GENERAL PARTICIPANT INFORMATION SHEET

Title:	Better Evidence And Translation for Calciphylaxis (BEAT-Calci)
Investigators:	Prof Meg Jardine (Co-ordinating Principal Investigator) *[Name]* (Principal Investigator) *[Name]* (Associate Investigator) *(if required by institution)*
Study Sponsor:	The University of Sydney
Coordinating Centre:	NHMRC Clinical Trials Centre
Site:	[Site name] (where PI will recruit)

1 Introduction

You are invited to take part in a clinical research study titled *Better Evidence And Translation for Calciphylaxis (BEAT-Calci)* because you have recently been found to have calciphylaxis. Calciphylaxis is a rare disease that is mainly seen in patients with kidney failure, who are receiving dialysis. In calciphylaxis, calcium builds up in the small blood vessels of fat and skin tissue. This can lead to blocked blood vessels, painful skin ulcers and sometimes complications including serious infections.

What is the purpose of this study?

Doctors are uncertain about the best way to treat calciphylaxis. There are many ways that doctors may approach the clinical care of people with calciphylaxis. These include pharmaceutical (or 'drug') treatment, changing dialysis frequency or type, wound care, surgery and so on. These represent different *types* of treatment, which your study team may refer to as treatment 'domains'.

At present, none of these approaches to manage calciphylaxis are supported by high-quality evidence. For each type of treatment, no single treatment is recognised as being better compared to others or to no treatment. The BEAT-Calci Trial aims to find the best treatment, or combination of treatments, for calciphylaxis. The study is using a design that is capable of answering many treatment-related questions within one study. The study is 'eternal', which means that participants will continue to be recruited until all possible treatments have been tested or the best treatment has been found. It is also 'adaptive' which means it is flexible. New treatment types or individual treatments can be added. Treatments that are not working can be removed.

You will be given a set of Participant Information Sheets/Consent Form that tell you about the study:

- General Participant Information Sheet – describes the overall study
- Domain Participant Information Sheets – describe the individual treatment types being tested

Please read this information carefully. If there is anything you do not understand or want to know more about, please ask us. Participation is voluntary. Before deciding whether or not to take part you might want to talk about it with a relative, friend, your kidney doctor or the dialysis staff.

Your participation is voluntary

Your participation in this study is completely voluntary and there will be no cost to you. If you choose to participate in this study, you may participate in all of the treatment types for which you are *clinically* suitable for, but you can choose which of these to take part in. If you choose to participate in this study, you must participate in at least one treatment type.

If you do not want to take part in this study, you do not have to. You should feel under no obligation to participate in this study. Choosing not to take part in this study will not affect your current and future medical care in any way. If you do not take part in this study, you will continue to receive routine clinical care. Your study doctor will discuss these options with you before you decide whether to take part in this study. You can also discuss the options with your local doctor.

If you decide that you do want to take part in the study, you will be asked to sign the Participant Consent Form. By signing it, you are telling us that you:

- Understand what you have read in the Participant Information Sheets
- Consent to take part in the research
- Consent to have the tests and treatments described in the Participant Information Sheets
- Consent to the use of your personal and health information as described in the Participant Information Sheets

Within the Participant Consent Form, you can indicate which parts of the BEAT-Calci Trial you would like to take part in. It is entirely up to you which options you choose. Your selection will not affect your care in the other parts of the study or your usual care.

You can withdraw at any time

If you choose to participate in the study, you are under no obligation to continue with the study. You may change your mind at any time about participating in the research. People withdraw from studies for various reasons, and you do not need to provide a reason. If you decide you do not wish to continue with any aspect of this study at any time, please call the study team to discuss your decision.

You can choose to withdraw from this study at any time by completing and signing the ‘Participant Withdrawal of Consent Form’. This form is to be completed by you and supplied to the study team if you choose to withdraw at a later date.

If you do withdraw from the study, the study doctor and relevant study staff will not collect additional personal information from you. You will be able to choose whether the study will destroy or retain the information it has collected about you. You should only choose one of these options. Where both boxes are ticked in error or neither box is ticked on the form, the study will destroy all information it has collected about you.Your study doctor will discuss how to manage any health risks and provide recommendations for your ongoing care.

Storage Retention & Destruction of your information

Your study data will be held in paper and electronic format at site and electronically by the NHMRC CTC. Electronic data will be held securely and processed on protected computers. Paper records will be stored and handled in a confidential manner e.g., in locked filing cabinets or lockable rooms. The study data will be kept for at least 15 years from the end of the study, after which it will be destroyed in a secure manner. Further information on how we maintain your confidentiality is described in section 11 of this Participation Information Sheet.

2 What does participation in this research involve?

If you choose to participate, you will be participating in a randomised controlled 'platform' trial. Sometimes, we do not know how to manage a condition; to find out the best way to manage calciphylaxis we need to compare various treatments. You will be put into a group by chance (or 'randomised', like rolling a dice) to receive different treatment/s. The treatment you receive may be a placebo, which is a medication with no active ingredients or a procedure without any medical cost.

If your calciphylaxis condition does not respond to the treatment assigned to you, your treatment may be "intensified". This may include changing or adding new treatments. Further information on this is contained in the individual Domain Participant Information Sheets.

If the study is suitable for you and you agree to participate, you will be asked to sign the Participant Consent Form before any study-related procedures can commence. If you agree to participate in this study, you agree to be involved in the visits described below.

You also agree to follow the instructions in this document and instructions provided by your study doctor. If you cannot, or do not wish to accept this responsibility, please advise your study doctor. The duration of your participation in the study is 26 weeks and includes the following visits:

a) Before starting in the study (Screening Visit)

If you decide to take part in the study, you will need to sign the Participant Consent Form before any study-related procedures can commence. The study team will confirm that the study is suitable for you by talking with you and reviewing your medical records.

At this initial screening visit, you will be given the opportunity to ask questions about the study and to decide if you wish to participate.

b) Start of study (Baseline Visit)

At the baseline visit, the following information will be collected or procedures performed:

1. Demographics (e.g. birth date, gender and ethnicity)
2. Medical history (e.g. kidney disease and dialysis history)
3. Details of your dialysis prescription and other calciphylaxis treatments
4. Details of your current medications (including any pain medication)
5. Short questionnaires to assess your health-related quality of life and any pain you may be experiencing
6. Your calciphylaxis wound/s will be photographed
7. Details of blood results from routine testing
8. An extra 16 mL blood sample will be collected if you are participating in an (optional) part of the study

This visit should take approximately one hour of your time.

c) Treatment start visit (Randomisation Visit)

Following enrolment in the study, you will be randomised to treatments in each of the treatment types ('domains') in which you are suitable for. This visit may or may not take place at the same time as your baseline visit. You will begin to receive study treatment/s at this visit.

d) During the Study (Follow-up Visits)

The study team will manage your follow-up visits to line up with your regular check-ups or dialysis sessions at your treating hospital, to avoid extra trips and to minimise any additional time spent at the hospital.

The follow-up assessments at weeks 2, 6, 8, 10 and 19 will be brief, involving:

1. Details of your current pain medications
2. Short questionnaire to assess any pain you may be experiencing

The follow-up assessments at weeks 4, 12 and 26 will involve:

1. Details of your dialysis prescription and other calciphylaxis treatments
2. Details of your current medications (including any pain medication)
3. Short questionnaires to assess your health-related quality of life and any pain you may be experiencing
4. Your calciphylaxis wound/s will be photographed

5. Details of blood results from routine testing
6. An extra 16 mL blood sample will be collected if you are participating in an (optional) part of the study

Any medical events or side effects will be recorded throughout the whole study.

Details of any additional laboratory testing of routine blood collections will be described in the relevant Domain Participant Information Sheets.

e) After the study (Post-study follow-up)

Following study completion, we ask that your caring medical team update us about your overall health status on a yearly basis for up to 5 years after the study. In addition, if you have consented to data linkage (optional), we will continue to obtain data about your health and use of health services through data linkage for up to 5 years. This long-term information is helpful in understanding mid- to long-term calciphylaxis outcomes.

3 What about the optional parts of the study?

The study has optional components to it:

1) Data Linkage

Data linkage brings together health information held by different local health authorities about the same individual. This information may include details about previous tests, treatments and healthcare provision. This helps researchers better understand people's health journey, which can improve treatment and health services delivery.

In BEAT-Calci, the research team are seeking to collect extra data about your health by linking study data with health databases and government data. This includes, but is not limited to:

- Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data;
- state government hospitalisation data
- state government data on emergency department visits
- state government mortality data
- Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data

Data linkage will be facilitated by the Data Linkage Unit in your state. These units link multiple sources of data and maintain a record linkage system that protects privacy. Data linkage of study data with your MBS and PBS data will only be undertaken by an agency authorised to link Commonwealth and State data. Further information about these units can be found on: http://www.phrn.org.au

If you consent to the data linkage of study data with your MBS/PBS data, you will be asked to sign an additional consent form authorising the study to access your complete

MBS/PBS data. MBS collects information on your doctor visits and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to Services Australia who holds the data confidentially.

All MBS/PBS data and linked datasets will be stored in Australia and will not be disclosed or stored overseas.

2) Biobanking

Biobanks are secure storage facilities that are set up so that researchers can collect, store and examine samples of material from humans (e.g. blood, urine, tissue, DNA or protein). This information can improve our understanding of health and disease and is used by the medical community to investigate if a patient is responding to a particular treatment.

If you agree to take part in this optional study component, additional blood samples will be collected from you. The samples will be labelled with a unique and anonymised study ID and stored confidentially at a central biobank. The samples will be used for a sub-study, which involves identifying specific genes (DNA), proteins in the blood or other markers, that are common in patients with calciphylaxis. This is novel and may lead to better insight for early diagnosis or personalised treatment options in future patients.

You should be aware that during this research, information may be discovered that has significant health implications for you (and possibly your genetic relatives). These are known as 'incidental findings'. There may also be implications for your life insurance policy that may include some exemptions. Please refer to the information from the Financial Services Council website on: https://fsc.org.au/policy/life-insurance/ or consult your financial advisor. You should consider the potential risks and think carefully before agreeing to participate in this optional study component. Feel free to discuss this further with your study team.

In the event that an incidental finding is made, the Trial Steering Committee will determine whether a finding is serious or not and refer the matter to your treating doctor at the time, who will contact you. You may require further tests, genetic or otherwise, to ensure the validity of the finding. These laboratory research studies are experimental, and the results will not be suitable for guiding decisions about your treatment. Accordingly, we do not plan to make all your individual results from these studies available to your study doctor.

All blood samples taken for biobanking, and associated health information, will be stored securely. While stored samples are completely anonymised in the biobank, they can be linked back to a specific individual through their treating hospital/doctor in conjunction with the biobank, who can de-code stored samples if necessary.

Access to samples in this study will be restricted; any external parties wishing to access the samples will require approval from the BEAT-Calci executive committee as well as an

ethics committee. Approval will only be provided after careful consideration by the BEAT-Calci executive committee of the scientific merit of, and clinical need for, the proposed research. Any blood samples left over at the end of the study will be destroyed.

You will retain the right to have your samples destroyed at any time by contacting your study doctor. If you decide to have your samples destroyed, any data or analyses that were done before the request cannot be removed. However, no additional analysis will be done on your samples, and all your remaining samples will be destroyed. The University of Sydney is responsible for organising the destruction of your samples at your request.

Your samples will never be sold. You will not benefit financially if this research leads to development of new treatments.

3) Consumer (Patient) Engagement

The BEAT-Calci research team has formed a committee, involving patients who will consult with the BEAT-Calci executive committee. The activities of this committee will be coordinated by research staff at the NHMRC CTC and will include reviewing and providing feedback on study materials and providing ongoing consumer feedback on the progress of the platform trial. This will be done through email, video conference and/or in-person meetings, whichever is most suitable for the consumer. If you are interested in being a part of the consumer (patient) engagement committee, please let your study team know.

4 What are the possible benefits of taking part?

This study aims to improve medical knowledge and may help patients in the future with calciphylaxis. The results of this study will provide doctors with important information about which treatments work best for wound healing in calciphylaxis. We currently do not know how well, or even whether, the treatments will help you, which is why the research is needed.

5 What are the possible risks and disadvantages of taking part?

Your study doctor or members of the study team will discuss any risks and inconveniences.

All medical treatments involve some risk of harm. The most common unwanted side effects associated with the treatments being tested are described in the Domain Participant Information Sheets. If you experience any side effects or new symptoms whilst on treatment, please discuss this with your study doctor. If you become unwell between hospital visits, please seek advice immediately, either from your treating hospital or from your GP. Please update the study team if you attend your GP or hospital for problems relating to calciphylaxis.

Other known risks in this study are around blood collection. Wherever possible, your blood will be collected at the time of dialysis to minimise the need for additional needles. For most people, blood collection does not cause any serious problems. However, it is possible you may feel some discomfort and there may be some bruising, swelling or bleeding where the needle enters the skin.

6 What if new information arises during this study?

This study is designed to be 'adaptive', allowing the introduction of new therapies into the study and making them more easily accessible to participants than if they were not in the study. Information about new treatment types will be documented in additional Domain Participant Information Sheets as they are incorporated into the BEAT-Calci Trial.

If new information becomes available during this study, your study doctor will discuss with you what it means and whether you want to withdraw or continue in the study. If you decide to continue in the study, we may ask you to sign an updated consent form.

On receiving new information, your study doctor might also consider it to be in your best interest interests to withdraw you from the study. If this happens, they will explain the reasons and arrange for your regular health care to continue.

7 Can I have other treatments during this study?

Whilst you are taking the assigned treatment/s for this study, you will continue to receive your usual standard of care from your kidney doctor and the dialysis staff. However, there are some medications and supplements that will need to be stopped prior to participating in the study. This includes, but is not limited to:

- Warfarin
- Calcium and Vitamin D supplements
- Calcium-based phosphate binders

Alternatives to these medications may be possible and your study doctor will discuss your individual treatment if this applies to you. We recommend you advise your GP of any proposed changes to your medication.

8 Could this study or my treatment be stopped unexpectedly?

Whilst unlikely, the researchers may stop the study or your participation in this study earlier than planned. This may be because the study management or health authorities feel the study needs to be stopped. If this is required, it will be discussed with you by your study doctor.

In addition to this, there are some circumstances where your study doctor may recommend pausing or modifying the study treatment, where it is in your best interest to do so (e.g. if you experience severe side effects). If treatment is permanently stopped, you can still continue to be a part of the study and will be encouraged to attend follow-up visits.

If the study is stopped early, the study team will contact you to explain the reasons for the decision and provide instructions for completing your study participation.

9 What happens when the study ends? How will I be informed of the results of this study?

At the end of your follow-up in this study, you will continue to receive your usual standard of care from your kidney doctor and the dialysis staff. If you require ongoing calciphylaxis management, it will be discussed with you by your kidney doctor at that time. Your doctor may or may not choose to continue one or some of the treatments tested in the study.

Once the study is complete and the results are known, a written plain-English summary of the results of the study will be made available to your study doctor for discussion with you. A summary of the results will also be published on the NHMRC CTC website http://www.ctc.usyd.edu.au (search for 'trial results'). In addition, a description of this study will be available on http://www.ClinicalTrials.gov. Public information is provided in such a way that you cannot be identified.

Results of the study may be used to register any successful products for the treatment of calciphylaxis.

10 What happens if I am injured as a result of participating in this study?

Every reasonable precaution will be taken to ensure your safety during the course of the study. If you suffer any injuries or complications as a result of participating this study, please contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. In Australia, if you elect to be treated as a public patient and are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication.

You do not give up any legal right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study.

11 What will happen to information about me?

Your study data will be held electronically by the NHMRC CTC and in paper and electronic format at site. The study data will be kept for at least 15 years from the end of the study, after which it will be securely destroyed. After the study ends, if you have consented to data linkage of MBS/PBS data with your study data, the MBS/PBS data will be securely destroyed within 7 years following the final study publication.

By signing the consent form, you consent to your study doctor and relevant study staff collecting and using personal information about you for the purpose of this study. Any information obtained in connection with this study that can identify you will remain confidential and will not be disclosed without your permission, except as required by law. The information collected in the study database will be identified by a code number. Only your study doctor and the study team will be able to link the code number to you personally. This information will only be used for the purpose of this study and it will only be disclosed with your permission, except as required by law. The coded information entered in the study database (except for MBS/PBS data and any study data linked with MBS/PBS data) will be stored in a 'cloud' server (a way of storing and accessing data electronically online rather than on a physical server), which is located outside Australia. The primary data storage location is Houston, Texas, USA. By signing the consent form, you agree to your coded information being stored overseas, for at least 15 years from the end of the study, per clinical trial regulation.
Information about you may be obtained from your health records held at this and other health services for the purpose of this study. Your participation in this study will be recorded in your health records. By signing the consent form, you agree to your study doctor and the study team accessing health records if they are relevant to your participation in this study.

Your health records and any information obtained during the study are subject to inspection, both remotely and at the location where it is held (for the purpose of verifying the procedures and the data) by authorised representatives of the NHMRC CTC, supporting commercial partners, the Australian Therapeutic Goods Administration , the approving Human Research Ethics Committee (HREC) and other relevant regulatory authorities, or as required by the law. By signing the Participant Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above (except for MBS/PBS data and any study data linked with MBS/PBS data).

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the study team. You also have the right to request that any information collected with which you disagree be corrected. Please contact your study team if you would like to access your information.

Once the results of the study are known, it is anticipated that the results of this study will be published and/or presented at meetings. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

12 Who is organising and funding the research?

This study is coordinated by the NHMRC CTC and sponsored by the University of Sydney.

Principal funding is through the Australian Government's Medical Research Future Fund. The study is collaborating with commercial partners, who are providing financial and/or product support for certain study 'domains'. This will be detailed in the Domain Participant Information Sheets, as applicable. The companies may benefit financially from this study if the study demonstrates benefits of the intervention/s within each domain.

The study site will receive a payment from the NHMRC CTC for undertaking this study.

No member of the study team will receive a personal financial benefit from your involvement in this study (other than their ordinary wages).

13 Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of Sydney Local Health District (SLHD).

This study will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007, updated 2018 and as amended from time to time)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

In other participating countries, the study will be carried out according to the applicable laws and regulations.

14 What do I do if I have a privacy complaint?

If you have a privacy complaint in relation to the use of your MBS/PBS data you should contact the Office of the Australia Information Commissioner. You will be able to lodge a complaint with them.

Website: www.oaic.gov.au
Telephone: 1300 363 992
Email: enquiries@oaic.gov.au
Mail: GPO Box 5218, Sydney NSW 2001

If you have a privacy complaint in relation to the use of general study data or your bio-specimens you should contact the Privacy Commissioner in your relevant state. You will be able to lodge a complaint with them.

State	New South Wales	Queensland	Victoria
Website	www.ipc.nsw.gov.au	www.oic.qld.gov.au	www.ovic.vic.gov.au
Telephone	1800 472 679	1800 642 753	1300 006 842
Email	ipcinfo@ipc.nsw.gov.au	enquiries@oic.qld.gov.au	enquiries@ovic.vic.gov.au
Mail	GPO Box 7011, Sydney NSW 2001	PO Box 10143, Adelaide Street, Brisbane, QLD 4000	PO Box 24274, Melbourne VIC 3001

15 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this study or if you have any medical problems which may be related to your involvement in the study (for example, any side effects), you can contact your clinical contact representative:

Name	*[Name]*
Position	Clinical Contact
Telephone	*[Phone number]*
Email	*[Email address]*

If you have any complaints about any aspect of the study, the way it is being conducted or any questions about being a research participant in general, then you may contact the reviewing HREC approving this research:

Name	Sydney Local Health District Human Research Ethics Committee – Concord Repatriation General Hospital
Position	Executive Officer
Telephone	02 9767 5622
Email	SLHD-ConcordEthics@health.nsw.gov.au

The conduct of this study at the *[name of hospital]* has been authorised by the *[name of Local Health District]*. Any person with concerns or complaints about the conduct of this study may also contact the Research Governance Officer *[or other officer]* on *[telephone number]* and quote protocol number *[insert local protocol number]*.

Thank you for taking the time to consider taking part. A copy of this information sheet and signed consent form will be given to you to keep.

*(add the following **OPTIONAL** sections if applicable for the institution)*

16 Teletrials

This clinical trial is being undertaken by *[name of primary site]* using the teletrial model, and you may participate in the trial at a site closer to your home using telehealth technology such as telephone, video, or computer (telehealth) conferencing to connect clinicians at one location to clinicians and patients in other locations. Some of your visits may be done locally, but you might also need to travel to another hospital or clinic for some visits. If this is required, your study team will explain when and where you will need to attend your study visits.

Health professionals at *[name of satellite site]* will communicate with *[name of primary site]* electronically, to conduct study visits and review your medical records. Any clinical information about you may be sent from *[name of satellite site]* to *[name of primary site]* using coding matching your Study ID. Your name and contact details will not be included. Telehealth communications between *[name of primary site]* and *[name of satellite site]* will be subject to the same confidentiality provisions as are in place for all telehealth consultations.

17 Required reporting about teletrials in the Australia Teletrial Program

The Australian Government Department of Health is sponsoring the expansion of a teletrial model across Australia though the Australian Teletrial Program (ATP), which means that across Australia, people may participate in clinical trials closer to home. This Program is coordinated by Queensland Health.

The ATP is required to report back to the Australian Government Department of Health about the difference teletrials make – especially to people from regional, rural or remote areas. Research teams from James Cook University and Queensland University of Technology will be assisting in evaluating the model and ATP reporting.

We will record your home postcode so that we can work out the remoteness category of where you live; but we will not include your postcode in any reports – we will only report the remoteness category.

With your consent, the research team will also collect the following information about your participation in this teletrial, and this will be used for ATP reporting: age, gender, cultural background, location of your study visits, and whether you finished the study. Your name and date of birth will not be recorded.

If you consent to information about your participation in teletrials being collected for ATP reporting, your information will be merged with information from all other Teletrial participants who have consented to this data collection for ATP reporting. Individual data will not be reported.

If you do not want information about your participation in teletrials to be collected and used for ATP reporting, you do not have to agree. You may still participate in a teletrial, and only your postcode information will be collected.

Information about your participation in teletrials will be stored on a server located within Queensland Health and will be protected in accordance with the Hospital and Health Boards Act 2011 (Qld), the Information Privacy Act 2009 (Qld) and the Australian Privacy Principles.

18 Teletrials withdrawal of consent

Participation in a clinical trial or a teletrial is voluntary. If you don't wish to take part, you don't have. If you wish to withdraw and have previously provided consent for additional information about you to be collected for ATP reporting purposes, you will need to decide if you want your information removed from the ATP database.