PARTICIPANT INFORMATION

STUDY TITLE: The evaluation of intra-venous autologous adipose derived mesenchymal stem cell therapy in the treatment of small joint osteoarthritis. A pilot study.

CHIEF INVESTIGATORS: **Associate Professor Julien Freitag** MBBS, BMedSci, FACSEP (Principal Investigator & Study Clinician),

- Charles Sturt University
- Melbourne Stem Cell Centre
- Magellan Stem Cells

Dr James Wickham PhD (Non-Clinical Scientific Investigator)

- Charles Sturt University

Dr Kiran Shah PhD (Non-Clinical Scientific Investigator)

- Magellan Stem Cells

Please read the following information carefully

This Participant Information Sheet gives detailed information about the research study, which the Principal Investigator and/or Study doctor will discuss with you. Once you understand the study and if you wish to participate, you will be asked to sign the consent form.

Invitation

You are invited to participate in a research study that aims to explore the preliminary safety and effectiveness of an intra-venous infusion of your own stem cells to treat small joint arthritis of the hand.

This study is being conducted by primary sponsor Box Hill Stem Cell Centre Pty. Ltd. trading as Melbourne Stem Cell Centre ("MSCC") and co-sponsor Magellan Stem Cells.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

Ask us if there is anything that is not clear or if you would like more information. You will be given as much time as required to ensure that you fully understand what is involved in the participation of this study. Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care, whether or not you take part.

Once you understand the study and the potential risks and discomforts associated with it, and if you decide to participate, you will be asked to sign the consent form.

By signing the consent form you are telling us that you:

- Understand what you have read

- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described

1. What is the purpose of this study?

The purpose of this study is to explore safety and potential benefit of the intravenous administration of your own stem cells in the treatment of small joint arthritis.

Mesenchymal stem cells (MSCs) are present throughout the body. Animal and human studies of MSCs have demonstrated that they have a key role in tissue repair and regeneration. Therefore, MSCs may be a potential treatment for patients with osteoarthritis of the joints. Intravenous administration may be a suitable method of treatment of small joint arthritis as these joints are not readily treatable – due to size - by injections directly into the joint.

2. Why have I been invited to participate in this study?

You have been invited to participate in this research as you have either been referred by a treating practitioner/doctor or have made a direct enquiry. You have also met the required inclusion/exclusion criteria.

Any of the following will exclude you from participating in the study: a known allergic reaction to medications, or anaesthetic agents; if you must take medications not allowed by the study (including over the counter medicines, dietary supplements and herbal remedies); if you have taken certain medications in a time period considered unacceptable by the study doctor or if you have a history of alcohol or drug abuse within 12 months before admission to the study; if you have had major surgery within the last 3 months or are planning surgery any time within the following 12 months; if you/your partner plan to donate ova, are pregnant or plan to become pregnant within the next 12 months; if you are not willing to comply with the contraceptive precautions required; if you are unable to restrain from strenuous activity not typical of your usual activity for the following 12 months; or for any other reason that your study doctor determines would exclude you from being able to meet the eligibility criteria for the trial.

3. What does this study involve?

3.1 How long is this study? How many other people will be in this study?

This study will take place at one clinical site (MSCC) in Melbourne, Australia. A total of 10 male/female subjects diagnosed with small joint osteoarthritis of the hand will take part.

If you qualify and decide to take part in this study, your part in the study is expected to last up to 15 months (the estimated amount of time from the Screening Visit through to the End of Study Visit at Month 12).

3.2 Overview of study

Participation in this study will require you to make a number of visits to MSCC for tests and procedures, MRI scans of your hand. In addition, you will be required to complete a series of web-based questionnaires. You will also complete Diary Cards for the purpose of recording adverse events/side effects and use of other medications.

Your health and the safety of the stem cell therapy will be evaluated through monitoring of samples taken of your blood (haematology, clinical chemistry, liver function tests), ECG ('heart trace'), physical examinations and recording of any side effects and medications taken.

The study doctor will talk to you about the things you must do or not do in order to be in this study. Please tell your regular doctor, health care providers and any emergency care providers that you will be in this research study.

The details of what will happen at each visit are described below.

Visit 1. Screening& Enrolment Visit (1 hour)

Prior to any procedures being performed, one of the study doctors will personally explain the study to you. You will be informed of the purpose of the study and of the risks and you will receive a copy of this Patient Information Sheet (PIS) and the Informed Consent Form (ICF) to keep as a record of the material explained to you.

You will be invited to sign a consent form.

To determine if you meet the conditions for participation in the study, the study doctor will perform some tests and procedures at no cost to you. The following procedures will be performed :

- The study doctor will review the entry criteria with you to find out if you qualify to be in this study.
- *The study doctor will complete a physical examination and arrange baseline blood tests, ECG (heart trace), urine pregnancy testing for females of child bearing age and imaging (MRI).*

You will be formally enrolled in the study if you meet all the inclusion criteria and none of the exclusion criteria.

Your General Practitioner will be informed of your participation in the study and they may divulge details of your past medical history to the Study Doctor, as they see relevant.

Visit 2. Adipose Tissue Harvest Procedure (3 hours).
You will undergo a mini-liposuction to harvest stem cells. Approximately 20-100 ml of abdominal fat will be taken following local anaesthetic in filtration. The harvested tissue will be processed to isolate and culture the stem cells for future injections. The isolated stem cells will be suitably stored meeting TGA biological product/treatment requirements. The isolation and culture of stem cells will take a period of 8weeks.

Visit 3. Post Adipose Tissue Harvest Procedure
You will be seen by the lipo-suction procedural doctor or study nurse as routine post operative care 1 week post the procedure.

Visit 4. Study Day 1 - Day of Intravenous Infusion of Stem Cell Therapy (2 hours)

On Day 1 you will attend the study site.

- The study doctor will again review the entry criteria with you to find out whether or not you still qualify to be in this study.
- Prior to administration of the stem cell therapy you will complete the following on-line questionnaires:
  - Numerical Pain Rating Scale (NPRS),
  - Disability of Arm, Shoulder and Hand score (DASH)
  - Quality of Life Score
  - Orebro Musculoskeletal Pain Questionnaire short form (OMSPQ-short)
  - Satisfaction with Treatment questionnaire,
  - Seven-point global perceived effect scale.

You will receive an infusion of stem cells. You will be monitored for 3 hours following this procedure.

After completion of all procedures and in the absence of any untoward events you will be allowed to leave the study site. You will be reminded to comply with dietary/lifestyle restrictions.

Visit 5-9 (Week 1 + Months 1,3,6 and 9) – Clinical assessment
At these visits you will attend the study site and the following procedures will be completed:

- The Diary Card you completed will be reviewed for any adverse events you have experienced, medicines you have taken, and any co-interventions you have used since the last study visit.
- You will have a brief physical examination, including assessment of your affected joint.
- Your vital signs will be measured.
- You will have an ECG (Month 1 only)
- You will give blood (up to 20 mL or 4 teaspoons) and urine for routine safety tests (Week 1, Month 1 and 3 only).
- You will complete online outcome questionnaires.
-

You will be asked about any co-interventions you have been using.

Visit 10 – 12 months – End of Study Visit

At Month 12 you will attend the study site. During the scheduled consultation, the following procedures will be performed:

- The Diary Card you completed for Months 9-12 will be reviewed for any adverse events you have experienced, medicines you have taken, and any co-interventions you have used since the last study visit.
- You will have a brief physical examination, including assessment of your affected joint.
- You will give blood (up to 20 mL or 4 teaspoons) and urine for routine safety tests.
- You will complete online outcome questionnaires.
- You will have an X-ray of the study joint.
- You will have an MRI of the study joint.

Once all procedures have been completed and providing you feel well, you will be discharged from the study. In the event that you require follow-up appointments due to any changes in your health during the study, you will be required to be available for follow-up until these changes return to normal, at the discretion of the Principal Investigator.

4. Are there benefits, risks or inconveniences to me for taking part?

If you agree to take part in this study, there may be no direct medical benefit to you from participating in this study.

Medical procedures may cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your doctor. Your doctor will also be looking out for side effects.

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information. This new information may mean that you can no longer participate in this research. If this occurs the person(s) supervising the research will stop your participation. In all cases, you will be offered all available care to suit your needs and medical condition.

4.1 Benefits

We cannot guarantee or promise that you will receive any benefits from your participation in this research.

4.2 Risks

If you do not understand what some of the potential side effects or risks mean, you are strongly advised to ask the study doctor or the study staff to explain them to you.

- **Blood collection**
  You will have blood collected from a vein in your forearm, via a needle and syringe. You may experience minor discomfort with the initial insertion and occasionally some bruising or irritation afterwards. These effects normally clear up completely within a few days. Procedures relating to blood collection can also occasionally

cause light-headedness or fainting. These reactions are usually mild, of short duration and limited to a feeling of weakness, accompanied by sweating, slowing of heart beat, and a decrease in blood pressure.

You will give a total of about 120 mL (approximately 6 tablespoons) of blood. This will not exceed the amount of blood normally donated by an individual during a single visit to a blood bank (approximately 500 mL). Additional blood samples may be taken, if needed, to check on your safety.

- **Harvesting Liposuction Procedure**
  The liposuction/lipoharvest will be performed in a day procedure centre and under local anaesthetic control. Approximately 20-40grams of abdominal fat will be harvested and transferred directly to the Magellan Stem Cells laboratory for the isolation of adipose (fat) derived stem cells.

  The liposuction harvest procedure may be associated with the following risks :
  a. Discomfort : It is possible that some participants may experience discomfort during the liposuction procedure. All liposuction will be performed after infiltration of a local anaesthetic tumescence which is an internationally accepted practice.
  b. Infection – participants will be monitored for adverse events such as infection. The risk of this occurring is low. Subjects will receive a single dose of intravenous antibiotics prior to the liposuction procedure.
  c. Bruising - participants may experience minor bruising at the site of liposuction.

- **Intra-venous MSC therapy**
  The intra-venous MSC therapy may be associated with the following risks :
  a. Discomfort: patients may experience some discomfort with insertion of the intra-venous canula.
  b. Infection: participants will be monitored for adverse events such as infection at the site of the cannula. If infection did occur participants will be referred to their treating doctor for assessment and prescription of antibiotics and treatment as deemed necessary. The risk of this occurring is low.
  c. Bruising: participants may experience minor bruising at the site of the cannula.
  d. Fever: Transient and self limiting fever has been noted in previous studies assessing intra-venous administration of MSCs.

  **Note : Medical doctors will perform all the procedures including the lipoharvest. They will have an equivalent of a Bachelor of Surgery and Bachelor of Medicine degree and will have current medical registration and medical indemnity. All doctors performing the liposuction/lipoharvest have completed a certification in fat harvesting for the purpose of stem cell isolation.*

- **MRI of the study joint**
  You will have had an MRI on your study joint performed at Screening and at the Month 12 visit to help see if there have been any changes.

  An MRI is a computerized scan performed in the radiology department that provides a 3-dimensional picture of the inside of the body using a strong magnetic field. An MRI scan is performed like a CT scan. It is performed in a large tunnel-shaped machine and uses radio frequency waves, like those in an AM/FM radio, and a powerful magnet. MRI uses non-ionizing radiation and is safe when used on subjects who are appropriately screened for conditions where an MRI cannot be performed.

  This procedure will take about 30 minutes. The MRI scans will be performed at Imaging Associates (Box Hill).

- **Reproductive Risks and Contraception**
  It is not known if or how the study drug may affect the embryo or foetus.

  Females
  You may not take part in this study if you are female and are breastfeeding, pregnant, think that you may be pregnant, or are trying to get pregnant. If you become pregnant or are breastfeeding, there may be risks to you and the baby that are not known at this time.

All women of child bearing age must have a negative urine pregnancy test before dosing.

You must not donate ova starting at Screening and for 90 days after injection of the Study Treatment.

You must use appropriate contraception (as detailed below) for 12 months following injection of Study Treatment. Discuss your birth control options with the study doctor. **Hormonal contraception by itself is not considered as being adequate for this study.**

If you suspect you are pregnant anytime during the study, or within 12 months after the injection of Study Treatment, you must immediately inform the study doctor. Do not wait until your next appointment. As the risk to you and your baby is unknown, it is desirable for you to agree to medical supervision during your pregnancy and for the baby after it is born. Your study doctor will work with the study Sponsor to organize this. You will be invited to sign a consent form to allow collection of confidential information about your health, the pregnancy and its outcome, for the purpose of determining any effects from the study.

Males
It is not known if the study drug will affect sperm or semen. You must not donate sperm or father a child for 30 days after the injection of Study Treatment. If your partner might become pregnant, you and your partner should use reliable forms of contraception for 30 days after the dose of study drug. **Hormonal contraception by itself is not considered as being adequate for this study.**

Please ask the study doctor if you have any questions about the methods of birth control that must be used while participating in this research study.

If your partner becomes pregnant within the 30 days after dosing, you should inform your study doctor immediately. As the risk to your partner and baby is unknown, it is desirable for your partner to agree to medical supervision during her pregnancy and for the baby after it is born. Your study doctor will work with the study Sponsor to organize this. Your partner will be invited to sign a consent form to allow medical supervision. The study Sponsor may also request your and your partner's consent to collect confidential information about her health and that of the baby, to allow monitoring of the pregnancy, the birth and the health of the child up to 3 months of age.

Acceptable contraceptive measures

For the purposes of this study hormonal contraception is allowed, but is considered inadequate unless combined with at least one other highly effective (i.e. less than 1% failure rate per year when used consistently and correctly) method.

Examples of contraceptive measures regarded as adequate for the purposes of this study include:

- Injected, implanted, oral hormonal methods of contraception combined with a condom/Intra-uterine device/diaphragm.
- Barrier methods of contraception (condom or occlusive cap [diaphragm or cervical/vault caps]) combined with spermicidal foam/gel/film/cream/suppository.
- Subjects who have undergone a bilateral tubal ligation/surgical sterilization.
- Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the Study Treatments and complies with the preferred and usual lifestyle of the subject.

- **Serious Adverse Reactions and Hospitalisation**

Although all possible precautions are taken to prevent serious adverse reactions (side effects), if such an event occurs, it may be in your best interest to be admitted to the hospital. Depending on the type of reaction, a medical specialist will be contacted to be primarily responsible for your treatment. In the event of hospital admission you will need to consent to access to your medical records for purposes pertaining to the study including assessment of adverse events (see Consent Form).

In case of a serious adverse reaction and subsequent hospitalization, the treating medical doctor will be allowed access to your medical records collected during the course of this clinical study in order to provide appropriate care.

- **Non-compliance of Participant Responsibilities**.
  As a study participant, you are responsible for following the study directions and those of your study doctor. Failure to do this may put you at harm which is not something we want to see happen. Responsibilities include returning promptly to the study clinic for all necessary study follow-up visits, reporting any changes in your medications (over-the-counter and prescription), and reporting any changes in how you feel to the study doctor and the study staff. If you experience any illness or discomfort during the study, you should notify your study doctor.

5. Illness or Injury

If as a result of being in this study you become ill or are injured, please immediately contact your study doctor. She or he will then give you all the necessary information and treatment and will inform the trial sponsor.

6. Compensation and medical treatment for trial-related injury

If you are injured as a result of your participation in this trial you may be entitled to compensation. The study is being conducted subject to the "Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial" published by Medicines Australia. A copy of this guideline can be obtained from the Medicines Australia website at http://medicinesaustralia.com.au/files/2010/09/Clinical-Trials-Compensation-Guidelines.pdf.

However, as guidelines, they do NOT in any way dictate the pathway you should follow to seek compensation. The Sponsor is obliged to follow these guidelines. It is recommended that you seek independent legal advice before taking any steps towards compensation for injury. Should you suffer injury as a result of drug administration or from any of the procedures carried out during this study, medical treatment will be administered

7. How is this study being paid for?

This study is being conducted by MSCC, Magellan Stem Cells and the Principal Investigator, Assoc. Prof. Julien Freitag. The study is sponsored by MSCC and Magellan. Your study doctor is not being reimbursed to conduct this study. He/she will not allow a conflict of interest to compromise their position or this research study.

8. Will taking part in the study (or travelling to) cost me anything and will I be paid?

You will not be paid for taking part in this study. All study-related tests will be provided at no cost to you.

There will not be reimbursement for cost of travel expenses.

9. What if I don't want to take part in this study?

Participation in this research is entirely your choice. Only those people who give their informed consent will be included in the project. Whether or not you decide to participate, is your decision and will not disadvantage you.

If you do decide to participate, you may withdraw from the project at any time without giving any reason and have the option of withdrawing any data if you wish.

10. What are the alternatives to participation in this study?

Your alternative is to not participate in the study.

Your regular doctor or the study doctor can answer any questions you may have about the relative risks and benefits of alternative therapy(ies) or any other matters concerning the study.

11. What if I participate and want to withdraw later?

It is important that you understand that your participation in this study is entirely voluntary. You will be informed in a timely manner if any information becomes available that may be relevant to your willingness to continue to participate in this study. Declining to participate or withdrawal from the study will involve no penalty or loss of medical benefits to which you would otherwise be entitled and your decline or withdrawal will not affect your selection for future studies.

If you decide to withdraw from the study you should contact your study doctor or his study staff as detailed in Section 17. They will recommend that you complete an Early Withdrawal Visit and possibly further safety Follow-up Visits as may be indicated in the interest of your health but again it would be for you to decide if you do/do not want to complete these assessments.

You may also demand that existing data arising from your participation are not used in the research project provided that this right is exercised within four weeks of the time from which you withdraw from the project. If this is the case, you are asked to complete a "Withdrawal of Consent Form" or to notify one of the researchers by e-mail or telephone that you wish to withdraw your consent for your data to be used in this research project.

Your participation in this study may be stopped at any time by the Principal Investigator or the Sponsor without your consent. This may be for reasons of your safety, or if you are not complying with the study restrictions as outlined to you. The Sponsor may decide at any time to stop the study, in which case you would be withdrawn.

12. Could this research be terminated unexpectedly?

This research project may be stopped for a variety of reasons, one of which may be due to decisions made in the commercial interests of the Sponsor, or by local regulatory/health authorities

13. How will my confidentiality be protected?

Your medical records, records relating to this study and any other information received will be kept strictly confidential. Information obtained during the course of the study will be retained in confidential files at MSCC.

Your name or any other personal identifiers will not appear on any documentation forwarded to the sponsor or be used in any reports or publications resulting from this study. Data from the study may be used in scientific presentations or reports, although your identity will not be revealed.

However, staff participating in your care, the sponsor and other agencies authorised by law, may inspect the records related to the study. By consenting to participate, access to your original medical records may be granted to representatives of the study sponsor, the study doctor, employees or agents of MSCC, members of the independent human research ethics committee, regulatory authorities and other agencies permitted by law, for verification of clinical study procedures and/or data, with the understanding that these records will be used only for the purpose of carrying out obligations relating to this clinical study. All information collected and retained by the sponsor of the study will be

confidential. "Sponsor" includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study.

On rare occasions, the law may also require disclosure to regulatory bodies or other third parties, for instance, if you are found to have a reportable disease such as hepatitis.

Your treating Doctor/s will be notified of your participation in this study and of any clinically relevant information noted by the study doctor in the conduct of this study.

In the event that you are admitted to hospital as a result of an adverse event resulting from this study, your treating doctor may require access to your study records.

It is important that the study itself remains confidential and that any accidental release of confidential information about the study is prevented. Before the study has begun, you are encouraged to discuss with friends and family to help you decide whether you want to participate. However, you should refrain from publicly disclosing details of the study (for example, the name of the Sponsor, the study drug, any information regarding other study subjects, or the study procedures). You are also not allowed to post or discuss these details of the study in any public forum, such as on social networking websites or blogs.

By signing the consent section, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

14. What will happen to the information that I give you?

Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purposes stated in this document. The results of this study may be used for regulatory purposes and/or published. ***In any publication and/or presentation, information will be provided in such a way that you cannot be identified and no personal details about you will be provided, except with your permission.***

The information will be re-identifiable. This means that we will remove your name and give the information a special code number. Only the research team can match your name to your code number, if it is necessary to do so. The key to this code will be kept by the Investigator and will not be released to the Sponsor.

We will keep your information for at least 15 years after completion of the study. It may be kept for longer if required by applicable laws and regulations, or if needed by the Sponsor (Magellan). After this time, the information will be destroyed.

A description of this clinical trial will be available on a publicly listed register (e.g. http://www.anzctr.org.au/; https://clinicaltrials.gov/), accessible via the internet. This register will not include information that can identify you. At most, the web site may include a summary of the results. You can search the applicable register at any time.

Once the study is complete and the results are known, a written plain English summary of the results of the study can be made available to you upon request. To obtain this, please contact one of the investigators listed in **Section 17.**

However, results may be suppressed for commercial reasons as the Sponsor of the project retains the rights to the data.

15. What will happen to my blood samples?

By consenting to take part in this study you also consent to the collection, storage and use of blood samples for the purposes mentioned previously.

Blood samples collected will be labelled as per routine practice. That is, that your name and date of birth may be used. Blood samples will be stored and processed by Melbourne Pathology (Australia). Following analysis, blood samples will be destroyed in accordance with local regulations and standard methods for disposal.

Additional blood samples may be taken during the study if the study doctor considers it is necessary to monitor for your health and safety.

You will be informed of any information obtained from the tests that could have an impact on your health and your general practitioner will be advised and will receive a copy of these test results.

16. Disclosure of Researchers' Potential Financial Interests

In addition to their scientific interests in this research project, the individuals conducting this stem cell study might profit financially from the research. There may be current or potential financial benefits to the Principal Investigator for the study (Assoc. Prof. Julien Freitag), the participating institution(s), Magellan and Melbourne Stem Cell Centre, and other research institutions or researchers arising from discoveries made through this research project. The Principal Investigator, Assoc. Prof. Julien Freitag, is a shareholder of both Magellan Stem Cells and Melbourne Stem Cell Centre. If you have any questions or concerns about these matters, please contact the persons listed below.

17. What should I do if I want to discuss this study further before I decide?

If you would like further information, please contact:

Assoc. Prof. Julien Freitag
Melbourne Stem Cell Centre
Level 2, 116-118 Thames Street
Box Hill North, VIC
Telephone: 03 9270 8000

Emergency Information:
In case of medical emergencies during the study you are advised to call 000.
In the event of urgent questions concerning discomfort or injury associated with the study, please telephone:

Assoc. Prof. Julien Freitag
Ph. 03 9270 8000
Ph. 0415 953 918 (after-hours emergency only)

18. Who should I contact if I have concerns about the conduct of this study?

Charles Sturt University's Human Research Ethics Committee has approved this project. This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007 and all updates), produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

If you have any complaints or reservations about the ethical conduct of this project you may contact the Committee through the Executive Officer:

The Executive Officer
Human Research Ethics Committee
Tel: (02) 6338 4628
E-mail: ethics@csu.edu.au

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

CONSENT FORM

The evaluation of intra-venous autologous adipose derived mesenchymal stem cell therapy in the treatment of small joint osteoarthritis. A pilot study.

Chief Investigators: Assoc. Prof. Julien Freitag (Principal Investigator), Dr James Wickham (Non-Clinical Scientific Investigator), Dr Kiran Shah (Non-Clinical Scientific Investigator)

- I agree to participate in the above research project and give my consent freely.
- I am 18 years of age or over.
- I understand that the project will be conducted as described in the Participant Information Sheet, a copy of which I have retained.
- I acknowledge that the nature, purpose, potential risks, discomforts and alternative treatments associated with it have been fully explained to my satisfaction by Dr _____. I understand them, and agree to take part.
- I acknowledge that the details of the procedures proposed have been explained to me as well as the anticipated length of time it will take, the frequency with which the procedures will be performed and an indication of any discomfort that may be expected.
- I consent to undergoing all tests and procedures as described in the Participant Information Sheet.
- I agree to adhere to the protocol requirements and restrictions as laid out in the Participant Information Sheet
- I understand that I must use effective contraception during the study. In the event of becoming pregnant (or a male participant's female partner becoming pregnant), I must inform the study doctor immediately.
- I understand that I am free to withdraw from the study at any stage and that this will not affect my medical care, now or in the future.
- Although I understand that the purpose of this research study is to improve the quality of medical care, it has also been explained to me that my involvement may not be of any direct benefit to me.
- I understand that access will be required to my medical records for the purpose of this study as well as for quality assurance, auditing and in the event of a serious adverse event and I consent to this access.
- I have been told that no information regarding my past medical history will be divulged to unauthorised third-parties so as to reveal my identity, and the results of any tests involving me will not be published so as to reveal my identity.
- I consent to my GP/treating doctor(s) being notified of my participation in this study and of any clinically relevant information noted by the study doctor as a result of my participation in this study.

- I have had the opportunity to have a member of my family or another person present while the study is explained to me.
- I have had my questions answered to my satisfaction

PRINT name of **Participant**: _____

Signature _____**Date*** _____ **Time:*** _____

PRINT name of **Witness to Participant's Consent**: _____

Signature _____**Date*** _____ **Time:*** _____

Declaration by Study Doctor

A verbal explanation of the research project, its procedures and risks has been given to the participant and I believe that the participant has understood that explanation.

PRINT Name of **Principal Investigator or nominee**: _____

Signature _____**Date*** _____ **Time:*** _____

* Each person who signs the consent form must personally enter the date and time for their signature.