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## Procedure and Guidelines to Access Banked Biospecimens

The goal of the Parkinson's Progression Markers Initiative (PPMI) is to identify, test and verify markers of progression for early-stage Parkinson's disease. To accomplish this goal, PPMI is collecting biospecimens, including urine, blood and cerebrospinal fluid (CSF) from participants (early stage Parkinson's disease (PD) subjects and healthy subjects). An inventory of PPMI biospecimens available through Coriell, the PPMI biorepository, will be maintained on the PPMI website. Comprehensive clinical and imaging data collected from PPMI research participants will also be available on the PPMI website to enable researchers to develop studies that might correlate biospecimen analysis with relevant subject data.

Several analyses of already identified analytes will be performed by PPMI investigators. Results of these studies will be made available on the PPMI website as soon as laboratory analyses are complete. Planned analyses will investigate the following analytics:

- Alpha-synuclein levels in CSF
- Urate levels in plasma
- DJ-1 levels in blood and CSF
- Tau, Phosphorylated tau, and beta-amyloid 1-42 in CSF

The PPMI study encourages interested investigators, whether associated with PPMI or not, to apply for use of PPMI biospecimens to verify potential PD progression biomarkers. **Please note: Stored samples are reserved for verification studies; samples should not be used for biomarker discovery work.** A list of biospecimen sources for discovery work can be found here.

**The PPMI Biospecimen Review Committee (BRC)** The BRC has been established to review applications seeking access to PPMI biospecimens. Following evaluation, the BRC will decide to accept or decline a proposal. The BRC will meet every other month and will review all Letters of Intent and Full Proposals received in time for the meeting. Please check here for a listing of submission dates coinciding with BRC meetings.

### **PROCEDURE TO APPLY FOR ACCESS TO BIOSPECIMENS**

***Please read the following section carefully to understand the process to apply for use of biospecimens (serum, plasma, DNA, RNA/miRNA, urine, CSF) collected as part of the PPMI study. In addition to applying for access to PPMI biospecimens, please note that applicants may also apply to MJFF for funding to perform the proposed studies. The review processes for biospecimen access and funding are separate; PPMI biospecimen access is determined by the PPMI BRC while MJFF will review all funding requests. Approval for use of PPMI biospecimens DOES NOT guarantee MJFF funding.***

There will be two stages to the application process: The Letter of Intent and the Full Proposal submission.

Rev June 10, 2010





PARKINSON'S  
PROGRESSION  
MARKERS  
INITIATIVE  
Play a Part in Parkinson's Research

## **Letter of Intent (LOI)**

Please note that the LOI is a required element of this application process.

Prospective applicants must submit an LOI online to <https://www.ppmi-info.org/specimens>. This link will also be provided on the MJFF website ([www.michaeljfox.org](http://www.michaeljfox.org)) under Funding Opportunities. LOIs are brief two-page summaries that outline the rationale for the proposed biomarker, the current evidence for testing of this biomarker, the current experience with the proposed assay as well as the number and type of samples the investigator is requesting. LOIs are not formal proposals *per se* but will act as a basis for selecting the most relevant and promising projects to be submitted for a Full Proposal. LOIs will be reviewed by BRC who will consider the criteria listed below when deciding whether to invite applicants to submit a Full Proposal. LOIs can be submitted at any time and will be reviewed by the BRC at their next scheduled meeting. Following that meeting, applicants will be informed whether they are invited to submit a Full Proposal.

### *LOI Evaluation Criteria*

- 1. Biomarker and Assay Rationale:** Is there sufficient evidence indicating that the biomarker can track with PD progression?
- 2. Preliminary Data and Validity of Assay:** Does the investigator have sufficient expertise working with the biomarker/assay? Is the biomarker truly ready to be 'verified'?
- 3. Feasibility:** Can PPMI provide the samples requested?

Applicants whose LOI are determined to best meet the criteria above will be invited to work with MJFF staff and the PPMI Steering Committee to submit Full Proposals. It is expected that invited applicants may work closely with PPMI investigators in shaping the final experimental design.

Because of the specific focus of these sample requests and selection criteria, the BRC does not expect to provide formal written critiques to applicants not invited to the full application stage. ***Projects that propose duplicate studies already being conducted by the PPMI Study will not be approved. A listing of on-going PPMI analyses can be found on the PPMI website at [www.ppmi-info.org](http://www.ppmi-info.org).***

Please note that applicants can indicate at the LOI stage whether they are requesting funding from MJFF to perform the studies proposed.

### **Full Proposal**

When applicants are notified via email as to whether they are invited to submit a Full Proposal, they will also receive feedback from MJFF that should be incorporated into the final proposal. Applicants will also be provided with instructions and all information necessary for submitting full proposals online. All proposals are treated with confidentiality by the BRC. Upon receipt, all proposals will be reviewed for completeness.

Full proposals will not exceed four pages in length and will include further information on the experiments proposed and the type/amount of samples requested. Applicants will also

Rev June 10, 2010





PARKINSON'S  
PROGRESSION  
MARKERS  
INITIATIVE

Play a Part in Parkinson's Research

submit information on key personnel working on the experiments, and if applying for MJFF funding, a budget and budget justification.

Proposals will be evaluated by the BRC based on the review criteria listed below. If applicants are requesting MJFF funding, MJFF will evaluate the proposed budget and budget justification in parallel to the BRC's evaluation of the scientific proposal. Final decisions will be based on the outcome of these reviews. Please note that all decisions are final and no appeals process is available.

*Proposal Evaluation Criteria*

- 1. Biomarker and Assay Rationale:** Does the proposed biomarker have sufficient rationale for testing in the limited biological resources collected as part of the PPMI study? The following information on the proposed biomarker/assay should be discussed:
  - Stability of the biomarker in the current PPMI storage conditions
    - polypropylenetubes used in the PPMI study
    - multiple freeze/thaw cycles
    - without preservatives or additional reagents in sample processing
  - Reproducibility of the assay
  - Volume of sample required
  - Range of biomarker
  - Test-retest reliability of the assay
  - Previous use of assay in human samples
  
- 2. Experimental Plan and Feasibility:** Has sufficient technical groundwork been performed to justify the use of this valuable material? Are sample sizes justified based on power analyses? A data analysis plan incorporating analysis of the relevant aspects of the PPMI dataset (clinical, neuroimaging, etc) should be discussed.
  
- 3. Collaborative Team and Environment:** Do the investigator and collaborators possess the appropriate expertise to carry out the proposed work? Are all key areas of expertise adequately supported as needed? Does the organizational/institutional environment in which the work will be done contribute to the probability of success? Are materials, technologies and additional support personnel available to ensure progress? Do the proposed experiments take advantage of unique features of the environment or employ useful collaborative arrangements? Is there evidence of institutional support? Has the team agreed to the PPMI Data Sharing Policy and IP Guidelines?

**Post Review**

A Full Proposal will receive one of the following sample access decisions:

Rev June 10, 2010





PARKINSON'S  
PROGRESSION  
MARKERS  
INITIATIVE

Play a Part in Parkinson's Research

1. Approval of application with MJFF funding: After a positive review by the BRC and funding decision by MJFF, MJFF will direct the PPMI Biorepository to release specimens to the investigator once the administrative items listed below are complete.
2. Approval of application without MJFF funding: After a positive review by the BRC, MJFF will direct the PPMI Biorepository to release specimens to the investigator, once funding for the project is demonstrated and administrative items listed below are complete.
3. Project re-evaluation: If the current proposed project has merit but requires changes to the experimental design, the applicant will receive specific feedback from the BRC with the opportunity to re-apply for sample access at a later date.
4. Disapproval of the application: Application was not deemed to be of significant merit and/or the proposed assays were not of sufficient quality to justify use of the limited PPMI samples.

Approved projects will obtain biological material and related information (data) from the PPMI biorepository at Coriell. Before any biospecimens or data will be released to the investigator(s) the following administrative items must be completed by the investigator(s):

- acknowledgment and acceptance of [PPMI Biospecimen Use Agreement](#) by the investigator(s), including compliance with the IP policy/guidelines outlined within the Agreement
- Receipt of regulatory approval (i.e. IRB) by the relevant institution(s) to handle/work with the biospecimens
- Signed Material Transfer Agreement between Coriell and the investigator's institution.

Comment [s1]: Link.

To ensure that experiments occur on a timely basis, investigators will be required to complete the administrative necessities outlined above within three months of receipt of BRC approval.

### **Data Obtained from PPMI Samples**

Biospecimens will be shipped from Coriell to the receiving investigator in a blinded fashion. The samples are matched to a unique Coriell Identification number. When the analyses are completed the investigator will submit a report of the analyses by subject to the BRC. Upon approval, the BRC will provide a "code" that will match the unique Coriell ID with the PPMI ID so the investigator will then be unblinded and have the opportunity to match the data to the clinical data in the PPMI database. Within two months of receiving the code, the investigator must resubmit his/her data/analyses to the BRC, with the understanding that this information will be deposited into the PPMI study database so that it may be mined by the Research Community.

### **CONFIDENTIALITY POLICY**

MJFF and the BRC treats all Letters of Intent (LOI), Full Proposals, research projects and associated research information (collectively, the "Confidential Information") in confidence using no less than reasonable care in protecting such Confidential Information from

Rev June 10, 2010





PARKINSON'S  
PROGRESSION  
MARKERS  
INITIATIVE

Play a Part in Parkinson's Research

disclosure to third parties who do not participate in the grant review process and MJFF assessments. All Confidential Information will be used by the BRC, MJFF and its grant reviewers ("Reviewers") only internally for the purposes of reviews and assessments, and will be shared only in accordance with its sharing policy stated herein. Notwithstanding Reviewers' obligations regarding such Confidential Information, such obligations cover any information retained in their unaided memories and may not be used without the permission of the disclosing party. Notwithstanding the foregoing, the obligations governing the disclosure and use of Confidential Information do not apply with respect to Confidential Information that it can be demonstrated:

- (a) was generally known to the public prior to the effective date when the LOI was submitted; or
- (b) becomes generally known to the public through no unlawful or unauthorized act of omission by any recipient of Confidential Information, or in violation of this review process; or
- (c) was independently developed by any recipient prior to the effective date of this review process; or
- (d) was disclosed to a recipient by a third party who has the right to make such disclosure.

If any recipient of Confidential Information is requested to produce any of the Confidential Information pursuant to a legal or governmental proceeding, such recipient shall give the applicant or other owner of such Confidential Information (the "Discloser") as much prior notice of such requirement as is reasonably practicable under the circumstances and shall use its reasonable efforts to assist the Discloser of such Confidential Information in objecting to such request. If a recipient is compelled to disclose any of the Confidential Information pursuant to such legal or governmental proceeding, such recipient shall use its reasonable efforts to assist Discloser in obtaining confidential treatment for such Confidential Information, will disclose only that portion of the Confidential Information which is responsive to the order, and will provide the Discloser with any copies of Confidential Information so disclosed; provided that such Confidential Information shall remain confidential until it falls into one of the categories specified in this Section entitled "CONFIDENTIALITY."

#### **CONFLICTS OF INTEREST**

Principal investigators and their paid collaborators submitting applications for access to PPMI biospecimens may be excluded from serving on the BRC and/or MJFF Grant Review Committee (GRC) that reviews their proposal. However, non-applicants who are invited to serve on the BRC/ GRC may still have a conflict of interest that arises during the grant review process. A BRC/GRC member is judged to have a conflict of interest if (1) he or she is a collaborator, sub-contractor, and/or consultant with an investigator that has a grant application before the BRC/GRC, (2) the application is from the reviewer's own institution

Rev June 10, 2010





PARKINSON'S  
PROGRESSION  
MARKERS  
INITIATIVE

Play a Part in Parkinson's Research

regardless of whether or not reviewer has had any involvement in preparing the application, (3) the member, his/her immediate family, or close professional associate(s) has a financial or vested interest in the outcome of the proposed research (even if no significant involvement is apparent in the proposal being considered), or (4) the BRC/GRC member has been involved in discussions regarding the application, is a provider of services, cell lines, reagents, or other materials, or writer of a letter of reference for the applicant. BRC and GRC members may also identify additional conflicts outside of those listed above.

When a conflict of interest is deemed to be present, the BRC/GRC member will be ineligible to review the proposal and will be asked to leave the room when the proposal is discussed during the review process, including when it is scored. Nor will the results of the review be made known to the conflicted reviewer until after the entire review process is complete. BRC and GRC members are also urged to avoid any actions that might give the appearance that a conflict of interest exists, even though he or she believes there may not be an actual conflict of interest.

Rev June 10, 2010

