



Parkinson's
Progression
Markers
Initiative

PPMI *Operations* *Manual*

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1.0 GENERAL INFORMATION

Study Management Contacts

Institute for Neurodegenerative Disorders (IND) Site Management Core (SMC) Study Contacts

Whom to Call	Reason to Call
IND Senior Director <u>Bridget McMahon</u> Phone: +1 443-695-5220 Email: bmcmahon@indd.org Senior Associate <u>Jessica Dimos</u> Phone: +1 203-645-9163 Email: jdimos@indd.org Senior Associate <u>Jillian Ricci</u> Phone: +1 203-430-6160 Email: jricci@indd.org	Questions regarding protocol, day-to-day study operations, IRB/ethics submissions, training, electronic regulatory document management (Florence eBinder™) system, site visits
Project Team Specialist <u>Cari Rainville</u> Phone: +1 203-215-9611 Email: crainville@indd.org	Event coordination (conference calls, site visits), surveys, general project support

Medical Monitor Contact

Whom to Call	Reason to Call
PPMI Medical Monitor <u>Andrew Siderowf</u> Phone: +1 215-280-2396 Email: Andrew.Siderowf@penntmedicine.upenn.edu	Urgent (e.g., after hours) questions about participant safety and enrollment (e.g., SAE reports, eligibility); generally, communications around adverse event reporting and eligibility can be addressed to the SMC who will triage as needed to study leadership, including the medical monitor.

Michael J Fox Foundation for Parkinson's Research Study Contacts

Whom to Call	Reason to Call
Senior Associate Director, Research Cohorts <u>Alyssa Reimer</u> Phone: 212-509-0995 Ext. 327 Fax: 212-509-2390 Email: areimer@michaeljfox.org	Questions regarding contracts
Research Cohorts Officer <u>David Bresnahan</u> Phone: 212-509-0995 EXT: 223 Email: dbresnnahan@michaeljfox.org	Questions regarding site payments, document translations, Greenphire, or recruitment & retention materials

PPMI 2.0 Study Core Primary Contacts

Whom to Call	Reason to Call
Pathology Core <u>Laura Heathers</u> Phone: 317-274-5080 Fax: 317-278-1100 Email: laeheath@iu.edu <u>Kumar Mantravadi</u> Phone: 317-278-6412 Fax: 317-278-1100 Email: kmantrav@iu.edu	Questions regarding Pathology Core and brain donation
Imaging Core <u>Andrew Serrano, MBA</u> Phone: 203-990-1638 Fax: 203-508-1564 Email: aserrano@invicro.com <u>Leanna Rodriguez</u> Phone: 215.458.4331 Email: lrodriguez@invicro.com	Questions regarding the MRI or DaTSCAN processes, procedures, transfer of scans. Questions or issues regarding ordering, shipping or receipt of DaTSCAN study drug.

Whom to Call	Reason to Call
<p>Biorepository Core <u>Danielle Smith, BS</u> Phone: 317-274-5744 Fax: 317-278-1100 Email: dchampag@iu.edu</p> <p><u>Karla Gonzalez, BS</u> Phone: 317-278-1148 Fax: 317-278-1100 Email: gonzalka@iu.edu</p>	<p>Questions regarding Biorepository Core: sample processing and shipments</p>
<p>IU Participant Coordination Core (IUPCC) <u>Laura Heathers</u> Phone: 317-274-5080 Fax: 317-278-1100 Email: laeheath@iu.edu</p> <p><u>Michelle Totten (UPSIT Screening)</u> Phone: 317-278-1189 Fax: 317-278-1100 Email: mictott@iu.edu</p> <p><u>Audra Myers (Travel Coordination)</u> Phone: 317-278-9034 Fax: 317-278-1100 Email: audmyers@iu.edu</p>	<p>Questions regarding Genetic Coordination Core</p>
<p>Genetic Coordination Core <u>Laura Heathers</u> Phone: 317-274-5080 Fax: 317-278-1100 Email: laeheath@iu.edu</p> <p><u>Paige Webb</u> Phone: 317-274-5713 Fax: 317-278-1100 Email: paiawebb@iu.edu</p> <p><u>Cheryl A Halter, MS CCRC</u> (Site Testing Questions) Phone: 317-274-5734 Fax: 317-321-2002 Email: chalter@iu.edu</p>	<p>Questions regarding Genetic Coordination Core</p>

Whom to Call	Reason to Call
<p>FOUND Study <u>Cheryl Meng</u> Phone: 415-221-4810 ext 23807 Fax: 415-353-9060 Email: chencheryl.meng@ucsf.edu</p> <p><u>Primi Ranola</u> Phone: 415-571-4808 Fax: 415-353-4275 Email: primi.ranola@ucsf.edu</p> <p><u>Kathleen Comyns</u> Email: kathleen.comyns@ucsf.edu</p>	<p>Questions regarding FOUND Study</p>

Study Personnel

Each site has identified one primary investigator and one primary coordinator on record; however, due to the number of participants and variety of activities involved as part of the PPMI 2.0 Clinical study, the investigator may appoint MDS-UPDRS-credentialed sub-investigators, as well as co-coordinators to the study team. Investigators may designate additional study personnel who will be conducting neurocognitive assessments, specimen blood draws and processing, skin biopsies, imaging, and CSF collection and processing, and regulatory management.

Please note the importance of consistency of study personnel.

It is essential to maintain consistency in ratings as much as possible throughout the study by having the same investigator or sub-investigator, coordinator/co-coordinator and other raters, as applicable, follow the same participant from screening through all subsequent follow-up visits. In instances where this is not possible, it will not be considered a protocol deviation, but close adherence is requested.

All key site personnel (e.g., investigator, sub-investigator, coordinator, co-coordinator) involved in the conduct of the study, including those conducting assessments and/or entering data in EDC, will require a Blackfynn EDC login account, and must have a completed Delegation of Responsibilities Form located in Florence, the electronic trial master file system (eTMF). Additional staff who are involved in the study (e.g., lead nuclear medicine PI, imaging manager, proceduralists, e.g., physician performing LP only, individual responsible for regulatory documents, etc.), but are not completing data entry do not require an EDC login account; however, they must have a Delegation of Responsibilities Form. The Delegation of Responsibilities Form must be updated whenever there is a change to the study team staff (including new additions, departures and role changes). The Delegation of Responsibilities Form must be signed electronically by both the staff person and the primary site investigator (or in the instance of departed staff, the investigator only).

Documentation of Site Personnel for PPMI

PPMI will utilize a web platform called HubSpot as the contact resource management (CRM) system. Site personnel will provide their contact information on the HubSpot website via on-line forms, using either an initial contact form or a change form (for departures or changes to roles or responsibilities). Examples of these forms can be found in the Florence PPMI General Study File > Study Contacts subfolder. It may be helpful to review the form in advance of online completion. The form can be completed on behalf of other team members (e.g., a designated site staff member may complete for other site staff).

Initial staff contact entry:

- The SMC will provide the site coordinator with a link to the HubSpot website to complete a contact form for each key personnel staff member (the coordinator can share the link with other staff members for their completion, if desired).
- The SMC will review and approve completed contact forms in HubSpot and notify site if there are any queries.
- Once the form is reviewed as complete, the SMC will post a copy to Florence in the Investigator Site File under study contacts.

Staff changes (role or responsibility changes, staff departures):

- Site staff will notify the SMC of role or responsibility changes and departures by submitting a ticket in Hubspot.

Global site contact listing

- A global PPMI 2.0 study contact list will be placed in the Florence PPMI 002 General Study File folder for reference and updated periodically.
- This listing is for PPMI purposes only and not for sharing outside PPMI.

Delegation of Responsibilities Form

- After initial site selection, all investigator changes must be first approved by the Steering Committee, or designee. Please contact SMC who will liaise with leadership to facilitate the approval process.
- Changes in coordinator and any other site staff will be reviewed by the SMC to ensure appropriate training and applicable document collection is completed to facilitate the change.
- Complete the Delegation of Responsibilities form for new staff additions, or when there are changes to roles or delegated responsibilities.

IND SMC Office Closings

In general, the IND SMC will be closed for the US holidays listed below. A date-specific schedule is posted in the Florence PPMI 02 General Study Binder. If you have an emergency on a day we are closed, please call the Medical Monitor at +1 215-280-2396.

New Year's Day (January 1)

Martin Luther King Observance (3rd Monday in January)

President's Day (3rd Monday in February)

Spring Holiday (April 2, 2021)

Memorial Day (4th Monday in May)

Independence Day (July 4 and possible day before or after)

Labor Day (1st Monday in September)

Columbus Day (2nd Monday in October)

Thanksgiving (4th Thursday and Friday in November)

Christmas (December 25)

2.0 OBTAINING INFORMED CONSENT

Prodromal Participants

Sites receiving referrals for Prodromal participants will need to obtain consent from these individuals at two timepoints – first at the Screening Visit when the primary activity will be to complete the DaTscan to determine eligibility to proceed to Baseline. Participants who return to the site will need to give informed consent for the main PPMI 2.0 Clinical protocol Baseline and follow up visit activities.

All Other Cohorts

All newly enrolled PPMI participants will give informed consent using the main PPMI 2.0 Clinical protocol consent.

Designation of Research Proxy

Designation of a research proxy is voluntary; thus, identification of a substitute decision maker is not required to participate in PPMI 2.0. A research proxy may be identified or changed at any point during study participation; however, if a participant is no longer able to provide ongoing consent to participation and a research proxy has not yet been identified, the participant must be withdrawn from the study. It is understood that state and international laws, regulations, and institutional policy might vary on terminology and designation of a research proxy (e.g., Legally Authorized Representative is a commonly used term, which may be inclusive of a “research proxy”). As such, consent forms and signatures to document when a research proxy gives ongoing consent on behalf of the participant should be implemented as applicable.

3.0 ENROLLMENT

Participant Profile Information

When a participant provides consent to participate, the following required participant identifiers will be collected in the EDC system:

- First name
- Last name
- Email address
- Date of birth
- Sex

In addition, the following (optional) identifiers will be collected:

- Middle name
- City/municipality of birth
- Country of birth

Participant ID Assignment

A participant ID number will be assigned to all PPMI program participants. Active PPMI participants transitioning in to this PPMI Protocol will keep their previously assigned PPMI ID number. Newly enrolled participants will be assigned a six-digit ID number when a participant profile is created in the EDC system. The six-digit ID number will be generated and assigned automatically in the EDC system. If a participant

screen-fails or decides not to enroll in the study, their ID number will NOT be re-used. The PPMI participant ID number will be used to identify a participant on all study-related documents.

Globally Unique Identifier (GUID) Number

Participant's identifiers may be used to generate a GUID number. Use of this ID can track an individual's participation across multiple studies without storing any personally identifiable information. The protected system used to create the GUID uses an algorithm of data element inputs, such as those collected in the participant's profile and produces an electronic "fingerprint" output. The system stores only the "fingerprint" and clears the individual's inputted data elements from memory. The participant is then assigned a 9-digit Unique ID Number that is associated with their electronic "fingerprint."

Activities Prior to Enrollment

PD/Healthy Controls (recruited locally at site):

Once a potential participant provides written information consent and Screening activities are then conducted, the following additional activities should be noted:

- The Imaging Core will make the determination based on the SPECT DaTscan results whether the participant is eligible to proceed to the Baseline visit. The site must receive confirmation of eligibility from the EDC system before any baseline activities may be completed.
- Before a participant is considered enrolled into the study (i.e., an eligible participant who counts towards the total enrollment goal), the site investigator (or sub-investigator) and coordinator should review the Inclusion/Exclusion eCRF to assess that the participant meets all eligibility criteria and complete the Inclusion/Exclusion page in EDC. Any uncertainty regarding the participant's eligibility should be referred to the IND SMC Site Manager prior to completing the Baseline visit in the EDC.

Prodromal/PD with Genetic Mutation:

Potential participants for the prodromal cohort, as well as potential participants with a diagnosis of PD with a genetic mutation, will be referred by the IU Participant Coordination Core (IUPCC) to an imaging site to begin the PPMI Clinical protocol activities and described below. Note that PD participants with a genetic mutation who are identified directly by the site will follow the pre-enrollment activities as outlined in the section above.

- The potential participant will first provide informed consent for the screening visit and DaTscan imaging.
- The Imaging Core will provide SPECT DaTscan results that will assist with the eligibility determination (whether the participant is eligible to proceed to the Baseline visit).
- If the participant is eligible to proceed to the Baseline visit, and the participant agrees to continue follow up in PPMI 2.0 Clinical, the IUPCC will refer the participant to the clinical site. The clinical site may be the same as the imaging site, or it may be different from the imaging site, depending on geographic location. [Confirmation of eligibility based on DaTscan imaging must be documented in the EDC system before any baseline visit activities may be completed.](#)
- The participant must provide informed consent to the PPMI 2.0 Clinical protocol prior to completing any baseline visit activities.

- Before a participant is considered enrolled into the study (i.e., an eligible participant who counts towards the total enrollment goal), the site investigator (or sub-investigator) and coordinator should review the Inclusion/Exclusion eCRF to assess that the participant meets all eligibility criteria and complete the Inclusion/Exclusion page in EDC. Any uncertainty regarding the participant's eligibility should be referred to the IND SMC Site Manager prior to completing the Baseline visit in the EDC.

Ineligible Participants/Screen Fails:

A participant will be considered enrolled into PPMI 2.0 Clinical if the participant consents to participate, all eligibility criteria are met, and the screening and baseline visits are completed in the EDC system. If a participant does not complete enrollment, no other study activities should be completed, and the individual should be marked as a screen fail in one of the following two ways:

1. If a participant declines further participation in PPMI 2.0 Clinical prior to completing a baseline visit, the “*Screen Fail*” electronic case report form (eCRF) should be completed in the EDC baseline visit and this should be documented in Question #1 on the eCRF.
2. If a potential participant does not meet all eligibility criteria, they will be considered a screen-fail and the “*Screen Fail*” eCRF should be completed in the applicable visit in the EDC system.

Protocol Waivers

Purpose: A protocol waiver (eligibility exception or eligibility waiver) is a prospective decision to permit accrual of a subject who does not satisfy the approved inclusion/exclusion criteria for enrollment. Protocol waivers may be granted at the discretion of the PPMI Clinical Monitor.

A protocol waiver will be documented via a Note to File (NTF). The NTF will be generated by the PPMI Site Management Core (SMC) and uploaded to the respective Investigator Site File in Florence.

Procedures:

The site staff will contact SMC in advance of the participant's enrollment. Information to be provided by the site includes participant ID, cohort, and eligibility criterion that is being requested. If requested in advance of participant ID assignment (i.e., creation of the participant's profile in EDC), the site will follow up with SMC, once available, for the SMC to finalize the NTF.

Once a request is made, the SMC will follow the steps below:

- Contact PPMI Clinical Monitor to review and approve the request.
- Notify Blackfynn of approved waiver; Blackfynn to provide data entry guidance for the site, as applicable.
- Notify the site of the approval, if granted; SMC to prepare documentation of the approval via a note to file (NTF), using the current NTF template (located in Florence <https://v2.researchbinders.com/#/app/teams/5e149516d0d359160449be32/documents/5fbc5e057ecde5003b07759c/versions/1>).
- Once the participant ID is supplied, finalize the NTF. The NTF will detail the request and approval.
- The NTF file name convention will be PPMI 002 NTF Site ###_PPT [insert Participant ID] DDMONYYYY

- SMC to upload completed NTF to Florence site folder under *Other, Notes to File Misc.*
- Upon completion of upload, SMC to apply electronic signature to document in Florence.
- SMC to notify site of request for e-signed (SMC and Site representative) NTF in Florence by assigning the task for electronic signature (coordinator or investigator). Supporting documentation (e.g., communication of approval of waiver) will also be filed in Florence using PPMI 002 NTF Site ### PPT [insert Participant ID] DDMONYYYY.
- SMC to maintain log of NTFs issued with site #, participant ID, date issued, and reason for waiver.

4.0 IMAGING

Refer to the SPECT Imaging Trial Operations Manual for details regarding the DaTscan™ product (ordering, storage, administration and accountability).

Ordering DaTscan™ (US Sites)

The Imaging Core will supply the GE Healthcare (GEHC) Dose Order Form created for each PPMI 2.0 site. Instructions provided by GEHC outline the ordering process and will be provided along with the order form. Each form includes the specific code for the PPMI study. The form will highlight to GEHC that the dose is to be supplied at no charge.

Placing a new DaTscan™ dose order (US Sites)

- Currently DaTscan™ dose is produced on Monday, Tuesday, Wednesday and Thursday for injection on the day following production (barring holidays and production site shutdowns). DaTscan™ is available for delivery and injection Tuesday – Friday.
- GEHC requires a lead time of three business days to place a DaTscan™ order. Orders should be placed by 11am EST three business days prior to injection.
- For each participant scheduled for imaging, you will need to request 1 vial.
- The participant cohort must be selected on the form.
- Please review the form to confirm the accuracy of the order information.
- All sites must place dose orders with GEHC using the order form provided which will highlight that the vials are to be free of charge for the PPMI study.
- Upon receipt of the order form, GEHC will provide you with an order confirmation via email or fax. If you do not receive an acknowledgement, please contact GEHC as instructed on the order form. Site's should file the order confirmation in the participant's study record.

Order Cancellation (US Sites)

- GEHC requires a minimum of three working days to cancel a DaTscan™ dose order.
- Requests for cancellation should be made by 11am EST three business days prior to the date of the scheduled delivery by contacting GEHC at the number provided on the order form.
- GEHC should also be notified if the delivered dose was not used as planned or if a dose needs to be replaced.

Shipment to Sites (US Sites)

For each shipment received, you will need to complete the DaTscan™ Acknowledgment of Receipt Form (see appendix) and record the number of packages received (vials in this case). Please file this completed document with your source documents.

DaTscan™ will be delivered on the day of injection. DaTscan™ may be delivered to sites via FedEx or a local delivery service. If DaTscan™ is delivered to your site via FedEx, the shipment is expected to arrive in accordance with the times specified by the delivery service.

NOTE: Each DaTscan™ vial will contain 5 mCi at 12:00 pm Eastern Time the day of delivery. If a participant is scheduled for injection past 12:00 pm Eastern Time, additional vials may need to be ordered to ensure the appropriate amount of radioactivity is available at the time of the injection.

Ordering DaTscan™ (EU Sites)

- There is an internal system in place to accommodate a differential coding between imaging centers normal 'paid-for' vials and PPMI orders.
- All sites must place dose orders with GEHC using the order form provided which will highlight that the vials are to be free of charge for the PPMI study.
- The participant cohort must be selected on the dose order form.
- GEHC's Customer Service teams have been notified to expect and authorize free of charge vials to each of these centers.
- GE requires a lead time of two business days prior to injection to place a new DaTscan™ orders. Orders should be placed by 11am local time two business days prior to injection.
- Orders should be cancelled by 11am local time two business days prior to the requested delivery date (EU only).
- GEHC should also be notified if the delivered dose was not used as planned or if a dose needs to be replaced.

Storage of DaTscan™

DaTscan™ should be stored at room temperature and is not to be frozen. Appropriate radiation precautions should be observed during the preparation and storage of the agent. Aseptic technique using sterile syringes and needles should be used.

Administration of DaTscan™

DaTscan™ should only be used by qualified personnel with the appropriate government authorization for the use and manipulation of radionuclides within a designated clinical setting.

DaTscan™ is a 5% (v/v) ethanolic solution for intravenous injection and should be used without dilution. Clinical efficacy has been demonstrated across the range 3 to 5 mCi (111 to 185 MBq). Do not exceed 5 mCi (185 MBq) and do not use when the activity is below 3 mCi (110 MBq).

To minimize the potential for pain at the injection site during administration, a slow intravenous injection (about 15 to 20 seconds) via an arm vein is recommended.

The dose should be assayed in a 10 ml syringe filled to a standard volume of 6 ml. In order to avoid geometry effects on determination of actual injected dose following injection of DaTscan™, the syringe should be reassayed.

Participants should be pretreated with saturated iodine solution (10 drops in water) or perchlorate (1000 mg,) prior to DaTscan™ injection. Participants are to be imaged 4 +/- 0.5 hours following the injection. Specifically bound activity washes out from striatal binding sites slowly, but not negligibly, hence every effort should be made to maintain a consistent imaging time post injection of DaTscan™.

Accountability of DaTscan™

After each injection day complete the DaTscan™ Acknowledgement of Receipt Form and the Investigational Medicinal Product Accountability Log (see appendix) and file with your source documents.

NOTE: In the event there is a problem with the DaTscan™ during the study (e.g., issues with delivery or administration), the site should notify GEHC and the Imaging Core. Once the issue is resolved, the Imaging Core will convey information to the IND SMC as necessary.

5.0 SOURCE DOCUMENTATION

Instructions for Source Documentation

PPMI 2.0 will use a direct-data-entry, electronic data capture (EDC) system designed and managed by Blackfynn. **It is expected that all study visit data will be entered during the study visit, except in the instance a paper source document is expected to be completed (e.g., certain assessments, as described below).** Tablet devices will be provided by the study for completion of data collection in the EDC system during study visits. Most study assessments allow for direct data entry into the EDC; therefore, the electronic case report form (eCRF) is the expected source for those assessments. An eCRF is an auditable electronic record designed to record data required by the clinical study protocol. eCRFs may have special display elements, electronic edit checks, and other properties or functions, and are used for both capture and display of the data. Given the nature of the assessment, some will need to be completed on paper copy and the data will then be promptly entered into the EDC system. For these assessments, the paper source CRF should be kept in the participant's study record.

Sites should always use the tablet and direct-data-entry EDC system unless the site encounters extenuating circumstances, such as internet interruption during the study visit. If needed, sites may use paper copy CRFs to record information collected during the study visit and then promptly input the data into the EDC system. A full set of CRFs will be uploaded to the PPMI 002 General Study File (Case Report Form folder) in Florence. If paper copy CRFs are completed for a study visit, these CRFs should be kept as the source documents in the participant's study record.

Detailed instructions for the EDC system can be found in the user help area within the EDC system.

Assessments & Instructions for eCRF Completion

Refer to the PPMI 2.0 Assessments Manual for detailed instructions regarding assessments with alternating versions, administration of study assessments, and completion of eCRF's.

Types of Visits

Several types of visits may be conducted in PPMI 2.0 and the type of each visit should be documented on the *Visit Status* eCRF at the end of every study visit. Detailed information about each visit type can be found in the "Study Visit Procedures" (Section 10) of the PPMI 2.0 Clinical Protocol. Please contact an IND SMC Site Manager if you need more guidance around which type of visit should be conducted and documented.

Assessment and Study Supply Ordering

Refer to the *Assessments Source Documents* sub-folder under ASSESSMENTS in the Florence PPMI 002 General Study File binder.

- This folder contains the "PPMI 2.0 Cognitive Assessment Instruction and Paper Source Bundle", which will be printed by the site and contains the following assessments: Benton Judgment of Line Orientation (scoring sheet), Letter Number Sequencing, Lexical Fluency (F, A, S), Montreal Cognitive Assessment, Modified Semantic Fluency (Animals Only), and Symbol Digit Modalities Test.

- In addition, paper booklet source documents for the Modified Boston Naming Testing, Hopkins Verbal Learning Test-Revised, and Trail Making Test will be provided to sites by the IUPCC. The IUPCC will also provide the UPSIT kits. When a site is activated in PPMI 2.0, IUPCC will send an initial bulk shipment of these assessment booklets and kits. Additional biospecimen kits and assessment supplies may be ordered using the online kit module at <https://kits.iu.edu/ppmi>.

6.0 SIGNIFICANT STUDY EVENTS

There are important events that might occur during a participant's follow up in the study, such as initiation of PD medication, a new diagnosis made by the Investigator, an SAE, pregnancy, or death. This information will be captured within the study database as described below and may result in additional follow up with the site.

Initiation of PD Medication

Please refer to the PPMI 2.0 Clinical Protocol section 10.4 for guidance on scheduling a "Need for PD Therapy Visit". Once a site has been notified that a participant has initiated the use of PD medication, this should be documented, and the applicable medication information recorded in the LEDD Medication Log.

Adverse Event Reporting

Site staff should assess for adverse events according to the PPMI 2.0 Clinical protocol.

- Document the adverse event telephone follow-up on the *Adverse Event Telephone Assessment* in EDC.
- Document all adverse events occurring within the study procedure adverse event reporting period on the *Adverse Event Log* in EDC.
- If an adverse event might be associated with more than one study procedure, repeat the recording of the AE to indicate each relationship on a separate row.
- If there is any change in severity over the course of an ongoing adverse event, each change in severity is entered on a new row.

Serious Adverse Event Reporting-PPMI002 Clinical Protocol

The Investigator should assess whether an adverse event meets the criteria of "Serious Adverse Event" according to the PPMI 2.0 Clinical protocol. Any event assessed as "serious" is documented on the *Adverse Event Log* in EDC. Such events will be 'flagged' in the EDC database and the SMC will be notified, which might result in additional follow up with the site regarding the event. Sites are responsible for reporting SAEs to GE Healthcare as instructed below.

➤ Reporting Requirements to GE Healthcare following DaTscan™ injection

The **PPMI GE Healthcare SAE Report Form** template is available in the Florence PPMI General Study File under Safety Reporting. Completed reports and related communications should be filed in your Florence Investigator Site File in the Safety Reports folder.

In the event of an adverse event following administration of the imaging agent (¹²³I-DaTscan™), the site will notify **BOTH** GE Healthcare and PPMI of the following:

- **Any SAE occurring within 24 to 48 hours following injection**, regardless of relatedness to DaTscan™, must be reported **immediately**, but no later than 24 hours of becoming aware of an event, using the PPMI GE Healthcare SAE Report Form.
- An SAE occurring **more than 24 hours following injection AND related** (“related” is defined as unlikely, possible, probable, or definite) to administration of DaTscan™, must be reported directly to GE using the PPMI GE Healthcare SAE Report Form.

Complete the **PPMI GE Healthcare SAE Report Form** and email the form to **BOTH** GE Healthcare Pharmacovigilance and PPMI Site Management Core. If email is not feasible, you may use the telephone number listed below.

GE Healthcare Pharmacovigilance	PPMI Site Management Core
Email: gpv.drugsafety@ge.com	Email: PPMI_SAE@indd.org
Safety Telephone Numbers: <ul style="list-style-type: none"> • US and Canada: 800 654-0118, Option 2, then Option 1 • Other countries: + XX [appropriate country code] 774-843-3800, Option 2, then Option 1 	

Serious Adverse Event Reporting-PPMI 004 Early Imaging

The Investigator should assess whether an adverse event meets the criteria of “Serious Adverse Event” according to the PPMI 2.0 Early Imaging (AV-133) protocol. Any event assessed as “serious” is documented on the *Adverse Event Log* in EDC. Such events will be ‘flagged’ in the EDC database and the SMC will be notified, which may result in additional follow up with the site regarding the event. Sites are responsible for reporting SAEs to PPMI Site Management Core (SMC) and Invicro as instructed below.

➤ *Reporting Requirements following [¹⁸F] AV-133 injection*

The most current version of the **PPMI 2.0 Early Imaging (AV-133)-004 SAE Report Form** template is available in the Florence PPMI 004 - Early Imaging General Study File under Safety Reporting. Completed reports and related communications should be filed in your Florence Investigator Site File in the Safety Reports folder.

In the event of an adverse event following administration of the imaging agent ([¹⁸F] AV-133), the site will notify **BOTH** Invicro **and** SMC of the following:

- **Any SAE occurring within 24 to 48 hours following injection**, regardless of relatedness to [¹⁸F] AV-133, must be reported **immediately**, but no later than 24 hours of becoming aware of an event, using the PPMI 2.0 Early Imaging (AV-133)-004 SAE Report Form.

Complete the **PPMI 2.0 Early Imaging (AV-133)-004 SAE Report Form** and email the form to **BOTH** Invicro and SMC.

Invicro Email: safetyreporting@invicro.com	PPMI Site Management Core Email: PPMI_SAE@indd.org
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Conclusion from Study Participation

If a participant concludes study participation following completion of the Baseline visit, refer to the protocol “Premature Withdrawal Visit” section for information about what study activities might be needed. Document the information and reason for withdrawal from the study on the *Conclusion of Participation* eCRF in EDC. The SMC may follow up with the site to obtain additional information as necessary.

Report of Pregnancy

If a participant is confirmed as pregnant, document this on the *Report of Pregnancy* eCRF in EDC. If this pregnancy occurred within 30 days following administration of DaTscan™, the information must be reported immediately, but no later than 24 hours of becoming aware of the event. The SMC may follow up with the site to obtain additional information as necessary.

Participant Death

If a participant death occurs, document this on the *Conclusion of Participation* eCRF in EDC. The SMC may follow up with the site to obtain additional information as necessary.

7.0 LABORATORY SPECIMEN MANAGEMENT

Refer to the Covance Lab Manual for instructions and details regarding processing and shipping PPMI 2.0 clinical labs.

Refer to the Biospecimen Collection and Processing Manual for instructions and details regarding collection of the PPMI 2.0 research samples.

A copy of both manuals will be filed for your reference in the Florence eBinder PPMI 002 General Study File in the Laboratory, Central folder and in the Biorepository folder, respectively.

Pregnancy Test Kits

Per the protocol, women of childbearing potential must have a urine (or serum if required by the site) pregnancy test prior to injection of DaTscan™. The result must be confirmed as negative prior to proceeding with the injection. Sites should use their local lab for testing and supplies as these are not supplied or processed through Covance. Special requests can be made with prior approval from SMC.

8.0 SITE MANAGEMENT

Site Management Plan

Site management of PPMI 2.0 sites will be conducted on behalf of the PPMI Leadership by the Site Management Core (SMC) at the Institute for Neurodegenerative Disorders (IND), in coordination with other PPMI study cores (e.g., Indiana Participant Coordination, Biorepository and Pathology Cores, Imaging, Data Management and Analytics Core, and Statistical Core and service providers (e.g., Covance), via ongoing support, review and oversight of site engagement, performance and data quality from site initiation through study conclusion to ensure:

1. The rights and well-being of human participants are protected.
2. The reported study data are attributable, legible, contemporaneous, original, accurate and complete.
3. The conduct of the study follows the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).

These activities will be conducted via ongoing site engagement, on-site visits and remote interactions as described below. Site visits will occur approximately annually at a mutually agreeable time and for the purpose of face-to-face engagement and review of study activity, followed by a summary of discussions and any action items.

1. Site Visits
 - a. Pre-Study Visit (on site or remote) to review site interest, capabilities and resources
 - b. Site Initiation Remote Visit (pre-study activation call)
 - c. Interim Site Visits
 - d. Closeout Visit
2. Remote Activities
 - a. SMC/site interaction (e.g., routine or ad hoc calls, communications, web-based meetings, newsletters)
 - b. SMC/IUPCC, Biorepository and Pathology Core calls
 - c. Training (protocol, procedures, systems as required)
 - d. Centralized regulatory document management and monitoring, via Florence eBinders™ system
 - e. Centralized data monitoring
 - i. Compliance review in coordination with Indiana University Biorepository Core
 - ii. Blackfynn EDC ongoing review and report generation
 - iii. Remote review of data metrics
 - f. Safety Management
 - i. Safety assessments

- ii. Adverse and serious adverse event reporting
- 3. Other activities
 - a. PPMI Annual Meetings
 - b. Special events

Site Activation Process

1. Requirements for Site Activation
 - a. Administrative/Regulatory (e.g., IRB/Ethics approval, site contracts)
 - i. SMC will work with sites throughout the IRB/Ethics submission process,
 - ii. SMC will review the site's draft consent(s) for acceptability prior to IRB/Ethics submission.
 - iii. The SMC will request the date of IRB/Ethics review to track progress towards approval, if site is not able to use the central IRB.
 - iv. MJFF will issue contract documentation to the site and notify SMC when contracts are both released and executed to help monitor progress.
 - b. Site Qualification and Role-Based Training
 Role-specific training and, as applicable, certification will be required prior to activation. See Table 9.1 (Section 9) for typical training and certification requirements for PPMI. Training will be provided in various formats, whether live, web-based or self-paced learning options, or if obtained outside of PPMI (e.g., MDS-UPDRS and Human Participants Research training), certification will be uploaded by the site to Florence.
 - c. Regulatory documents received and approved
 Documents will be supplied to the PPMI SMC via upload or email into the electronic site investigator file in the Florence eBinders™ system, the regulatory document management system. SMC will review and, if applicable query the documents, and approve.
 - d. Study supplies (e.g., lab kits, paper assessments, tablets)
 - i. Paper source documents for purchased or licensed assessments that cannot be made available electronically due to copyright considerations will be supplied to the site by the IU Biorespository Core.
 - ii. In addition, the site will download from the Florence eBinders™ system the source documents requiring completion on paper (e.g., participant completed worksheets) before transcribing participant data into the EDC. The remainder of study assessments are directly entered in the Blackfynn electronic data capture system during the participant study visit.
2. Site Initiation Visit (Pre-activation call with SMC) and follow up. This call will be a check-in to be sure everything is in good order for the site to begin seeing participants in PPMI, as well as an opportunity to ask questions and exchange information. Follow up communications to include:
 - a. Site activation approval letter. A formal communication of approval will be issued to the site. Upon receipt, this document should be filed in the Florence investigator site folder under SMC correspondence.
 - b. SMC to be made aware of first scheduled participant visit, to ensure availability for questions or issues during the visit. Site-specific feedback from these visits will be solicited and helpful in supporting other sites as they begin protocol activities

9.0 ESSENTIAL DOCUMENTS & ELECTRONIC TRIAL MASTER FILE (eTMF) SYSTEM

Essential Documents

PPMI is utilizing Florence eBinders™ for regulatory, also referred to as essential, document management, a regulatory compliant, web-based document management system, for the filing of PPMI essential study documents. For purposes of the PPMI Clinical protocol (PPMI 002), these will be housed in the PPMI 002 binder in Florence in two designated folders, as follows:

PPMI 002 General Study File: The **PPMI 002 General Study File** folder serves as a study portal for general study documents, is accessible to all fully trained users who are granted access by the SMC, and will contain study documents and templates for reference and downloading or duplicating, as needed. Contents are described in the table below and may be updated to meet future study needs.

Sub-Folder	General Description of Contents
ASSESSMENTS	<ul style="list-style-type: none">Worksheets for select patient-reported assessments –to be printed (these are complemented by purchased booklets and forms supplied to sites by the IU Biorepository Core)Assessments Manual Current and Prior Versions
BIOLOGICS MANUAL	Current and Prior Versions
CASE REPORT FORM	<ul style="list-style-type: none">Set of unique CRFs (as study requires direct data entry; for backup only)Current and Prior Versions
FLORENCE	Guidance documents
GLOBAL COMMUNICATIONS	General communications
IMAGING TECHNICAL OPERATIONS MANUAL	Current and Prior Versions
INFORMED CONSENT, MODEL	Current and Prior Versions
LABORATORY, CENTRAL	Covance manual Current and Prior Versions
NEWSLETTERS	Site and participant newsletters
OPERATIONS MANUAL	Current and Prior Versions
PRESENTATION MATERIALS	Miscellaneous presentation materials
PROTOCOL_CENTRALLY APPROVED	Current and Prior Versions
RECRUITMENT_RETENTION RESOURCES	Current and Prior Versions
SAFETY REPORTING	Safety Reporting Form Template
STUDY CONTACTS	Global contacts list

Sub-Folder	General Description of Contents
STUDY DOCUMENT TEMPLATES	<ul style="list-style-type: none"> • Delegation of Responsibilities Form • Note to file re contract location • Not to file template (general)
TRAINING	Reference to training materials, resources, platform

PPMI Investigator Site File: Each PPMI site will have a site-specific electronic folder in Florence (***named PPMI 002 - Site XXX Site Name – Investigator Site File***) for the purpose of regulatory document management. Documents required for PPMI will be uploaded into this system. This folder and its subfolders are accessible to trained members of the site only, along with the SMC who will have monitoring oversight of and provide support for its use, as well as approval of documents submitted for inclusion. This electronic binder replaces the need for a paper regulatory binder. Contents are described but are not limited to those described in the table below and may be updated to meet future study needs.

Sub-Folder	General Description of Contents
01. SITE CONTACT INFORMATION	Personnel-Specific form samples (this data will be entered directly into the PPMI contacts resource management system, HubSpot); SMC upload contact form for reference.
02. AGREEMENTS	<i>Placeholder*</i> for Note to file denoting institutional location of site contract (template provided in General Study File)
03. PROTOCOL	Current and Prior Approved Versions
04. INFORMED CONSENT	Current and Prior Approved Versions
05. PARTICIPANT-FACING ASSESSMENTS	Current and Prior Approved Versions (e.g., copies of paper-sourced participant worksheets)
06. RECRUITMENT_RETENTION RESOURCES	Current and Prior Approved Versions
07. CASE REPORT FORM (CRF)	Current and Prior Approved Versions (blank set of unique forms)
08. INSTITUTIONAL REVIEW BOARD (IRB)_INDEPENDENT ETHICS COMMITTEE (EC)	<ul style="list-style-type: none"> • PPMI 1.0 Continuing Review and Study Closure Acknowledgment (for 1.0 sites) • IRB_EC Approval Letters; Correspondence; Progress Reports; Correspondence (to/from), Safety Reports • IRB_EC Roster (if not using WIRB as IRB)
09. STUDY PERSONNEL	<ul style="list-style-type: none"> • Curriculum Vitae • Delegation of Responsibilities Forms • Licenses
10. TRAINING	Documentation of training (Protocol, Assessments, Biorepository, Blackfynn EDC, Certifications (e.g. MDS-UPDRS), Clinical and Biorepository Lab Training, Florence Binders, Human Research Education)
11. SITE VISITS	<ul style="list-style-type: none"> • Correspondence • Site Visit and Action Items Logs
12. IMAGING	<ul style="list-style-type: none"> • Imaging Approvals to scan (MRI and SPECT) • Technical Site Setup Report

Sub-Folder	General Description of Contents
13. CLINICAL LABORATORY	<ul style="list-style-type: none"> • Lab Credentials (e.g., CLIA, CAP) • CV lab director • Local lab normal references (e.g., if local lab is utilized, e.g., for PT/PTT at other than screening visit)
14. BIOLOGICAL RESEARCH SAMPLES	<ul style="list-style-type: none"> • Biological Sample Handling • Shipping Records • Manual
15. SAFETY REPORTS	SAE reports
16. CORRESPONDENCE	Essential Correspondence with IU, MJFF, SMC, Other
17. TABLET	<ul style="list-style-type: none"> • PPMI 2.0 Site Tablet Receipt and Acceptance Form (or note to file if site is using own device) • Miscellaneous, including notes to file if not required elsewhere in site folder <p>This folder is set up as a place to send emails with important documents directly into the tool using a contact created in the user's email address book. From there, communications can be moved to their intended location within the site's folder (see PPMI Florence User Guide Quick Tip).</p> <p>This is a folder set up as a workspace, where multiple documents can be imported at the same time via email or uploaded for later filing (i.e., moving to the appropriate folder (see PPMI Florence User Guide Quick Tip).</p>
18. OTHER	
19. COMMUNICATIONS	
20. FOR FILING	

**Placeholders are digital “sticky notes” that hold a place for an expected Document. Users use these to indicate that they will need to fill Folders with specific key Documents, such as CVs, training, ICFs, approvals, etc.*

PPMI Document and Training Requirements (for Sites and Personnel by Role)

Site-specific and personnel-specific document requirements for site activation and maintenance are outlined in the Operations Manual Appendix 9. Essential Documents Guide in the Florence **PPMI 002 General Study File > OPERATIONS MANUAL folder**.

Refer to Florence User Guide and Quick Start Guide in the PPMI 002 General Study File > FLORENCE folder.

Guidance Regarding PPMI Regulatory Document Completion

The following section summarizes document requirements.
Please utilize file naming recommendations, as requested.

Delegation of Responsibility Form (files to be named DR_Last Name_First Initial)

A Delegation of Responsibility Form (DR form) must be completed for each research staff member upon assignment of any PPMI 2.0 project activities. Specifically, a DR form must be completed for any of the following staff members:

- the Site Investigator (SI)

- any Sub-Investigators (Sub-Is)
- Study Coordinators (SCs, primary and co-coordinator(s))
- Rater(s) (clinician or nurse)
- Proceduralists (for lumbar punctures or skin biopsies)
- Regulatory Managers/Staff
- Data Entry
- CRC/CTU Supervisor or Manager
- Imaging Lead
- Lab Managers (for specialized research specimen processing)

For assessments or procedures managed by personnel outside the immediate research team (the SI, Sub-Is, SCs), a DR form can be completed for the Supervisor or Manager and is not required for everyone involved with the assessment/procedure. For example, the Supervisor or Manager of Lab collections, processing and/or shipping biospecimens would complete a DR form and not all lab personnel. This guidance applies to:

- Imaging Department (MRI/DaT)
- Lab Department

The DR form should be filled out and saved as a draft with the start date blank and pending e-signatures to assist the Site Management Core (SMC) with determining the applicable training and regulatory documents required. Notify the SMC once each DR form is drafted for review.

The start date is the date that the staff member completes the applicable training.

For example, the start date used on the DR form for the SI, Sub-Is, and SCs is the date protocol training is completed by that staff member. Applicable training for a staff member may consist of training in any of the following:

- Protocol
- Neuropsychiatric/cognitive
- MDS-UPDRS
- Florence (electronic Trial Master file)
- Blackfynn (EDC)
- Biosample collection, processing and shipment
- Imaging

To complete the DR form, enter the start date (based on the date training is completed) and then have the form e-signed in Florence (via addendum) by both the staff member and the investigator.

The DR form is to be updated when:

- A research staff member departs from the program
- If the role or responsibilities of a research staff member changes

Curriculum Vitae (files to be named *CV_Last Name_First Initial*)

- A 'stamped' electronic signature is to be applied to the document from within the Florence system after uploading to the Florence **Binders > PPMI 002 – PPMI 002 Site xxx Site Name - Investigator Site File > 09 STUDY PERSONNEL > Curriculum Vitae** folder.
- Refer to Florence eTMF Electronic Workflows and eSignature Guidance for instructions on applying eSignatures (this guidance is located in Florence **Binders > PPMI 002 > PPMI 002 General Study File > FLORENCE**
- Each site file has a number of pre-placed placeholders; additional requested CVs can be added to the folder without needing a placeholder.
- Curriculum vitae (CV) must be on file for the following staff members:
 - the Site Investigator (SI),
 - any Sub-Investigators (Sub-Is),
 - Study Coordinators (SCs, primary and co-coordinator(s)),
 - Cognitive Rater(s), not including any of the above, Proceduralists (for lumbar punctures or skin biopsies)
 - Imaging Lead (Director or Manager of the local imaging center(s) that will be involved in PPMI)

NOTE: Please ensure before submitting the CV has the business (not home) address as well as the current professional title and institutional affiliation where the PPMI study is taking place.

Licenses (File to be named *License_Last Name_First Initial DDMMYYYY*) – DATE IN FILE NAME SHOULD BE EXPIRY/RENEW BY DATE

A license must be on file for the following staff members:

- the Site Investigator (SI),
- any Sub-Investigators (Sub-Is),

If the following staff members have a license, the license must be on file:

- Study Coordinators (SCs, primary and co-coordinator(s)) (i.e., RN, NP, PA),
- Cognitive Rater(s), not including any of the above, as applicable (i.e., psychology)
- Proceduralists (i.e. RN, NP, PA, MD, DO)

Training

The following training activities will be provided and managed by PPMI:

- **Florence eBinders™**- Training for Florence will be conducted via review of a recorded video. Training must be on file for each staff member requiring a Delegation of Responsibility Form. The minimum training required is the Find and Sign training to permit viewing of documents and ability to apply electronic signatures (typically, Investigators will opt for this training). Following completion of Florence training, the staff member must sign an attestation form, by eSignature or otherwise, and ensure it is on file. **Blackfynn EDC** - Training for Blackfynn EDC will be conducted by Blackfynn. A training certificate must be on file for each staff member requiring access to the EDC for data entry, query resolution or eCRF signing, specifically:
 - the Site Investigator (SI),

- any Sub-Investigators (Sub-Is),
- Study Coordinators (SCs, primary and co-coordinator(s)),
- Cognitive Rater(s)
- **Biorepository** - Training for the Biorepository will be administered by the PPMI Biorepository Core (BRC) at Indiana University (IU), via web-conference, self-paced review of a recorded training session, or one-on-one training. The IU BRC will notify SMC of each staff member completing the training. This training specifically applies to any coordinator or lab manager, under whose direction staff are handling the biorepository collection, processing and/or shipment.
- **Clinical lab (Covance)** - Training for the central clinical lab will be administered by Covance and a recording will be made available for sites. In addition, there will be training modules associated with use of the Covance eSite This training specifically applies to any coordinator or lab manager handling the sample collection, processing and/or shipment.
- **Protocol and Assessments** - Protocol and assessment training will be conducted via web-conference, recorded video or one-on-one training. Refresher training may be required. Training on any amendment to the protocol or assessment procedures will be conducted as needed. Attestation of training will be completed, uploaded and electronically signed by each 'trainee' to **PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File 11. TRAINING. Recommended file name Florence_Last Name_First Initial**

Training on the protocol and assessments is required for:

- the Site Investigator (SI),
- any Sub-Investigators (Sub-Is),
- Study Coordinators (SCs, primary and co-coordinator(s)),
- Cognitive Rater(s)

Documentation of the following training, though training is not provided by PPMI, is required and will be the site responsibility:

- **MDS-UPDRS** - Training will need to be on file for any designated staff member administering the MDS-UPDRS. This may apply to:
 - the Site Investigator (SI),
 - any Sub-Investigators (Sub-Is),

Training can be completed at <https://mds.movementdisorders.org/updrs/> and the certificate uploaded into Florence.

File to be named **MDS-UPDRS_Last Name_First Initial** and uploaded into the following folder: **Binders PPMI 002 > PPMI 002 - Site xxx Site Name - Investigator Site File > 11. TRAINING > Certifications (MDS-UPDRS)**

- **IATA** - This training specifically applies to any coordinator or lab manager shipping the biorepository, pathology and/or central lab samples and will need to be on file for the applicable staff members.

Certificate to be uploaded into Florence.

File to be named ***IATA_Last Name_First Initial*** and uploaded into the following folder: ***Binders PPMI 002 > PPMI 002 - Site xxx Site Name - Investigator Site File > 11. TRAINING > IATA***

- **Human Participants Research (HSR) Training** – Training will need to be on file for:
 - the Site Investigator (SI),
 - any Sub-Investigators (Sub-Is),
 - Study Coordinators (SCs, primary and co-coordinator(s)),
 - Cognitive Rater(s)

Certificate to be uploaded into Florence.

File to be named ***HSR_Last Name_First Initial*** and uploaded to the following folder: ***Binders PPMI 002 > PPMI 002 - Site xxx Site Name - Investigator Site File > 11. TRAINING > Human Participants Education***

SMC and site staff can manage document due and expiration dates within Florence. It is recommended that this tool be used as a reminder for when updated documents need to be placed in Florence.

eTMF System

As noted above, the Florence eBinders™ system, an electronic trial master file platform, is the regulatory document management for PPMI that will be utilized for PPMI protocols. This system eliminates the need for paper documents and binders with built in mechanisms for Part-11 compliant eSignatures to be applied, where required. Only authorized users with secure permission-based access control from the IND Project Team and Site Management Core and at the site will have access to the site-specific folder in Florence. The system allows the study team and site team to maintain an automated audit trail with document version control. The SMC team will access, review and approve documents remotely for monitoring purposes. The SMC Team may assign tasks to specific staff to help manage requests (e.g., due dates, expirations).

There will be two site user roles: 1) Site Staff and 2) Site Staff_Signing Authority. The Site Staff_Signing Authority role has more limited access (permits view of all documents and the ability to provide electronic signatures). Following completion of applicable Florence training, the study team will authorize and assign access based on the site user's role. Certifications of training will be filed in ***Binders PPMI 002 > PPMI 002 Site xxx Site Name - Investigator Site File > 11. TRAINING > Florence***.

Participant Transfer Process

When a PPMI participant wishes to continue participation at a different site, whether out of need or interest, the following steps will be performed by the transferring and new sites, the SMC, MJFF and Blackfynn to facilitate the participant's transfer. *Participant must have been reconsented and a visit completed at the original site prior to transferring to another site. In addition, the new site must have IRB approval of the same protocol version as the transferring site for the transfer to take place.*

Transferring Site Activities	
1	Contact SMC if a participant transfer is being discussed. <ul style="list-style-type: none">SMC to provide transferring site with potential site nearest the participant's desired location.
2	Confirm participant wishes to transfer to site provided; notify SMC. <ul style="list-style-type: none">SMC to contact new site coordinator to confirm site can accept the transfer; if so, SMC to provide transferring site contact information to new site coordinator. Obtain written permission from participant to share name and contact information with new site coordinator before providing to new site coordinator.
3	Contact new site coordinator to provide participant's contact information, study visit schedule, and any other pertinent information (e.g., legally authorized representative).
4	Contact participant to confirm transfer. Provide new site coordinator contact information to participant should they have questions or concerns. <ul style="list-style-type: none">If applicable, discuss the importance of establishing a clinical care provider (e.g., if relocating).Follow up with new site to ensure participant has been successfully contacted by new site and that the transfer will proceed; confirm with SMC.Once SMC gives approval to proceed, the new site may proceed to reconsent the participant*.
5	Ensure all participant's data is up to date and complete in EDC and, importantly, <u>all queries must be resolved before participant is consented at the new site</u> . Blackfynn to confirm with transferring site and SMC when query resolution is complete. <ul style="list-style-type: none">Prior to SMC completing the transfer workflow in CTMS, Blackfynn will provide the transferring site with a .pdf export of any completed visit CRFs. The export will only include PPMI ID. This will allow the transferring site to maintain a copy of completed visit records since they will no longer have access to the participant data once the transfer is complete. Blackfynn will include SMC on all site correspondence for reference.<u>Important</u>, once participant is officially 'transferred', transferring site no longer has access to participant's data in EDC.Complete this step to ensure appropriate processing of site payment for visits completed.*SMC to confirm above activities completed, SMC to email new site (cc transferring site) to give approval to proceed with consent of participant, below.

(New site activities continued below)

New Site Activities

1	<p>Following SMC approval to proceed, contact participant to introduce yourself and discuss next steps, including reconsent to new site-specific current consent form(s); electronic consent via DocuSign is preferred</p> <ul style="list-style-type: none"> Notify SMC when consent has been completed. <i>Once consent obtained, new site assumes responsibility for the participant and transferring site is relinquished of these responsibilities.</i> SMC (or designee) to transfer participant to new site in EDC. SMC to notify new site, transferring site, applicable cores and vendors, e.g., Imaging Core, Biorepository Core, IU Travel Core, Pathology Core, Blackfynn, LONI of the participant's new site assignment and successful transfer.
2	<p>Enter reconsent data in EDC (into next planned study visit) once SMC notifies new site that the transfer is complete in EDC, and next visit is imminent. (Note: do not mark visit as "complete" at this time, unless a visit is also completed. The visit start date will be entered as the date of reconsent.)</p>
3	<p>Schedule participant's next visit if not conducted at the time reconsent obtained.</p>

Instances Where Transfer is not Complete

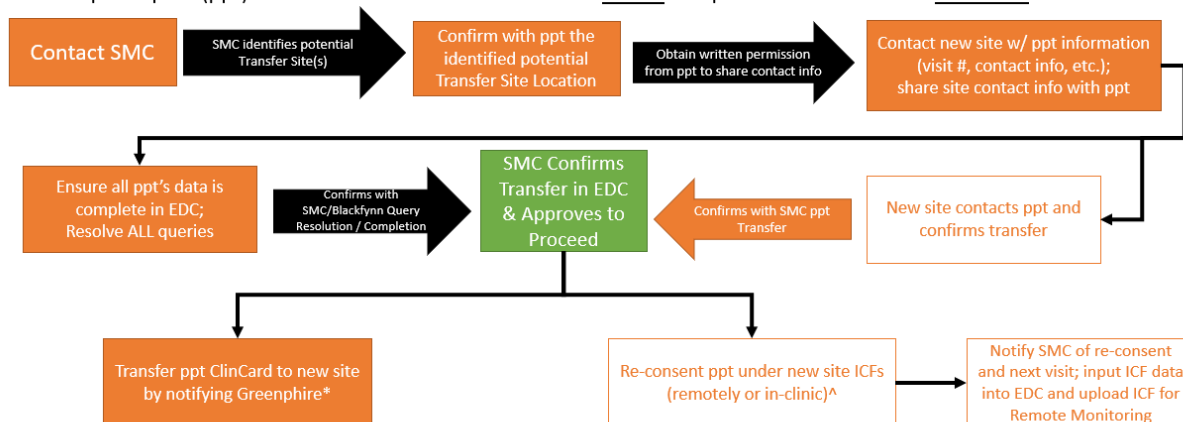
1	<p>Participant unable to be reached by new site.</p> <ul style="list-style-type: none"> Transferring site to follow up with participant to determine continued interest in transferring.
2	<p>Participant changes mind about transfer.</p> <ul style="list-style-type: none"> If participant relays this decision to new site, notify SMC and transferring site. Transferring site to follow up with participant to confirm participant's decision to remain at the current site.
3	<p>Participant decides to withdraw from PPMT altogether.</p> <ul style="list-style-type: none"> If this decision is relayed by the participant to the new site, the new site must convey that back to the transferring site. Transferring site to discuss decision with participant and determine if participant is willing to have another visit before concluding participation in EDC.

Other

1	<p>Transfer of Greenphire ClinCard</p> <ul style="list-style-type: none"> To transfer a participant's ClinCard to new site, transferring site will notify ClinCard Support via email to request transfer, cc'ing MJFF (David Bresnahan dbresnahan@michaeljfox.org), SMC representative and the new site coordinator. MJFF will approve the transfer and the Greenphire Support team will execute the transfer.
2	<p>As always, if any questions, do not hesitate to reach out to your SMC representative.</p>

PPMI Participant Site Transfers

When a participant (ppt) wishes to transfer to a different site **AFTER** completion of PPMI visit at **CURRENT** site:



*To transfer a participant's ClinCard to new site, transferring site will notify ClinCard Support via email to request transfer, cc'ing MJFF (David Bresnahan dbresnahan@michaeljfox.org), SMC representative and the new site coordinator.

^Once ppt is re-consented under the new site's ICFs, new site assumes responsibility for the participant (ongoing AE's, etc.) and transferring site is relinquished of these responsibilities.

SECTION 4- APPENDIX

DaTscan™ Drug Order Form US Sites (EXAMPLE)

GE Healthcare INC.		PPMI	
ORDER FORM (Investigator Sponsored Trial)		SITE #xxx	
IST Reference: 09-DAT-001		Site PI: InsertName	
Project code: 71998200			
AGREEMENT STATEMENT: GE Healthcare has agreed to supply doses of DaTscan at no cost for the PPMI project as specified in the Agreement between GE Healthcare and the Michael J Fox Foundation / Institute of Neurodegenerative Disorders (Chief Investigator: Ken Marek, MD)			
<u>PLEASE COMPLETE ALL DETAILS BELOW</u>			
Item Code: 1186529		<u>PLEASE TICK APPLICABLE COHORT:-</u>	
Quantity Requested:		<input type="checkbox"/> Original Cohort	
Date of Delivery:		<input type="checkbox"/> Prodromal Cohort	
		<input type="checkbox"/> Genetic Cohort	
<u>INSTRUCTIONS:</u>			
Orders must be placed by 11am EST THREE (3) business days before required delivery date.			
Please note that DaTscan is only available for delivery Tuesday – Friday			
** Submit your order via fax: Insertnumber **			
SAP Sold to account number: xxxxxx		SAP Ship to account number: xxxxx	
Delivery Address:		ATTN:	
		Address 1	
		Address 2	
		Address 3	
<u>Insert Site Contact Details</u>		Name:	
Tel:		FAX:	
		Email:	
Please direct any questions, concerns or cancellation requests to: xxxxxxxx			
Please note cancellation requests must be made before 11am EST three business days prior to delivery date			

Customer Service, please send confirmations to fax: xxxxxxxxxxxxxx			
as well as datscan@indd.org and FOC.Confirmations@qe.com			

DaTscan™ Drug Order Form EU Sites (EXAMPLE)

ORDER FORM
(PPMI Project – 09-DAT-001)

Project code: 71998200

AGREEMENT STATEMENT: GE Healthcare has agreed to supply DaTSCAN™ to [insert centre name] at no cost for the PPMI project, as stated in the Agreement between GE Healthcare and the Michael J Fox Foundation / Institute of Neurodegenerative Disorders.

PLEASE TICK WHICH COHORT THIS ORDER APPLIES TO:-

- ☐ Original Cohort
☐ Prodromal Cohort
☐ Genetic Cohort

ITEM CODE: ???
SAP CODE: ???
COST CENTRE: xxxx

Quantity Requested: [PI to complete]

Delivery Date: [PI to complete]

INSTRUCTIONS:

Product to be ordered by 11am, a minimum of two working days before delivery date. Please send the completed order form to your local Customer Services, either by fax or email as follows:-

Tel: xxxxx

E-mail: [xxxxx](#)

DELIVERY DETAILS (please complete):

Name of person for delivery of IMP: _____

Ship to:

Fax: _____ Email: _____

***** For completion by Customer Services*****

SALES ORDER NUMBER: _____ Order Loaded by: _____

- ☐ Request sent to Eindhoven
☐ Confirmation received from Eindhoven
☐ Customer informed
☐ FOC invoice issued

Copy of order confirmation to be emailed to:
foc.confirmations@ge.com
datscan@indd.org

SECTION 9- APPENDIX

Table of Documents

The following table lists the documents by site and by personnel role that will be filed in Florence. Detailed instructions for Florence, including instructions for providing electronic signatures for certain documents can be found in the User Guide and Quick Start Guides in **PPMI 002 General Study File > FLORENCE**.

Site-Specific Documents

Document	Comment
Note to file denoting institutional location of site contract	<ul style="list-style-type: none"> • DUPLICATE Template located in Florence Binders > PPMI 002 > PPMI 002 General Study File > STUDY DOCUMENT TEMPLATES • <i>File to be named: PPMI 2.0 Site XXX Contract Location DDMMYYYY Note to file</i> • Fill placeholder and apply Investigator eSignature to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 02 AGREEMENTS > PPMI 2.0 Site XXX Contract Location DDMMYYYY Note to file
Protocol, IRB/Ethics approved	<ul style="list-style-type: none"> • If possible, please rename file to: PPMI 002 Site XXX IRB_EC Approval DDMMYYYY (with date representing date of approval) • Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 03 PROTOCOL> Current Approved Protocol
Informed consent(s), IRB/Ethics approved	<ul style="list-style-type: none"> • If possible, please rename file to: PPMI 002 Site XXX Main/Prodromal ICF_DDMMYYYY (insert version date) Approval DDMMYYYY (with date representing date of approval) • Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 04 INFORMED CONSENT > Current Approved Informed Consents • Advanced directive, HIPAA (if separate) and any other applicable consent documents may be filed here (and named similarly).
Participant-Facing Assessments, IRB/Ethics approved	Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 05 PARTICIPANT-FACING ASSESSMENTS > Current Approved Version(s)
Recruitment Retention Resources, IRB/Ethics approved	Upload to Florence Binders > PPMI 002 > PPMI 002- Site XXX Site Name - Investigator Site File > 06 RECRUITMENT_ RETENTION RESOURCES/Current Approved Version(s)

Document	Comment
Case Report Form (CRF), blank unique set download from General Study File	DUPLICATE from Florence Binders > PPMI 002 > PPMI 002 General Study File/ CASE REPORT FORM/Current Version to <u>PPMI 002 - Site xxx Site Name Investigator Site File 07 CASE REPORT FORM (CRF)</u>
IRB/Ethics Committee (EC) Approval Letter)	Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 08 INSTITUTIONAL REVIEW BOARD (IRB)_INDEPENDENT ETHICS COMMITTEE (EC) > Current Approved Protocol/Approval Letters
Imaging approval to scan	Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 10 IMAGING > IMAGING APPROVALS
Local lab (if using) CLIA, CAP, CV Medical Director, references normal ranges	<ul style="list-style-type: none"> For sites using local labs for screening. Note <u>all sites</u> will use central lab (Covance) Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 13. CLINICAL LABORATORY > Lab_Miscellaneous
Site Tablet Receipt and Acceptance Form (iPad)	Fill placeholder and apply eSignature to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File > 17 TABLET > PPMI 2.0 Site Tablet Receipt and Acceptance Form (also acceptable to upload signed and scanned version)

Personnel-Specific Documents

Document	Inv/ Sub-I	Coord/ Co-Coord	Cognitive Rater	Imaging	Proceduralist	Regulatory Manager	Other	Comment
Staff Contact Form (completed in HubSpot, the PPMI Contact Resources Management System)	X	X	X	X	X	X	X	<ul style="list-style-type: none"> Sample Located in Florence Binders > PPMI 002 > PPMI 002 General Study File Site to complete contact forms in HubSpot for each team member SMC to place printout of approved contact in this folder for future reference

Document	Inv/ Sub- I	Coord/ Co- Coord	Cognitive Rater	Imaging	Procedur- alist	Regulatory Manager	Other	Comment
Delegation of Responsibilities form	X	X	X	X	X	X	X	<ul style="list-style-type: none"> • DUPLICATE Template located in Florence Binders > PPMI 002 > PPMI 002 General Study File > STUDY DOCUMENT TEMPLATES • Files to be named PPMI 002 Site XXX DR – Last Name_First Initial • Upload and apply eSignatures of staff personnel and PI to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name > 09 STUDY PERSONNEL > Delegation of Responsibilities Forms (may fill placeholders if provided; otherwise, upload into folder)
Curriculum Vitae (includes current role, institution/address)	X	X	X	X	X			<ul style="list-style-type: none"> • File to be named PPMI 002 Site XXX CV_Last Name_First Initial • Upload and apply eSignature to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name > Investigator Site File > 09 STUDY PERSONNEL > Curriculum Vitae • Fill placeholders if applicable; otherwise, upload into folder
Professional License/Renewals (as applicable)	X	X	X	X*	X			<ul style="list-style-type: none"> • Upload to Florence Binders > PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File 09 STUDY PERSONNEL/ Licenses_Renewals • Fill placeholders if applicable; otherwise upload into folder
Florence (full or Find & Sign, as applicable)	X	X	X	X	X	X	X	Upload training certification to appropriate folder in Florence, under PPMI 002 > PPMI 002 - Site XXX Site Name - Investigator Site File 11. TRAINING
Blackfynn EDC	X	X	X				X	
Certification (MDS-UPDRS) – designated rater(s)	X	(X)					(X)	
Biorepository training (Coord, Lab Manager if applicable)		X					X ¹	
Central clinical lab (Covance) training		X					X ¹	

Document	Inv/ Sub- I	Coord/ Co- Coord	Cognitive Rater	Imaging	Procedur- alist	Regulatory Manager	Other	Comment
IATA training (for persons shipping any biosamples)		X					X ¹	
Human Subjects Research Training (e.g., CITI, GCP)	X	X	X					
Protocol, Assessments	X	X	X					
Other	as required							

¹ If labs collected/processed/shipped from site's lab, lab manager requires training