Project Title: Systems Medicine of Mitochondrial and biochemical Parkinson’s Disease and other related movement disorders (SysMedPD)

Protocol
Version 1.1

04/10/2017

Co-Chief Investigators: Prof. Anthony Schapira and Prof Huw Morris

Study Administrator: Dr Philip Campbell

Reference Codes:
UCL Sponsor Code: 17/0126

Start Date of study: 1/3/17
Project Duration: 5 years

Abbreviations: Parkinson’s disease – PD; idiopathic Parkinson’s disease – IPD; cerebrospinal fluid (CSF); PD patients with detectable mitochondrial dysfunction – mito-PD; PD patients without detectable mitochondrial dysfunction – amito-PD;
PROTOCOL VERSIONS

<table>
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<tr>
<th>Version Stage</th>
<th>Versions No</th>
<th>Version Date</th>
<th>Protocol updated &amp; finalised by;</th>
<th>Appendix No detail the reason(s) for the protocol update</th>
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<td>12/4/17</td>
<td>AS, HM, PC</td>
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<td>04/10/2017</td>
<td>AS, HM, PC</td>
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DECLARATIONS

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the Research Governance Framework 2005 (as amended thereafter), the Trust Data & Information policy, Sponsor and other relevant SOPs and applicable Trust policies and legal frameworks.

I (investigator) agree to ensure that the confidential information contained in this document will not be used for any other purposes other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I (investigator) also confirm that an honest accurate and transparent account of the study will be given; and that any deviations from the study as planned in this protocol will be explained and reported accordingly.

Chief Investigator:
Signature: [Signature]
Date 21/06/2017
Print Name (in full): Professor Anthony Henry Vernon Schapira
Position: Head of Department and Professor of Clinical Neurosciences

On behalf of the Study Sponsor:
Signature: [Signature]
Date 22/06/2017
Print Name (in full): Suzanne Emerton
Position: Sponsorship Officer
1. Trial Personnel

Co-investigators
Dr Philip Campbell, UCL  p.campbell@ucl.ac.uk

2. Summary

Title: Systems Medicine of Mitochondrial and biochemical Parkinson’s Disease and other related movement disorders
Short title: SysMedPD
Objectives: Stratification of PD patients based on biochemical markers to develop novel neuroprotective therapeutic approaches.
Type of trial: Basic science study with human subjects
Trial design and methods: Genetic analysis, biological material sampling, biochemical assays, cell line generation.
Trial duration per participant: 24 months (up to 3 study visits in 2 years)
Estimated total trial duration: 5 years (includes 2 years for additional data analysis)
Planned trial sites: Multi-site (Royal Free Hospital Trust and National Hospital for Neurology and Neurosurgery, UCLH NHS Trust)
Total no. participants planned: 160
Main inclusion/exclusion criteria:
   Inclusion – Affected by Parkinson’s disease (PD) or a related disorder or unaffected by PD or related disorder for control cohort
   Exclusion – Participants with dementia, under 18 years of age.
Statistical methodology and analysis:
Screening for genetic mutations associated with PD, biochemical analysis of biosamples (blood components and tissue) by a variety of methods (Seahorse, flow cytometry etc) to stratify patients into groups with and without dysfunction in the studied biochemical process (e.g. mitochondrial dysfunction). Statistical analysis will include univariate and multivariate statistics such as principal component analysis, linear mixed models, partial least squares regression and ANOVA simultaneous component analysis.
3. Introduction

3.1 Background: Parkinson’s disease (PD) is a progressive neurological disorder that is increasingly prevalent with age, with the incidence rising from approximately 4 people per 10,000 in their forties to 2 in 100 over the age of eighty. Besides motor symptoms, such as tremor, rigidity, bradykinesia, and postural instability, PD patients often experience a variety of non-motor symptoms, such as fatigue, depression, sleep disturbance, and dementia.

Although symptomatic treatments exist to partially compensate for motor dysfunction, no neuroprotective treatment has yet been established to slow PD progression, which inevitably renders patients incapable of living independently. Compared to age- and sex-matched controls, PD patients are about 5 times more likely to require nursing home care and this care costs about 5 times more than average nursing home care. This, combined with the European demographic shift toward an increasingly larger fraction of aged individuals, creates a social and economic challenge to develop new medications to slow the progression of PD.

Our understanding of the aetiopathogenesis of PD has rapidly developed in the past two decades, but this has not yet translated into any clinically established neuroprotective treatment that slows disease progression. There is a growing consensus that the failure of previous efforts is mainly due to the aetiopathogenic diversity of PD and the estrangement of existing preclinical models from clinical PD. For example, it is known that mutations in mitochondrial genes can cause monogenic PD and biochemical evidence indicates that in a proportion of cases, idiopathic PD is associated with detectable mitochondrial dysfunction.

Therefore, our focus is on monogenic forms of PD that involve mitochondrial abnormalities as a primary (e.g., Parkin, PINK1), or secondary (e.g., LRRK2, GBA1) phenomenon, in order to extrapolate to idiopathic PD (IPD) patients with and without mitochondrial dysfunction (Mito-IPD and Amito-IPD, respectively). Biochemical pathways focusing on, but not restricted to mitochondrial function, will be assessed using a variety of techniques including biochemical assays on blood, urine, CSF and tissue samples. We will explore both the relevance and measurement of specific biochemical pathways in Parkinson’s and related disorders.

The main overall objective is to stratify PD patients based on dysfunction in biochemical pathways related to PD. This will aid in developing new candidate neuroprotection compounds to slow the progression of neurodegeneration.

3.2 Ethical considerations: The primary ethical considerations here are accurate informed consent, data security and potential adverse events related to study procedures, which will be monitored through the study.

3.3 Risks/benefits: This is a basic science study involving procedures to human participants. The primary risks of this study will be:

(1) Potential adverse events related to study procedures which will be mitigated by careful monitoring throughout the study.
(2) Causing increased anxiety about risk to family members of developing PD, which will be mitigated (i.) the provision of NHS-based genetic counselling and support where needed and (ii.) patient and public engagement through education about the results and implications of research as the study progresses.

4. Objectives

To identify participants with known monogenic forms of PD and related disorders (PINK1, parkin, GBA, LRRK2) for biochemical assessment of blood, urine, CSF and tissue samples to identify defects in specific biological pathways (e.g. mitochondrial dysfunction). The most informative of these assays will then be applied to participants without genetic mutations (IPD) to stratify them based on dysfunction in these biochemical pathways.

5. Study design

It is planned that 160 participants will be recruited to the study (comprising 100 with idiopathic Parkinson’s disease, 30 with genetic forms of Parkinson’s disease and 30 healthy control subjects). This is based upon power calculations conducted by the University of Luxembourg (who constructed the initial EU study proposal).

Participants will be asked to take part in up to 3 visits, one at baseline where a full assessment including clinical assessment and biosamples donation will take place, an optional visit for skin biopsy and/or CSF sampling and one further visit 1-2 years post entry into the study for repeat assessment and biosamples collection for participants with PD only. Data and samples will be collected in a standardised format and, following site based subject anonymization, will be entered onto a secure web-based database. To develop a patient registry, subjects can provide consent for permission to be contacted if further/additional research projects were to become available.

All participants must consent to the core protocol of clinical assessment and blood and urine donation. CSF and skin biopsy consent is highly desirable but optional. Skin biopsies will be requested from some study participants including unselected PD patients, healthy controls and PD patients with defined genetic and/or biochemical phenotypes. If participants are identified as being in particular cohorts of interest post baseline assessment/sampling analysis (e.g. the mito-PD or amito-PD groups) then cell lines generated from skin biopsies from these participants will be used to create advanced cell models, such as induced pluripotent stem cells and dopamingeric neurons for further biochemical analysis and validation of initial findings. All monogenic PD participant skin biopsy samples will be used to generate such models.

Patients will be asked if they want to be informed of the availability of NHS genetic or biochemical tests which emerge as a result of this research. Participants will not be made aware of the cohort they fall into as currently this will not change their medical care, however consent will be sort to re-contact patients based on the results of this study if these results suggest they will be eligible for novel therapies for PD or would be eligible to take part in future studies or clinical trials related to Parkinson’s disease. Control subjects will be asked to
complete baseline clinical assessments and donate biosamples but will not be asked to return for any further study visits.

**Table 1 – SysMedPD overview**

<table>
<thead>
<tr>
<th>Study personnel administered</th>
<th>Visit 1</th>
<th>Visit 2 (optional)</th>
<th>Visit 3 - 24-48 months (for those affected by PD only)</th>
</tr>
</thead>
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<tr>
<td>Demographic information</td>
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<td>CSF</td>
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<tr>
<td>Skin biopsy</td>
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</table>

**5.1 Inclusion/exclusion criteria:**

**Inclusion**

1. Diagnosed with PD, or a related condition (e.g. Parkinson’s plus, dystonia, tremor) or healthy control participant

2. Age 18 years or over

**Exclusion**

1. Lack of capacity to consent to participate in the project
Additional lumbar puncture and skin biopsy exclusion criteria

1. Anticoagulants such as warfarin
2. Known coagulation abnormalities – known coagulopathy
3. Lumbar spinal surgery within 6 months prior to assessment, or any lumbar spinal surgery that interferes with anatomy of the inter-vertebral space (LP).
4. History of chronic or repeat CSF leakage following previous lumbar puncture or history of spontaneous or traumatic intracranial hypotension (LP)
5. Active infectious process
6. Allergy/hypersensitivity to local anaesthetic

5.2 Recruitment: Participants will be identified in the following ways:

a) By the study team from existing biobank studies that UCL is collaborating on, where the patient has consented to be re-contacted.

b) By the clinical care team/ their treating physicians through movement disorder and neurology clinics in the course of normal clinical care.

c) Participants may contact the study team directly, for example after reading adverts on PD charity websites, in this instance participants will need to complete and return a ‘permission to contact form’ to the study team.

d) Participants friends/spouses who plan to attend study/clinic visits with the participant may also be approached to join the study as control subjects. This will be done by the study team. During study visits participants can be given permission to contact forms and information leaflets to give to friends/spouses who they feel may want to enrol in the study as a control subject

Participants will be provided with written information on the study before they participate, either via email or regular post. The primary research clinics will be based at the Royal Free London Foundation Trust and UCLH. Participants will be approached by their caregiver in the course of normal clinical care or by caregivers holding registries of patients who have agreed to be contacted for research purposes.

5.3 Consent: Written Informed consent will be obtained by individuals trained in GCP; and in consent procedures specific to this study. The consent process will be guided by a standard operating procedure (SOP). Standardised patient information sheets (PIS) and consent forms will be used. Participants can withdraw from the study any time without giving reasons.

5.4 Study assessments: Potential participants will sign an informed consent form prior to any study-related procedures, which will involve agreement to:

1. A brief structured clinical interview (30 mins) that will obtain details of patient demographics, PD history, past medical history, medication history, family history and environmental exposures (based on MERQ-PD questionnaire). This will also include reviewing participants NHS records.
2. A structured clinical examination (15mins) consisting of the following standardised examinations:
   a. MDS-UPDRS
   b. Montreal Cognitive Assessment (MoCA)
   c. Handwriting and spiral drawing assessment

Examinations may be videotaped for confidential research analysis, for example validation of clinical diagnosis, and rating scale assessment by another member of the research team.

3. Standardised validated patient self-completion questionnaires (20mins – can be done at home) including Epworth sleepiness scale (ESS), Parkinson’s disease sleep scale 2 (PDSS2), WHO Quality of Life scale short version (WHOQol – BREF), Hospital Anxiety and Depression scale (HADS) and Scales for Outcomes in Parkinson’s disease - Autonomic (SCOPA-AUT).

5.5 Biosamples: All participants will be invited to donate blood, urine and CSF at the initial study visit. All samples will be taken and stored using a standardised protocols. Participants will be asked to fast for 10-12 hours where possible before biosamples are taken. All samples will be labelled with a unique study identifier.

   a. Blood – each participant will be invited to donated up to 100mls of blood for DNA, analysis, RNA analysis, storage of immortalised peripheral blood lymphocytes (PBLs) (see below), plasma and serum samples, and extraction of blood cells (red blood cells, white blood cells and platelets) for biochemical assessment (such as mitochondrial function).

   b. Urine - a mid-stream urine sample will be collected from each participant

   c. CSF – Consent to CSF sampling is highly desirable but optional. For participants who agree to donate CSF a lumbar puncture will be performed. An information sheet on lumbar puncture will be provided to the participant. Local protocols should include the ability to perform a blood patch if necessary for persisting low-pressure headache. Lumbar punctures for CSF collection are performed using a small calibre needle in either a sitting or lateral decubitus position. CSF is obtained via gravity flow into polypropylene tubes. The first 0.5-1ml will be discarded due to potential contamination with blood. 5-10ml of CSF will then be collected for storage. Participants who are having a lumbar puncture as part of their routine clinical care, treatment or as a research procedure will be asked if they will donate surplus CSF for research purposes.

   d. Skin biopsy – Skin biopsy consent is highly desirable but optional. A proportion of participants will be asked to donate a skin biopsy. Skin biopsies will yield both skin and underlying fat samples. The area for biopsy will be scrubbed with 70% isopropyl alcohol and local anaesthetic will be instilled prior to removal of a skin and underlying fat sample by sterile punch biopsy instrument (4-6mm depending on the participant’s build). The skin will be closed with steristrips in most cases. Occasionally it is anticipated that a single stitch will be required and if this is the case the participant will be instructed to attend their GP surgery to
have the stitch removed by the practice nurse in one week’s time. The patient will be given an information sheet on post skin biopsy management. Skin punch will be carried out by clinically qualified personnel at all centres or where appropriate, at the participant’s home. The skin and fat sample will be transferred to the laboratory for further processing. Here fibroblast (from skin) and adipose stem cell (from fat) lines will be established using standard methods.

5.6 Controls: Individuals who are not blood relatives of the patient are eligible to participate as an unaffected control. Typically this will be the spouse or a close friend of the affected SysMedPD patient, but not their son, daughter or sibling. Permission to contact forms and patient information leaflets will be given to participants in the study to pass onto friends/spouses who would be eligible to enrol as control subjects. Alternatively, at study/clinic visits where a participant is accompanied by a friend/spouse who would be eligible to enrol as an unaffected control, the study team will invite the individual to take copies of the participant information sheet and consent form, as well as a ‘permission to contact form’. If they would like to enrol then they can return the permission to contact form to the study team. Finally unaffected controls can contact the study team directly, for example after reading adverts on PD charity websites. In this instance they would need to complete and return a ‘permission to contact form’ to the study team. Unaffected individuals can participate by completing study questionnaires/assessment and donating blood samples, and if possible CSF collection and skin biopsy. They will not be required to undergo a second follow up visit.

6. Sample analysis/processing

6.1 Screening for genes related to PD: Blood samples will be sent to UCL Institute of Neurology Neurogenetics Lab for DNA extraction and storage to be carried out in accordance with the analytical plan agreed with the Chief Investigator. The Neurogenetics Laboratory will process, store and dispose of blood samples in accordance with all applicable legal and regulatory requirements, including the Human Tissue Act 2004 and any thereto. Genetic analysis may include large scale sequence, copy number and single nucleotide variant analysis. Similarly RNA will be extracted from whole blood and analysed using RNA sequencing (RNAseq).

6.2 ECACC: Consent will also be sought for a coded blood to be sent to the European Collection of Cell Cultures - Porton Down (ECACC) for storage of peripheral blood lymphocytes (PBLs) and ultimately the preparation of immortalised cell lines for affected individuals only. No personal identifiers will be sent with this sample. However to enable the cell line to be of optimal use to the research community, strictly limited details of the subject will accompany the sample, specifically sex, race and year of birth. No further personal identifying details will be released to ECACC. The code linking the samples will be kept strictly confidential by the research group, on the encrypted NHS computer system in a folder whose access restricted by the study PI. Subjects can request withdrawal of their samples from ECACC at any point. The European Collection of Cell Cultures will process, store and dispose of blood samples in accordance with all applicable legal and regulatory requirements, including the Human Tissue Act 2004 and any amendments thereto. The custodian and Human Tissue Act Designated
Individual for ECACC is Julie E. Russell (MSc C.Biol MSB) - Head of Culture Collections for Public Health England (PHE) (contact details: email: julie.e.russell@phe.gov.uk; direct telephone: +44 (0) 1980 612661)

6.3 Assessment of biochemical pathways: This will involve analysis of plasma, serum, urine, CSF, blood cellular components and tissue taken from participants. If participants have already donated samples to another approved study lead by the principle investigators or their collaborators (such as the Clinical Neurological Disorders DNA and Serum Research Bank - CANDAS), and there is consent to use samples in collaborating projects, then these samples will be requested from the CANDAS study to reduce patient burden. Various pathways thought to be involved in PD (such as mitochondrial dysfunction) will be investigated using a range of laboratory techniques such as flow cytometry, seahorse extracellular flux analysis and metabolomic analysis. The aim is to use these pathways to stratify participants into cohorts with and without dysfunction in the studied biochemical pathway.

6.4 Collaboration – incoming data/samples: The research group may analyse anonymous samples provided by collaborators where an MTA is in place and where samples have been collected with appropriate local ethical approval.

6.5 Collaboration – outgoing samples: The research group will collaborate with national and international groups engaged in neurology research, principally in the EU for analysis as above. This project is part of a large European wide project involving multiple sites across Europe and is being funded primarily by an EU ‘Horizon 2020’ grant. This will involve sharing anonymised samples for specific analysis which will be carried out at other sites, e.g. “metabolomics” in the Netherlands. Pseudo-anonymised data will accompany the samples. Appropriate material transfer agreements (MTAs) will be used. Participants will be asked whether they consent to sharing of their pseudo-anonymized data.

7. Feedback to participants and the Wider Community

7.1 Individual based: Participants will be asked at the time of entry to the study whether they would wish to be informed if the project discovers they have a genetic mutation related to PD that has a validated NHS genetic test. If they elect to be informed, they will be contacted by letter. This will allow the individual to seek formal NHS (or equivalent) neurogenetics disease gene confirmation via an accredited genetics service and for potentially at risk family members to seek predictive counselling and testing via an NHS clinical genetics service if they wish. It will be emphasized that research results cannot be used for diagnosis or genetic counselling but that the appropriate NHS services will be used and that we will link closely with normal NHS care. The main genetics services with which we will work will be the Neurogenetics clinic, National Hospital for Neurology and Neurosurgery and Royal Free Hospitals. Where an individual does not want feedback, no communication of specific research findings will be made.

Participants will also be asked at time of entry into the study whether they would consent to be re-contacted based on results (genetic or biochemical) generated from this study should these results indicate they would be eligible for new research studies or therapies for
Parkinson’s disease. The contact will involve providing information about new studies with no commitment to enter these studies.

7.2 Incidental identification of health problems: There is the potential to detect unexpected, unrelated pathology in individuals undergoing clinical evaluation and clinical test. In such a case, the clinical research team will discuss the situation with the study participant and advise they see their GP to discuss whether specialist referral to assess and potentially treat these symptoms is appropriate. Relevant results will also be fed back to the participant’s GP with their consent. This possibility will also be made clear in the consent form signed by the study participant.

7.3 Scientific publication of results: will be via written reports to scientific journals. These publications will involve publication of anonymized information in scientific journals and the results of the research listed above.

8. Adverse events

All adverse events will be recorded in the case records. Adverse events may include side effects from the assessments performed but may also include signs or symptoms that may or may not be related to the study procedures. Appropriate local procedures will be in place for reporting of adverse events.

8.1 Reporting Serious Unexpected Adverse Events: All Serious Unexpected Adverse Events to a research subject in the study must be reported immediately to the sponsor using the following email address research-incidents@ucl.ac.uk.

A Serious Adverse Event
- Results in death
- Is life Threatening
- Requires Hospitalisation or prolongation of hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect
- Any other serious medical occurrence

Serious Adverse Events will be documented from the point of enrolment until the patient is exited from study. Information recorded and reported shall include
- A description of the event
- The date of event onset
- The relatedness of the event to the procedure
- The expectedness of the event
- The outcome of the event
- The date the event was first noticed by, or reported to the investigator

All ongoing Serious Adverse Events will be followed-up until the last study visit.

8.2 Reporting Incidents: All incidents must be reported through the appropriate Trust incidents reporting system. Where no Trust is involved the incident should be reported by completing form at http://www.ucl.ac.uk/jro/postapproval
Where the study is being conducted at UCLH then the incidents should be reported through Datix.

An incident in a research study is
- Something that should not have happened OR
- Something that should have happened but didn't

Which significantly effects any of the following
- The rights and well-being of the research subject
- The scientific value of the study
- The compliance of the study with all relevant legal rules or ethics guidance including the Data Protection Act and the Human Tissue Act.
- The reputation of UCL

This includes a requirement to report all serious breaches of protocol or GCP (if applicable).

9. Data and sample management

9.1 Storage of data: Patient identifiable source data will be stored in clinical subject folders in locked cabinet/locked room at study centres. Electronic scanned copies of primary consent forms and primary NHS records (e.g. NHS copy clinic letters, discharge summaries, previous genetic tests and scans) will be stored on the main NHS data store or on the secure database. Personally identifiable data will be transferred by mail, fax or 256-AES encrypted digital communication.

Participants will have a unique study ID generated using a standard labelling procedure. A ‘code-break’ will exist on the secure network if the need to identify a patent is required. Only the study primary investigators (Prof Anthony Schapira and Prof Huw Morris) and the study co-ordinator (Dr Philip Campbell) will have access to this ‘code-break’.

The main study database will be held in pseudo-anonymised form (study number) on a web application called REDCap, which is PHP software with a MySQL database back-end, created by Vanderbilt University for creating and managing online databases and surveys. It is tried and tested and popular among research institutions particularly for use in managing clinical studies and trials, longitudinal studies and surveys. REDCap has password protected and granular access to data and software modules, as well as logging and audit trails of any activity. It enforces a robust security model, with password requirements/expiry and time-outs, and any communication is encrypted through SSL. The database will be on a Linux server virtual machine hosted on a secure cloud hosting service. The web host, network connection and storage is Information Governance Toolkit compliant and ISO27001 certified following data security best practice. The database server will be backed up to two separate locations with server redundancy, meaning if one server goes down then a mirror will be up instead. No patient identifiable data will be held on this web based system.

Personally identifiable information will be held on a database which is separated from the main study database, with access restricted to the study coordinator and chief investigator.
The Study Coordinator will be responsible for enforcing a secure and robust system for maintaining coherent de-identified participant IDs at the central database.

Study clinical and genetic data will also be stored in pseudo-anonymised form with study code number on University (UCL) computer systems or other secure database.

Anonymised data with study code and year of birth may be shared with external collaborators as indicated above. Participants' personal data, including their name, postcode, date of birth and NHS number will be shared with the NHS Health and Social Care Information Centre in order to provide information about their health status. Storage and handling of data will follow Standard Operating Procedures. The databases will be maintained until 2037 for genetic/epidemiological research, under the custodianship of Prof. Anthony Schapira or Prof. Huw Morris to enable the long term follow up of participants recruited in this study. It may become important for participants to be re-contacted if new treatments or NHS tests become available as a result of this research.

9.2 Archiving: UCL recognises that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that he will archive the study master file at Royal Free for the period stipulated in the protocol and in line with all relevant legal and statutory requirements. The Principal Investigator agrees to archive the site’s study documents for 10 years following the study end, and in line with all relevant legal and statutory requirements.

At the end of the research all existing biosamples from the study will be transferred to the Clinical Neurological Disorders DNA and Serum Research Bank (CANDAS) at UCL, under the custodianship of Prof Huw Morris (co-principle investigator of this study).

9.3 Sample handling: Plasma, serum, urine, CSF and peripheral blood lymphocytes (PBLs) will be stored in secure freezers at the Royal Free Hospital Clinical Neuroscience Laboratories; Royal Free Hospital Biobank or National Hospital for Neurology Neurogenetics Laboratory.

9.4 Blood/DNA/RNA: will be extracted and then stored in a local or collaborating DNA/RNA lab (e.g. Institute of Neurology Neurogenetics lab, Department of Clinical Neuroscience Laboratory Royal Free Hospital) and/or processed at the European Consortium for Cell Cultures (ECACC), Salisbury, Wiltshire.

9.5 Cell lines: will be stored at Royal Free Hospital Clinical Neuroscience Laboratories; Royal Free Hospital. Cell lines may be submitted for bio-banking at ECACC (see section 6.2), StemBANCC, and collaborating laboratories in the UK and worldwide.

StemBANCC is a large-scale international multi-site partnership in the area of stem cell research. It brings a consortium of 35 partners together who share their experience in the field. It is a resource for developing new disease models and testing new therapies, funded by several partners including the UK Medical Research Council. It is a consortium which includes UCL and is overseen by a Scientific Ethical and Advisory Board and managed by Dr Zameel Cader, University of Oxford.
9.6 **Quality assurance:** An ongoing record of completion of study procedures will be kept. Protocol changes and personnel changes will be notified to REC, Local Trusts and other appropriate organizations.

9.7 **Insurance:** University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital’s duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

**10. Training**

The Chief Investigators will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files. Written Informed consent will be obtained by individuals trained in GCP. MDS-UPDRS assessment will only be carried out by those trained to do.

**11. Intellectual property**

Intellectual property agreements have been agreed regarding this project, see section 8 (page 18) of signed final version of consortium agreement for the project ‘SysMedPD’.

**12. Supply of equipment**

UCL owned research equipment (e.g Department of Clinical Neuroscience video recorder) will be used.

**13. Statement of Compliance**

The Chief Investigators will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki and in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.