PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research

Operations Manual
PPMI Genetics Study

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Play a Part in Parkinson's Research

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SECTION 1: OVERVIEW

Who are we looking for?

- Individuals with and without PD, who have a *LRRK2* or *SNCA* mutation.

How can people be screened?

- Site Screening: PPMI study sites can directly recruit subjects and send blood samples for genetic mutation testing. Sites with Amendment 7 approval may also send saliva samples for genetic mutation testing.
- Widespread Recruitment Initiative (WRI): This is a web-based recruitment method coordinated by the Michael J. Fox Foundation for Parkinson's Research and the Genetics Coordination Core (GCC) at Indiana University. The current focus is the identification of individuals at increased risk for a *LRRK2* mutation. Screening for *SNCA* mutations is not currently available. This initiative is only available in English. Potential participants are referred to the website where they undergo an online consenting process and complete a series of screening questions. Those who meet eligibility criteria are sent a saliva kit for genetic mutation testing. Subjects who test positive for a *LRRK2* mutation are referred to a PPMI site for enrollment.
    - https://www.michaeljfox.org/page.html?ppmi-genetics

Who is eligible for genetic testing?

- A person with PD, meeting either of the following criteria:
    - From an ethnic or geographic group known to have a relatively high risk of a *LRRK2* (such as people of Ashkenazi Jewish or Basque descent) or *SNCA* mutation
    - Having a 1st degree relative (parent, sibling, child) with a positive *LRRK2* or *SNCA* mutation test

  Note: All PD subjects must be willing to be informed of their testing results.

- A person without PD, meeting either of the following criteria:
    - From an ethnic or geographic group known to have a relatively high risk of a *LRRK2* (such as people of Ashkenazi Jewish or Basque descent) or *SNCA* mutation and having a 1st degree relative (parent, sibling, child) with PD. *This person must be willing to be informed of their genetic mutation testing results.*
    - Having a 1st degree relative (parent, sibling, child) with a positive *LRRK2* or *SNCA* mutation test. *This person may choose if they wish to learn their genetic mutation testing results.*

What are the two study arms?

- Genetic Cohort
    - PD or Unaffected
    - More intensive arm
    - Schedule of events similar to PPMI de novo PD and HC cohorts.

- Genetic Registry
  - PD or Unaffected
  - Subjects evaluated at less frequent intervals, fewer study visits and assessments.

SECTION 2: INFORMED CONSENT FORMS

There are multiple consent forms utilized in the genetic study. To determine which is appropriate for use with a participant with a LRRK2 or SNCA mutation, begin by determining if the individual has or has not undergone previous genetic mutation testing and can provide test results.

Individuals who have not undergone previous genetic mutation testing:

PD Status	Risk Factor	Research Subject Information and Consent Form
PD	And either of AJ ancestry or have a family member with a *LRRK2* mutation	Genetic Testing in Individuals With Parkinson's Disease
Unaffected	And are of AJ ancestry and have a family member with PD	Genetic Testing in Individuals Without Parkinson's Disease With Family Members With Parkinson's Disease
Unaffected (Added with AM7)	And have a family member with a *LRRK2* or *SNCA* mutation	Genetic Testing in Individuals Without Parkinson's Disease Who Have Family Members With a *LRRK2* or *SNCA* Mutation

Once these individuals have undergone genetic mutation testing the site will be notified of study arm assignment. Participants will sign a PPMI study consent form for the study arm in which they agree to participate.

Note: Participants assigned to the Genetic Cohort may elect to participate in the Genetic Registry.

PD status	Final arm assigned	Research Subject Information and Consent Form
PD	Genetic Cohort	PD Genetic Cohort Research Participants
PD	Genetic Registry	PD Genetic Registry Research Participants
Unaffected	Genetic Cohort	Unaffected Genetic Cohort Research Participants
Unaffected	Genetic Registry	Unaffected Genetic Registry Research Participants

Individuals who have undergone previous *LRRK2* or *SNCA* genetic mutation testing and have documentation of their positive results will sign the appropriate consent below. They will not need to sign a second PPMI study consent at the time of their first visit, unless they decline participation in the Genetic Cohort but agree to participate in the Genetic Registry.

PD status	Mutated gene	Time since diagnosis	Research Subject Information and Consent Form
PD	*LRRK2*	≤ 7	PD Genetic Cohort Research Participants
PD	*LRRK2*	> 7	PC Genetic Registry Research Participants
PD	*SNCA*	≤ 7	PD Genetic Cohort Research Participants
PD	*SNCA*	< 7	PD Genetic Registry Research Participants

PD status	Mutated gene	Current age	Research Subject Information and Consent Form
Unaffected	*LRRK2*	≥ 50	Unaffected Genetic Cohort Research Participants
Unaffected	*LRRK2*	< 50	Unaffected Genetic Registry Research Participants
Unaffected	*SNCA*	≥ 30	Unaffected Genetic Cohort Research Participants
Unaffected	*SNCA*	< 30	Unaffected Genetic Registry Research Participants

SECTION 3: GENETIC TESTING

Overview

Individuals will be recruited who have either a confirmed *LRRK2* or *SNCA* mutation or are at increased risk to carry a mutation. Individuals without previous genetic testing results will undergo genetic testing and, based on test results, age, diagnosis, and duration of disease, may be centrally assigned to a study arm.

Screening

The first part of recruitment is to identify those individuals with an increased risk of having a *LRRK2* or *SNCA* mutation. It is anticipated that screening methods to identify individuals at an increased risk of carrying a *LRRK2* or *SNCA* mutation will vary widely across sites but all individuals will be screened as described in the PPMI protocol and operations manual. Individuals who are at an increased risk of having a *LRRK2* or *SNCA* mutation will undergo genetic testing. Individuals with a diagnosis of PD must be willing to be informed of their genetic test results. Individuals who are unaffected can choose if they wish to learn their genetic test results.

A complementary approach to screening at a PPMI site is the Widespread Recruitment Initiative (WRI), coordinated by the Genetic Coordination Core (GCC) at Indiana University. This initiative uses a web-based survey approach to identify individuals at increased risk of a having a *LRRK2* mutation and acquire genetic testing on these individuals. The current focus of the WRI is the identification of individuals at increased risk for a *LRRK2* mutation. Screening for *SNCA* mutations is not currently available through the WRI. This initiative is only available in English. All individuals completing this screening must learn the results of their genetic testing. The WRI is described in detail in Section 4.

SECTION 3A: SUBJECTS WITHOUT EXISTING GENETIC TESTING

Overview

PPMI subjects who meet the study criteria and are at increased risk of carrying a *LRRK2* or *SNCA* mutation will be identified. These participants will provide a blood or saliva sample that will be tested for *LRRK2* or *SNCA* mutations.

Identify Potential Subjects

Two guides were created to help sites identify individuals who are at increased risk of carrying a *LRRK2* mutation. The individuals who meet the criteria on these guides are appropriate to recruit into the PPMI study.

- *Guide for Molecular Screening for Individuals with PD* (Appendix A: Guides for Molecular Screening)
- *Guide for Molecular Screening for Individuals without PD* (Appendix A: Guides for Molecular Screening)

Consent Subject

- Subject signs the appropriate consent form:
  - *Genetic Testing in Individuals with Parkinson's Disease* ***or***
  - *Genetic Testing in Individuals without Parkinson's Disease With a Family Member with Parkinson's Disease* ***or***
  - *Genetic Testing in Individuals Without Parkinson's Disease Who Have Family Members With a LRRK2 or SNCA Mutation*
- These consents allow the site to obtain a blood or saliva sample and send the sample for genetic testing.

Complete Necessary Forms

- Complete the ***Genetic Mutation Testing form*** (Appendix D) and the ***Laboratory Requisition Form*** (Appendix E).
- The ***Genetic Mutation Testing form*** and the ***Laboratory Requisition Form*** are faxed or emailed to the GCC using the ***GCC Cover Sheet*** (Appendix F).
- The ***Genetic Mutation Testing form*** is entered by the site into eClinical.
- The GCC will verify that there are no missing data and/or discrepancies between the eClinical data and the forms they receive. Sites will be contacted by the CTCC regarding any missing data and/or discrepancies.

Draw and Ship Sample

- Record the PPMI Subject ID, sex, year of birth and site number on the tube label.
- Draw 10ml purple top EDTA tube or collect a saliva sample using an Oragene saliva collection kit.
- The ***Laboratory Requisition Form*** (Appendix E) is sent with the sample to the laboratory. This form gives information about the sample collection, the subject, and which genetic mutation test is requested.
- Shipping information can be found in Appendix G.

Results

- Sites will receive a weekly email report from the GCC with genetic testing results.
    - Sites will provide genetic testing results to the PPMI study subject if they wish to be informed.
- GCC is responsible for entering genetic testing results into eClinical.
    - If there are no outstanding data discrepancies, entering the genetic testing result into eClinical will trigger study arm assignment.
- Once study arm is assigned, an automatic email notification is sent to the site and the GCC.

SECTION 3B: SUBJECTS WITH EXISTING *LRRK2* or *SNCA* GENETIC TESTING RESULTS

Overview

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

Identify Potential Subjects

- Subjects with existing genetic testing results will be asked to provide a copy of their report and will not need to provide a blood sample.

Consent Subject

- Subject signs the appropriate consent form
  - *PD Genetic Cohort Research Participants* ***or***
  - *Unaffected Genetic Cohort Research Participants* ***or***
  - *PD Genetic Registry Research Participants* ***or***
  - *Unaffected Genetic Registry Research Participants*

Obtain Results from Subject and Complete Necessary Forms

- Obtain a copy of the genetic testing results from the subject.
- Complete the ***Genetic Mutation Testing form*** (Appendix D) form. Fax or email this form to the GCC, along with the subject's existing genetic mutation test results, using the ***GCC Cover Sheet*** (Appendix F).
  - All identifiable information on the genetic testing results must be redacted (blacked out) before the results are sent to the GCC.
  - The PPMI Subject ID number must be written on each page of the genetic testing results.
- Enter the ***Genetic Mutation Testing form*** into eClinical.
  - The GCC will verify that there are no missing data and/or discrepancies between the eClinical data and the forms they receive. Sites will be queried by the CTCC regarding any missing data and/or discrepancies.

GCC Review and Interpretation

- The GCC will review the genetic testing results and determine whether or not the subject carries a *LRRK2* or *SNCA* mutation.
- Sites will receive an email report from the GCC with the interpretation of the genetic testing results.
- If the result is not for a *LRRK2* or *SNCA* mutation, the subject may be screened (Section 3A)

Results

- GCC will enter the final result into eClinical.
- If there are no outstanding data discrepancies, entering the genetic testing result will trigger study arm assignment.
- Once study arm is assigned an automatic email notification is sent to the site and the GCC.

SECTION 4: PRESCREENING THROUGH THE WIDESPREAD RECRUITMENT INIATIVE

Overview

The Widespread Recruitment Initiative is designed to provide web-based recruitment and screening of participants. The current focus is the identification of individuals at increased risk for a *LRRK2* mutation. Screening for *SNCA* mutations is not currently available. This initiative is only available in English.

Driving subjects to the site

The Michael J. Fox Research Foundation for Parkinson's Research has developed study materials that can be distributed within the clinic, at support groups, community events, synagogues, etc. These cards provide the Michael J. Fox Research Foundation for Parkinson's Research website address where individuals can begin the screening process.

Initial screening

Potential participants are directed to the Michael J. Fox Research Foundation for Parkinson's Research website (www.michaeljfox.org/ppmi/genetics) where they complete an initial screen for eligibility. Those who meet eligibility requirements are then directed to the Indiana University website where they are guided through online consenting. They are then asked additional screening questions (similar to those used in the *Guide for Molecular Screening for Individuals with PD* and the *Guide for Molecular Screening for Individuals without PD*). Individuals are immediately told whether they do or do not qualify to receive a saliva kit for genetic mutation testing.

Sample collection

Subjects qualifying for a saliva kit are contacted by the GCC study coordinator. The GCC study coordinator will complete the ***Genetic Mutation Testing form*** and confirm the participant's responses and mailing address. Subjects are then sent a saliva kit which, after being filled, is returned to the GCC at Indiana University.

LRRK2 testing

The GCC study coordinator will ship the saliva sample to Massachusetts General Hospital (MGH) for *LRRK2* mutation testing. Genetic testing results will be returned to the GCC on a weekly basis. The GCC genetic counselor will contact each participant who provided a saliva sample and explain their genetic testing results. A letter will be sent to each subject, summarizing the genetic testing results. For those individuals with a positive *LRRK2* mutation test, the GCC genetic counselor will confirm that the subject agrees to have their contact information provided to the PPMI site.

Site referral and study arm assignment

For those individuals who carry a *LRRK2* mutation and have given permission for their contact information to be shared with their local PPMI site, the GCC genetic counselor will complete a ***PPMI Genetics Referral form*** (Appendix H). This form will be faxed to the appropriate PPMI site along with the completed ***Genetic Mutation Testing form*** and the ***GCC Genetic Counseling Checklist***. The site will enter the ***Genetic Mutation Testing form*** into eClinical.

After the site has entered the ***Genetic Mutation Testing form*** into eClinical, the GCC study coordinator will enter genetic testing results into eClinical. Study arm assignment will be triggered by entering the genetic testing results. The site will receive an automated email,

with the study arm assignment. At this point, the site will contact the subject, discuss the study and study arm assignment and schedule a study visit.

The PPMI site will fax the ***Genetics Referral form*** back to the GCC after completing the bottom portion, which indicates if the subject has had an appointment scheduled at the site, declined further participation, or cannot be reached by the PPMI site for scheduling.

SECTION 5: STUDY ARM ASSIGNMENT

Overview

Study arm assignment is based on PD status, mutation status, age, and whether or not the subject wishes to know their mutation status. Study arm assignment cannot be made if there is discrepant information or an incomplete data field.

Not all individuals who are screened will be eligible to enroll in a study arm. Study arm assignment is generated at the CTCC based on data entered by the sites and test results entered by the GCC. Study arm assignment will be transmitted to the site via email from the CTCC. Study arm assignments are: Genetic Cohort PD, Genetic Cohort-Unaffected, Genetic Registry-PD and Genetic Registry-Unaffected.

PD Status	Know or Want to Know Gene Status	Gene Status	Mutation	Disease Duration (from Diagnosis)	Age	Study Arm
PD	Yes	+	*LRRK2* or *SNCA*	≤7 years	≥ 18	Genetic cohort
PD	Yes	+	*LRRK2* or *SNCA*	>7 years	≥ 18	Genetic registry
PD	Yes	-	Not applicable	NA	NA	Excluded
Unaffected	Yes	+	*LRRK2*	NA	≥ 50	Genetic cohort
Unaffected	Yes	+	*SNCA*	NA	≥ 30	Genetic cohort
Unaffected	Yes	+	*LRRK2*	NA	< 50	Genetic registry
Unaffected	Yes	+	*SNCA*	NA	< 30	Genetic registry
Unaffected	Yes	-	Not applicable	NA	NA	Excluded
Unaffected	No	+	*LRRK2*	NA	≥ 50	90% Genetic cohort 10% Genetic registry
Unaffected	No	+	*SNCA*	NA	≥ 30	90% Genetic cohort 10% Genetic registry
Unaffected	No	+	*LRRK2*	NA	< 50	Genetic registry
Unaffected	No	+	*SNCA*	NA	< 30	Genetic registry
Unaffected	No	-	*LRRK2*	NA	≥ 50	85% Genetic registry 15% Genetic cohort
Unaffected	No	-	*SNCA*	NA	≥ 30	85% Genetic registry 15% Genetic cohort
Unaffected	No	-	*LRRK2*	NA	< 50	Genetic registry
Unaffected	No	-	*SNCA*	NA	< 30	Genetic registry

- The CTCC has created an algorithm that assigns study arm based on the rules in the chart above.
- GCC confirms that there is no discrepant or missing data. If there are no data discrepancies, then entry of the genetic mutation test result triggers the algorithm to automatically assign study arm.
- The GCC enters the genetic testing result from the testing laboratory or from review of existing genetic test results.
- An email with the subject's study arm assignment will be sent to both the site and the GCC.

SECTION 6: FAMILY HISTORY SUBSTUDY

Overview

One of the goals of evaluating the PD related gene mutations in *LRRK2* and *SNCA* is to enroll multiple members of the same family into PPMI. For future analyses, we would like to know how participants are related to each other. The GCC will conduct the Family History substudy of PPMI, which will gather family history information using an Indiana University protocol. Sites are only responsible for providing PPMI participants with a Family History Packet and completing the Family History Packet Distribution fax.

Family History Packet

Subjects screened by the GCC through the Widespread Recruitment Initiative will be sent a Family History Packet before being referred to a PPMI site. The site will be informed that this packet has been given to the subject.

Subjects screened by a PPMI site will provide a Family History Packet to the subject at their baseline visit.

Packets will include:

- Family History Packet Distribution fax
- Introductory cover letter with a consent/substudy reply form
- Indiana University informed consent for the Family History Substudy
- Indiana University HIPAA form
- Family History Questionnaire (FHQ)

Complete the Family History Packet Distribution form (Appendix I)

- This form is completed by the site and faxed to the GCC.
- This form links the family history packet number to the subject's PPMI Study ID.

SECTION 7: APPENDICES

PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research

PPMI2 Guide for Molecular Screening for individuals **WITH** PD

(This form should be used for individuals with PD and is retained at PPMI site)

This guide can be used by sites to identify individuals with PD who have an increased risk for a LRRK2 mutation. People with PD must be willing to be informed of their testing results.

1. Does this individual have a positive LRRK2 G2019S gene test?

☐ Yes ☐ No ☐ Unknown

For individuals with **PD** a **positive response to question 1** triggers a request for the subject to enroll in the PPMI study; a blood sample for additional LRRK2 testing is not needed.

A **positive response to question 2 or 3** triggers a request for the subject to provide a blood sample for LRRK2 testing.

2. Does this individual have a 1st degree relative with a positive LRRK2 G0219S gene test?

☐ Yes ☐ No ☐ Unknown

3. Is this individual from an ethnic or geographic group known to have a high risk of LRRK2 (such as people of Ashkenazi Jewish descent)?

☐ Yes ☐ No ☐ Unknown

PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research

PPMI2 Guide for Molecular Screening
for individuals **WITHOUT** PD
(This form should be used for individuals without PD and is retained at PPMI site)

This guide can be used by sites to identify individuals who have an increased risk for a LRRK2 mutation.

For individuals **without PD**, a positive response to **question 1** triggers a request for the subject to enroll in the PPMI study; a blood sample for additional LRRK2 testing is not needed.

1. Have you had a positive LRRK2 G2019S gene test?

☐ Yes ☐ No ☐ Unknown

OR

For individuals **without PD**, a positive response to **BOTH question 2 and 3** triggers a request for the subject to provide a blood sample for LRRK2 testing. ***These individuals must be willing to learn their testing results.***

2. Are you of Ashkenazi Jewish ancestry?

☐ Yes ☐ No ☐ Unknown

3. Do any of your following relatives have PD?

☐ Father ☐ Mother ☐ Full Sibling ☐ Children

OR

A positive response to **question 4** triggers a request for the subject to provide a blood sample for LRRK2 testing. ***These individuals may choose to be informed or remain unaware of their testing results***.

4. Do you have a 1st degree relative (father, mother, full sibling, child) with a positive LRRK2 G0219S gene test?

☐ Yes ☐ No ☐ Unknown

Individual at Increased Risk Without Existing Genetic Testing

Identify Potential Subjects

1. Identify individuals with PD at increased risk of having a mutation who meet any of the following criteria. Individuals with PD must be willing to be informed of their testing results.
    a. 1st degree relative with a positive LRRK2 or SNCA gene test
    b. From an ethnic or geographic group known to have a relatively high risk of a LRRK2 (such as people of Ashkenazi Jewish or Basque descent) or SNCA mutation
2. Identify individuals without PD at increased risk of having a mutation who meet any of the following criteria.
    a. From an ethnic or geographic group known to have a relatively high risk of a LRRK2 (such as people of Ashkenazi Jewish or Basque descent) or SNCA mutation and has a 1st degree relative with PD and is willing to be informed of their testing results
    b. 1st degree relative with a positive LRRK2 or SNCA gene test. Subject may choose to be informed or remain unaware of their testing results.
3. Describe the PPMI study to identified individuals.

Consent Subject

1. Have interested participants sign appropriate consent
    a. *Genetic Testing in Individuals With Parkinson's Disease* **or**
    b. *Genetic Testing in Individuals without Parkinson's Disease who have a family member with PD* **or**
    c. *Genetic Testing in Individuals Without Parkinson's Disease who have family members with a LRRK2 or SNCA mutation*
        i. Assign PPMI Subject ID from block of subject IDs provided by the CTCC.
        ii. The original IC is retained by the site.

Complete Necessary Forms

1. Complete the Genetic Mutation Testing form and the Laboratory Requisition form.
2. Use the GCC Cover Sheet to fax or email the Laboratory Requisition form and the Genetic Mutation Testing form to the GCC.

Draw and Ship Sample

1. Collect sample.
    a. Record the PPMI Subject ID, sex, year of birth and site number on the tube label.
    b. Draw 10ml purple top EDTA tube **or**
    c. Collect saliva sample using an Oragene saliva collection kit
    d. See sample collection and shipping instructions in Appendix F.
2. Ship sample and Laboratory Requisition form to laboratory.
3. Enter the Genetic Mutation Testing form into eClinical.

Return of Genetic Testing Results and Study Arm Assignment

1. Genetic test results are sent directly to the GCC from the testing laboratory.
    a. GCC emails test results to site.
    b. Email from CTCC, to both the site and the GCC, reporting subject's study arm assignment.

2. Provide subject with genetic testing results (If appropriate)
3. Consent subject to appropriate study arm
    a. Give subject the appropriate consent for study arm
        i. PD Genetic Cohort Research Participant or
        ii. Unaffected Genetic Cohort Research Participants or
        iii. PD Genetic Registry Research Participants or
        iv. Unaffected Genetic Registry Research Participants
    b. If the subject was assigned to the Genetic Cohort arm but declines, they are offered the Genetic Registry arm.

Conduct Screening Visit

1. Complete the Screening/Demographic Form. Record the study arm into which the subject actually consents on this CRF.
2. Enter the Screening/Demographic Form into eClinical.

Individual at Increased Risk With Existing Genetic Testing Results

Identify Potential Subjects

1. Identify individuals at increased risk of having a mutation.
    a. PD and unaffected individuals verified through previous genetic testing to have LRRK2 or SNCA mutation do not require retesting.
    b. May choose to use either the Guide for Molecular Screening for Individuals with PD or the Guide for Molecular Screening for Individuals without PD. These guides are retained at the site and are not entered into eClinical.
2. Describe the PPMI study to identified individuals.

Consent Subject

1. Have interested participants sign appropriate consent.
    a. *PD Genetic Cohort Research Participants* **or**
    b. *Unaffected Genetic Cohort Research Participants* **or**
    c. *PD Genetic Registry Research Participants* **or**
    d. Unaffected Genetic Registry Research Participants
2. Assign PPMI Subject ID from block of subject IDs provided by the CTCC.
3. The original IC is retained by the site.

Obtain Results from Subject and Complete Necessary Forms

1. Ask the subject to mail their genetic test results to the clinic.
    a. Provide pre-addressed return envelope.
2. Upon receipt of results from the subject, complete the Genetic Mutation Testing form.
    a. Copy subject's genetic test results and redact any identifying information.
    b. Record the PPMI Subject ID on each page of the genetic testing results.
    c. Use the GCC Cover Sheet to fax or email the Genetic Mutation Testing form and the subject's redacted genetic test results to the GCC.
3. Enter the Genetic Mutation Testing form into eClinical.

GCC Review and Interpretation

1. GCC reviews and interprets genetic test results.
    a. GCC checks for missing data and/or discrepancies. After addressing any missing data and/or discrepancies, GCC enters results into eClinical.
    b. GCC emails results of test review to site.
    c. If there are no outstanding discrepancies the CTCC algorithm will assign study arm.
    d. Email from CTCC, to both the site and the GCC, reporting subject's study arm assignment.

Return of Genetic Testing Results and Study Arm Assignment

1. Provide subject with genetic testing results.
2. Consent subject to appropriate study arm.
    a. If the subject agrees to participate in the study arm to which they were assigned, they will not need to sign a new consent.

b. If the subject was assigned to the Genetic Cohort arm but declines, they are offered the Genetic Registry arm. This subject will need to sign a new consent.
c. Give subject the appropriate consent for study arm.
    i. *PD Genetic Registry Research Participants* **or**
    ii. *Unaffected Genetic Registry Research Participants*

3. Conduct Screening Visit.
    a. Complete the Screening/Demographic Form. Record the study arm into which the subject actually consents on this CRF.
    b. Enter the Screening/Demographic Form into eClinical.

PPMI2

1 5 4 **GENETIC MUTATION TESTING FORM** 0 1

SUBJECT ID | | | | | | VISIT NO G M U

INITIALS | | | SITE NO | | | VISIT DATE | | (MM) | | (DD) | | | | | (YYYY)

A. ☐ Check box if subject has signed consent

B. Date informed consent was signed: B. | | (MM) | | (DD) | | | | | (YYYY)

1. Date of birth: 1. | | (MM) | | (DD) | | | | | (YYYY)

2. Gender (0 = Female of child bearing potential, 1 = Female of non-child bearing potential, 2 = Male) 2. ☐
Women who are surgically sterile (hysterectomy or tubal ligation) or post-menopausal (last menstruation was 1 year or more prior to Screening Visit) are considered to be of non-child-bearing potential.

3. Subject PD Status (1 = PD, 2 = Unaffected) 3. ☐

3a. If q3 is 1 = PD, duration of disease (years) 3a. ☐☐
(If less than one year, enter 1)

3b. If q3 is 2 = Unaffected, does the subject know or desire to know their gene test results? (0 = No, 1 = Yes) 3b. ☐

4. Does the subject have a first degree relative (father, mother, sibling, child) with a LRRK2 mutation? (0 = No, 1 = Yes) 4. ☐

5. Does the subject have a first degree relative (father, mother, sibling, child) with a SNCA mutation? (0 = No, 1 = Yes) 5. ☐

6. Does the subject have a first degree relative (father, mother, sibling, child) who is also participating in the study? (0 = No, 1 = Yes) 6. ☐

1 5 4 **GENETIC MUTATION TESTING FORM** 0 1

SUBJECT ID | | | | | | VISIT NO G M U

7. Did the subject have previous genetic testing from which a copy of the results were provided to the site? (0 = No, 1 = Yes) 7. ☐

7a. If q7 is 1 = Yes, where was the testing completed? 7a. ☐
(1 = MGH, 2 = 23andMe, 3 = Other _____)

7b. If q7 is 1 = Yes, were de-identified testing results sent to GCC? (0 = No, 1 = Yes) 7b. ☐

7c. If q7b is 1 = Yes, date results sent 7c. ☐☐ (MM) ☐☐ (DD) ☐☐☐☐ (YYYY)

If subject has not had previous genetic testing, complete questions 8 - 10

8. Was a sample collected? (0 = No, 1 = Yes) 8. ☐

8a. If q8 is 1 = Yes, type of sample collected: 8a. ☐
(1 = Blood, 2 = Saliva (Amendment 7 or later), 3 = DNA (Specific sites only))

8b. If q8 is 1 = Yes, date of sample collection: 8b. ☐☐ (MM) ☐☐ (DD) ☐☐☐☐ (YYYY)

9. If q8a is 1 = Blood, volume drawn: 9. ☐☐ ml.

10. If q8 is 1 = Yes, sample is being shipped to: 10. ☐
1 = Massachusetts General Hospital
2 = Other, specify _____

Comments:

_____

_____

_____

GCC Cover Sheet

Use this form to request review of genetic testing results,
or to notify GCC that a blood sample has been sent for testing.

Fax#: 1-317-278-4507 or email chalter@iu.edu

To:

Cheryl A. Halter, MS, CCRC
Indiana University
Hereditary Genomics
Phone: 1-317-274-5734
FAX: 1-317-278-4507
E-mail: chalter@iu.edu

From:

Site#: ☐ ☐ ☐

Contact Name: _____

Contact Email: _____

Contact Phone: _____

Contact Fax: _____

Date faxed: ____ / ____ / ____
Month Day Year

# of Pages Faxed: _____

☐ **Sending genetic testing results for review**

☐ **Sending notification that a blood sample has been sent for testing**

Sending Genetic Results:

- Complete the Genetic Mutation Testing Form and enter into eclinical.
- Redact any identifiable subject information from the genetic testing results report.
- Record the PPMI Subject ID on each page of the genetic testing results report.
- Fax the Genetic Mutation Testing Form along with the subject's redacted genetic testing results to the GCC.

Sending Blood Sample:

- Complete the Genetic Mutation Testing Form and enter into eclinical.
- Complete the Laboratory Requisition Form.
- Fax the Genetic Mutation Testing Form and the Laboratory Requisition to the GCC.

PPMI Laboratory Requisition Form

To:
Massachusetts General Hospital
Neurogenetics DNA/
Biochemical Diagnostic Lab
Center for Human Genetic Research
CPC Building North, Suite 5300
185 Cambridge Way
Boston MA 02114
Phone: 617-726-5721
Email: kaburke@partners.org

From:
Site#: ☐☐☐
Institution: _____
Address: _____
Address: _____
City, State, Zip: _____
Contact Name: _____
Phone: _____
Fax: _____
Email: _____

PPMI Subject ID: ☐☐☐☐☐

MGH#:		(Completed by MGH)

Date Collected: _____ Male ☐ Female ☐ Year of Birth: _____

Sample Type (Check One): Blood ☐ Saliva ☐ DNA ☐

DNA Test Requested: ☐ LRRK2 G2019S ☐ Other (please list): _____

Billing Information:

Institution: Michael J Fox Foundation for Parkinson's Research
Address: Grand Central Station, P O Box 4777
City, State, Zip Code: New York, NY 10163-4777
Contact Name: Sohini Chowdhury
Phone: 212-509-0995 X 206 Fax: 212-509-2390
Email: schowdhury@michaeljfox.org

Comments:

PPMI Sample Collection and Shipping Information

1. General Blood Draw Information

- Draw 1 10ml EDTA purple topped Vacutainer tube for each subject.
- Record the subject ID, sex and year of birth on the pre-labeled EDTA purple topped Vacutainer tube.
- Invert each tube 8-10 times to mix additive; do not shake tubes.
- Samples should be shipped **ambient** (room temperature), within 24 hours of being drawn.
- Do not ship samples on Friday.

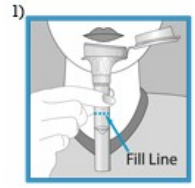
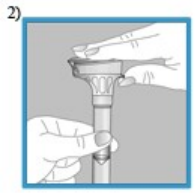
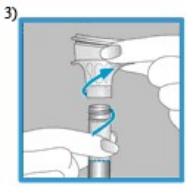
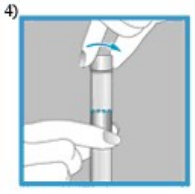
2. Blood Draw Kit

- Blood kits will be prepared by the GCC and shipped to sites. The number of kits sent to each site will be determined by that site's available storage space and the anticipated number of screening visits. Site coordinators will be responsible for informing the GCC of the number of kits the site requires as well as requesting additional kits as needed. Additional kits may be requested by email to PPMI@iu.edu.

- Each kit includes: 1 pre-labeled 10 ml purple topped EDTA Vacutainer tube, a small plastic canister, a segmented absorbent pouch, cushioning material (bubble wrap) and a cardboard shipping box. A ***Laboratory Requisition*** form, a ***Genetic Mutation Testing CRF*** and a ***GCC Fax Cover Sheet*** are also included.
- Each box is pre-labeled with a biohazard symbol label and a Biological Substance Category B label.

3. Saliva Collection Instructions

- **Remember: Do NOT remove plastic film from the lid.** Do not eat, drink, smoke, or chew gum for 30 minutes prior to giving your sample. You do NOT need to rinse your mouth prior to giving your sample. Most people take between 2 and 5 minutes to deliver a saliva sample following steps 1 to 5 below. Before spitting, relax and rub your cheeks gently for 30 seconds to create saliva.

	**STEP 1** Please write the date of sample collection where indicated on the tube label. Do NOT remove the plastic film from the lid of the container. Spit until the amount of liquid saliva (not bubbles) reaches the fill line shown in picture #1. Do NOT fill above the line.
	**STEP 2** Once the saliva level reaches the fill line, hold the tube upright with one hand. Close the lid with the other hand (as shown) by firmly pushing the lid until you hear a loud click. The liquid in the lid will be released into the tube to mix with the saliva. Make sure that the lid is closed tightly.
	**STEP 3** Hold the tube upright. Unscrew the tube from the funnel.
	**STEP 4** Pick up the small cap for the tube. Use the small cap to close the tube tightly.
	**STEP 5** Shake the capped tube for 5 seconds. Discard or recycle the funnel. Place sample in the provided specimen bag for shipment to Indiana University (IU).

To review a video of the saliva collection procedure, please visit:
http://www.oragene.com/flash/OG-500UserInstructions.swf

4. Saliva Collection Kit

- Saliva kits will be prepared by the GCC and shipped to sites. The number of kits sent to each site will be determined by that site's available storage space and the anticipated number of screening visits. Site coordinators will be responsible for informing the GCC of the number of kits the site requires as well as requesting additional kits as needed. Additional kits may be requested by email to PPMI@iu.edu.

5. Shipping Instructions

1. Complete the ***Laboratory Requisition Form***, the ***Genetic Mutation Testing CRF*** and the ***GCC Fax Cover Sheet***.

2. Record the subject ID, sex and year of birth on the pre-labeled sample.

    a. **For Blood:**
        i. Place filled blood tube into the segmented absorbent pouch.

        ii. Roll segmented absorbent pouch with tube(s) and place into canister.

        iii. Place the ***Laboratory Requisition Form*** into the cardboard shipping box.

        iv. Roll canister in cushioning material (bubble wrap) and place into cardboard shipping box.

        v. Place the entire cardboard shipping box into a Federal Express Diagnostic Specimen Envelope and seal the Specimen envelope.

b. For Saliva:

i. Place the filled Oragene saliva collection tube into the provided specimen bag.

ii. Seal the specimen bag and place it into the padded envelope.

iii. Seal the padded envelope

iv. Place the padded envelope into a Federal Express Diagnostic Specimen Envelope and seal the Specimen envelope.

3. Affix the pre-printed shipping label to the Diagnostic Specimen Envelope.

4. Ship samples are shipped to:

Massachusetts General Hospital
Neurogenetics DNA/Biochemical Diagnostic Lab
Center for Human Genetic Research
CPC Building North, Suite 5300
185 Cambridge Way
Boston MA 02114
Phone: 617-726-5721
Email: kaburke@partners.org

5. Ship Fed Ex Standard Overnight.

6. **Do not ship samples on Friday.**

7. If you do not have a regularly scheduled Fed Ex pick, call 1-800-463-6339 to arrange for a carrier pick-up.

8. Fax ***Genetic Mutation Testing CRF*** and the ***Laboratory Requisition Form*** to the GCC using the ***GCC Fax Cover Sheet.***

GCC Genetic Counseling Checklist

PPMI Subject ID _____ Date of Counseling _____

Subject Name _____

PD ☐	Unaffected ☐	LRRK2+ ☐	LRRK2- ☐

The following information was obtained and discussed with this subject as part of the genetic counseling session:

☐ Assessment of the subject's understanding of the study was performed

☐ Basic rationale behind studying the genetics of Parkinson disease was reviewed

☐ Results of LRRK2 genetic studies were disclosed

☐ A clinical description of Parkinson disease was reviewed

☐ Causes and genetic aspects of Parkinson disease were discussed

☐ The implication of the test results to the subject's disease or disease risk was reviewed

☐ A de-identified three generation pedigree was obtained and a risk assessment to family members was provided based on the subject's mutation status, disease status, and family history

☐ Privacy/confidentiality of test results were discussed

☐ PPMI study overview was provided

☐ A family history sub-study packet has been mailed to the subject

Additional Comments

PPMI Family History Packet Distribution form

This form is used to track this packet and to help link family members together.

Please record below the **PPMI Subject ID, Sex and Year of Birth**.
Record the date the packet was given to the subject.
Fax or email this form to: **Fax#: 1-317-278-4507 PPMI@iu.edu**

To:
Genetic Coordination Core
Indiana University
Hereditary Genomics
Phone: 1-888-830-6299
FAX: 1-317-278-4507
E-mail: PPMI@iu.edu

From:
Site#: ☐☐☐
Contact Name: _____
Contact Phone: _____
Contact Fax: _____
Contact Email: _____

Date Packet Given to Subject: ____ / ____ / ____
Month Day Year

PPMI Subject ID: ☐☐☐☐☐ PPMI Packet ID: **Pre-assigned**

Male ☐ Female ☐ Year of Birth: ☐☐☐☐

Comments: