



Summary of the National Institute of Neurological Disorders and Stroke Parkinson's Disease Biomarkers Program Consortium Meeting September 9, 2013 Bethesda MD

In September 2012, the National Institute of Neurological Disorders and Stroke (NINDS) awarded nine projects under the Parkinson's Disease Biomarkers Program (PDBP), a Program focused on promoting the discovery of biomarker candidates for early detection and measurement of disease progression. On September 9, 2013, PDBP Principal Investigators (PIs), clinical and data management experts from each PDBP site, representatives from non-government organizations and NINDS staff gathered to discuss the progress and challenges during the first year of the Program. A summary of the meeting discussion is given below.

Overview of Performance - Year 1

Site Recruitment and Biospecimen Collection

- Subject recruitment has been remarkable: As of August 2013, a total of 373 subjects have been enrolled across the 6 actively recruiting sites. This represents 27% of the PDBP recruitment goal. (More recent figures can be found [here](#))
- Sites have begun entering clinical data into the DMR and making good progress
- The PDBP biospecimen collection housed at the NINDS Repository continues to expand: As of August 2013, 373 DNA and RNA samples, 303 whole blood samples, 280 plasma samples, 254 serum samples and 60 CSF samples
- Reference pools for plasma and serum that can be used for normalization and standardization across sites, platforms and assays have been developed and housed at the NINDS Repository

PDBP Data Management Resource (DMR)

The DMR commenced in November 2012 when ProFoRMS, a system for electronic data entry, was launched and became available for data entry in February 2013. Newly added features include the Query tool and the Repository order manager tool.

- The Query tool allows users to search for data (defined in terms of CDEs) across all studies. Before data can be queried, however, it must first be moved from ProFoRMS to the long-term data repository – a process known as 'locking'. All sites have been trained to do this. The Query tool also enables investigators to search for biospecimens included in the NINDS Biorepository catalog file.



- The order manager tool allows investigators to request biospecimens collected by the PDBP. Requests for access to clinical data and biospecimens are adjudicated by the Data Access Committee (DAC) and Biospecimen Resource Access Committee (BRAC) respectively. Demo videos and ordering details will all be available on the PDBP public website.
- The DMR staff strives to provide excellent customer service and is constantly trying to improve the DMR user experience. To this end, a few enhancements have been made to ProFoRMS: GUID generation (has been made faster), keyboard data entry (made easier, Tab switching is now better ordered), and tablet data entry (now debugged)

Award Certificates/Acknowledgements

- Andrew West, Rachel Clark, Ashlee Rawlins (University of Alabama): most subjects enrolled and most data entered into the DMR
- Richard Dewey, Dwight German, Heather Askew, Julia Koch (UT Southwestern): most biospecimens collected
- Amy Snyder (University of Florida): leadership on clinical coordinator calls
- Clemens Scherzer (Harvard), Jing Zhang (University of Washington): PDBP steering committee chairs

NINDS Biorepository Update

- Over 6000 PDBP samples in the NINDS Repository which include baseline and follow-up visits
- Biospecimen quality control has been established for DNA, RNA, plasma, serum and CSF
 - For DNA, it was suggested that for identity/gender confirmation, replacing MSATs with SNPs may be more informative.
 - For plasma and serum, hemoglobin concentration is measured to ascertain site-to-site variation. Measuring other analytes will be useful (see 'Analytes to be measured across PDBP' below) and a proposal on the analytes to be assessed is currently being assembled by the PDBP Executive Committee.
- Samples become available for distribution following QC tests.

Data and Biospecimen Access

- Requests for data access are reviewed by the Data Access Committee (DAC). Similar to the format used at dbGaP, the DAC ensures that the Data Use Certification (DUC) is signed by both the requestor and the institutional business official and the research project is reasonable. Once these conditions are satisfied the requestor will be given access to the data.



- Similar to dbGaP policy, beginning November 2013 there will be a one year embargo on DMR data. Approved PIs can view the data but are not allowed to publish on that data for one year.
- Requests for biospecimens will be reviewed by the Biospecimen Resource Access Committee (BRAC). More stringent criteria will be used because biospecimens are non-renewable resources. The committee will comprise NINDS staff and experts in statistics, biomarker discovery, consent and banking requirements.
- Ordered samples will be blinded and can only be unblinded after data is submitted back to the DMR.

Looking Forward to Year 2

Suggestions for Enhancing recruitment and retention

- Have a physician talk to the subject about lumbar puncture
- Consider providing a budget to reimburse travel costs (this will enable recruitment from a wider radius)
- Tag teams to collect clinical data (to reduce total time)
- Use support groups

Data Management Resource

- New functionality is planned for November and include: the MIPAV tool to allow for upload of imaging data and the genomics tool which permits upload of large data files
- Legacy data will be directly uploaded into the long term data repository from spreadsheets.
- User feedback is critical to improving the DMR

Analytes to be measured across PDBP

Measurement of specific analytes in biospecimens collected across PDBP sites will be useful in assessing site-to-site variability. Some analytes will be valuable for QC, others could have potential biomarker interest. The testing platform needs to be discussed for each of these analytes.

CSF Analytes to be considered

- Hemoglobin (Hb)
- alpha synuclein (a-syn)
- Tau (total Tau, phospho Tau)
- A-Beta (A β)
- Total protein

Plasma analytes to be considered

- Fasting lipid profile
- Hemoglobin
- Platelet markers (soluble CD40L, platelet factor 4)
- Inflammation marker (CRP)
- Urate
- Microparticles