your clothing and wear a hospital gown that will provided for you. You will have an intravenous (IV) line with a short catheter placed in a vein for an injection of 8-12 mCi of Avid Radiopharmaceuticals Amyvid ([18F]-florbetapir), a radioactive imaging dye for amyloid in the tissues of your body, also known to bind to myelin. You will then receive a PET scan on the entire-body scanner which will last from 10 to 20 minutes and will begin 50 minutes after you receive the injection. This 10-20 minute PET scan will be followed by a CT scan, which will take less than 1 minute on the same scanner. After completion of the entire-body PET-CT scan, the IV line will be removed, and you can get up and off the scanner bed. The total amount of time for this visit to the medical imaging center for the Amyvid PET scan with CT may be approximately a half day.

What happens if I decide to withdraw from the study?

The decision to participate is voluntary. You can choose not to participate or you may decide to volunteer now and then later withdraw from the study for any reason at any time. You can inform the study team at BHA in writing at the address listed on the first page of this form. Any data collected prior to your withdrawal from the study will belong to the clinical trial, and may be used for research by BHA. The study doctor or sponsor can stop your participation at any time without your consent for the following reasons: if it appears to be medically harmful to you, if you fail to follow directions for participating in the study, if it is discovered that you do not meet the study requirements, if the study is canceled, or for administrative reasons.

What are my alternatives?

The EPSMS clinical trial has been designed, managed, and will be conducted for research purposes only. Your only alternative is simply not to participate in this study. PET scans with Amyvid can be obtained outside the study, but it is not likely that it could be performed with an entire-body PET-CT scanner unless done as part of the study.

How will my privacy be protected?

We will do our best to make sure that your health and management information collected during the course of this research study will be kept private. However, we cannot guarantee total privacy. Records of your participation on this study, your progress and data from the images submitted while you are on the study will be kept in a confidential form at the BHA research office. All data sent to BHA over the internet will be secured so that other people cannot read it. Your personal identifying information will be stored separately from the study data that will be analyzed. Study information may be given out if required by law. If information from this study is published or presented at medical scientific meetings, your name and other personal information will not be used.

Who will be allowed to see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. However, the researchers will do their best to make sure that any information that is released will not identify you. There are government regulatory organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are: the Centers for Medicare & Medicaid Services (CMS), and the Institutional Review Board (IRB) for BHA, a group of people who review the research with the goal of protecting the participants who

volunteer for the study. Specifically, the principal investigator, referring physicians, the statistical team coordinating collection and analysis of data, and members of the IRB will have access to the records. De-identified information may be provided as required by law.

How will confidentiality be maintained?

Any paper records obtained, received and/or produced concerning your health care and personal health information will be stored in locked cabinets in locked rooms only accessible by the study coordinator and principal investigator. Your PET scan will be collected and archived at BHA, stripped of all identifying information, for use in future research in the EPSMS clinical trial, and will be accessible only to researchers on the study team analyzing the data. The analysis database and image archive for the EPSMS clinical trial will contain only unique identifiers (your own identification number that is not linked directly to your name or any other personal health information) for you in order to protect and conceal your identity. These electronic computerized records will be secured behind both hardware and software firewalls and multi-factor authentication and authorization systems (the equivalent of two or more means of identifying the individual who obtains access). This electronic database will be used to analyze the data, manage and conduct the research study, ie, answer the medical scientific questions posed by the investigators.

Whom can I call with questions, complaints, or if I'm concerned about my rights as a research subject?

If you have questions, concerns, or complaints regarding your participation in this study, you should contact your treating or referring physician and also the principal investigator, Dr. Carl Taswell, identified on the first page of this consent form. If you have any questions about your rights as a clinical trial research subject, and/or concerns or complaints regarding this pilot study, you should write to Dr. Carl Taswell, Brain Health Alliance, 8 Gilly Flower St, Ladera Ranch, CA 92694. You may also email him at ctaswell@BrainHealthAlliance.org or call him at 1(949)481-3121. Additional information to help you understand clinical trial research can be found online at https://clinicaltrials.gov/ct2/about-studies/learn. A description of this clinical trial will be available on ClinicalTrials.gov as required by US Federal Law. The EPSMS clinical trial has been assigned the identifier NCT04390009 by ClinicalTrials.gov. This website will not include any information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. You may also contact the UC San Diego Office of IRB Administration at 858-246-4777 or irb@health.ucsd.edu to inquire about your rights as a research subject or to report research-related problems.

PET Scan Results

If you agree to participate in the EPSMS clinical trial, and you do complete a PET imaging test with an entire-body PET scanner and the Amyvid imaging dye, please let us know if you wish to be informed of your PET scan results with regard to amyloid in the grey matter of the brain, myelin in the white matter of the brain and nervous system, both amyloid and myelin, or neither. If you wish to be informed of any results, regarding either amyloid and/or myelin, then you must also spend some time (both before and after the PET scan) talking with a doctor who will provide the necessary education and counseling with respect to disclosure of the imaging results from the PET scan.

YES, I wish to be informed about the results from my PET scan concerning the white matter of the brain and nervous system related to myelin.
_____ (sign initials)

YES, I wish to be informed about the results from my PET scan concerning the grey matter of the brain related to amyloid.
_____ (sign initials)

YES, I wish to be informed about the results from my PET scan concerning comparisons with my past PET, MRI, and/or CT scans that I request be studied for retrospective analysis.
_____ (sign initials)

NO, I do not want to be informed about the results from my PET scan.
_____ (sign initials)

EPSMS Clinical Trial

I have read this consent form or had it read to me. As required for informed consent, I have discussed it with the BHA research study team (represented by Discussant), and with my study partner, and our questions have been answered to our satisfaction. I agree voluntarily to participate in the EPSMS clinical trial, assisted and accompanied by my study partner, until I or my study partner decide otherwise. I understand that I do not give up any of my legal rights by signing this consent document, and that both I and the medical imaging center that will perform my PET scan will be given a copy of this signed form, and the original signed form will be retained by Brain Health Alliance. I understand that I will receive a copy of this consent document, the local imaging center consent document, and a copy of the California State “Experimental Subject’s Bill of Rights” to keep.

Participant’s signature: _____
Name: _____ Date: _____
Phone: _____ Email: _____

Study partner’s signature: _____
Name: _____ Date: _____
Phone: _____ Email: _____

Discussant’s signature: _____
Name: _____ Date: _____
Phone: _____ Email: _____