**Operations Manual:**

**PPMI Screening & Travel Cores**

**Screening**

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**Team Information**

Website: <https://pdnexus.org/our-team.html>

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**SECTION 1: OVERVIEW**

**Remote Enrollment**

* Individuals may be identified as eligible for remote screening activities through:
  + PPMI Online
  + Direct communications or in-person events
  + Other Michael J Fox Foundation efforts
* All interested participants will be funneled to the Indiana University (IU) portal (<https://portal.pdnexus.org/>) to begin screening activities.

**Remote screening activities**

* **Olfaction Testing**: Eligible, unaffected participants are asked to complete olfaction testing by means of a smell identification kit (UPSIT).
* **Genetic Testing**: Affected and unaffected participants are asked to provide a saliva sample for testing. Participants that have previously undergone testing for pathogenic Parkinson’s disease (PD) variants are asked to provide a copy of their test results in lieu of testing.

**Clinical site referral**

* **PD participants**: Participants with PD may be referred to a site for additional participation based on their genetic results and disease duration.
* **Unaffected participants**: Unaffected participants may be referred to a site for additional participation based on their screening results and questionnaire responses.

**SECTION 2: INFORMED CONSENT AND PORTAL ACCESS**

Individuals are directed to login to the PPMI Participant Portal, where they will be given the opportunity to read through the consent form(s) and ask questions before electronically signing.

Eligibility for each activity is determined by information provided through the PPMI Online surveys or the referral source. Family history, disease status and duration, age, and other factors are all taken into consideration. Unaffected individuals may be eligible for olfaction testing only or for genetic and olfaction testing. Affected individuals will only need to undergo genetic testing.

Once participants have signed the consent, they will be asked to provide their demographic and contact information. Those eligible for olfaction testing will also be asked to complete a short screening questionnaire.

**SECTION 3: GENETIC TESTING**

**Overview**

To be eligible for clinical enrollment based on genetic test results, participants must come through Indiana University for genetic testing or results review. Participants without previous testing for pathogenic PD variants of interest may be provided a saliva collection kit for testing. Participants with previous testing may provide their reports directly to IU for eligibility review. Clinical sites may provide previous testing reports for locally identified participants to IU for review. Clinical sites may also refer enrolled participants to IU for confirmatory genetic testing in instances where PPMI analysis has identified a pathogenic PD variant(s).

**SECTION 3A: PARTICIPANTS WITHOUT EXISTING GENETIC TESTING RESULTS**

**Overview**

Eligible participants that have not had previous genetic testing, or whose testing did not include pathogenic PD variants of interest, will be asked to provide a saliva sample for testing. Participants must be willing to be informed of their results to undergo testing.

**Kit Distribution**

Participants are shipped a saliva collection kit which includes:

* Saliva collection tube
* Instructions for collecting sample
* Sample form to be filled out by participant and returned with collected sample
* Biohazard specimen bag for collected sample
* Return envelope with prepaid shipping label

**Sample Collection and Return**

Participants are asked to fill the collection tube with saliva (not including bubbles) to the indicated fill line. Once collected, the participant closes the attached funnel lid to release a preserving solution. The funnel lid is then replaced with a small cap and gently inverted to combine the two liquids. Once mixed, the tube is placed in the specimen bag and returned in the provided envelope.

**Sample Testing**

Returned samples are accessioned at the IU Biobank and shipped to a CLIA lab for extraction and analysis. Results are typically ready in 6 weeks after they are received by the lab and a results report is provided to IU for each participant.

**SECTION 3B: PARTICIPANTS WITH EXISTING GENETIC TESTING RESULTS**

**Overview**

PPMI participants who report previous genetic testing will be asked to provide a copy of their genetic testing results. Results will be centrally reviewed by the screening core to confirm mutation status and study eligibility.

**Eligible Results**

Participants with results that show testing for PD variants of interest will be offered the opportunity to speak with a genetic counselor about their results.

**SECTION 3C: PARTICIPANTS WITH EXISTING GENETIC TESTING RESULTS IDENTIFIED AT A CLINICAL SITE**

**Overview**

PPMI participants who are recruited locally and report previous genetic testing will be asked to provide a copy of their genetic testing results. Results will be provided to IU by the site for review by the screening core to confirm mutation status and study eligibility.

**Results Upload**

Sites that locally identify an individual to enroll based on genetic results will need to submit a copy of the participant’s results to the screening core through the online upload instrument ([here](https://redcap.uits.iu.edu/surveys/?s=DF989ATPMY)). The report should have the participant’s name and other identifiable information redacted. Lab and testing information should still be readily visible.

**Results Review**

Results will be reviewed by the screening core to confirm genetic status and enrollment eligibility. Once the report has been reviewed, the screening core will communicate its determination to the site.

**SECTION 3D: PARTICIPANTS IDENTIFIED AS NEEDING CONFIRMATORY GENETIC TESTING**

**Overview**

Longitudinally enrolled PPMI participants may have PD pathogenic variants identified through ongoing research analysis. For sites based in the USA, these individuals can be referred for confirmatory clinical testing and genetic counseling through IU. For sites based outside of the USA, the site team should coordinate local clinical testing.

**IU Referral**

Sites will be notified by a representative from the PPMI Consensus Committee of participants who have been identified with a pathogenic PD variant. Sites will be instructed to contact their participants to notify them of these findings, and if interested, submit a participant referral to the IU team ([here](https://ppmi.iu.edu/genetic_referral)).

**IU Coordination**

Upon referral receipt, IU will contact participants and coordinate a pre-test consult with a genetic counselor. If agreeable to further genetic testing, the IU team will coordinate consenting, sample collection, lab testing, and results disclosure.

**SECTION 4: GENETIC COUNSELING**

**Overview**

Participants that undergo genetic testing through IU will be provided with genetic counseling as part of their results disclosure. Participants that have previously been tested for pathogenic PD variants of interest will also be offered genetic counseling.

**Genetic Counseling Scheduling**

Once results have been received, a coordinator will contact the participant to schedule a genetic counseling appointment. Once scheduled, the coordinator will follow up with an email to confirm the appointment and provide a link to a pre-counseling informational video.

**Genetic Counseling Session**

The genetic counseling session is conducted either through video or by phone, depending on participant preference. Participants are encouraged to include family members and caregivers if they would like. During the discussion, the genetic counselor will discuss the participant’s genetic results, family history, and PD status. Participants will also have an opportunity to ask questions and request additional resources.

**Genetic Counseling Follow Up**

After the genetic counseling session is complete, participants will receive a summary of their discussion and a copy of their results. Additional information about the genetics of PD and PD-related research will also be provided.

**SECTION 5: PPMI CLINICAL ELIGIBILITY**

For individuals enrolled in IU’s PPMI remote data collection study, PPMI Clinical eligibility is determined in a multi-step process and calculated using an algorithm maintained by the PPMI data management team. The algorithm evaluates several different risk factors to determine eligibility.

**SECTION 5A: PPMI CLINICAL ELIGIBILITY: PD**

Individuals with a Parkinson’s disease diagnosis and an identified PPMI-eligible pathogenic variant(s) will be referred to a PPMI site for a combined Screening and Baseline visit.

**SECTION 5B: PPMI CLINICAL ELIGIBILITY: Prodromal**

The data management team will notify IU when participants are determined as eligible for in-person clinic visits. From this determination, the IU team will contact participants for further PPMI review and to complete additional phone screening to ensure they aren’t precluded from undergoing DaT screening. The study team will balance travel preferences and site availability to refer participants as rapidly as possible to an approved referral site.

**Site Referral**

Once an eligible participant is ready to proceed, the IU team will assign them to a site in the electronic data capture system and securely transfer the participant’s information to the referral site. The site will be responsible for completing required scheduling through their institution.

**Baseline Eligibility**

Post-DaT eligibility results are communicated with the site and the IU team. IU coordinating staff will contact participants to discuss eligibility results. Ineligible individuals are encouraged to continue PPMI Online participation, while those who are eligible are invited to longitudinally enroll in the PPMI Clinical study. The team review the next steps for a baseline visit, as well the anticipated schedule for yearly in-person/virtual visits. IU notifies the site if an eligible participant agrees to continue or declines. If the participant decides to continue, IU securely transfers information to the site, after which the site schedules the baseline visit.

**SECTION 6: TRAVEL COORDINATION**

**Overview:**

The IU Travel Core works closely with participants, sites, and the travel vendor to optimize travel itineraries. The team provides education to participants on PPMI reimbursement guidelines and helps manage reimbursement for out-of-pocket expenses incurred from visits.

**Planning**

Sites are responsible for completing required scheduling through their institution for PPMI visits. Once complete, sites must submit a Travel Request Form providing the visit details (see [here](https://redcap.uits.iu.edu/surveys/index.php?s=NFWLATWJJN)). This is required for all cancellations and reschedules too. Once received, IU coordinating staff contacts the participant to discuss travel and reimbursement needs. Participants requiring additional services (fights, hotels, car services, etc.) are put in direct contact with the travel vendor to finalize an itinerary. This itinerary is shared with the participant and IU team. Once reviewed for accuracy, it is provided to the site team. After the visit and travel are complete, participants receive instructions on how to claim any out-of-pocket expenses.