Participant Information Sheet

Study title:	**A prospective observational cohort study of patients with calcium pyrophosphate deposition (CPPD) disease in the Auckland Region**		
Locality:	**The University of Auckland**	Ethics committee ref.:	2025 EXP 21801
Investigators:	**Dr Vicky Tai, Prof Nicola Dalbeth, Assoc Prof Greg Gamble**	Contact phone number:	0223683154

You are invited to take part in a study investigating how patients with CPPD disease are affected by this condition. Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form at the end of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 10 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

CPPD disease is a painful inflammatory arthritis caused by the deposition of calcium pyrophosphate crystals in and around the joints. CPPD disease is one of the most common forms of arthritis, affecting up to 7% of the population. CPPD disease is more common in the elderly and as the population ages, it is likely to become a condition of public health importance. At present, however, the disease remains poorly understood.

We are establishing a cohort of patients with CPPD disease in the Auckland Region who will be followed longitudinally to improve our understanding of this condition. Specifically, we will be investigating the following:

1. Patterns of disease activity (ie. flares) in patients with CPPD disease
2. Patients' perceptions of CPPD disease and the impact CPPD disease has on their quality of life
3. Imaging features of CPPD disease on both X-rays and ultrasound
4. Long-term health outcomes associated with having CPPD disease
5. Identifying biomarkers in blood samples from patients that may be implicated in the development of CPPD disease

WHO CAN TAKE PART IN THE STUDY?

Adults (≥18 years) who fulfil the classification criteria for CPPD disease based on symptoms, imaging findings +/- joint aspiration will be eligible to take part in the study. Additionally, participants need to be able to provide informed consent, attend two in-person study visits at the University of Auckland's Clinical Research Centre, and complete forms/questionnaires in English.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

If you are eligible to participate in the study and agree to taking part by signing the consent form, you will be asked to attend the Clinical Research Centre at the University of Auckland's Grafton Campus for two in-person study visits spaced 6 months apart.

At the baseline visit, you will complete a study questionnaire with the researcher. The questionnaire will collect information on your demographics (eg. age, gender, ethnicity, occupation), the duration that you have had CPPD disease, how frequently you experience flares of CPPD disease, family history of CPPD disease, the medications you are currently taking and other health conditions you may have. Additionally, you will be asked to complete some questionnaires looking at how CPPD disease is affecting your life and your understanding of CPPD disease. After completing the questionnaires, you will have a joint examination by the study doctor to assess for tenderness and swelling, followed by an ultrasound of your wrists and knees to assess for features of CPPD disease and joint inflammation. You will also have a blood sample taken to test CRP (a marker of inflammation) and stored for future biomarker analysis. Finally, you will be asked to attend the Radiology Department at Auckland City Hospital or Beyond Radiology Grafton for X-rays of your hands, wrists and knees. The first study visit is expected to take between 2-3 hours (depending on waiting times at the Radiology Department).

At the 6-month follow-up visit, you will be asked to complete a follow-up questionnaire which has similar questions to the baseline questionnaire. You will then have a joint examination by the study doctor to assess for tenderness and swelling, followed by an ultrasound of your wrists and knees to assess for features of CPPD disease and joint inflammation. Another blood sample will be taken and stored for future biomarker analysis. The follow-up visit will be shorter and should take no longer than 1.5 hours.

Between the two study visits, you will be asked to keep a flare diary to monitor how active your CPPD disease has been. This involves recording the days where you experience flares of CPPD disease, which joints are involved, the pain score for each day of the flare, medications used to manage the flare, and medical encounters/hospital admissions related to the flare. You may choose to complete the flare diary on paper or online. We will send you weekly texts/emails to remind you to fill out the flare diary. At the 3-month mark, the study doctor will also contact you by phone to review the flare diary and to answer any questions that you may have.

Beyond the two study visits, we hope to continue following you to assess longer-term health outcomes related to having CPPD disease. With your consent (optional), this will involve us having ongoing access to your health records and contacting you periodically by phone so that we can see how your health has been.

WHAT WILL HAPPEN TO MY BLOOD SAMPLES?

You will have a blood sample taken at the first study visit which will be sent to LabPlus to test for CRP (a marker of inflammation).

Blood samples taken at the baseline and 6-month visits will also be stored and may be used to measure other biomarkers implicated in CPPD disease. These samples will be stored in secure freezers within the Clinical Research Centre at the University of Auckland and will only be accessible to the study investigators. With your consent, samples may also be sent to a laboratory overseas for testing if required.

If you wish a karakia to be performed at the time that your blood samples are disposed, please indicate your wish on the consent form. Please note, however, that a karakia may not be possible for blood samples that have been sent overseas.

Genetic Testing (optional):

In recent years, there has been growing interest in identifying genes implicated in the development of CPPD disease. We would like to contribute to genetic studies in CPPD by storing blood samples (DNA/RNA) from patients with CPPD disease for future genetic analysis. Blood samples may be sent to a laboratory overseas for genetic testing. If you wish to participate in this genetics study, we will ask you to complete a separate Genetics Testing Consent Form located at the end of this Information Sheet. Participation in this genetics study is optional.

WHAT WILL HAPPEN TO MY INFORMATION?

During this study the investigators will record information about you and your study participation. This includes the results of any study assessments eg. questionnaire responses, examination findings, ultrasound/X-ray findings and blood test results. If needed, information from your hospital records and your GP may also be collected.

Identifiable Information

Identifiable information is any data that could identify you (e.g. your name, date of birth, or address). Only the study investigators will have access to your identifiable information.

We will advise you and your GP of any abnormal test results found as part of the study that have implications for future health. This could include results of blood tests, or abnormal x-ray or ultrasound findings.

In one of the study questionnaires (called the EQ-5D-5L), you will be asked to indicate your level of anxiety/depression. If you indicate that you are severely or extremely anxious/depressed, we will undertake a brief assessment to see if you are at risk of harming yourself. If you are, then we will refer you to the Mental Health Crisis Team and inform your GP. If you are not at risk of harming yourself, we will still inform your GP that you are significantly anxious/depressed and encourage you to seek help from your doctor. We will also provide you with the contact details of the Mental Health Crisis Team and free telephone counselling services (eg. Lifeline NZ).

De-identified (Coded) Information

To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by the study. Instead, you will be identified by a code. The investigators will keep a list linking your code with your name, so that you can be identified by your coded data if needed.

The results of the study will be published or presented, but not in a form that would reasonably be expected to identify you. It is up to you whether you consent to your de-identified x-ray or ultrasound images (without your personal details) being used for training or publication purposes by indicating on the relevant section of the Consent Form.

Future Research Using Your Information.

If you agree, your de-identified (coded) information may be used for future research related to CPPD disease. You will not be told when future research is undertaken using your information. Your information may be shared with other research groups, including overseas. Your information may also be added to information from other studies, to form much larger sets of data.

Your information may be used indefinitely for future research unless you withdraw your consent. However, it may be extremely difficult or impossible to access your information, or withdraw consent for its use, once your information has been shared for future research.

Security and Storage of Your Information.

Your identifiable information will be held in secure storage facilities at the University of Auckland during the study. Your de-identified (coded) information will be entered into electronic case report forms and stored on the REDCap database which is hosted on secure servers at the University of Auckland with access controlled by unique user ID and password with two-factor authentication and full electronic tracking log. All storage will comply with local and/or international data security guidelines.

Special Note on X-ray and Laboratory Results

Your X-ray images and reports will be stored in your clinical records against your National Health Index (NHI) so that other clinicians may view these if needed for your clinical care. Additionally, your identifiable information along with the X-ray images and reports will be stored with the radiology provider.

Similarly, your laboratory results (CRP) will be stored in your clinical records against your NHI so that other clinicians may view these if needed for your clinical care. Additionally, your identifiable information along with the laboratory results (CRP) will be stored by LabPLUS, Auckland City Hospital.

WHO PAYS FOR THE STUDY?

Participation in this study is free. The costs for the ultrasound scans, blood tests and x-rays will be covered by us. We will provide you with a $50 supermarket voucher following each study visit as a koha. Parking is available for free for study participants at the University of Auckland's Clinical Research Centre.

WHAT ARE THE POSSIBLE RISKS OF THIS STUDY?

This study will involve the sampling of blood. A blood sample taken may hurt a little, and some people get a small bruise where the needle goes in. Occasionally the needle hole can become infected, but this is very rare. Most people have no problems. If you ever faint with blood samples or when you see

blood, please let the study doctor know beforehand. That way we can be ready for this and take the sample while you are lying down.

This study involves radiation exposure from X-rays of the hands, wrists and knees which will take place at the first study visit. As part of everyday living, everyone is exposed to a small amount of background radiation that comes from soil, rocks, outer space and within the body itself. The radiation dose you will receive in this study is about the amount that you receive over 1 day from background radiation. This radiation exposure is necessary for us to obtain information about the health of your bones and joints. The risk from this dose is small.

The ultrasound scans do not involve radiation exposure. Ultrasound scanning is safe and painless. Sound waves are used to obtain images of your joints. This technology is the same as that used to scan a pregnant woman and has no known side effects.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, which is unlikely, you would be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT ARE MY RIGHTS?

Your participation is entirely voluntary (your choice). You do not have to take part in this study and if you choose not to take part, it will not affect any future care or treatment. If you do agree to take part, you may withdraw from the study at any time without having to give a reason and this will in no way affect your future health care. If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

<u>Implications of genetic testing</u>

If you agree to participate in this study, you do not have to agree to your blood sample being used for genetic testing. If you do agree to your blood sample being used for genetic testing, we will ask you to complete an additional Genetic Testing Consent Form (located at the end of this Information Sheet) stating you agree to the storage and testing of your genetic samples.

Please note that the researchers are not allowed to sell or export your genetic material. The researchers, however, may need to send a small amount of your genetic material (DNA/RNA) to a laboratory overseas where genetic testing will be conducted. The samples can only be used for research related to CPPD disease.

The cultural issues associated with storing your blood samples, sending them overseas and undertaking genetic analysis on them should be discussed with your family/whānau as appropriate.

We understand that storing blood samples and performing genetic testing on them is a culturally significant activity for Māori as it is linked to whakapapa and the continuation of Māori as a nation. For some Māori, tissue and genetic material are considered tapu and imbued with wairua. Please be assured that we will treat your samples as taonga and will ensure that they are transported and stored securely, with access limited to research staff. To avoid problems at a later stage, however, we encourage you to discuss your participation in the genetic testing component of the study with your family/whānau. We are happy to meet with you and your family/ whānau to discuss the study further if required, prior to you giving consent. Additionally, Māori cultural support is available through He Kamaka Waiora (contact details available at the end of this information sheet).

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

You may withdraw from the study at any time without providing a reason. If you decide to withdraw from the study, no further data/blood samples will be collected from you. Data/blood samples collected prior to your withdrawal will, however, continue to be processed and analysed for the purposes of the study.

We are happy to give you information about the progress of the study and about future studies at your request at any time. We will keep you informed of the results of the study. Please note that there may be a delay between your study visits and publication of the results.

WHO IS FUNDING THE STUDY?

This study is funded by the Health Research Council of New Zealand. Dr Vicky Tai is a recipient of the Health Research Council Clinical Research Training Fellowship.

WHO HAS APPROVED THE STUDY?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The [insert Committee name] has approved this study.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr Vicky Tai (Rheumatologist & PhD Candidate)
Phone: 0223683154
Email: cppdstudy@auckland.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone:	0800 555 050
Fax:	0800 2 SUPPORT (0800 2787 7678)
Email:	advocacy@advocacy.org.nz
Website:	https://www.advocacy.org.nz/

For Māori cultural support please contact:

He Kamaka Waiora (Maori Health Services)
Phone: (09) 307 4949 ext 29200

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email: hdecs@health.govt.nz
Phone: 0800 400 569 (Ministry of Health general enquiries)

Consent Form

Please read the following carefully before signing and dating this Consent Form

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.
I have been given sufficient time to consider whether or not to participate in this study.
I have had the opportunity to use a legal representative, whānau/ family support or a friend to help me ask questions and understand the study.
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.
I know who to contact if I have any questions about the study in general.
I understand my responsibilities as a study participant.
I understand the compensation provisions in case of injury during the study.
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
I agree to local laboratory testing of my blood sample for CRP (a marker of inflammation).
I agree to the storage of my blood samples for future biomarker analysis.
I consent to the research staff collecting and processing my information, including information about my health from my medical records.

I consent to my GP or current provider being informed about my participation in the study.		
I consent to my GP or current health provider being informed about any significant abnormal results obtained during the study.		
If I decide to withdraw from the study, I agree that the information and blood samples collected from me up to the point when I withdraw may continue to be processed and analysed for the purposes of the study.		
I wish to have my blood samples disposed of with an appropriate karakia	Yes ☐	No ☐
I agree to my blood samples being sent overseas for testing and I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste. Please note that a karakia may not be possible when disposing of blood samples that have been sent overseas.	Yes ☐	No ☐
I consent to my de-identified X-ray and ultrasound images being used for training and publication purposes	Yes ☐	No ☐
I agree to providing the contact details of whānau/family or close friends that can be contacted when I cannot be reached.	Yes ☐	No ☐
I wish to receive a summary of the results from the study.	Yes ☐	No ☐
I agree to the researchers having ongoing access to my health records beyond the 6-month study visit and to contact me periodically by phone regarding my health	Yes ☐	No ☐
I agree to my de-identified data/blood samples being made available to other researchers for future research and I understand that I may not receive the results from future studies.	Yes ☐	No ☐
I agree to being contacted about future studies related to CPPD disease.	Yes ☐	No ☐

Declaration by participant:
I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by member of research team:
I have given a verbal explanation of the research study to the participant and have answered the participant's questions about the study. I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date:

Genetic Testing Consent Form

Please read the following carefully before signing and dating this Consent Form

I have read, or have had read to me in my first language, and I understand the implications for genetic testing as outlined in the Participant Information Sheet.		
I have been given sufficient time to consider whether or not to participate in the genetic testing component of this study.		
I have had the opportunity to use a legal representative, whānau/ family support or a friend to help me ask questions and understand the study.		
I am satisfied with the answers I have been given regarding the study and I have a copy of this Genetic Testing Consent Form and the Information Sheet.		
I understand that taking part in the genetic testing component of this study is voluntary (my choice).		
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.		
I know who to contact if I have any questions about the genetic testing involved in this study.		
I understand my responsibilities as a study participant.		
I agree to the storage of my blood samples (DNA/RNA) for future genetic testing.	Yes ☐	No ☐
I agree to my genetic samples (DNA/RNA) being sent overseas for genetic testing.	Yes ☐	No ☐
I agree to laboratory testing done on DNA/RNA to be performed on my blood samples.	Yes ☐	No ☐

Declaration by participant:
I hereby consent to take part in the genetic testing component of the study.

Participant's name:

Signature: Date:

Declaration by member of research team:
I have given a verbal explanation of the genetic testing component of the study to the participant and have answered the participant's questions about it. I believe that the participant understands the genetic testing component of the study and has given informed consent to participate.

Researcher's name:

Signature: Date: