



Parkinson's  
Progression  
Markers  
Initiative

# Operations Manual

## PPMI Pathology Core

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## SECTION 1: OVERVIEW

Individuals who have been consented for the PPMI Clinical study are eligible to participate in brain donation through the Pathology Core. The brain tissue collected at the time of death undergoes neuropathological analysis and characterization of disease progression, which allows researcher to compare data and samples collected during the longitudinal visits with the postmortem findings. In addition, representative tissue specimens are made available to approved researchers for future studies related to Parkinson's disease (PD). For USA sites, donation planning is centralized through Indiana University and neuropathologic evaluation is completed by Stanford University.

**An overview of Pathology Core activities is shown below:**



## SECTION 2: INTRODUCING PATHOLOGY CORE TO PARTICIPANTS

Site teams play a critical role in introducing brain tissue donation to participants during clinical visits or during any other outreach. Participants who indicate that they are interested in learning more will agree to have their contact details shared with the team at Indiana University. A referral is not an agreement to participate, but an opportunity for the participant to learn more about the program before deciding if they would like to enroll.

If a participant is already enrolled in a separate brain donation program, we ask that the site team still discuss brain donation through PPMI. The Pathology Core team can work with the participant to learn details of the external donation program and determine if dual enrollment is feasible. The Pathology Core has successfully coordinated with external banks for dual enrollment, sharing of tissue/data, and serving as a backup if a primary donation bank cannot perform removal.

The following talking points summarize useful items to discuss with the participant when approaching them about referral to the Pathology Core:



- **“Information for your Family”**
  - The examination of brain tissue is a definitive way to link brain functional changes with physical findings
  - Evaluation can provide a confirmation of PD diagnosis
  - Families will receive a letter summarizing the results of the evaluation of the brain tissue
  
- **“Help Advance PD Research”**
  - The PPMI study has collected an extensive set of data and bio-specimens from research participants during longitudinal visits, which researchers can compare with postmortem analysis and understand how neuropathological findings correlate with disease presentation
  - Brain tissue is pivotal to understanding PD progression, but researchers have limited access to this type of tissue (which makes it all the more valuable)
  - The participant’s donation of brain tissue can be used for research studies to better understand the link between changes in the brain, physical findings, and genetic risk factors
  
- **“No cost to your Family”**
  - PPMI covers all additional costs related to the removal and analysis of brain tissue

### **SECTION 3: REFERRING PARTICIPANTS TO THE PATHOLOGY CORE**

If the participant is interested in learning more and agrees to a referral of their contact information to the Pathology Core, then the site coordinator submits a REDCap referral with the participant’s and legally authorized representative (LAR), if applicable, contact information (see below). The link to the online referral form can be found on the site channel in MS Teams.





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## PPMI Pathology Core Referral

Use this survey to submit a referral for brain donation planning to the PPMI Pathology Core. **Please do not resubmit old referrals that have already been sent to the Pathology Core team.** If you have any questions or concerns about completing this form, email the Pathology Core team at [ppmipath@iu.edu](mailto:ppmipath@iu.edu).

PPMI Site	<input type="text"/>
Participant's PPMI ID	<input type="text"/>
Participant's Date of Birth	<input type="text"/>  M-D-Y
Participant's Name	
First Name	<input type="text"/>
Last Name	<input type="text"/>
Middle Initial	<input type="text"/>

### Participant Contact Information

Primary Email	<input type="text"/>
Secondary Email	<input type="text"/>
Mobile Phone	<input type="text"/>
Home Phone	<input type="text"/>
Work Phone	<input type="text"/>
Preferred method of contact	<input type="checkbox"/> Mobile <input type="checkbox"/> Home <input type="checkbox"/> Work
Comments	<div><p>Please include any important information related to reaching this participant (only available after a certain time, primary language is not English, etc.)</p><input type="text"/></div> <p>Expand </p>
Submitter's Email (will receive a receipt of referral)	<input type="text"/>



If the participant is already in declining health at the time of referral, we request this information is flagged to the Pathology Core team so planning can be immediately prioritized. If the team has difficulty contacting the participant, follow up with the site coordinator may be required to clarify contact details and/or assist in future outreach.

#### **SECTION 4: INFORMED CONSENT AND DONATION PLANNING**

When communicating with newly referred participants, the study team will explain the Pathology Core's role in PPMI, the brain donation process, and answer any questions. If the individual would like additional time to consider participation, the study team will provide them with materials and resources for review and follow up at a later date. If the participant doesn't have questions and is agreeable to continue, they will be offered the opportunity to complete consent, authorization, and planning forms through a web-based platform or through paper materials mailed to their provided address. It is possible that the referred participant is in cognitive decline and unable to complete these documents, in which case, their LAR may do so on their behalf.

Once these forms are completed, the study team will identify a local specialist to assist with brain removal at time of death. If a funeral home and/or nursing home has been identified by the participant, the study team will contact these facilities to determine the most appropriate process for brain removal. The Pathology Core will then compile this information into a Brain Donation Plan and disseminate this summarized plan to the participant, next of kin, removal specialist, funeral home, and nursing home in order to ensure all applicable parties are aware of the participant's wish to donate. Pathology Core staff ensure the information in Brain Donation Plans is kept up to date by contacting participants, funeral homes, long term care facilities and removal specialists annually.

The following wallet card is given to participants and their family to facilitate brain donation at time of death:

Because there are many pieces to organize for a successful donation, it is important to plan for donation well in advance. In cases where the participant is in rapidly declining health or had died without finalizing donation plans and there is a desire to donate, the Pathology Core team will make every effort to try to facilitate collection.

#### **SECTION 5: BRAIN COLLECTION AND TISSUE ANALYSIS**

Upon death, the donation plan will be activated so that the brain tissue can be removed as quickly as possible. Depending on the time elapsed between death and removal (referred to as the postmortem interval, or PMI), separate protocols may be enacted for optimal preservation of brain



tissue. A small cerebellum sample will be sent to Indiana University for DNA extraction, while the remaining whole brain will be shipped to Stanford University, where it will undergo neuropathological evaluation and tissue storage. After analysis is complete, the Pathology Core coordinates preparation for a Clinicopathological Cases Conference (CPC) presented by the Stanford Neuropathologist, a clinician from the donor's PPMI site and a genetic counselor from Indiana University to review the case. A lay research summary will be available to provide to the PPMI participant's listed next of kin. The data generated from the case will also be added to the existing dataset and transferred to the Laboratory of Neuro Imaging (LONI). Qualified researchers may submit requests for brain tissue and distribution of samples will be coordinated by the Indiana University and Stanford University teams.

## **SECTION 6: ADDITIONAL COMMUNICATIONS BETWEEN SITES AND PATHOLOGY CORE TEAM**

For ease of reviewing the status of referred participants, sites can refer to their *Site Reports* on MS Teams. These reports detail the following information for all participants referred from the site:

- How the referral was received (site vs. participant-initiated referral)
- Decline/ Withdrawn / Lost to Follow-up status
- Consent status
- Donation Plan Status
- Notifications of death (if applicable)
- Additional flags for the site team

The Pathology Core team may request site staff approach participants that have been lost to follow up at their next site visit to inquire if they are still interested in brain donation. The Pathology Core team will immediately inform sites when learning that a referred participant has died and if collection was successful. It is also requested that the site team alerts the Pathology Core if they learn that a participant is in declining health or has died.

## **SECTION 7: INTERNATIONAL OPERATIONS**

For non-USA sites, donation activities are managed by the site team and/or coordinated through an established local brain donation program. Several non-USA PPMI sites have been identified that can leverage existing infrastructure for brain donation activities. The Pathology Core team will provide guidance to these participating sites to ensure harmonization on practices and collected data, assist in reconciling neuropathological data from all PPMI collections, as well as oversee transfer of data to LONI.