Human Research Ethics Application

Application Management Information
Application ID: AL00133
Created date: 26/09/2019
Originating Application ID: AL00133
**This is the earliest application from which this application (AL00133) was copied.*
Parent Application ID: AL00133
**This is the immediate predecessor from which this application (AL00133) was copied.*
Version Number: 4
Application submitted to: Adventist Health Care Limited; Adventist Health Care Human Research Ethics Committee.

The applicant has requested that this ethics application be considered under the Low risk review pathway.

Section 1 – Core Information

Pre-application conditions

The applicant/s have acknowledged that:

1. The HREA has been designed for ethics review of human research, as defined in the National Statement.
2. Adequate resources must be available to conduct this research project.
3. All relevant institutional polices pertaining to the conduct of this research project should be considered and adhered to.
4. Research activities must not commence until ethics approval (and site authorisation, if appropriate) has been provided.

Project Overview

Q1.1 Project Title:

Evaluation of dose of Photobiomodulation (Light) Therapy and Physiotherapy for improving quality of life outcomes and mobility in Parkinson's Disease (Sydney)

Q1.2 Summary of the research project:

Parkinson's disease (PD) is the second most common degenerative neurological disease resulting in a substantial economic cost to the Australian community. Standard medical treatment for PD is drug therapy and sometimes surgical deep brain stimulation (DBS) with concomitant physiotherapy. Each has potentially deleterious side effects. Photobiomodulation therapy (PBMt) is a safe alternative that has been shown in animals to reduce dysfunction from PD and to protect nerves. There are no published data for the efficacy of PBMt in humans with PD. This Sydney arm of a Phase 1 single blinded clinical trial will evaluate a series of single cases to understand escalating dose requirements and application site for using PBMt . Outcomes will be assessed with same standardised physical tests (as in Brisbane arm) of gait and balance performance, upper limb dexterity and tremor, and Unified Parkinson's Disease Rating Scale (UPDRS). Results will inform a Phase 2 clinical trial.

Q1.3 Which category/ies of research best describes the project?

Series of single case participant, researcher-blinded studies (researcher in this case is the

researcher who will analyse the data)

Q1.4 In what environments will the research be conducted?

- 🕐 **Clinic(s)**
- ○ Community centre(s)
- ○ Cultural/religious organisation(s)
- ○ Hospital(s)
- ○ Online
- ○ Private residence(s)
- ○ Professional organisation(s)
- ○ Public place(s)
- ○ Research institute(s)
- ○ School system(s)
- ○ University(ies)
- ○ Workplace(s)

Q1.5 What organisation/entity has overall responsibility for this project?

Equally: Griffith University, and North Shore Musculoskeletal and Laser Physiotherapy

Q1.6 Describe how this research project is currently, or will be, funded.

Philanthropic funding ($50,000) provided by a private donor (confirmed). Photobimodulation devices will be donated or purchased at cost price. Other equipment has been purchased for other arms of the trial (Brisbane and Adelaide) and is available. Researchers provide their time for no cost

Q1.7 Anticipated starting date of the research project:

16/10/2019 12:00:00 AM

Q1.8 Anticipated duration of the research project:

9 Months

Project Team

Name: **Dr Ann Liebert**

Q1.9.4 Email Address:

ann.liebert@outlook.com

Q1.9.5 Is this person the contact person for this application?

Yes

Q1.9.5.1 Email Address:	ann.liebert@outlook.com
Q1.9.5.2 Telephone Number:	0409311887
Q1.9.5.3 Mailing Address	Australasian Research Institute, San Hospital, Wahroonga, NSW 2076

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Honorary Director of Photomolecular Research, Australasian Research Institute, San Hospital
Adjunct Senior Lecturer, Sydney University
Principal, North Shore Musculoskeletal and Laser Physiotherapy Centre, Artarmon, NSW
Photobiomodulation Clinic, Specialist and GP Centre, San Hospital

Q1.9.8 Staff ID *(optional)***:**

Q1.9.9 ORCID Identifier *(optional)***:**

Q1.9.10 Position on the research project:

Co-ordinating Principal Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

Yes

Q1.9.12 Research activities Dr Ann Liebert will be responsible for:

Planning and design of study protocol; treatment of participants; collection of data; data analysis and interpretation; Writing of reports.

Q1.9.13 Expertise relevant to the research activity:

Dr Ann Liebert is a a registered physiotherapist and physiotherapy/photobimodulation researcher with a track record of research and publications. She has delivered numerous papers at national and international conferences in this field. She is Vice-President of the Australian Medical Laser Association, on the scientific committee of the World Association for Photobiomodulation Therapy, and a Board Member of the North American Association for Photobiomodulation Therapy. She also has many years of experience in the delivery of photobiomodulation therapy.

Name: **Prof Liisa Laakso**

Q1.9.4 Email Address:

liisa.laakso@mater.uq.edu.au

Q1.9.5 Is this person the contact person for this application?

No

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Senior Research Fellow, Mater Hospital, Brisbane
Conjoint lecturer, University of Queensland

Q1.9.8 Staff ID *(optional)***:**

Q1.9.9 ORCID Identifier *(optional)***:**

Q1.9.10 Position on the research project:

Chief Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

No

Q1.9.12 Research activities Prof Liisa Laakso will be responsible for:

Provide advice on protocol, particularly with reference to applications of PBMt; data analysis and interpretation of results; assistance in drafting report

Q1.9.13 Expertise relevant to the research activity:

Prof Liisa Laakso is a registered physiotherapist and physiotherapy academic/researcher with a long track record of publications and grants in the field of photobiomodulation therapy (PBMt). She has delivered numerous papers at national and international conferences in this field. Prof Laakso has served on the Laser Safety Committee of the Royal Brisbane and Women's Hospital. Dr Laakso has been Vice-President of the Australian Medical Laser Association, President of the World Association for Laser Therapy, a member of the North American Association for Photobiomodulation

Name: **Prof Hosen Kiat**

Q1.9.4 Email Address:

hosen.kiat@chi.org.au

Q1.9.5 Is this person the contact person for this application?

No

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Professor of Cardilogy, Maquarie University

Q1.9.8 Staff ID *(optional)***:**

Q1.9.9 ORCID Identifier *(optional)***:**

Q1.9.10 Position on the research project:

Chief Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

No

Q1.9.12 Research activities Prof Hosen Kiat will be responsible for:

Assessing participants for cardiac health; data analysis; writing report

Q1.9.13 Expertise relevant to the research activity:

Prof Kiat is a world renowned cardiologist with extensive experience in both research and treatment of patients.

Name: **Dr Brian Bicknell**

Q1.9.4 Email Address:

brian.bicknell@acu.edu.au

Q1.9.5 Is this person the contact person for this application?

No

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Honorary Fellow, Australian Catholic University, North Sydney

Q1.9.8 Staff ID *(optional)***:**

Q1.9.9 ORCID Identifier *(optional)*:

Q1.9.10 Position on the research project:
Chief Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?
No

Q1.9.12 Research activities Dr Brian Bicknell will be responsible for:
microbiome analysis; report writing

Q1.9.13 Expertise relevant to the research activity:
Dr Bicknell is an experience microbiologist with expertise in this type of analysis and reporting of results.

Name: **Dr Roberta Chow**

Q1.9.4 Email Address:
robertachow103@gmail.com

Q1.9.5 Is this person the contact person for this application?
No

Q1.9.6 Is this person a student on this project?
No

Q1.9.7 Institutional affiliation and position:
Brain and Mind Centre, Sydney University
Photobiomodulation Clinic, Specialist and GP Centre, San Hospital

Q1.9.8 Staff ID *(optional)*:

Q1.9.9 ORCID Identifier *(optional)*:

Q1.9.10 Position on the research project:
Associate/Assistant/Sub-/Co- Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

Q1.9.12 Research activities Dr Roberta Chow will be responsible for:
Participant diagnosis; data collection; data analysis; report writing

Q1.9.13 Expertise relevant to the research activity:

Dr Chow is an experienced and world renowned and respected researcher in the field of photobiomodulation with many publications. She is also a specialist pain doctor with extensive experience in photobiomodulation therapy

Name: **Dr Greg Bennett**

Q1.9.4 Email Address:

gregorybbennett@gmail.com

Q1.9.5 Is this person the contact person for this application?

No

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Specialist Gerontologist, San Hospital

Q1.9.8 Staff ID *(optional)***:**

Q1.9.9 ORCID Identifier *(optional)***:**

Q1.9.10 Position on the research project:

Associate/Assistant/Sub-/Co- Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

No

Q1.9.12 Research activities Dr Greg Bennett will be responsible for:

Patient diagnosis

Q1.9.13 Expertise relevant to the research activity:

Dr Bennett is an experienced Gerontologist with expertise in the diagnosis and treatment of Parkinson's disese

Name: **Prof John Mitrofanis**

Q1.9.4 Email Address:

john.mitrofanis@sydeny.edu.au

Q1.9.5 Is this person the contact person for this application?

No

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Dept Anatomy, Sydney University

Q1.9.8 Staff ID *(optional)*:

Q1.9.9 ORCID Identifier *(optional)*:

Q1.9.10 Position on the research project:

Associate/Assistant/Sub-/Co- Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

No

Q1.9.12 Research activities Prof John Mitrofanis will be responsible for:

performing functional MRI; interpreting MRI data; report writing

Q1.9.13 Expertise relevant to the research activity:

Prof Mitrofanis is a senior academic and researcher with many years of experience in Parkinson's disease manifestations and experimental models of Parkinson's disease. He also has previously performed the required fMRI testing protocol.

Name: **Sharon Tilley**

Q1.9.4 Email Address:

tilley.sharon@gmail.com

Q1.9.5 Is this person the contact person for this application?

No

Q1.9.6 Is this person a student on this project?

No

Q1.9.7 Institutional affiliation and position:

Principal Physiotherapist, Lymphoedema and Laser Therapy Clinic, Adelaide

Q1.9.8 Staff ID *(optional)*:

Q1.9.9 ORCID Identifier *(optional)*:

Q1.9.10 Position on the research project:

Investigator/Researcher

Q1.9.11 Does this person have authorisation to sign the application on behalf of all members of the research team?

No

Q1.9.12 Research activities Sharon Tilley will be responsible for:

data collection

Q1.9.13 Expertise relevant to the research activity:

Sharon Tilley has been involved in a previous arm of this trial in Adelaide and has expertise in the administration of the tests that the participants will undergo

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Disclosure of interests

Q1.10 Do any members of the research team (including persons not listed in this application), have any financial or non-financial interests related to this research?

Yes

Q1.10.1 Explain the nature and extent of the interests and to which member of the team they apply.

Dr Ann Liebert who is the Principal Coordinating Investigator is married to Dr Brian Bicknell (Chief Investigator) who, in turn, is the Australian representative for one of the PBM devices (Irradia Midcare laser) that will be utilised in the study. The PBM device is being purchased through Dr Bicknell's contacts with Irradia Sweden.

Q1.10.2 Explain how you intend to manage these interests and any potential conflicts that may arise.

The devices to be utilised in the research (the Irradia Mid-Laser) have already been used as part of other research being undertaken in Brisbane and Adelaide. Dr Bicknell's role in the Sydney arm of the study is derived from his biochemical microbiology expertise and specifically for assessing the faecal microbiome samples of participants in order to evaluate whether the intervention has had any impact on the participant microbiome over the course of the study. No conflict is perceived as all faecal samples will be coded at entry and exit to the testing, and Dr Bicknell will therefore be blinded to the sampling regimen.

Restrictions

Q1.11 Are there any restrictions or limits on publication of data or dissemination of research outcomes of this project?

No

Evaluations

Q1.12 Has the scientific or academic merit of the research project been evaluated?

No

Q1.13 Has this research project had prior ethics review?

Yes

Q1.13.1 Name of ethics committee	Griffith University; Griffith University Human Research Ethics Committee
Q1.13.2 Outcome of ethics review	Approved
Q1.13.2.1.1 Name of HREA attachment containing evidence of the outcome of the prior ethics review *(optional)*	Sydney trial ethics approval email.pdf

Q1.14 Will any further or additional specialised review of this application be sought?

No

Setting of research

Q1.15 Will this project be conducted at multiple sites?

Yes

Q1.16 Will separate institutional approvals or authorisations be required prior to commencing research at each site?

Yes

Section 2 – Research Details and Participants

Q1.17 The following research methods will be used in the research project:

Research Method	Status
Action research	✗
Biospecimen analysis research	✗
Data linkage research	✗
Ethnographic research	✗
Epidemiological research	✗
Interventional/Clinical Trials research	✓
Observational research	✗
Survey/Interview/Focus Group research	✗
Textual analysis research	✗
None of the above	✗

Q1.18 The research will be conducted with the following:

Participation	Status
Human beings (via active participation), including their associated biospecimens and/or data.	✓
Human biospecimens only	✗
Data associated with human beings only (i.e. as the primary object of research)	✗

Q1.19 The research will involve the following participants:

Participants	Status
Women who are pregnant and the human fetus	✗
Children and young people	✗
People highly dependent on medical care who may be unable to give consent	✗
People with a cognitive impairment, intellectual disability or mental illness	✗
People in dependent or unequal relationships	✓
People who may be involved in illegal activities	✗
People in other countries	✗
Aboriginal and Torres Strait Islander peoples	✗

Method Specific Questions

Interventional/Clinical Trials Research

M6.1 Briefly describe the intervention/s that you will be using.

The intervention is photobiomodulation therapy (PBMt) applied to the abdomen and spine in people with Parkinson's Disease self-referred or referred by Geriatrician for physiotherapy (with diagnosis confirmed by medical specialist). Images of the application methods are appended. A low dose of light is applied to specific points on the abdomen and neck to stimulate the body's gut-brain axis. The participant feels nothing with the treatment. Further details regarding the device to be trialled can be found in the Appended Project Description.
PBMt has been used in humans for a wide range of conditions such as musculoskeletal disorders, inflammatory conditions and neurogenesis. PBMt is a safe, non-invasive, and non-thermal modality that is based on a substantial body of research dating back to the 1960s [1]. The mechanisms of action are proposed to involve the stimulation of mitochondria by the absorption of photons in cytochrome c oxidase, resulting in increased ATP production [2], leading to reduced oxidative stress, anti-inflammatory effects [3], improved cellular energy, increased synthesis of enzymes [4], and increased focal cerebral blood flow [5, 6]. Most encouraging, recent research has reported neuroprotection against degeneration, stimulated by PBMt in animal models of PD [7-9].
To date, the basic science research, and anecdotal clinical evidence offer support for the benefits of PBMt in PD [1, 10-14]. In a monkey model in which a Parkinson's Disease state was modelled by a neurotoxin, the application of PBMt reduced the signs of movement dysfunction as well as promoted neural protective responses and in some cases neuroregeneration of impaired nerve cells [11]. Further research reports PBMt is well tolerated and may be valuable in improving sleep-wake cycles in patients with PD [10]. PBMt has also been shown to be safe. Studies have applied both transcranial (e.g., WARP-LED) or intracranial (e.g., optical fiber device) methods to deliver light therapy at power intensities ranging from 1–700 mW/cm2 and have reported no adverse effects on brain tissue structures and function [3, 15]. The applicability of PBMt, the positive animal study responses and the lack of side effects [16-20] suggest that PBMt could provide a viable adjunct to current treatments for PD in humans. No study has yet explored this method of treatment for normalising movement in humans. We propose to undertake a Phase 1 trial of PBMt in a series of patients to best identify the type of application, place of application and dose rate that may produce positive changes in clinical signs and functional capacity of people with PD. In the Sydney arm of the trial (specific to this HREA) participants will receive PBMt to the abdomen and spine only, whereas in the Brisbane arm of the trial, participants will receive PBMt to the head only and in the Adelaide arm, participants receive PBMt to the head, neck and abdomen. The findings from each arm will be used to determine application procedures for a future Phase 2 clinical RCT.
References:
[1] Saltmarche AE, Naeser MA, Ho KF, Hamblin MR, Lim L (2017) Significant Improvement in Cognition in Mild to Moderately Severe Dementia Cases Treated with Transcranial Plus

Intranasal Photobiomodulation: Case Series Report. Photomedicine and Laser Surgery, 35-41
[2] Huang Y Y, Chen A C, Carroll J D, et al. Biphasic dose response in low level light therapy[J]. Dose Response, 2009,7(4):358-383.
[3] Chung H, Dai T, Sharma S K, et al. The nuts and bolts of low-level laser (light) therapy[J]. Ann Biomed Eng, 2012,40(2):516-533.
[4] Manteifel' V M, Karu T I. [Structure of mitochondria and activity of their respiratory chain in subsequent generations of yeast cells exposed to He-Ne laser light][J]. Izv Akad Nauk Ser Biol, 2005(6):672-683.
[5] Nawashiro H, Wada K, Nakai K, et al. Focal increase in cerebral blood flow after treatment with near-infrared light to the forehead in a patient in a persistent vegetative state[J]. Photomed Laser Surg, 2012,30(4):231-233.
[6] Schiffer F, Johnston A L, Ravichandran C, et al. Psychological benefits 2 and 4 weeks after a single treatment with near infrared light to the forehead: a pilot study of 10 patients with major depression and anxiety[J]. Behav Brain Funct, 2009,5:46.
[7] Johnstone D M, Moro C, et al. Indirect application of near infrared light induces neuroprotection in a mouse model of parkinsonism - an abscopal neuroprotective effect[J]. Neuroscience, 2014,274:93-101.
[8] Peoples C, Spana S, Ashkan K, et al. Photobiomodulation enhances nigral dopaminergic cell survival in a chronic MPTP mouse model of Parkinson's disease[J]. Parkinsonism Relat Disord, 2012,18(5):469-476.
[9] Shaw V E, Peoples C, Spana S, et al. Patterns of Cell Activity in the Subthalamic Region Associated with the Neuroprotective Action of Near-Infrared Light Treatment in MPTP-Treated Mice[J]. Parkinsons Dis, 2012,2012:296875.
[10] Videnovic A, Klerman E B, Wang W, et al. (2017) Timed Light Therapy for Sleep and Daytime Sleepiness Associated With Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol 74:411-18.
[11] Darlot F, Moro C, El M N, et al. Near-infrared light is neuroprotective in a monkey model of Parkinson Disease. Ann Neurol, 2016,79(1):59-75.
[12] Pitzschke A, Lovisa B, Seydoux O, et al. (2015) Red and NIR light dosimetry in the human deep brain. Physics in Medicine & Biology, 60(7):2921-37.
[13] Moro C, Massri N E, Torres N, et al. Photobiomodulation inside the brain: a novel method of applying near-infrared light intracranially and its impact on dopaminergic cell survival in MPTP-treated mice. J Neurosurg, 2014,120(3):670-683.
[14] Vos M, Lovisa B, Geens A, et al. (2013) Near-infrared 808 nm light boosts complex IV-dependent respiration and rescues a Parkinson-related pink1 model. PLoS One, 8(11):e78562.
[15] Moro C, Massri N E, Torres N, et al. (2014) Photobiomodulation inside the brain: a novel method of applying near-infrared light intracranially and its impact on dopaminergic cell survival in MPTP-treated mice. J Neurosurg, 120(3):670-683.
[16] Purushothuman S, Johnstone D M, Nandasena C, et al. (2015) Near infrared light mitigates cerebellar pathology in transgenic mouse models of dementia. Neurosci Lett, 591:155-159.
[17] Johnstone D M, Mitrofanis J, Stone J. (2015) Targeting the body to protect the brain: inducing neuroprotection with remotely-applied near infrared light. Neural Regen Res, 10(3):349-351.
[18] Farfara D, Tuby H, Trudler D, et al. (2015) Low-level laser therapy ameliorates disease progression in a mouse model of Alzheimer's disease. J Mol Neurosci, 55(2):430-436.
[19] Purushothuman S, Johnstone D M, Nandasena C, et al. (2014) Photobiomodulation with near infrared light mitigates Alzheimer's disease-related pathology in cerebral cortex - evidence from two transgenic mouse models. Alzheimers Res Ther, 6(1):2.
[20] Tuby H, Hertzberg E, Maltz L, et al. (2013) Long-term safety of low-level laser therapy at different power densities and single or multiple applications to the bone marrow in mice. Photomed Laser Surg, 31(6):269-273.

M6.2 Is your intervention related to the prevention, diagnosis, treatment or management of a health condition?

Yes

M6.2.1 Do you consider that you are conducting a clinical trial?

Yes

M6.2.1.1 What does the clinical trial involve the use of?

- ○ Drug
- ◷ Device
- ○ Xenotransplantation
- ○ Other

Use of a clinical trial device/s

The following details are provided for the use of *Irradia MID 2.5 laser* in the research project.

M6.2.1.1.2.1 Approved Name

Irradia MID 2.5 laser

M6.2.1.1.2.2 Trade Name (if any) *(optional)*

M6.2.1.1.2.3 Manufacturer of device

Spectra Analytic Irradia AB

M6.2.1.1.2.4 Supplier of device

SUMOLite Pty Ltd trading as Irradia Australia

M6.2.1.1.2.5 Approved therapeutic indication, duration in Australia

treating pain and accelerating healing

M6.2.1.1.2.6 Known adverse events

nil

M6.2.1.1.2.7 Known contra-indications or warnings

nil

M6.2.1.1.2.8 Is this the first use of the device in humans?

No

M6.2.1.1.2.9 Is this the first use of the device in patients?

No

M6.2.1.1.2.10 Is the device included on the Australian Register of Therapeutic Goods (ARTG)?

Yes

M6.2.1.1.2.10.1 Under what name is the device registered?

Irradia MID laser

M6.2.1.1.2.10.2 ARTG Number

ARTG #168734

M6.2.1.1.2.11 Is the application of the device proposed in this project different from the application/s of the device included on the ARTG?

No

M6.2.1.1.2.12 Has the device been registered/licensed/approved for marketing for this indication by an international regulatory authority (other than the Australian Therapeutic Goods Administration)?

No

M6.2.1.1.2.13 Has the device been registered, licensed or approved for marketing for other indications by an accepted international regulatory authority (other than the Australian Therapeutic Goods Administration)?

No

M6.2.1.1.2.14 Has the device been reviewed for investigational or research uses by an international regulatory authority?

No

M6.2.1.2 Does the clinical trial differ from standard care?

Yes

M6.2.1.2.1 How the clinical trial differ from standard care?

All consenting participants will receive the standard physiotherapy usually provided for Parkinson's Disease. Over and above the standard care, consenting participants will receive the photobiomodulation (PBM) therapy as an adjunct.

M6.2.1.3 Will trial participants be exposed to ionising radiation to which they would not have been exposed to if they did not participate in the trial?

No

M6.2.1.2.4 Will your clinical trial be conducted under either the Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX) scheme?

Neither

M6.2.1.2.5 Who is the sponsor of the clinical trial?

Dr Ann Liebert

M6.2.1.2.6 Provide the following details for each site where the clinical trial will be conducted.

M6.2.1.2.6.1 Name of Site:	North Shore Musculoskeletal and Laser Physiotherapy Clinic
M6.2.1.2.6.2 Individual responsible at site:	Dr Ann Liebert

M6.2.1.2.6 Provide the following details for each site where the clinical trial will be conducted.

M6.2.1.2.6.1 Name of Site:	Photobiomodulation Clinic, Specialist and GP Centre, San Hospital
M6.2.1.2.6.2 Individual responsible at site:	Dr Ann Liebert

M6.2.1.2.7 Select the phase or class of your clinical trial.

Phase 1

M6.2.1.2.8 Has this clinical trial been registered on a Primary Registry in the WHO Registry Network?

Yes

M6.2.1.2.8.1 Provide the clinical trial registration number/identifier.

373999

M6.2.1.2.9 Do you intend to make the trial intervention available to participants after the completion of the trial?

No

M6.2.1.2.10 Explain how and when participants will be informed about post-trial access to the trial intervention.

It is not known whether the intervention will have a beneficial effect. It is not known what dose regimen or site of application may have a beneficial effect. This trial is to determine these factors as a Proof of Concept in a clinical model. Depending on the outcomes, the team will progress to a Phase 2 clinical trial. It is unlikely that participants in this trial will have continued access to the device once the Phase 1 trial is completed although Dr Liebert may continue to use it as part of her physiotherapy protocols in her Sydney practice. All participants will continue to have access to the standard physiotherapy for which they were originally referred.

M6.3 With regard to your answers above, describe any ethical considerations related to your use of the intervention/s in this research project and your plans for addressing these issues.

The research team understands its responsibilities to potential research participants in this proposed trial. We understand that the participants will be in a dependent relationship (patient and physiotherapist) and will be mindful about not coercing patients to take part in the trial. Steps for reducing this potential are embedded in to the recruitment process. The research has however, gained media interest in recent months and potential participants in Sydney have been in contact with the researchers to express their interest in being involved in the trial. We are aware that a number of matters are required including: confirmation of diagnosis and rigorous adherence to inclusion/exclusion criteria.

The team members are aware also that for people with a non-curable, neurodegenerative condition such as Parkinson's Disease, they may feel more 'motivated' than normal to take part in a study of an innovative device that has received recent attention in mainstream media. Strict attention will be paid to participant selection criteria in order to ensure participant safety.

The members of the research team and advisory panel have extensive experience, (a) utilising PBM therapy for a range of diverse clinical conditions (including transcranial and cranial applications in individuals with headache and conditions such as dementia); and (b) investigating PBM therapy in animal models of induced Parkinson's Disease. Their experience is informed by clinical use as well as research track records in the field and they have carefully considered the safety and efficacy of the proposed therapy before embarking on the methodology described herein. In particular, the team members have decided to take a pharmaceutical industry approach to translating the animal studies into a clinical model, something never before done in such a stringent way in the field of PBM therapy. The reason for doing so is based on the fact that PBM therapy has not previously been applied to the brains of people with Parkinson's Disease with the specific intent of altering movement dysfunction

Participant Specific Questions

People in dependent or unequal relationships

P5.1 Describe any potentially detrimental effects on people in dependent or unequal relationships who may participate in your research, and how will you manage them.

The researchers understand that the participants will be in a dependent relationship (patient and physiotherapist) and will be mindful about not coercing patients to take part in the trial. Steps for reducing this potential are embedded in to the recruitment process. The research has gained media interest in recent weeks and potential participants in Sydney have been in contact with the researchers to express their interest in being involved in the trial. These individuals have been placed on a waiting list until ethical approval to commence the trial has been gained. We are aware that a number of matters are required including: confirmation of diagnosis and rigorous adherence to inclusion/exclusion criteria, and an appropriate enrolment procedure. Any specialist referrals from the trial Geriatrician will be accepted at the North Shore physiotherapy practice by the Administration team who will organise an appointment at the clinic that suits the patient. Prior to a patient's arrival at the clinic, standardised forms will be sent to the patient for completion in preparation for the initial physiotherapy assessment. Included will be two Participant Information Sheets (one for the patient and one for their nominated carer, e.g., spouse). These will inform the potential participants of the Parkinson's Disease Research project at North Shore Physiotherapy and invite them to read the enclosed information sheet. The information sheet for the patient with Parkinson's Disease will clarify that the physiotherapy that they receive will not be affected by their participation (or otherwise) in the study and that usual physiotherapy protocols will be followed. It will be made clear that their consent is required to participate in the PBMt component of the study as well as to allow all of their assessment data to be used in a de-identified manner for analysis. If patients wish to learn more information, the information sheet will indicate to them to contact the administrative team prior to their first physiotherapy appointment. Should a patient indicate an interest in participating in the trial, the Principal Coordinating Investigator will contact them by phone, answer any questions and further explain the project and determine eligibility to participate in the project. Patients with Parkinson's Disease as well as their nominated carer will be asked to re-read the Participant Information Sheet and bring the consent form for signing to their first appointment. The carer will also have a consent form to sign. All participants will be informed that they can withdraw from the project at any time without any impact on their physiotherapy treatment. An additional appointment will be diarised with thePrincipal Coordinating Investigator on the same day as their initial physiotherapy appointment.

Recruitment Questions

Q2.1.1 Indicate how you will identify and recruit participants for your research, referencing any relevant sections of your Project Description/Protocol as appropriate.

The recruitment strategy (including the inclusion and exclusion criteria) are included in the accompanying Project Description. Herein however, we have summarised the following:
Screening for eligible participation in the trial will take place by phone if a patient contacts the trial site for further information and before written consent. Further screening may be necessary at the first appointment.
The initial approach to potential participants is enacted through the North Shore Physiotherapy clinic's usual protocols. That is, in writing. Normally, all specialist referrals are accepted at the North Shore physiotherapy practice by the Administration team who organise an appointment that suits the patient. Prior to a patient's arrival at the clinic, standardised forms are sent to patients for completion in preparation for the initial physiotherapy assessment. For the purposes of this study, in addition to these forms, two Participant Information Sheets will be sent to the patient (one for them and one for their nominated carer (e.g., spouse). This will inform the potential participants of the Parkinson's Disease Research project at North Shore Physiotherapy and invite them to read the enclosed information sheet. If patients wish to learn more information, the information sheet will direct them to contact the administrative team at North Shore Physiotherapy prior to their appointment. Should a patient indicate an interest in participating, the Principal Coordinating Investigator will contact the patient by phone, answer any questions and further explain the project and determine eligibility to participate in the project. Patients with Parkinson's Disease as well as their nominated carer will be asked to re-read the Participant Information Sheet and bring the consent form for signing to their first appointment.
Participants receive the recruitment documentation either by mail or email depending on information available to the physiotherapy practice at the time of referral.
A potential participant will have time to consider participation in the trial between receipt of the Participant Information Sheet, the telephone discussion with thePrincipal Coordinating Investigator North Shore Physiotherapy (above) and the first appointment. The length of this period can be up to four weeks before an appointment time becomes available.
As a result of recent Sydney media interest in the treatment, a number of potential trial participants have already made enquiries about taking part in the research. The contact details for these individuals have been stored until such time as ethics approval has been obtained, at which point these individuals will be contacted and the above screening, recruitment, enrolment process will be enacted. Critical to this process will be ensuring that the individuals have been reviewed by their treating specialist, have confirmation of their diagnosis and been recommended for physiotherapy for their Parkinson's Disease.

Q2.1.2 How will your recruitment strategy take account of the ethical considerations relevant to the specific people you are recruiting?

The researchers have taken in to account the following ethical considerations related to recruitment:

- As this is a Phase 1 case series to evaluate Proof of Concept (that is, the potential efficacy and safety) of PBM therapy in Parkinson's Disease (PD), we intend to recruit only a small number of participants (12) with PD to the Sydney arm of the trial, sufficient to understand what influence remote application of the PBMt may have on symptoms and the threshold dose required to influence any change in the proposed outcome measures. From the Brisbane, Adelaide and Sydney arms of the trial, the extent of the effect on outcome measures, the best application site and the 'best dose' from the case series will be used to develop a Phase 2 clinical trial to understand the dose ranging issues before progressing to a Phase 3 randomised controlled clinical trial.
- The researchers contend that the recruitment strategy is fair and promotes distributive

justice as all patients with PD who are interested and/or referred for physiotherapy at North Shore Physiotherapy will be offered the opportunity to take part in the study if they meet the recruitment criteria and consent to do so. The researchers contend that the process developed for recruitment will eliminate any undue influence, coercion or exploitation of potentially eligible participants.

The matter of the unequal relationship (between patient and physiotherapist) has been specifically addressed elsewhere in this application.

- Participants in the study will not receive any payments but will have the opportunity to receive an adjunctive therapy (over and above standard physiotherapy) that may have a theoretical benefit (based on the results of studies in primates and mice).

The exclusion criteria are not based on specific groups who would otherwise be eligible to participate in and may wish to be included in this project. Incidental recruitment of people with an indigenous background is possible. Any potential participants whose first language is not English will not be excluded unless they are unable to provide fully-informed consent. All steps will be taken to explain the study to such potential participants in order that they can make appropriate decisions regarding consent.

Consent Questions

Q2.2.1 Indicate by reference the relevant section/s of your Project Description/Protocol that address/es consent.

The researchers have provided information in the Project Description and taken in to account the following ethical considerations related to consent:

- Consent will be obtained in writing by the Principal Coordinating Investigator at the first physiotherapy appointment at North Shore Physiotherapy and after the patient has had: (a) adequate time to read the participant information sheet and consent form at leisure at home prior to the first appointment; and (b) the opportunity to speak with the Principal Coordinating Investigator either by phone or in person at the first appointment.
- Administrative staff at North Shore Physiotherapy will issue participant information sheets and consent forms either by email or post.
- As the waiting list for treatment for Parkinson's Disease at North Shore Physiotherapy can be up to one month, participants will have adequate time to consider their potential participation, and seek further information from the PINSP between the time they receive their paperwork and the time of the first appointment.
- The Principal Coordinating Investigator will obtain consent from participants and their carers.

Q2.2.2 Will you be obtaining consent from some or all participants to participate in the research?

Yes for all participants

Q2.2.2.1 What is the scope of consent that you will be seeking?

- Specific
- Extended
- Unspecified

Q2.2.2.2 How will consent be obtained?

- Written

- Verbal
- Implied

Q2.2.2.3 Are you proposing to obtain consent using limited disclosure?

No

Q2.2.3 Are family members, authorised representatives or any others involved in the participants' decision to participate in the research?

Yes

Q2.2.3.1 Outline the family members, authorised representatives or others that will be involved in the participants' decision to participate in the research and the extent of their involvement.

Under other circumstances, the researchers would not exclude individuals with a cognitive impairment, an intellectual disability, or a mental illness. However, as this research specifically seeks to measure change in cognition as part of PD as well as seeking to specifically alter neurological performance indicators mediated at the level of the brain, we have decided to limit the extent to which such factors might be affected by the intervention. Thus, patients with cognitive impairment of <24 as measured by the Montreal Cognitive Assessment (MOCA) score will be excluded. Those with slight impairment (MOCA score 24 or more) may be included and so a family member or carer may become involved in the participant's decision to participate in the research.
For all of the research participants with PD, a nominated carer (e.g., spouse/family member) who lives with the PD Participant will also be required to consent to participation in the study to provide 3rd party observations and to mark in a trial diary observations or noted changes in parameters of interest. It is likely therefore that participants will discuss consent to take part with a nominated person who lives with them thus also addressing the matter of dependent relationship status.

Q2.2.4 Will there be an opportunity to confirm or re-negotiate consent during the research project?

Yes

Q2.2.6 Describe any ethical considerations related to the approach to consent that you will be seeking and your strategies for addressing and managing these issues.

Participants may withdraw from the study at any time without giving a reason, and without prejudice. Such withdrawal will have no effect on the participant's relationship with any of the researchers or the organisational affiliations of the researchers (being North Shore Physiotherapy, the Photobiomodulation Clinic at the San Hospital or Griffith University).
Regarding the dependent relationship status (patient and physiotherapist) it is expected that there will be no pre-existing relationship between participants and researchers but this cannot be guaranteed as people with PD may have had treatment at North Shore Physiotherapy previously. The researchers have devised a recruitment and consent method that should avoid any matters related to an unequal relationship. This has been addressed elsewhere in this application.
For participants with cognitive matters limiting appropriate participation, for those whose first

language is other than English and for those with cultural issues, the researchers will encourage the participation of an appropriate advocate as part of the recruitment/consenting process, as well as attendance at sessions.

Q2.2.7 Are you proposing to use an opt-out approach with respect to some or all of the participants?

No

Q2.2.8 Are you requesting a waiver of the requirement for consent with respect to some or all participants?

No

Risk Questions

Q 2.3.1 Describe the risks and burdens associated with your research, referencing any relevant sections of your Project Description as appropriate.

To date, the basic science research, and anecdotal clinical evidence offer support for the benefits of PBMt in PD (Shaw et al 2012; Johnstone et al 2014, Johnstone et al, 2015; Darlot et al, 2016). In a monkey model in which a Parkinson's Disease state was modelled (induced) by a neurotoxin, the application of PBMt reduced the signs of motor dysfunction as well as promoted neural protective responses and in some cases neuro-regeneration of impaired nerve cells (Darlot et al, 2016). Further research reports PBMt is well tolerated and may be valuable in improving sleep-wake cycles in patients with PD (Loddo et al; 2017; Videnovic et al., 2017). PBMt has also been shown to be safe in other applications. Studies have applied both transcranial (e.g., WARP-LED) or intracranial (e.g., optical fiber device) methods to deliver light therapy at power intensities ranging from 1–700 mW/cm2 and have reported no adverse effects on brain tissue structures and function (Moro et al, 2014; Hamblin, 2016; Saltmarche et al, 2017).

The PBMt devices are of low intensity and because of this, the light emitted is not able to cause damage, pain or discomfort at the region on which it will be used. As is the case for PBMt applied in other conditions (such as pain) it is possible that up to 15% of people experiencing PBM therapy for the first time may experience some sensitivity to the therapy in the form of temporary dizziness, nausea or increased pain. Any such symptoms, if they occur, would occur in the first 2 hours directly after treatment, and all such reactions are NOT considered to be dangerous. Any such reactions will subside within 2 hours of first appearing.

The outcome measurements that will be utilised are used as standard clinical evaluation tools are are controlled to cause the minimum of discomfort. Further information regarding the measures is available in the Project Description.

Q 2.3.2 Describe how these risks will be mitigated and managed.

The researchers do not foresee any direct risks from the PBMt however, as this is the first human trial of PBMt for PD movement effect mitigation, they have built in to the research design a number of risk mitigation strategies:

- Particpants will be made aware of the small chance of a reaction to PBM treatment before they begin treatment. If a participant experiences any discomfort, dizziness, nausia or increased pain after the first PBM treatment they will be encouraged to contact the trial coordinator at the Northshore Physiotherapy Clinic for reassurance regarding the temporary nature of the reaction. The participants will also be informed of their right to withdraw from the study without prejudice and without giving a reason to do so. Should the partipants wish to continue, they will be re-assured that sensitivity symptoms would be expected to decrease in intensity with repeated treatments.
- If at any time, a participant decides that they do not wish to continue with PBMt treatment for any reason, they are free to withdraw from the study without providing a reason and without prejudice to their ongoing treatment at North Shore Physiotherapy, Photobiomodulation Clinic at the San Hospital or any relationship with Griffith University or the referring specialists/doctors.
- All participants will have telephone access to the principal researchers should any adverse physical or psychological reactions occur. Such responses will be triaged over the phone and recommendations for appropriate follow-up will be made directly to the patient and/or carer.
- Clinical information will be kept confidential within the patient's chart as per normal physiotherapy clinic protocols.
- Patients will be provided with free parking for attendance at the North Shore Physiotherapy clinic for the duration of the study (the costs for free parking will be borne by the clinic as part of grant funds)
- The attendance (number of appointments) for PBMt at the physiotherapy clinic has been determined according to known evidence and PBMt will be applied when the participant is attending for usual physiotherapy appointments.
- The burden of assessment of the participants is no more than would occur under usual circumstances and is necessary in order to determine progress. That is, the type of assessment is the same as that which is carried out in the usual physiotherapy setting. Without the assessments detailed in the Project Description, it might not be possible to identify objective deterioration requiring withdrawal from the study nor identify factors requiring attention in any subsequent research. However, as Parkinson's Disease can cause unwanted psychological burden, in the event that a participant's involvement in this study raises any concerns for them, we suggest in the participant information sheet that they should contact their referring doctor or either of the following support services:
    - Beyond Blue 1300 22 4636
    - Lifeline 13 11 14

(People in dependent or unequal relationships specific question)

Q 2.3.P5.1 How will you ensure that a person declining to participate in, or deciding to withdraw from, research will not suffer any negative consequences?

For a person who declines to participate in or decides to withdraw from the research, the risks of negative consequences are mitigated by the fact that:

- Recruitment is initially at arms-length from the researchers and treating physiotherapists;
- The PBMt is in addition to (or over and above) the physiotherapy being delivered by the treating physiotherapist and so will reduce the time spent at the physiotherapy appointments likely therefore to be considered positively; and
- The researchers will only collate data from outcome measures once the patient's involvement in the study is complete.

Benefit Questions

Q2.4.1 Describe the benefits associated with your research, referencing any relevant sections of your Project Description as appropriate.

The potential benefits, if any, include:

- to participants: Based on animal studies and the work of Videnovic et al (2017) (see Project Description) we expect at least some temporary improvement in the movement-related and cognitive aspects of PD as well as of sleep. It is not possible to know how long such improvement might last beyond the end of the study.
- to PD groups: Information gleaned from this Phase 1 pilot study will inform a Phase 2 study for which we will further recruit individuals with Parkinson's Disease. The results from the Phase 2 study will in turn inform a larger Phase 3 clinical RCT. At each stage, we expect to publish the results in an international peer-reviewed journal and/or present the results at an appropriate international conference.
- to researchers and to the advancement of knowledge: We expect that the results of the Phase 1 pilot study will contribute to knowledge necessary to advance the use of PBMt in further clinical translational research in people with Parkinson's Disease. We expect also that the research will provide information that will inform PBMt research for other brain-related neurodegenerative disorders including dementia as well as in functional neurological disorder, stroke and traumatic brain injury. The research team and advisors are already in discussion regarding follow-up studies for PD and other brain-related disorders.
- to communities, to society: Based on the expectations noted above, the program of research that may arise from the current translational Phase 1 pilot study has the potential to provide non-pharmacological, non-invasive adjuvant therapies for a range of brain-related disorders that will contribute to the health and wellness of Australia's ageing population. More importantly, the research will provide evidence either to support or refute media claims regarding the potential efficacy of light-based therapies for brain-related disorders.

The device to be tested in the Sydney arm of this novel study is already on sale in Australia. The Irradia device is presently available only to health practitioners. We are aware that since a story appeared in The Weekend Australian magazine in October 2017 (discussing the possible benefits of light therapy for Parkinson's Disease), many consumers have purchased similar devices despite the lack of any real evidence to support its safety and efficacy. People with neurological conditions that restrict quality of life and limit life span are vulnerable to wild claims. Although the research team is expecting to see and measure benefit from the therapy under investigation, we retain a sense of academic scepticism until the translational work can be completed in an orderly manner. We will therefore not be making any recommendations about the intervention or its availability to participants or patients until the results are unequivocal. This may not be possible to know until at least a Phase 2 trial has been completed.

Q2.4.2 Explain how benefits of this research justify any risks or burdens associated with the research.

As noted in the response to Q2.4.1, the device to be investigated in this study is already on sale in Australia. This study seeks to start the process to understand if PBMt has a role to play in the adjuvant therapy for PD, at what type of dosing regimens, the site for such or whether recommendations need to be made to avoid the therapy as an expensive waste of time.
We do not believe that the risks or burdens associated with the research outweigh the benefits because:

- -safety of PBMt has already been established in animal models, and in other studies of transcranial applications of PBMt. However, we remain interested in understanding if this is truly the case in this translational work in people with PD
- efficacy of PBMt in a number of brain-related conditions has previously been established, and so we have an expectation that some form of benefit is likely (even in the short-term) for participants
- all participants will receive established / standard physiotherapy throughout the study and so will not be at a disadvantage therapeutically
- the study intervention will be bundled in to the costs for standard treatment (i.e., there will be no additional cost to the participants) and parking charges will be waived

Q2.4.3 How will you manage participants' expectations of the perceived benefit of participating in the research?

As noted previously, the therapy under investigation has received recent media attention so it is possible that patients may be aware of the therapy. We have specifically addressed this matter in the participant information sheet. Moreover, patients will be made aware that whether or not they obtain benefit from the PBMt, they should expect to obtain improvement in their symptoms from the standard program of physiotherapy that each will receive.

Section 3 – Data and Privacy

Data Characteristics

Q3.1 Indicate the type of information/data you will be collecting for this project.

- 🕐 Personal information
- ○ Sensitive information
- 🕐 Health information
- ○ Not personal information

Q3.2 Indicate the type of information/data you will be using in this project:

- 🕐 Personal information
- ○ Sensitive information
- 🕐 Health information
- ○ Not personal information

Q3.3 Indicate the degree of identifiability of information/data you will be collecting for this project.

- ○ Individually identifiable information
- 🕐 Re-identifiable (coded) information
- ○ Non-identifiable information

Q3.4 Indicate the degree of identifiability of information/data you will be using in this project.

- ○ Individually identifiable information
- 🕐 Re-identifiable (coded) information
- ○ Non-identifiable information

Q3.5 Describe any ethical considerations relating to the collection and/or use of the information/data in this project.

The outcome data will be identified according to a study protocol code for the purposes of anonymising the data, and entered in to a study database for the purposes of statistical analysis. The participant study codes will be held securely under lock-and-key on a master sheet and matched to the participants' clinical identifier details (name and date of birth). The researchers have decided to make participant data re-identifiable in order to be able to communicate with any participants should any adverse events be identified during the course of the research study (although the latter is not expected we believe it is prudent to have such a mechanism in place as part of a Phase 1 pilot study). The master sheet will be destroyed at the completion of the study thus making participant data un-identifiable at the conclusion of the study. Only the primary investigators named on this project will have access to the data.
Each participant's carer will be asked to maintain a study diary to record observations regarding the participant's progress outside of the clinic setting. Such data includes: sleep patterns; initiation of conversation; level of independence in transfers and activities of daily living (such as sit to stand, in and out of a car, walking speed); speed and volume of speech; and perception of mood. The diary information will have a study code, and information will be transcribed directly in to the research database. The diary data will not be accessible to the physiotherapist who is providing the standard care to the participant. Any information of relevance to the physiotherapist will be the subject of the usual physiotherapeutic relationship and gleaned from conversations between the patient participant and his/her physiotherapist as part of that relationship (not from research diary information).

Q3.6 Identify the source/s of the information/data that you will be collecting and/or using in this project.

- 🕐 Individual participants and/or relatives or associates of participants
- 🕐 Medical/health/mental health record
- ○ Electoral roll
- ○ Held by a law enforcement agency
- ○ Publicly held database (Commonwealth)
- ○ Publicly held database (State or local)
- ○ Privately held database

Q3.6.1 Has the data custodian/s, if any, agreed to provide access to the data for use in the proposed research?

- ○ Data custodian has approved access to data
- ○ Data custodian has not provided approval
- 🕐 No data custodian identified

Q3.7 Describe any ethical considerations relating to the source of information/data as indicated in the response to the previous question.

Any information relevant to the study screening process or the outcome measures for this study will be obtained only from the patient and/or their carer, and from the patient participant's physiotherapy record at North Shore Physiotherapy. This is made clear in the participant information sheet.
The researchers will not access any other records

Q3.8 Was the information/data that you are using previously collected for a purpose other than research?

No

Activities Planned for/with Data

Q3.9 Do you plan to disclose any personal information/data in this project to a third party?

No

Q3.10 How will you protect the privacy of participants and non-participants in any notes and/or publications arising from your research?

The investigators named on the front of the participant information and consent document will be the only people, other than the participants, with access to the research records.
Participants with PD will have access to their own data and to diary data only and on request. Participant carers will only have access to their diary data on request. There will be no cross-over of access by participants to any other data.
The research records will be stored in a secure place without reference to participant names. The records will be coded and these codes will be used throughout the analysis of the results to ensure that the researchers are the only people who could match results with participant names.
Once the study is complete, all information that could be identifiable will be destroyed, and only the coded (de-identified) data will be kept for the period required by the AHCL HREC.

For the purposes of potential publication, the following statement is included in PICF:
"If the results of the study are published in a scientific journal, your identity will not be revealed. Participants will not be referred to by name during research reports or study discussions."

Q3.11 Are there any restrictions on your ability to assure the confidentiality of participants?

No

Q3.12 Do you plan to share any individual research results obtained during this research to the participants?

Yes

Q3.12.1 Describe any ethical considerations relating to the sharing of individual research results with the participants.

The following paragraph is included in PICF for the participant with Parkinson's Disease:
Confidentiality
You will be assigned a study code under which all of your study results will be recorded. The results of the tests that you will undergo as part of your treatment program at North Shore Physiotherapy will be de-identified with your study code and stored electronically for analysis at a later date. During the study, if we find out information important and relevant to you/your health, we will be able to re-identify and contact you if needed. All results will be kept confidential and all identifying data will be destroyed at the end of the study. If the results of the study are published in a scientific journal, your identity will not be revealed. Participants will not be referred to by name during research reports or study discussions. All data will be kept in the possession of the investigators. De-identified hard copies of data collection sheets will be stored in a central storage location at North Shore Physiotherapy for 15 years. Electronic information will be stored on an external hard drive (USB) and a university computer file, protected by password access. Only researchers associated with this research will have access to the files. No data will be identifiable after the conclusion of the trial. All data collection forms will be destroyed after 15 years.
The following paragraph is included in PICF for the nominated / consenting carer:
Confidentiality
You will be assigned a study code under which all of your observations will be saved. All results will be kept confidential, however, the participant with Parkinson's Disease will have access to your diary notes should they make such a request. For the purposes of privacy and confidentiality of the participant with Parkinson's Disease, you may not have access to their health research data. If the results of the study are published in a scientific journal, your identity will not be revealed. Participants will not be referred to by name during research reports or study discussions. All data will be kept in the possession of the investigators. De-identified hard copies of data collection sheets will be stored in a central storage location at North Shore Physiotherapy for 15 years. Electronic information will be stored on an external hard drive (USB) and a university computer file, protected by password access. Only researchers associated with this research will have access to the files. No data will be identifiable after the conclusion of the trial. All data collection forms will be destroyed after 15 years.

Q3.13 Describe how you will handle any secondary or incidental findings that arise from the analysis of personal information/data.

Although not expected, it is conceivable that secondary or incidental findings relevant to participants may arise during the course of this research (e.g., matters relevant to safety or dosing with PBMt), or during the analysis of data associated with the research. Should that occur, the researchers would be obliged under their health practitioner registration to make

such information known to the participants. It is for this reason that participant information will be re-identifiable until the end of the research (described elsewhere). The researchers have included a statement to this effect in the Confidentiality section of the PICF:
“During the study, if we find out information important and relevant to you/your health, we will be able to re-identify and contact you if needed.”

Q3.14 Describe how the information/data will be stored, accessed, archived and/or destroyed.

The researchers have included a paragraph to cover matters of information/data storage, access, archiving and destruction in the Confidentiality sections of the PICFs:

Confidentiality

You will be assigned a study code under which all of your study results will be recorded. The results of the tests that you will undergo as part of your treatment program at North Shore Physiotherapy will be de-identified with your study code and stored electronically for analysis at a later date. During the study, if we find out information important and relevant to you/your health, we will be able to re-identify and contact you if needed. All results will be kept confidential and all identifying data will be destroyed at the end of the study. If the results of the study are published in a scientific journal, your identity will not be revealed. Participants will not be referred to by name during research reports or study discussions. All data will be kept in the possession of the investigators. De-identified hard copies of data collection sheets will be stored in a central storage location at North Shore Physiotherapy for 15 years. Electronic information will be stored on an external hard drive (USB) and a university computer file, protected by password access. Only researchers associated with this research will have access to the files. No data will be identifiable after the conclusion of the trial. All data collection forms will be destroyed after 15 years.

Q3.15 Describe any ethical considerations relating to the storage of, access to or destruction of information/data in this project.

The researchers have taken in to account the confidentiality and privacy matters relevant to ethical management of research data by:

- arranging that research data will kept initially in re-identifiable form until the end of the study but then stored in de-identified form at the conclusion of the study
- de-identified research data will kept for a period of 15 years
- all research data once transferred to the research database (in either re-identifiable or de-identified form) will kept on a password-protected external hard drive (for back-up purposes) and a Griffith University computer
- only the researchers associated with the research will have access to the data files
- if a participant seeks to gain access to their personal data, this will be possible on request up until the end of the study only. After this time, all data will become de-identified and only able to be reported in aggregate form. Should a participant request access to their personal data before the end of the study, this will be arranged under the supervision of one of the researchers
- carer participant diary data will be accessible to the participant with Parkinson’s Disease, as this may be relevant to their psychological or physical well-being. The diary data will not be accessible to the treating physiotherapist. For privacy and confidentiality, the carer participant will not have access to the health research information of the participant with PD.
- at the end of the research study, the Master sheet that will allow re-identification of participants will be destroyed by deleting the file from the external hard drive and university computer, as well as deletion of any data from the computer recycling bin and cookies

Any hard copies of data collection forms will be destroyed at the end of the study or once all

data has been transferred to the computer database (whichever is soonest)

Q3.16 Will the outcomes of this project be disseminated to the participants?

Yes

Q3.16.1.1 Describe how the outcomes of the project will be disseminated to the participants, or refer to the relevant section/s of your Project Description/Protocol which deals with this matter.

As per PICF:
"Feedback
Once the results of the study have been analyzed we will be submitting the findings of the study to an international peer reviewed journal for potential publication. If you wish, you may opt to receive notification when the study is published and a report outlining the results."
Further:
"In signing below, I agree to participate in The PBM Parkinsons' Disease Trial and give my consent freely.

- I understand that I can contact the Adventist HealthCare Ltd Ethics Committee if I have any concerns about the ethical conduct of the project.
- I understand that if I have further questions, I am free to contact the research team.
- I wish / do not wish to receive information about the publication of the study results.
- I wish / do not wish to receive information about my personal results."

Q3.16.1.2 Describe any ethical considerations relating to any dissemination of outcomes to the participants.

After the completion of the research, no participants will be identifiable within the research database (see PICF **Confidentiality** section):

- "If the results of the study are published in a scientific journal, your identity will not be revealed. Participants will not be referred to by name during research reports or study discussions."
- Only aggregated data will be reported. If requested, only individual data for a particular participant will be available only to them and to no-one else outside of the researchers.

Q3.17 Describe any foreseeable future activities for which information/data collected and/or used in this project may be made available.

The researchers have no plans at present to share data outside of the research team. We expect to utilise the outcomes of the research to inform future study design and methods in this field of research. As elements of the data that becomes available from this research may have implications for future clinical innovation, the researchers do not foresee that the information gleaned from this Phase 1 pilot study will be made broadly available. We will re-evaluate the need for custodian consent for data sharing as this program of research progresses. To comply with the NHMRC statement on data sharing, we have included within the PICF, the following privacy statement:
"Privacy statement
The conduct of this research involves the collection, access to and / or use of your identified personal information. The information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal or other regulatory authority requirements. A de-identified copy of this data may be used for other research purposes. However, your anonymity will at all times be safeguarded. "

Q3.18 Describe any ethical considerations relating to the planned or possible future use of information/data in this project.

Ongoing custody of the non-identifiable research data/information will be vested in the researchers, specifically Dr Ann Liebert and Prof Laakso. Dr Liebert and Prof Laakso will have

primary access to the research data (during and beyond the completion of the study) which can then be made available to the other named researchers. Intellectual property will be shared equally between the named researchers as each has had specific input in to the intellectual processes, design, methods and statistics detailed in the Project Description.
As the program of research progresses, it may become evident to the researchers that non-identifiable data could be used in future research. Although this is not expected presently, the Privacy statement detailed in Q3.17 should be interpreted appropriately.

Section 4 – Attachments and Declarations

Attachments

The following documents have been attached to this HREA.

Project Description/Protocol

See attachment *Protocol Parkinson's trial Sydney Arm.pdf*

Other attachments

Attachment File Name	Attachment Description
Sydney trial ethics approval email.pdf	approval of HREA from Griffith U=niversity
LL03211_Output Form_v1_1.pdf	Griffith University HREA
PICF Group 1.docx	PICF group 1
PICF Group 2.docx	PICF group 2
PICF Group 3.docx	PICF group 3
PICF Group 1 and 3 carers.docx	PICF carers of groups 1 and 3
cover letter.docx	cover letter
Sydney trial ethics approval email.pdf	Evidence of prior ethics review by Griffith University; Griffith University Human Research Ethics Committee.
	Ethically defensible plan for the management of risks related to xenotransplantation research.

Investigator Team Declarations

The research team has certified that:

- All information in this application and supporting documentation is correct and as complete as possible;
- I have read and addressed in this application the requirements of the National Statement and any other relevant guidelines;
- I have familiarised myself with, considered and addressed in this application any relevant legislation, regulations, research guidelines and organisational policies;
- All relevant financial and non-financial interests of the project team have been disclosed; and
- In the capacity of a supervisor, as applicable, I have reviewed this application and I will provide appropriate supervision to the student(s) in accordance with the arrangements specified in this application and those associated with the student's educational program.

Dr Ann Liebert

Sign here:……