Participant Information Sheet

The Parkinson's Progression Markers Initiative (PPMI) Clinical

TITLE: The Parkinson's Progression Markers Initiative (PPMI) Clinical - Establishing a Deeply Phenotyped PD Cohort

PROTOCOL NO.: 002
WIRB® Protocol #20200597

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STUDY-RELATED PHONE NUMBER(S): 0191 2081250

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is unclear or if you would like more information. Take time to decide whether or not you wish to take part.

VOLUNTARY PARTICIPATION

Your participation in this research study is voluntary. You are under no obligation to participate in this study and your medical care at this site will in no way be affected by your decision to participate or not to participate. You may decide to stop your participation in this study at any time, but you may be asked to return for a final visit. If you do leave the study early, the information you have already provided will be kept confidential.

PURPOSE OF THE STUDY

The purpose of this study is to continue to obtain information from people with and without Parkinson's disease (PD) so that researchers may better understand how Parkinson's disease progresses, in order to inform better treatments. The information collected in this study is for research and not for clinical care. This study is an expansion of the PPMI study that has been ongoing for nearly ten years.

Information collected from this study includes:

- clinical information
- brain imaging scans
- samples of blood, urine, cerebral spinal fluid, and skin biopsy
- information from digital applications (such as an application on your smart phone)
- self-reported information from questionnaires you complete online

You will also be asked if you are interested in enrolling in a brain and tissue bank, if you wish to donate your brain after your death.

The information in this study will be used to help develop biomarkers for PD. Biomarkers are measures that tell us something about PD. We are working on biomarkers in PD because they may help to understand how the disease changes over time. Having good biomarkers for PD may also be useful in developing new treatments and may help to improve clinical care in the future. In this study, we will measure biomarkers that may be related to the way PD develops and changes over time.

WHY HAVE I BEEN CHOSEN?

You have been invited to participate in this study because you have been identified as one of the following groups:

- PPMI Study Participant – you are actively involved in the PPMI study and would like to continue your participation in this expanded PPMI Clinical study.
- Healthy Control – a healthy adult without a neurological disorder such as Parkinson's disease (PD).
- Prodromal – an adult who may be at increased risk for PD. This means you might be part of the PPMI Remote study where you already answered questions about your health. Otherwise, you were identified for the PPMI study by this site. You may have a sleep problem called REM Behavior Disorder (RBD) or a known genetic variant associated with PD, and you had testing of your sense of smell. As part of this study, we will evaluate whether individuals with RBD or a genetic variant associated with PD and/or a decrease in sense of smell may be more likely to have brain imaging results showing a reduction in dopamine function. Dopamine is a brain chemical that is affected in individuals with PD or other neurologic conditions.
- PD – an adult with early Parkinson's disease (PD), with or without a genetic variant.

STUDY PROCEDURES

We will maintain a separate research record for you, the information in the research record will not be available to you until the research is completed. The research record will not be made part of your routine medical records. You will be informed about the overall results of the study but, in general, you will not receive your own research test results, unless we find something of urgent medical importance to you.

As part of this study, we will collect your first name, last name, email address, sex (male or female), and date of birth. You will be assigned a unique PPMI study ID number. This number will be used to identify your PPMI research information and samples. In addition, we may also create a globally unique identification (GUID) number that will be assigned

to your research information. This number can be used to connect your research information to other studies in which you participate that might also use a GUID, without storing your personally identifying information. To receive this number, we will additionally ask for your city (municipality) of birth, and country (province) of birth. This information will be entered into a secure database to create the GUID number. The GUID number itself cannot be used to reconstruct your personally identifying information. The personally identifying information you provided will not be shared with other researchers.

At screening (or later visit if you are a Prodromal participant), you will be asked to identify a substitute decision maker (also known as a "research proxy" or a Legally Authorized Representative (LAR)). This person will help you decide whether it is a good idea for you to continue participation in this study if at a future time the investigator believes that you can no longer make decisions about ongoing participation. Choosing a substitute decision maker is voluntary. We will collect the information to identify your substitute decision maker on a separate form. You can change your mind about having a substitute decision maker, and/or change the person(s) you name at any time.

There are additional, separate optional research activities related to the PPMI program that you will be asked to do, such as completing on-line questionnaires and completion of assessments on a smart phone application. We may discuss these activities with you at your Screening visit or at a follow up visit. If you decide to participate in those optional activities, you will be asked to sign a separate consent for those activities.

STUDY ACTIVITIES

You will be asked to complete study activities depending on the group you are in as described below:

Active PPMI Participant Groups Transitioning into PPMI

- If you are transitioning from the previous PPMI study, you will not be required to complete a Screening or Baseline visit. You will continue to be followed on a visit schedule like PPMI for a minimum of 5 years.
- At your first visit in-person visit as part of this study (PPMI Clinical), you will be asked to update information about you and your family history so we can make sure your information is current. You will also be asked to complete other follow-up visit activities described below for your group.

Healthy Control / Parkinson's Disease / Parkinson's Disease with Genetic Variant Groups

- Screening Visit - A screening evaluation will take place to make sure you qualify to be part of the study. This visit may take up to 8 hours or will be spread over more than 1 day if more convenient. At this visit we will collect the following information:
    - Review of you and your family's medical history
    - PD diagnosis history (if applicable)
    - Physical examination and vitals, including blood pressure, pulse,

temperature, height and weight
    - A neurological examination and confirmation of diagnosis
    - Information about your ability to perform daily activities and to measure your movement
    - Review of any medications you are currently taking
    - A measure of your thinking and memory
    - Blood tests to make sure there are no abnormal results and you can be in the study
    - A brain scan looking at dopamine producing cells using SPECT imaging (Section 6 below). Your eligibility for this study will depend on the amount of dopamine levels shown on the SPECT scan.

- Baseline Visit – If you are eligible to continue with study visits, you will return to the site within 60 days of your screening visit. This visit may take about 6-8 hours or will be spread over more than 1 day if more convenient. We will collect the following information:
    - Your vital signs including blood pressure, pulse, temperature, height and weight
    - Information about your health and medications you are taking
    - Information about your neurological condition
    - Questionnaires about your ability to perform daily activities and to measure your movement
    - Questionnaires to measure your thinking, memory, moods and behaviors
    - Your ability to smell
    - A blood draw and a urine sample for storage and research tests (Section 1 and Section 2 below). The blood sample will also be used for DNA analysis (DNA contains genetic information about the development and functioning of humans).
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    - Lumbar puncture to collect cerebral spinal fluid for storage and research tests (Section 3 below)
    - You may be asked to undergo a skin biopsy to evaluate potential biomarkers (Section 4 below)
    - A brain scan using magnetic resonance imaging (MRI) (Section 5 below)

- Follow up Visits – Once all Baseline visit procedures are completed and you are enrolled in the study, you will be asked to return every 6 months for the first 2 years. After two years, visits will be conducted every 6 months remotely (for example, by phone or videoconference) and annually in the clinic. You will be asked to be followed for a minimum of 5 years of study visits.

    - The 6-month in clinic visits in the first 2 years will take about 2-4 hours and will include the following activities:
        - Your vital signs including blood pressure, pulse, and temperature
        - Information about your health and medications you are taking
        - Information about your neurological condition

        - Questionnaires about your ability to perform daily activities and to measure your movement
        - Questionnaires to measure your thinking, memory, moods and behaviors
        - A blood draw and urine sample for storage and research tests (Section 1 and Section 2 below)

    - Annual in clinic visits will take about 6-8 hours or will be spread over more than 1 day if more convenient and will include the following activities:
        - Your vital signs including blood pressure, pulse, temperature, height and weight
        - Information about your health and medications you are taking
        - Information about your neurological condition
        - Questionnaires about your ability to perform daily activities and to measure your movement
        - Questionnaires to measure your thinking, memory, moods and behaviors
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        - Blood sample and urine sample for storage and research tests (Section 1 and Section 2 below)
        - Lumbar puncture to collect cerebral spinal fluid for storage and research tests (Section 3 below)
        - You may be asked to undergo a skin biopsy (every 2 years) to evaluate potential biomarkers (Section 4 below)

    - Remote 6-month visits will begin following year 2 and will take about 1-2 hours and will include the following activities:
        - Information about your health and medications you are taking
        - Questionnaires about your ability to perform daily activities and to measure your movement
        - Questionnaires to measure your thinking, memory, moods and behaviors

    For Participants with PD: During this study if your treating physician prescribes a medication for your PD, please contact the study team BEFORE starting the medication and advise your treating physician of your participation in the study. If possible, we would like to evaluate you and conduct some study tasks before you start PD medication.

Prodromal Group:

- Baseline Visit – Once your screening visit is complete and you have been notified that you are eligible to continue in PPMI Clinical. You will be asked to complete a Baseline visit within 60 days of your Screening visit. This visit may take about 6-8 hours or will be spread over more than 1 day if more convenient. We will collect the following information:
    - Review of you and your family's medical history

- Physical examination and vitals including blood pressure, pulse, temperature, height and weight
- A neurological examination and confirmation of diagnosis
- Information about your ability to perform daily activities and to measure your movement
- Information about your health and review of any medications you are currently taking
- Blood test to make sure there are no abnormal results and you can be in the study
- A blood draw and a urine sample for storage and research tests (Section 1 and Section 2 below). The blood sample will also be used for DNA analysis (DNA contains genetic information about the development and functioning of humans).
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- Questionnaires to measure your thinking, memory, moods and behaviors
- Your ability to smell
- Lumbar puncture to collect cerebral spinal fluid for storage and research tests (Section 3 below)
- You may undergo a skin biopsy to evaluate potential biomarkers (Section 4 below)
- A brain scan using magnetic resonance imaging (MRI) (Section 5)

- Follow up Visits – Once all Baseline visit procedures are completed and you are enrolled in the study, visits will be conducted every 6 months remotely (for example, by phone or videoconference) and annually in the clinic. You will be asked to be followed for a minimum of 5 years of study visits.

    - Remote 6-month visits will take about 1-2 hours and will include the following activities:
        - Information about your health and medications you are taking
        - Questionnaires about your ability to perform daily activities and to measure your movement
        - Questionnaires to measure your thinking, memory, moods and behaviours

    - Annual in clinic visits will take about 6-8 hours or will be spread over more than 1 day if more convenient and will include the following activities:
        - Physical examination and vital signs including blood pressure, pulse, temperature, height and weight
        - Information about your health and medications you are taking
        - Information about your neurological condition
        - Questionnaires about your ability to perform daily activities and to measure your movement
        - Questionnaires to measure your thinking, memory, moods and behaviours
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- A blood sample and urine sample for storage and research tests (Section 1 and Section 2 below)
- Lumbar puncture to collect cerebral spinal fluid for storage and research tests (Section 3 below)
- You may be asked to undergo a skin biopsy (every 2 years) to evaluate potential biomarkers (Section 4 below)
- A brain scan using magnetic resonance imaging (MRI) (Section 5 below)

You may notice new symptoms during the study. If you are concerned about any changes or symptoms, please inform the study personnel. The study doctor will regularly conduct neurologic testing at study visits and any changes will be recorded. You will not be provided a clinical diagnosis as part of this research study. However, the study doctor may recommend you follow-up with your primary doctor or make a referral for other clinical care, if appropriate.

If you are diagnosed with PD or other neurodegenerative disorder during this study, please contact the study team. If possible, we would like to evaluate you and conduct some study tasks to evaluate the diagnosis. Depending on when you were last seen, this study visit may include the same activities as a yearly visit and may also include a SPECT imaging DaTscan and MRI imaging scan. If you are diagnosed with PD and your treating physician prescribes a medication for you, please contact the study team BEFORE starting the medication. If possible, we would like to evaluate you and conduct some study tasks before you start PD medication.

DESCRIPTION OF PROCEDURES

Section 1 – Blood Samples

Blood samples will be collected from a vein in your arm or hand to test for abnormalities and for research purposes. When a blood sample is collected at a Screening visit, less than half a Tablespoon full of blood will be collected. At Baseline and each in-person follow up visit, no more than 4 Tablespoons full of blood will be collected.

For the Baseline and follow up in-person visits, you will be asked to fast (no food and only drinks such as water, clear tea or black coffee) for at least 8 hours prior to the blood draw being completed. If it is not possible for you to fast, we will provide you with a list of foods for a low-fat diet and ask that you choose items from that menu the day of your blood draw.

Blood samples that are collected to test for abnormalities are sent to a central lab for processing and testing. This sample will be destroyed once the test is completed.

The blood samples that are collected for storage in a central repository for research purposes will be tested now and in the future for the following reasons:

- Measure the amount of proteins and other molecules found in blood that may reflect brain function or indicate changes in brain function. For example, the

amount of protein in blood may be an early sign to help diagnose PD and track disease progression.
- Look at the genetic material in people with PD compared to people without PD.
- Identify genes that may be important in the progression of PD.
- Use the blood to look at other measurements that have not yet been identified.

Section 2 – Urine Samples

Urine samples (about a tablespoon) will be collected at Baseline and up to 10 additional times during your participation. The urine samples will be shipped for storage in a central repository for research purposes now and in the future. The samples will be used to measure the amount of different chemicals in urine for participants with PD as compared to participants at risk for PD and those without PD. Samples will also be tested to determine whether there are any changes over time as PD progresses.

Section 3 – Lumbar Puncture

You will undergo a lumbar puncture (LP) to obtain cerebral spinal fluid (CSF) samples. CSF is the fluid that surrounds the brain. Studying this fluid may help researchers learn about what is going on in the brain. This procedure will be done for all groups at Baseline and up to 6 additional times during your participation, depending on when you enrolled. At the follow up visits, we may ask you to provide a blood sample before the LP is done to make sure you are not at an increased risk of bleeding.

A lumbar puncture involves inserting a small needle in your lower back. For this procedure, the study staff will help position you either on your side or sitting up, whichever is most comfortable for you. First your skin will be cleaned with antiseptic. The study doctor will inject a small amount of local anesthetic to numb the area. To avoid an allergic reaction, please let the study staff know if you have ever had a reaction to a local anesthetic (such as while at the dentist). Once numb, a very thin needle will be inserted into the spinal canal in your lower back. Up to 20 milliliters (about one and a half tablespoons) of spinal fluid will be removed for analysis and storage.

After the LP is completed, we will discuss with you any side effects that you may have experienced before you leave. You will also be contacted 2-3 days after the LP to discuss any side effects that you may have experienced since the LP was completed.

Section 4 – Skin Biopsy

If you are an active PPMI participant transitioning into this study, you may be asked to undergo a skin biopsy to collect up to two skin samples at your first in person visit. If you are a newly enrolled participant, you may be asked to undergo a skin biopsy to collect up to two skin samples at your Baseline visit, as well as Year 2 and Year 4 of participation. Skin samples will be taken for research tests looking at alpha-synuclein and other proteins and molecules related to PD or other neurological conditions.

We will place a needle into your skin and inject a local anesthetic to make the area numb. We will then take up to two skin samples from the back of your neck. The piece of skin of each biopsy will be about 3 millimeters in diameter, or about the size of an apple seed.

Although very rare, the study doctor may need to close the area with stitches. The skin biopsy process will take about 30 minutes.

After the skin biopsy is completed, we will discuss with you any side effects that you may have experienced before you leave. You will also be contacted 2-3 days after the skin biopsy to discuss any side effects that you may have experienced since the skin biopsy was completed.

Section 5 – MRI Brain Imaging Procedures

Magnetic Resonance Imaging (MRI) Scan
You will have an MRI scan at the baseline visit. If you are a Prodromal or PD participant, it is anticipated that you will also have an MRI at Year 1, Year 2 and Year 4. The MRI scan will look at the structure of your brain. You will lie inside a magnetic resonance scanner, which is like a narrow tube, for about 40 minutes while pictures of your brain are taken.

Section 6 – SPECT Brain Imaging Procedures

Dopamine Transporter DaTscan™ SPECT Imaging Scan
You will be asked to have an imaging procedure that will obtain pictures of your brain using single photon emission computed tomography (SPECT) using a radioactive substance called DaTscan™. The scan will be done to measure the function of those cells in your brain that produce dopamine (a chemical that sends messages between nerve cells in the brain). People with PD show a decrease in the number of cells that produce dopamine compared to people with no neurological disorder.
You will be asked to have a dopamine transporter SPECT scan at the Screening visit to determine your eligibility to continue being followed in the study. A central reading facility at Invicro in New Haven, Connecticut, in the USA will review your scan.

To lessen your burden, a previously acquired DaTscan may be used in place of a newly acquired Screening scan. The previous scan must have been acquired within 6 months of the PPMI scheduled Screening DaTscan and must meet the PPMI study requirements.

If you are a Prodromal or PD participant, it is anticipated that you will also have a SPECT scan at Year 1, Year 2 and Year 4.

The following procedures will be done:

- Women of childbearing potential will have a urine pregnancy test that must show a negative result prior to DaTscan™ injection.
- Before the injection of DaTscan™ you will take some medication, called Potassium iodide (either as Lugol's solution or Potassium Iodide tablets), by mouth to protect your thyroid gland. These medications contain iodine. To avoid an allergic reaction

to this solution, please tell study staff if you have ever had a reaction to iodine. If so, we will give you a different medicine if available

- You will have an intravenous line (IV) started in a vein in your arm through which the DaTscan™ will be injected.
- You will return about 4 hours later.
- Small markers will be attached with adhesive (a glue-like material) to the outside of your head. These markers allow us to better position the images of your head when we look at the results of the scan. The markers will be taken off at the end of the scanning session.
- An imaging procedure will be used to obtain pictures of the activity in your brain using single photon emission computed tomography (SPECT). You will lie on a narrow table and your head will be placed in the SPECT camera. The SPECT camera takes a "picture" of the radiation given off by the drug. A picture of your brain will be taken for about 30 minutes and could take up to 1 hour if your body moves during the scanning.
- After the SPECT scan is completed, we will discuss with you any side effects that you may have experienced before you leave.
- You will also be contacted 2-3 days after the scan to discuss any side effects that you may have experienced since the imaging visit.

NUMBER OF PARTICIPANTS

- About 4,500 participants will be eligible and invited to participate in this study. Locally, about 30 participants will be included.
- There will be about 50 study centres around the world (e.g., United States, Europe, Israel) enrolling participants for this study.

RISKS OF PARTICIPATION

Some of the questions you will be answering are personal and may make you feel uncomfortable or upset. You do not have to answer any questions that you do not want to. You may get frustrated or feel tired when completing some of the questionnaires or other study activities.

For patients with PD, if you are currently taking medications and stop PD medications so that you may be eligible for participation in this study, you may no longer experience the benefits of those medications on your symptoms. In particular, you might experience a recurrence of your tremor and slowness of movements at the level they were before starting PD medications. You may also feel stiffer, especially if stiffness rather than tremor is your main symptom. There is also a rare possibility that you may have side effects from the withdrawal of medications currently in use, including fever, rigid muscles, unusual body movements, and confusion.
You should discuss these risks with your primary care physician or the physician who prescribed these medications.

Risks of Blood Draws: Blood draws may cause pain and bruising at the site where the blood is taken. Sometimes people can feel lightheaded or even faint after having blood taken. There is a risk that someone could use information from the blood sample you

submitted, to identify you if it were matched with another blood sample provided by you. However, any user of a blood sample you provide in this study must agree not to use it to try to identify you.

Risks of Lumbar Puncture: You may experience pain from the lumbar puncture site from where the needle enters to take the spinal fluid. There is also a risk of infection or bleeding. After the lumbar puncture, you may get a headache, to minimize the risk of a headache, the doctor will use a small needle and may prescribe bedrest for one or more hours after the procedure. If a headache occurs, it is usually mild and can be controlled by bedrest, drinking lots of fluids, and pain medication. Rarely, the headache is severe and requires additional treatment with a "blood patch." In this procedure, a small amount of your own blood is injected into the lumbar puncture site. This procedure is generally effective in stopping the headache.

You must inform your study investigator if you are allergic to local anesthesia (lidocaine) or to Betadine. Although very rare, it is possible to have an allergic reaction to the local anesthetic used for the lumbar puncture. Signs of an allergic reaction include swelling and/or a rash on your skin where the anesthetic was injected. To minimize any possible risk, the lumbar puncture will be done by a staff person who is specifically trained in the procedure.

You may become anxious about the lumbar puncture procedure, If you are extremely anxious about the procedure, the study doctor may prescribe an anti-anxiety medication (called a benzodiazepine, such as lorazepam (Ativan), alprazolam (Xanex)) for you to optionally take prior to the lumbar puncture.

Risks of Skin Biopsy: During the skin biopsy procedure, you might experience some pain and discomfort from the injection of the local anesthetic and/or the biopsy procedure. The local anesthetic will be used to minimize the pain or discomfort. There is a small risk that the biopsy site might change colour. The skin biopsy might leave a scar. There is also a possibility of infection or bleeding at the biopsy site. The study doctor will explain how to watch for any signs of these problems. Although very rare, it is possible to have an allergic reaction to the local anesthetic (lidocaine) or betadine. Signs of an allergic reaction include swelling and/or a skin rash on your skin where the anesthetic was injected.

Risks of MRI: The magnetic resonance scanner takes pictures of your brain based on electromagnetic waves. There is no radiation exposure as part of this procedure. You may hear loud noises such as knocking or hammering during the MRI. **Please inform the study doctor if you have metal implants (screws, plates or clips) or if you have a pacemaker.**

You may become anxious while in the magnetic resonance scanner. If you do suffer from claustrophobia, please notify the study doctor. If you are extremely anxious about the procedure, the study doctor may prescribe an anti-anxiety medication (called a

benzodiazepine, such as lorazepam (Ativan), alprazolam (Xanex)) for you to optionally take prior to the MRI.

Risks of anti-anxiety medications (benzodiazepines, such as lorazepam (Ativan) or alprazolam (Xanex)): Anti-anxiety medications can cause drowsiness, confusion, dizziness, blurred vision, weakness, slurred speech, difficulty walking, gait imbalance or difficulty breathing. If you take this medication prior to MRI or LP you will be monitored and transportation home will be arranged (you will no longer be able to drive for at least 8 hours after taking such medication, and possibly longer).

Risks of DaTscan™: DaTscan™ has been given to more than 500,000 people. The most common side effects of DaTscan™ are headache, increased appetite and dizziness. However, it is important for you to know that the injection of DaTscan™ may involve risks that are not known at this time. In order to take pictures of your brain, DaTscan™ gives off ionising radiation that the camera sees. The amount of radiation from one scan is equal to the natural background radiation you receive over two years by simply living in the UK. If you have PD, you will receive 4 scans. This is equivalent to 8 years of average natural background radiation in the UK. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. The chances of the radiation causing cancer or birth defects are believed to be very small. We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their life. Taking part in this study will increase the chances of this happening to you from 50% to 50.08% if you have one scan only (healthy control) or to 50.3% if you have 4 scans (person with PD).The insertion of the IV may feel uncomfortable and may leave a bruise. You'll need to lie very still under the camera for about 30 minutes or up to an hour, which may cause back pain, headache, dizziness or fatigue.

Female Participants: If you are female and become pregnant while taking part in the study you must tell your study doctor immediately. If the pregnancy occurred within 30 days of the DaTscan™ injection, you will be asked to have a urine pregnancy test within 7 days of reporting the pregnancy. If the test result is positive, this will be reported to GE Healthcare (the supplier of the DaTscan™). You may choose to continue your participation in PPMI during your pregnancy; however, you will not have MRI, DaTscan imaging, or lumbar puncture during your pregnancy. If you are not still being followed in the study, you may be contacted in the future to find out the result of the pregnancy. There might be risks to your unborn child if you are pregnant or if you become pregnant during the study. **Because of these risks, you must not participate in this study if you are pregnant, or plan to become pregnant during the research study period or are breast-feeding a child.**

Male Participants: If you are male and your partner becomes pregnant in the 30 days after you received DaTscan™ injection, you must tell your study doctor immediately. We will ask that you return to our site with your partner who will be asked to sign a consent form to have a urine pregnancy test. If your partner agrees, the pregnancy test must be

done within 7 days of signing consent. There might be risks to the unborn child if your partner becomes pregnant during your study participation.

Risk of Potassium Iodide: Potassium Iodide comes in a number of forms. These include tablets and solutions (e.g. Lugol's solution). Lugol's solution is 10 drops of a saturated solution of potassium iodide. With either form participants may experience a metallic or bitter taste in their mouths from the iodine. Participants with allergies to iodine might get itching, a rash, bloating, severe blood pressure changes (shock), and death if given iodine. Participants who are allergic to iodine will be administered an alternative solution such as potassium perchlorate, if available..

Loss of Confidentiality: Participation in this research carries a risk of loss of confidentiality regarding your genetic information and possibly your diagnosis. It may not be in your best interest if, for example, insurance companies or your employer become aware of such information. Every effort in compliance with applicable law will be made to maintain your confidential information and protect personal information obtained as a result of this study.

We would like you to follow the Schedule of Activities as close as possible to collect all the possible information to understand how the disease progresses. However, should you, any time during the study, find any of the examinations described above like the lumbar punctures or the skin biopsy too troublesome, invasive, or uncomfortable, we will be happy to discuss this with you and try to minimize the discomfort as much as possible. If that is still not acceptable to you, you will be allowed to continue the study without the implicated examination.

There may be risks or side effects which are unknown at this time.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. 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.

BENEFITS OF PARTICIPATION

You will not benefit directly from being in this research study. However, new information may be generated by the study that will support development of better treatments for Parkinson's disease.

ALTERNATIVES

This is not a treatment study. Your alternative is to not participate.

COMPENSATION FOR INJURY

If you think you have been injured by being in the study, your study doctor will treat you or will refer you for treatment.

The NHS will provide medical care for any emergency medical problem that you may

experience as a direct result of your participation in this research.
Decisions regarding care and compensation for any other research related injury will be made on a case-by-case basis and will be dealt with by the Sponsor of the study (Michael J. Fox Foundation).

COSTS

There will be no cost to you to participate in this study.

PAYMENT FOR PARTICIPATION

You will be paid for completing study visits based on the following schedule:

- Around £80 (the equivalent of $100) for a Screening visit
- Around £160 (the equivalent of $200) for a Baseline visit
- Around £126 (the equivalent of $150) for Month 6 and Month 18 visit (for PD and Healthy Control groups)
- Around £160 (the equivalent of $200) for each annual visit that occurs thereafter

REIMBURSEMENT FOR PARTICIPATION

You will be reimbursed for reasonable out of pocket expenses after submission of receipts to the study team (for example, costs for travel related to the study). You will be provided a guideline that will outline expenses that would qualify for reimbursement for this study. Such reimbursed expenses are not taxable.

A company called Greenphire will act as an agent of PPMI to manage the payment and reimbursement process using the ClinCard system. You may elect to receive funds to the provided ClinCard. You may also choose to have funds deposited directly to a bank account of your choice. When a visit is completed, or expenses are submitted for reimbursement, funds will be approved and electronically credited to your ClinCard or bank account within 2-5 days after being approved in the system.

Additionally, through Greenphire, you will have the option to receive updates related to appointment reminders, payment reminders and updates via text message and/or email message (standard text messaging rates will apply). You will have the opportunity to opt-in to receive these messages. If you choose to receive messages and decide later that you want to stop these messages, you will have the ability to opt-out.

Greenphire will collect information about you, including name, address, and date of birth. If you choose to receive funds through the direct deposit option, Greenphire will also collect your banking information. All information is stored in a secure fashion and is deleted from their system once the study has been completed and the funds on the card have been exhausted. Your information will not be shared with any other third parties and will be kept completely confidential. You are not required to provide your mobile phone or email address to use a ClinCard.

By registering with the Greenphire system and receiving funds directly to the bank account you identified or to use the ClinCard as your reimbursement method, you consent to participate in the Greenphire program.

CONFIDENTIALITY OF RECORDS AND AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

The team at Clinical Ageing Research Unit makes every effort to keep the information collected from you private and confidential. In order to do so, we will label study information with a study identification number instead of your name, store information in a secure manner, and restrict access to study personnel only. Sometimes, however, researchers need to share information that might identify you with people that work for the facility, regulators, or the study sponsor.

What information may be used and given to others?
The study team will use your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Results of laboratory or other medical tests

Also, any information about you collected during the study, from your initial screening visit through your last study contact, will be used for the study and for future research as described in the Future Use of Research Information and Samples section.

Who may use and give out information about you?

- Personnel from the Clinical Ageing Research Unit
- The study investigator and the study staff
- The Michael J. Fox Foundation for Parkinson's Research, the sponsor of the study

Your information may be given to:

- The Department of Health and Human Services agencies.
- National and international medicine regulatory agencies such as the Medicines and Healthcare products Regulatory Agency (MHRA), and the European Medicines Agency (EMA) might need to inspect study records at some point during the study or even after it has been completed. If this occurs, every effort will be made to keep identifying information about you private.
- National and international governmental agencies who regulate research activities
- Study staff at the Institute for Neurodegenerative Disorders, in New Haven, Connecticut, in the USA (representatives who maintain, manage, and monitor information collected in the study)
- Research monitors (representatives who visit each study site to make sure the study is being conducted according to regulations)
- The University of California, San Francisco, in the USA (representatives who maintain and manage data for the FOUND sub-study).

- Study staff at Indiana University, in the USA (representatives who maintain and manage participant information as part of the Participant Core, Biorepository Core, and the Genetics Core, and the Pathology Core).
- Blackfynn, LLC, Philadelphia, Pennsylvania in the USA (representatives who maintain and manage information collected for the study).
- The Informatics Core at the Laboratory of Neuro Imaging (LONI), University of Southern California, in the USA (representatives who maintain, manage, and monitor the central data repository).
- The Imaging Core at Invicro, in New Haven, Connecticut, in the USA (representatives who maintain and manage the imaging data)
- Scientists working on cures, therapies and products and services that may benefit Parkinson's disease and other patients. These scientists may work at for-profit companies, academic medical centers, or non-profit organizations.
- The Michael J. Fox Foundation for Parkinson's Research, the sponsor of the study and other entities that MJFF may designate to hold and transfer data
- The City and East Research and Ethics Committee, the local Research and Development Office, and the Institutional Review Boards at WCG IRB, in the USA, (committees that review research as required by regulations to make certain your rights as a research participant are protected)
- DocuSign, an electronic platform used to obtain and document consent

Why will this information be used and/or given to others?

- To do the research
- To study the results
- To see if the research was done correctly
- To perform additional research studies, which may involve development of cures, therapies and products and services for the benefit of Parkinson's disease and other patients.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

How long will this permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
Yes. You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study investigator. Upon receiving the written notice, the study team will no longer use or disclose your health information and

you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?
Yes. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
Not necessarily. While every effort is made to comply with applicable law to make sure that your health information remains protected, there is a risk that your information could be accessed by persons without appropriate permission. In addition, various applicable laws allow for your health information to be given to others not specifically within the permission you provide through this form.

FUTURE USE OF RESEARCH INFORMATION AND SAMPLES

This study involves the collection of samples such as blood, DNA, urine, skin, and CSF, as well as research information. Any samples collected in this study, and your research information, will be used for current study analysis and stored for future research. The purpose of storing these samples and research information is to make them available to scientists who are trying to develop new tests, treatments, and ways to prevent diseases. These samples and research information may be shared with other scientists for studies of PD, other neurological conditions, other types of disorders, or other biomedical research studies.

The clinical research information collected from you will be sent to the Laboratory for Neuro Imaging at the University of Southern California in Los Angeles, California. If we previously collected information from you in PPMI, that information will be combined with the new information we collect for this study. The research information will be stored indefinitely for research purposes. There will be no personal identifiers attached with your research data that is shared with other researchers.

Blood samples, DNA, urine, skin, and CSF that are collected for research purposes will be shipped to a central repository. These samples will not be destroyed once the study is completed (they will be stored indefinitely). Prior to storage and analysis, your DNA, blood, urine, skin, and CSF samples that were coded at our site will be labeled with a new unique code (double coded). Your name or other information that may identify you will not be attached to the stored samples.

You can change your mind at any time about the storage of your samples. Contact the site investigator and let him or her know that you no longer want your samples stored and they will be removed and destroyed. However, in some cases, it may be impossible to locate and stop such future research on your specific sample if all identifiers were stripped from your sample prior to the sample being provided to other researchers.

Your samples and research information collected from or about you may be used in additional research studies involving PD, other neurological conditions, other types of disorders, or other biomedical research studies. These additional studies may involve development of cures, therapies and products and services for the benefit of PD and other patients. Your samples and research information may be transmitted to scientific researchers worldwide. Your samples and study data will only be used for research and will not be sold. Requests by other researchers to access coded samples and clinical research data will be scientifically reviewed according to criteria set by The Michael J. Fox Foundation for Parkinson's Research, the sponsor of this study.

COMMERCIAL PROFIT

We will use your information and/or samples for research only. However, the results of this research might someday lead to the development of products or services (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product or service) that could be sold by a company. You will not receive money from the sale of any such product or service.

RETURN OF RESEARCH RESULTS

In general, we will not give you any individual results from your participation in the study. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

NEW STUDY INFORMATION

If we discover any new information that might make you change your mind about continuing in this study, we will let you know.

SPONSOR SUPPORT

This site is receiving payment from The Michael J. Fox Foundation for Parkinson's Research for conducting this research study.

CONTACT PERSONS

For more information concerning this research, questions, concerns or complaints about the research, or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact**:** The Clinical Ageing Research Unit on 0191 2081250. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

This research is being overseen by City and East Research and Ethics Committee. This is a group of people who perform an independent review of research studies. You may want to contact them at cityandeast.rec@hra.nhs.uk if you have questions, concerns, or complaints relating to the following:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.

- You want to talk to someone else about the research.
- You have questions about your rights as a research subject

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