



Operations Manual PPMI Genetics Study

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SECTION 1: OVERVIEW

Who are we looking for?

- Individuals with and without PD, who have a *LRRK2*, *GBA* 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. Sites with Amendment 9 approval will be able to screen for *LRRK2*, *GBA* and *SNCA* mutations.
- **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 of having a *LRRK2* or *GBA* mutation. Screening for *SNCA* mutations is not currently available through the WRI. The WRI 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* or a *GBA* mutation are referred to a PPMI site for enrollment.
 - o <https://www.michaeljfox.org/page.html?ppmi-genetics>

Who is eligible for genetic testing?

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





- o Having a 1st degree relative (parent, sibling, child) with a positive *LRRK2*, *GBA* 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
 - o PD or Unaffected
 - o More intensive arm
 - o Schedule of events similar to PPMI de novo PD and HC cohorts.
- Genetic Registry
 - o PD or Unaffected
 - o 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*, *GBA* 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 <i>LRRK2</i> , <i>GBA</i> or <i>SNCA</i> mutation	Genetic Testing in Individuals with Parkinson's Disease
Unaffected (Added with AM7)	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	And have a family member with a <i>LRRK2</i> , <i>GBA</i> or <i>SNCA</i> mutation	Genetic Testing in Individuals without Parkinson's Disease Who Have Family Members with a <i>LRRK2</i> , <i>GBA</i> or <i>SNCA</i> 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*, *GBA* 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.





Individuals with PD with *LRRK2*, *GBA* or *SNCA* mutation:

PD status	Mutated gene	Time since diagnosis	Research Subject Information and Consent Form
PD	<i>LRRK2</i> , <i>GBA</i> or <i>SNCA</i>	≤ 7	PD Genetic Cohort Research Participants
PD	<i>LRRK2</i> , <i>GBA</i> or <i>SNCA</i>	> 7	PD Genetic Registry Research Participants

Unaffected Individuals with *LRRK2* or *SNCA* mutation:

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

Unaffected Individuals with *GBA* mutation:

PD status	Mutated gene	Send UPSIT	Deficit	Current age	Research Subject Information and Consent Form
Unaffected	<i>GBA</i>	Yes	Yes	≥ 50	Unaffected Genetic Cohort Research Participants
Unaffected	<i>GBA</i>	Yes	No	≥ 50	Unaffected Genetic Registry Research Participants
Unaffected	<i>GBA</i>	No	No	< 50	Unaffected Genetic Registry Research Participants





SECTION 3: GENETIC TESTING – SUBJECTS RECRUITED BY THE SITE

Overview

Individuals will be recruited who have a confirmed *LRRK2*, *GBA* 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 will be assigned to a study arm.

Screening

The first part of recruitment is to identify those individuals with an increased risk of having a *LRRK2*, *GBA* or *SNCA* mutation. It is anticipated that methods to identify individuals at an increased risk of carrying a *LRRK2*, *GBA* 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*, *GBA* or *SNCA* mutation will undergo genetic testing. All individuals must be willing to find out their genetic test results with the exception of those who are unaffected and have a first degree relative with a known mutation.

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 having a *LRRK2* or *GBA* 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* or a *GBA* 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 RESULTS

Overview

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

Identify Potential Subjects

Two guides were created to help sites identify individuals who are at increased risk of carrying a *LRRK2* or *GBA* 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)
- *Guide for Molecular Screening for Individuals without PD* (Appendix B)

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*, *GBA* 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 E) and the ***Laboratory Requisition form*** (Appendix G).
- 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.

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 G) 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 I.





Results

- GCC is responsible for entering genetic testing results into eClinical.
 - o 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.
 - o If there are no outstanding data discrepancies the GCC study coordinator will enter the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
 - o Once study arm is assigned, an automatic email notification is sent to the site and the GCC.
- Sites will receive an email report from the GCC with genetic testing results after results are received by the GCC.
 - o Sites will provide genetic testing results to the PPMI study subject if they wish to be informed.
- **Unaffected individuals with a positive GBA mutation test who are < 50** will be eligible for the Genetic Registry.
- **Unaffected individuals with a positive GBA mutation test who are $\geq$ 50** will be asked to complete additional assessments to determine study arm assignment.
 - o They will be asked to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ) to determine study arm eligibility.
 - If the subject agrees, the site coordinator will mail the UPSIT and SRQ to the subject. The subject will complete the UPSIT and SRQ and return them to the site.
 - When the UPSIT and SRQ are returned to the site, the study coordinator will review the booklets and questionnaire for completeness. If any documents are incomplete the study coordinator will contact the subject to resolve any issues. Any incomplete booklets will be returned to the subject to be completed.
 - When all documents are complete, the site study coordinator will send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring. The Olfactory Core will QC all booklets and documents and will enter UPSIT and SRQ data into the Olfactory Core database and will post data to LONI. They will submit cohort eligibility information to the GCC. Those individuals who have a deficit on the UPSIT/SRQ will be eligible for the Genetic Cohort study arm and those individuals who do not have a deficit on the UPSIT/SRQ will be eligible for the Genetic Registry study arm.





SECTION 3B: SUBJECTS WITH EXISTING *LRRK2*, *GBA* 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 or saliva sample.

Consent Subject

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

Obtain Results from Subject and Complete Necessary Forms

- Obtain a copy of the genetic testing results from the subject.
 - o All identifiable information on the genetic testing results must be redacted (blacked out) before the results are sent to the GCC.
 - o The PPMI Subject ID number must be written on each page of the genetic testing results.
- Complete the **Genetic Mutation Testing form** (Appendix E) 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).
- Enter the **Genetic Mutation Testing form** into eClinical.

GCC Review and Interpretation

- The GCC will review the genetic testing results and determine whether or not the subject carries a *LRRK2*, *GBA* or *SNCA* mutation.
 - o Sites will receive an email report from the GCC with the interpretation of the genetic testing results.

Results

- GCC is responsible for entering genetic testing results into eClinical.
 - o 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.
 - o If there are no outstanding data discrepancies the GCC study coordinator will enter the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
 - o Once study arm is assigned, an automatic email notification is sent to the site and the GCC.





- **Unaffected individuals with a positive *GBA* mutation test who are < 50** will be eligible for the Genetic Registry.
- **Unaffected individuals with a positive *GBA* mutation test who are $\geq$ 50** will be asked to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ) to determine study arm eligibility.
 - o If the subject agrees, the site coordinator will mail the UPSIT and SRQ to the subject. The subject will complete the UPSIT and SRQ and return them to the site.
 - o When the UPSIT and SRQ are returned to the site, the study coordinator will review the booklets and questionnaire for completeness. If any documents are incomplete the study coordinator will contact the subject to resolve any issues. Any incomplete booklets will be returned to the subject to be completed.
 - o When all documents are complete, the site study coordinator will send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring. The Olfactory Core will QC all booklets and documents and will enter UPSIT and SRQ data into the Olfactory Core database and will post data to LONI. They will submit cohort eligibility information to the GCC. Those individuals who have a deficit on the UPSIT/SRQ will be eligible for the Genetic Cohort study arm and those individuals who do not have a deficit on the UPSIT/SRQ will be eligible for the Genetic Registry study arm.





SECTION 3C: SUBJECTS WITH PREVIOUS PPMI *LRRK2* GENETIC TESTING BUT NO *GBA* GENETIC TESTING

Overview

PPMI subjects who have previously provided a blood, saliva or DNA sample for *LRRK2* genetic testing in PPMI but were found not to carry a mutation are eligible for *GBA* N370S genetic testing with site approval of Amendment 9.

Identify Potential Subjects

- Subjects who previously screened **negative** for a *LRRK2* mutation are eligible for *GBA* N370S genetic testing with site approval of Amendment 9.

Consent Subject

- The site coordinator will contact subjects to discuss screening for the *GBA* N370S mutation.
- Subjects do not need to provide another blood or saliva sample. Genetic testing will be done using DNA from their sample already stored at Massachusetts General Hospital (MGH) Neurogenetics DNA/Biochemical Diagnostic Laboratory.
- 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*
- The site study coordinator will complete the **GBA Screening form** (Appendix H) and fax or email the form to the GCC study coordinator.
- MGH has asked that requests to screen stored samples for *GBA* N370S be sent in batches. The GCC study coordinator will gather batches of **GBA Screening forms** (Appendix H) together into a pdf file. This file will be emailed to MGH, requesting that stored DNA samples be screened for *GBA* N370S.

Results

- GCC is responsible for entering genetic testing results 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.
 - If there are no outstanding data discrepancies the GCC study coordinator will enter the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
 - Once study arm is assigned, an automatic email notification is sent to the site and the GCC.
- **Unaffected individuals with a positive *GBA* mutation test who are < 50** will be eligible for the Genetic Registry.
- **Unaffected individuals with a positive *GBA* mutation test who are ≥ 50** will be asked to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ) to determine study arm eligibility.





- o If the subject agrees, the site coordinator will mail the UPSIT and SRQ to the subject. The subject will complete the UPSIT and SRQ and return them to the site.
- o When the UPSIT and SRQ are returned to the site, the study coordinator will review the booklets and questionnaire for completeness. If any documents are incomplete the study coordinator will contact the subject to resolve any issues. Any incomplete booklets will be returned to the subject to be completed.
- o When all documents are complete, the site study coordinator will send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring. The Olfactory Core will QC all booklets and documents and will enter UPSIT and SRQ data into the Olfactory Core database and will post data to LONI. They will submit cohort eligibility information to the GCC. Those individuals who have a deficit on the UPSIT/SRQ will be eligible for the Genetic Cohort study arm and those individuals who do not have a deficit on the UPSIT/SRQ will be eligible for the Genetic Registry study arm.





SECTION 3D: SUBJECTS WITH EXISTING *LRRK2* GENETIC TESTING BUT NO *GBA* GENETIC TESTING

Overview

PPMI subjects, who previously provided genetic testing results which were reviewed for a *LRRK2* mutation but were found to be negative, are eligible to participate in the *GBA* testing protocol. If the genetic testing report includes results for *GBA* N370S, the individual will be consented for a central review of the test result. If the individual's genetic testing report does not include a result for *GBA* N370S, the subject can be consented for the collection of a blood or saliva sample under Amendment 9.

Identify Potential Subjects

- Subjects who previously provided existing genetic testing results for review, who were found to be negative for a *LRRK2* mutation are eligible for *GBA* N370S genetic testing results review with site approval of Amendment 9.

Consent Subject

- The site coordinator will contact subjects to discuss reviewing their existing genetic testing results for a *GBA* N370S mutation.
- 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*
- The site study coordinator will complete the **GBA Screening form** and fax or mail the form to the GCC study coordinator.

GCC Review and Interpretation

- The GCC will review the previously supplied genetic testing results and determine whether or not the subject carries a *GBA* N370S mutation.
- If the subject's previous genetic testing results do not include screening for a *GBA* N370S mutation, the subject would be asked to provide a blood or saliva sample for testing. This sample would be sent to MGH for *GBA* N30S only, screening. (See Section 3A for procedures for screening a blood or saliva sample.)
- Sites will receive an email report from the GCC with the interpretation of the genetic testing results.
- GCC is responsible for entering genetic testing results 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.
 - If there are no outstanding data discrepancies the GCC study coordinator will enter the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
 - Once study arm is assigned, an automatic email notification is sent to the site and the GCC.





- **Unaffected individuals with a positive *GBA* mutation test who are < 50** will be eligible for the Genetic Registry.
- **Unaffected individuals with a positive *GBA* mutation test who are ≥ 50** will be asked to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ) to determine study arm eligibility.
 - o If the subject agrees, the site coordinator will mail the UPSIT and SRQ to the subject. The subject will complete the UPSIT and SRQ and return them to the site.
 - o When the UPSIT and SRQ are returned to the site, the study coordinator will review the booklets and questionnaire for completeness. If any documents are incomplete the study coordinator will contact the subject to resolve any issues. Any incomplete booklets will be returned to the subject to be completed.
 - o When all documents are complete, the site study coordinator will send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring. The Olfactory Core will QC all booklets and documents and will enter UPSIT and SRQ data into the Olfactory Core database and will post data to LONI. They will submit cohort eligibility information to the GCC. Those individuals who have a deficit on the UPSIT/SRQ will be eligible for the Genetic Cohort study arm and those individuals who do not have a deficit on the UPSIT/SRQ will be eligible for the Genetic Registry study arm.





SECTION 4: PRESCREENING THROUGH THE WIDESPREAD RECRUITMENT INITIATIVE (WRI)

Overview

The Widespread Recruitment Initiative (WRI) 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* or *GBA* mutation. Screening for *SNCA* mutations is not currently available through the WRI. This initiative is only available in English.

Driving subjects to the site

The Michael J. Fox Foundation for Parkinson's Research has developed study materials that can be distributed within the clinic, at support groups, community events, synagogues, etc. These materials provide the Michael J. Fox 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 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 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 and/or *GBA* testing

The GCC study coordinator will ship the saliva sample to Massachusetts General Hospital (MGH) for *LRRK2* and/or *GBA* mutation testing. Genetic testing results will be returned to the GCC. The GCC will contact each subject and schedule a time to speak with the genetic counselor. The genetic counselor will then 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.

Subjects with positive *LRRK2* results

For individuals with a positive *LRRK2* mutation test, the GCC genetic counselor will provide the subject's genetic testing result and complete a **Genetic Mutation Testing form** (Appendix E). She will confirm that the subject agrees to have their contact information provided to the PPMI site. A letter will be sent to each subject, summarizing the genetic testing results.





Subjects with negative *LRRK2* and/or *GBA* results

For individuals with a negative *LRRK2* and/or *GBA* mutation test, the GCC genetic counselor will provide the subject's genetic testing result and inform the subject that they are not eligible to enroll in PPMI. A letter will be sent to each subject, summarizing the genetic testing results.

Subjects with positive *GBA* results (and negative *LRRK2* results)

- For **individuals with PD and a positive *GBA* mutation test**, the GCC genetic counselor will provide the subject's genetic testing result and complete a **Genetic Mutation Testing form** (Appendix E). She will confirm that the subject agrees to have their contact information provided to the site. A letter will be sent to each subject, summarizing the genetic testing results.
- For **unaffected individuals with a positive *GBA* mutation test who are < 50** the GCC genetic counselor will complete a **Genetic Mutation Testing form** (Appendix E). She will provide the subject's genetic testing result and confirm that the subject agrees to have their contact information provided to the site. A letter will be sent to each subject, summarizing the genetic testing results.
- For **unaffected individuals with a positive *GBA* mutation test who are $\geq$ 50** the GCC genetic counselor will provide the subject's genetic testing result and complete a **Genetic Mutation Testing form** (Appendix E). She will confirm that the subject agrees to have their contact information provided to the site. A letter will be sent to each subject, summarizing the genetic testing results.
 - o She will ask the individual to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ).
 - o If the subject agrees, the GCC study coordinator will mail the UPSIT and SRQ to the subject. The subject will complete the UPSIT and SRQ and return them to the GCC.
 - o When the UPSIT and SRQ are returned, the GCC study coordinator will review the booklets and questionnaire for completeness. If any documents are incomplete the GCC study coordinator will contact the subject to resolve any issues. Any incomplete booklets will be returned to the subject to be completed.
 - o When all documents are complete, the GCC study coordinator will send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring. The Olfactory Core will QC all booklets and documents and will enter UPSIT and SRQ data into the Olfactory Core database and will post data to LONI. They will submit cohort eligibility information to the GCC. Those individuals who have a deficit on the UPSIT/SRQ will be eligible for the Genetic Cohort study





arm and those individuals who do not have a deficit on the UPSIT/SRQ will be eligible for the Genetic Registry study arm.

- GCC is responsible for entering genetic testing results and cohort eligibility into eClinical.
 - o 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.
 - o If there are no outstanding data discrepancies the GCC study coordinator will enter the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
 - o Once study arm is assigned, an automatic email notification is sent to the site and the GCC.

Subjects with positive *LRRK2* and positive *GBA* results

- Individuals with both a positive *LRRK2* and a positive *GBA* result will be enrolled using the *LRRK2* protocol.

Site referral and study arm assignment

- For those individuals who carry a *LRRK2* and/or *GBA* 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 J). This form will be faxed to the appropriate PPMI site along with the completed ***Genetic Mutation Testing form*** (Appendix E) and the ***GCC Genetic Counseling Checklist*** (Appendix K). The site will enter the ***Genetic Mutation Testing form*** (Appendix E) 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.
- If there are no outstanding data discrepancies the GCC study coordinator will enter the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
- Once study arm is assigned, an automatic email notification is sent to the site and the GCC.
- The site will contact the subject, discuss the study and study arm assignment and schedule a study visit.
- The site will fax the ***PPMI Genetics Referral form*** (Appendix J) 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 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 GMU 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.

- The CTCC has created an algorithm that assigns study arm based on the rules in the chart below.
- GCC confirms that there is no discrepant or missing data. If there are no data discrepancies, then entry of the genetic mutation test result and cohort eligibility triggers the algorithm to automatically assign study arm.
- The GCC study coordinator enters the genetic testing result and cohort eligibility into eClinical. Completing this data entry will trigger study arm assignment.
- An email with the subject's study arm assignment will be sent to both the site and the GCC.





SECTION 5A: SUBJECTS WHO WANT TO KNOW THEIR GENETIC TESTING RESULTS

PD Status	Want to Know Gene Status	Gene Status	Mutation	Send UPSIT & SRQ	UPSIT/SRQ Deficit	Disease Duration (from Diagnosis)	Age	Study Arm
PD	Yes	+	<i>LRRK2</i> , <i>SNCA</i> or <i>GBA</i>	No	Not applicable	≤7 years	≥ 18	Genetic cohort
PD	Yes	+	<i>LRRK2</i> , <i>SNCA</i> or <i>GBA</i>	No	Not applicable	>7 years	≥ 18	Genetic registry
PD	Yes	-	Not applicable	No	Not applicable	Not applicable	Not applicable	Excluded
Unaffected	Yes	+	<i>LRRK2</i> or <i>GBA</i>	No	Not applicable	Not applicable	< 50	Genetic registry
Unaffected	Yes	+	<i>SNCA</i>	No	Not applicable	Not applicable	< 30	Genetic registry
Unaffected	Yes	+	<i>LRRK2</i>	No	Not applicable	Not applicable	≥ 50	Genetic cohort
Unaffected	Yes	+	<i>GBA</i>	Yes	Yes	Not applicable	≥ 50	Genetic cohort
Unaffected	Yes	+	<i>GBA</i>	Yes	No	Not applicable	≥ 50	Genetic registry
Unaffected	Yes	+	<i>SNCA</i>	No	Not applicable	Not applicable	≥ 30	Genetic cohort
Unaffected	Yes	-	Not applicable	No	Not applicable	Not applicable	Not applicable	Excluded





SECTION 5B: SUBJECTS WHO DO NOT WANT TO KNOW THEIR GENETIC TESTING RESULTS

PD Status	Want to Know Gene Status	Gene Status	Mutation	Send UPSIT & SRQ	UPSIT/SRQ Deficit	Disease Duration (from Diagnosis)	Age	Study Arm
Unaffected	No	+ or -	<i>LRRK2</i>	No	Not applicable	Not applicable	< 50	Genetic registry
Unaffected	No	+ or -	<i>SNCA</i>	No	Not applicable	Not applicable	< 30	Genetic registry
Unaffected	No	+	<i>LRRK2</i>	No	Not applicable	Not applicable	≥ 50	90% Genetic cohort
								10% Genetic registry
Unaffected	No	-	<i>LRRK2</i>	No	Not applicable	Not applicable	≥ 50	85% Genetic registry
								15% Genetic cohort
Unaffected	No	+	<i>SNCA</i>	No	Not applicable	Not applicable	≥ 30	90% Genetic cohort
								10% Genetic registry
Unaffected	No	-	<i>SNCA</i>	No	Not applicable	Not applicable	≥ 30	85% Genetic registry
								15% Genetic cohort

Continued on page 22





SECTION 5B: SUBJECTS WHO DO NOT WANT TO KNOW THEIR GENETIC TESTING RESULTS (Continued from page 21)

PD Status	Want to Know Gene Status	Gene Status	Mutation	Send UPSIT & SRQ	UPSIT/SRQ Deficit	Disease Duration (from Diagnosis)	Age	Study Arm
Unaffected	No	+ or -	<i>GBA</i>	No	Not applicable	Not applicable	< 50	Genetic registry
Unaffected	No	+	<i>GBA</i>	Yes	Yes	Not applicable	≥ 50	90% Genetic cohort
								10% Genetic Registry
Unaffected	No	+	<i>GBA</i>	Yes	No	Not applicable	≥ 50	85% Genetic registry
								15% Genetic cohort
Unaffected	No	-	<i>GBA</i>	Yes	Yes	Not applicable	≥ 50	85% Genetic registry
								15% Genetic cohort
Unaffected	No	-	<i>GBA</i>	Yes	No	Not applicable	≥ 50	85% Genetic registry
								15% Genetic cohort





SECTION 6: FAMILY HISTORY SUBSTUDY

Overview

One of the goals of evaluating the PD related gene mutations in *LRRK2*, *GBA* or *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.

For sites with Amendment 8 approval, subjects screened by a PPMI site will provide a Family History Packet to the subject at their baseline visit. Subjects enrolled before the site has received Amendment 8 approval will be given a Family History Packet at their study visit following approval of Amendment 8.

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 L)

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

European Family History Information

Family history information from subjects enrolled through non-English speaking sites may be provided as data files from the site, or directly from subjects, using translated documents provided by IU. Plans for collecting this information will be arranged on a site by site basis.





SECTION 7: APPENDICES

(Click on page number to move to that page.)

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Appendix A: Guide for molecular screening for individuals WITH PD

PPMI2 Guide for Genetic 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* or *GBA* mutation. People with PD must be willing to be informed of their testing results.

1. Does this individual have a positive *LRRK2* or *GBA* gene test?

☐

Yes

☐

No

☐

Unknown

A positive response to question 1 triggers a request for the subject to enroll in the PPMI study; a blood sample for additional *genetic* 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* and *GBA* testing.

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

☐

Yes

☐

No

☐

Unknown

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

☐

Yes

☐

No

☐

Unknown





Appendix B: Guide for molecular screening for individuals WITHOUT PD

PPMI2 Guide for Genetic 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* or *GBA* mutation.

A positive response to **question 1** triggers a request for the subject to enroll in the PPMI study; a blood sample for additional genetic testing is not needed.

1. Have you had a positive *LRRK2* or *GBA* gene test?

☐

Yes

☐

No

☐

Unknown

OR

A positive response to **BOTH question 2 and 3** triggers a request for the subject to provide a blood or saliva sample for *LRRK2* and *GBA* 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 or saliva sample for *LRRK2* and *GBA* 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* or *GBA* gene test?

☐

Yes

☐

No

☐

Unknown





Appendix C: Enrollment check sheet – subjects without existing genetic testing results

Identify Potential Subjects

- Guide for Molecular Screening for Individuals with PD (Appendix A)
- Guide for Molecular Screening for Individuals without PD (Appendix B)

Consent Subjects

- PD Genetic Cohort Research Participants **or**
- Unaffected Genetic Cohort Research Participants **or**
- PD Genetic Registry Research Participants **or**
- Unaffected Genetic Registry Research Participants

Complete Necessary Forms

- Genetic Mutation Testing form (Appendix E)
- Laboratory Requisition form (Appendix G)

Email or Fax Forms to GCC

- GCC Cover Sheet (Appendix F)
- Genetic Mutation Testing form (Appendix E)
- Laboratory Requisition form (Appendix G)

Draw and Ship Sample

- Record PPMI Subject ID, sex, year of birth and site number on tube label.
- Draw 10ml purple top EDTA tube or collect a saliva sample using an Oragene saliva collection kit.
- Send the Laboratory Requisition Form (Appendix G) with the sample to the laboratory.
- Shipping information can be found in Appendix I.
- Enter the Genetic Mutation Testing form into eClinical.

Return of Genetic Testing Results

- Genetic test results are sent directly to the GCC from the testing laboratory.
- GCC emails genetic testing results to site.

Study Arm Assignment

- **Unaffected individuals with a positive GBA mutation who are < 50** will be eligible for the Genetic Registry.
 - o GCC will enter genetic testing results, generating study arm assignment email.
- **Unaffected individuals with a positive GBA mutation test who are ≥ 50** will be asked to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ) to determine study arm eligibility.
 - o Mail UPSIT and SRQ to subject. Subject will return UPSIT and SRQ site.
 - o Review the booklets and questionnaire for completeness when they are returned.





- o When all documents are complete, send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring.
 - o Olfactory Core will QC all booklets and documents and will determine cohort eligibility.
 - o Results will be returned to the GCC.
- GCC will enter genetic testing results and cohort eligibility into eClinical, generating study arm assignment email.





Appendix D: Enrollment check sheet – subjects with existing genetic testing results

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 or saliva sample.

Consent Subjects

- PD Genetic Cohort Research Participants **or**
- Unaffected Genetic Cohort Research Participants **or**
- PD Genetic Registry Research Participants **or**
- Unaffected Genetic Registry Research Participants

Obtain Existing Genetic Testing Results

- Obtain a copy of existing genetic testing results from subject.
- Redacted (black out) all identifiable information on the genetic testing results before sending to GCC.
- Write the PPMI Subject ID number on each page of the genetic testing results.

Complete Necessary Forms

- Genetic Mutation Testing form (Appendix E) and enter into eClinical

Email or Fax Forms to GCC

- GCC Cover Sheet (Appendix F)
- Genetic Mutation Testing form (Appendix E)
- Subject's existing genetic testing results

GCC Review and interpretation

- The GCC will review existing genetic testing results and determine whether or not the subject carries a *LRRK2*, *GBA* or *SNCA* mutation.

Return of Genetic Testing Results

- GCC emails interpretation of existing genetic testing results to site

Study Arm Assignment

- **Unaffected individuals with a positive *GBA* mutation who are < 50** will be eligible for the Genetic Registry.
 - GCC will enter genetic testing results into eClinical, generating study arm assignment email.
- **Unaffected individuals with a positive *GBA* mutation test who are ≥ 50** will be asked to complete the University of Pennsylvania Smell Identification Test (UPSIT) and the Self Report Questionnaire (SRQ) to determine study arm eligibility.
 - Mail UPSIT and SRQ to subject. Subject will return UPSIT and SRQ to site.
 - Site Coordinator reviews booklets and questionnaire for completeness when they are returned.





- o When all documents are complete, send the UPSIT and SRQ to the Olfactory Core at the Institute for Neurological Diseases for scoring.
 - o Olfactory Core will QC all booklets and documents and will determine cohort eligibility.
 - o Results will be returned to the GCC.
- GCC will enter genetic testing results and cohort eligibility into eClinical, generating study arm assignment email.





Appendix E: Genetic Mutations Testing Form, page 1

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) (If less than one year, enter 1)								3a. ☐	
3b. If q3 is 2 = Unaffected, does the subject <u>know</u> or <u>desire to know</u> 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. ☐	
4a. Does the subject have a first degree relative (father, mother, sibling, child) with a GBA mutation? (0 = No, 1 = Yes)								4a. ☐	
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. ☐	



Appendix E: Genetic Mutations Testing Form, page 2

PPMI2									
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? (1 = MGH, 2 = 23andMe, 3 = Other _____)				7a. ☐					
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: (1 = Blood, 2 = Saliva (Amendment 7 or later), 3 = DNA (Specific sites only))				8a. ☐					
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: 1 = Massachusetts General Hospital 2 = Other, specify _____				10. ☐					
Comments: _____ _____ _____									



Appendix F: GCC cover sheet

GCC Cover Sheet

Use this form to request review of genetic testing results,
or to notify GCC that a blood or saliva 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:

Contact Name:

Contact Email:

Contact Phone:

Contact Fax:

Site#:

Date sent:

____ / ____ / ____
Month Day Year

of Pages Sent:

☐

**Sending genetic testing
results for review**

☐

**Sending notification that a
blood or saliva 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 or email 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 or email the Genetic Mutation Testing Form and the Laboratory Requisition to the GCC.





Appendix G: Laboratory requisition form

PPMI Laboratory Requisition Form

To:	From:	Site#:
Massachusetts General Hospital		
Neurogenetics DNA/	Institution:	
Biochemical Diagnostic Lab	Address:	
Center for Human Genetic Research	Address:	
CPC Building North, Suite 5300	City, State, Zip:	
185 Cambridge Way	Contact Name:	
Boston MA 02114	Phone:	Fax:
Phone: 617-726-5721	Email:	
Email: kaburke@partners.org		

PPMI Subject ID:						MGH#:	
						(Completed by MGH)	
Date Collected:		Male		Female		Year of Birth:	

Sample Type (Check One):	Blood		Test Requested (Check One):	LRRK2 G2019S	
	Saliva			GBA N370S	
	DNA			LRRK2 G2019S and GBA N370S	
			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
Email:	schowdhury@michaelifox.org
Phone:	212-509-0995 X 206
Fax:	212-509-2390





Appendix H: GBA screening form

PPMI Additional Screening for GBA N370S

Please record below the **PPMI Subject ID, Sex and Year of Birth.**

Email or fax or this form to: chalter@iu.edu Fax#: 1-317-278-4507

To:	From:	Site#: ☐ ☐ ☐
Cheryl A. Halter, MS, CCRC	Contact Name: _____	
Indiana University	Contact Email: _____	
Hereditary Genomics	Contact Phone: _____	
Phone: 1-317-274-5734	Contact Fax: _____	
FAX: 1-317-278-4507		
E-mail: chalter@iu.edu		

This subject has previously provided a blood, saliva or DNA sample for genetic screening or has provided previous genetic testing results for review. The subject has now consented to have their stored sample screened for GBA N370S or for review of previously provided existing results.

PPMI Subject ID:	☐	☐	☐	☐	☐	MGH#:
Male	☐	Female	☐	Year of Birth:		
Please Check one:						
☐	Stored DNA sample should be screened for a GBA N370S mutation					
☐	Existing genetic testing results should be reviewed for a GBA N370S mutation.					





Appendix I: 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.



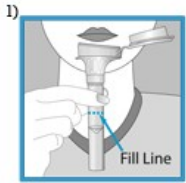
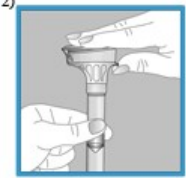
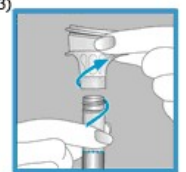
- Each kit includes: 1 pre-labeled 10 ml purple topped EDTA Vacutainer tube, a small plastic canister, a segmented absorbent pouch, cushioning material (bubble wrap) and a cardboard shipping box. A **Laboratory Requisition** form, a **Genetic Mutation Testing CRF** and a **GCC Fax Cover Sheet** are also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

- Complete the **Laboratory Requisition Form**, the **Genetic Mutation Testing CRF** and the **GCC Fax Cover Sheet**.
- Record the subject ID, sex and year of birth on the pre-labeled sample.
 - For Blood:**
 - Place filled blood tube into the segmented absorbent pouch.
 - Roll segmented absorbent pouch with tube(s) and place into canister.
 - Place the **Laboratory Requisition Form** into the cardboard shipping box.
 - Roll canister in cushioning material (bubble wrap) and place into cardboard shipping box.







Appendix J: Genetics referral form, page 1

PPMI GENETICS REFERRAL FORM

Clinical Site Notification of Eligible Subject for PPMI Screening Visit

Site number _____ Site Name _____

Coordinator _____

Coordinator Fax _____ Coordinator Email: _____

Notification Date _____

The individual identified below has been screened through the Widespread Recruitment Initiative of PPMI at Indiana University and is eligible for a PPMI screening visit as a part of the PPMI Genetic Cohort or Genetic Registry. Please contact the subject to schedule their visit. After the subject has been scheduled, enter the Genetic Mutations Testing Form (GMU) into eClinical then complete and fax or e-mail [this page](#) to the GCC for tracking purposes.

PPMI Subject ID _____

Subject Name _____

Address _____

Address _____

Phone1 _____ Phone2 _____

Email _____

Please check the appropriate box and add notes as indicated

Visit Scheduled ☐ Visit Date _____

Visit declined participation ☐ Reason _____

Subject did not return calls ☐ _____





Appendix J: Genetics referral form, page 2

PPMI GENETICS STUDY ARM ASSIGNMENT FORM

PPMI Subject ID _____

Year of Birth _____

Sex _____

Mutation: *LRRK2* G2019S ☐ *LRRK2* R1441G ☐
GBA N307S ☐ Other: _____ ☐

Subjects who know they have a <i>LRRK2</i> or <i>GBA</i> N307S mutation			Assignment
PD Subject – Duration	≤ 7 years	Cohort	
PD Subject – Duration	> 7 years	Registry	
Unaffected Subject – Age	≥ 50 years	Cohort	
Unaffected Subject – Age	< 50 years	Registry	
Unaffected Subject – Olfaction	Olfaction deficit	Cohort	
Unaffected Subject – Olfaction	No olfaction deficit	Registry	





Appendix K: GCC Genetic counseling checklist

GCC Genetic Counseling Checklist

PPMI Subject ID _____ Date of Counseling _____

Subject Name _____

PD	☐	Unaffected	☐	LRRK2+	☐	LRRK2-	☐
				GBA+	☐	GBA-	☐

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 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





Appendix L: Family history packet distribution form

PPMI Family History Packet Distribution form

Please record below the **PPMI Subject ID, Sex and Year of Birth.**

Record the date the packet was given to the subject.

Email or fax or this form to: chalter@iu.edu Fax#: 1-317-278-4507

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:

Family History Packet ID:

Pre-populated
by GCC

Date Packet Given to Subject:

/ /

Month Day Year

PPMI Subject ID:

Male

☐

Female

☐

Year of Birth:

Comments:

