Participant Information Sheet/Consent Form

University of Tasmania

Title	METHODS - A randomised controlled trial of methotrexate to treat hand osteoarthritis with synovitis
Short Title	METHODS study
Project Number	290/17
Project Sponsor	Monash University
Principal Investigators	Professor Flavia Cicuttini, Dr Andrew Teichtahl, Professor Graeme Jones, Dr Helen Keen, Dr Jessica Kasza, Dr Yuanyuan Wang, Professor Catherine Hill
Associate Investigators	Dr Benny Antony Dr Matthew Jiang
Location	Hobart

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have osteoarthritis and joint swelling (synovitis) in your hands. The research project is testing a new treatment for hand osteoarthritis. The new treatment is called methotrexate, a drug widely used to treat rheumatoid arthritis that has not been tested in osteoarthritis.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

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.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it 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.

You will be given a copy of this Participant Information and Consent Form to keep. The Participant Information and Consent form is 14 pages long in total. Please make sure that you have all the pages.

2 What is the purpose of this research?

Hand osteoarthritis is a common disabling condition resulting in pain and impaired function. Currently there is no treatment that slows the progression of hand osteoarthritis, so there is an urgent and unmet need for effective treatment. Joint swelling (synovitis) is common and present in approximately 50% of people with symptomatic hand osteoarthritis. Joints in hands with synovitis are three and half times more likely to have rapid joint damage than those without synovitis. Therapies targeting synovitis may offer a new approach to treating hand osteoarthritis. Methotrexate, the first line therapy for rheumatoid arthritis, is a well-established, low-cost drug with a well-described safety profile. It has been shown to improve both synovitis and symptoms in clinical trials of rheumatoid arthritis.

The METHODS study is a randomised clinical trial with the aim to compare the effect of methotrexate with an inactive dummy tablet (that is called a placebo) on slowing joint damage assessed by looking at change on X-rays and change in pain in people with symptomatic hand osteoarthritis and synovitis. If methotrexate is effective, it will offer a new way to treat hand osteoarthritis.

Methotrexate has been approved in Australia (Australian Government Department of Health, Therapeutic Goods Administration is the regulatory authority) to treat rheumatoid arthritis as well as other rheumatic conditions such as juvenile arthritis, lupus, psoriatic arthritis and polymyositis for more than 25 years. It is not approved to treat osteoarthritis and joint swelling of the hands. Therefore, it is an experimental treatment for hand osteoarthritis with synovitis. This means that it must be tested to see if it is an effective treatment for hand osteoarthritis with synovitis. The research team conducting this study are specialist rheumatologists extensively experienced in the clinical use of methotrexate.

A total of 125 participants will participate in this project. They will be randomly allocated into two groups, with one group receiving methotrexate and the other group receiving a placebo.

This research is a multicentre clinical trial being conducted by Monash University, University of Tasmania, University of Adelaide, and University of Western Australia. This research has been initiated by the study investigators, Professor Flavia Cicuttini, Dr Andrew Teichtahl, Professor Graeme Jones, Dr Helen Keen, Dr Jessica Kasza, Dr Yuanyuan Wang, Professor Catherine Hill, Associate Professor Anita Wluka, and Associate Professor Stephane Heritier.

This research has been funded by the National Health and Medical Research Council.

3 What does participation in this research involve?

If you agree to participate in the study, we will ask you to do the following:

1. Participation in this trial will initially involve a screening process. You will be screened for your suitability for the study over the phone by answering simple questions about your health. If you meet the inclusion criteria, a Participant Information Sheet will be mailed out to you. You will have an interview with the Clinical Trial Coordinator and a study doctor at the Menzies Institute for Medical Research, during which any question can be answered. If you agree to participate in the study, you will be asked to provide consent, by signing the consent form. You will undergo clinical assessments and complete questionnaires. In order to further assess your eligibility for the study, you will have a blood test at either the Menzies or Hobart Pathology, and have a chest X-ray (unless you have had a chest X-ray within the last 12 months) and hand X-rays (both hands) at Regional Imaging. If you are eligible after having blood tests and X-rays, you will undergo magnetic resonance imaging (MRI) of your study hand at the Royal Hobart Hospital to identify synovitis and eligibility for participation.

During these screening procedures, at any stage, if the researchers identify any reason that would put you at increased risk by being involved in the study, or any reason that would make it inappropriate for you to participate in the study, you will be asked not to continue in the study.

2. If you are eligible to participate, you will be randomly assigned to either the treatment or the control group. The term “randomised” means you will not have a choice regarding which group you are in, and you will have equal chance of receiving the active study medication or placebo. The treatment group will receive methotrexate (10 mg once a week for 4 weeks, followed by 20 mg once a week for the rest of the study, if there is no toxicity as determined at the physician’s discretion) and the control group will receive a placebo (one tablet once a week for 4 weeks, followed by 2 tables once a week for the rest of the study, if there is no toxicity as determined at the physician’s discretion). A placebo is a medication with no active ingredients. It looks like the real thing but is not. All study particpants will also take a vitamin B tablet (folic acid 5 mg) on days other than when study medication is taken (i.e. 6 times per week). Folic acid supplementation has been shown to reduce the potential side effects of methotrexate. As this is a double-blind trial, neither you or the study investigator will know which treatment you are receiving until the study is completed. However, in certain circumstances the study investigator may find out which treatment you are receiving.

3. The trial will go for two years as the effects of methotrexate on the progression of hand osteoarthritis will take this long to be measured adequately. During the trial you will attend the Menzies for 7 study visits in total - at screening/baseline, 4 weeks, 3, 6, 12, 18, and 24 months later, and have 5 telephone interviews in total after you are randomised: at 2 and 8 weeks, and 9, 15, and 21 months. Each study visit will take about 60 minutes, and each telephone interview will take about 10 minutes. We can provide an attendance certificate signed by the research investigator for each study visit.

4. The following measurements will occur during the study period.
   - A blood test will occur at screening, 2, 4, 8 and 12 weeks, and then every 3 months.
   - Hand X-rays of both hands will occur at screening and 24 months; a chest X-ray will be performed at screening.
   - A hand MRI will be performed at screening and 24 months. MRI scan will take about 30 minutes.
   - Questionnaires: information about yourself (employment, education, smoking history, marital status, parity, knee symptoms, quality of life – at screening and 24 months); medical history including vaccination, medications, allergies, and alcohol history (at screening and every 3 months); hand pain and function (at screening, 3, 6, 12, 18, and 24 months)
   - Measurement of height, weight, and girth (hip and waist) will occur at screening and 24 months; cardiovascular (including blood pressure), respiratory, gastrointestinal and skin examination will occur at screening, 12 and 24 months; hand grip strength and tender/swollen joint count will occur at screening, 3, 6, 12, 18, and 24 months.
   - Safety and adverse events will be recorded at 2, 4, 8 and 12 weeks, and then every 3 months; pill counts will occur at 4 weeks, 3, 6, 12, 18, and 24 months.

The following table shows you the procedures that are done at each study visit and telephone interview.

	Screening		Double blind period											
	Screening / baseline assessment	Post-screening	MRI & randomisation	Week 2	Week 4	Week 8	Months 3	Months 6	Month 9	Month 12	Month 15	Month 18	Month 21	Month 24
Visit/phone contact	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
Informed consent	X													
Eligibility blood tests		X												
Safety blood tests				X	X	*X*	X	X	X	X	X	X	X	X
Telephone follow-up				*X*		*X*			*X*		*X*		X	
Clinical visit	X				X		X	X		X		X		X
Hand x-ray		X												X
Chest x-ray		X												
Hand MRI			X											X
Medical history	X						X	X	*X*	X	*X*	X	X	X
Medications and allergies[1]	X				X		X	X	*X*	X	*X*	X	X	X
Employment and education history	X													X
Smoking history	X									X				X
Alcohol history	X			*X*	X	*X*	X	X	*X*	X	*X*	X	*X*	X
Marital status and number of pregnancies	X													X
Questionnaires														
Hand pain	X				X		X	X		X		X		X
Hand osteoarthritis and function	X						X	X		X		X		X
Health assessment	X						X	X		X		X		X
Knee pain, function, and quality of life	X													X
Physical examination														
Height, weight, waist and hip circumference	X													X
Grip strength	X						X	X		X		X		X
Hand examination	X				X		X	X		X		X		X
Chest and skin examination and blood pressure	X									X				X
Compliance with medication and side effects				*X*	X	*X*	X	X	X	X	X	X	X	X
Dispense medication			X					X		X		X		
Pill count					X		X	X		X		X		X

X-ray involves exposure to a very small amount of radiation to create pictures of the inside of your body. The images show the parts of your body in different shades of black and white. This is because different tissues absorb different amounts of radiation. In this study you will have hand and chest x-rays for us to assess your eligibility for the study and to investigate the effect of methotrexate on the progression of your hand osteoarthritis.

MRI stands for magnetic resonance imaging. A MRI scanner is a machine that uses electromagnetic radiation (radio waves) in a strong magnetic field to take clear pictures of the inside of the body. Electromagnetic radiation is not the same as ionising radiation used, for example, in X-rays. The pictures taken by the machine are called MRI scans. We will ask you to lie on a table inside the MRI scanner. The scanner will record information about your study hand. It is very important that you keep very still during the scanning. When you lie on the table, we will make sure you are in a comfortable position so that you can keep still. The scanner is very noisy and we can give you some earphones to reduce the noise. Some people may experience symptoms of claustrophobia from lying in a confined space. If you do experience discomfort at any time during the scan, you will be able to alert staff by pressing on a call button provided to you.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

Free parking at the Menzies Institute will be provided for participating in the research project related clinic assessments.

It is necessary that your family doctor be advised of your decision to participate in this research project. We will inform your family doctor of your participation in this study, as they need to know that you are participating in this research project.

If you choose to withdraw from this study before 24 months, you will be requested to have an early hand x-ray and MRI scan. You may also be asked to attend a follow-up visit to allow collection of information regarding your health status (questionnaires and physical examination).

4 What do I have to do?

You will be required to swallow 1 whole study medication tablet once a week for the first 4 weeks and then 2 whole study medication tablets once a week for the rest of the study, on the same day each week, with a drink of water. It would be preferable to take the tablets on an empty stomach. However if nausea is a problem, taking them at mealtime can help to reduce this side effect. It is a good idea to specify and diarise the day of the week that you will take your tablets to avoid making mistakes. You will also be required to take folic acid (another tablet) once a day with a drink of water on the days other than when study medication is taken. You will need to commit to taking the investigational drug regularly. You will need to attend all the study visits.

Whilst involved in this study, you should avoid drinking too much alcohol since if you are in the group taking methotrexate, drinking large quantities of alcohol may increase your chance of methotrexate causing liver damage. Please do not consume any alcohol on the day of taking study medication and try to limit alcohol intake to no more than 2 standard drinks on other days.

Whilst involved in this study, you can take your regular medications. We will screen for medications unsuitable for this study. You will need to record all medications and complete a questionnaire at study visits. You may not be able to donate blood while you are in the study.

You should tell your doctor and study personnel if you are taking any other medications, including any that you buy without a prescription from a pharmacy, supermarket or health food

shop. Some medications may be affected by methotrexate or may affect how well methotrexate works. It is also important not to start taking any other medications during the study without talking to your doctor and research staff.

5 Other relevant information about the research project

A total of 125 participants with symptomatic hand osteoarthritis and joint inflammation, aged 40-75 years will be recruited from the community, about 30 participants from each study site – Melbourne, Hobart, Adelaide, and Perth. The project will have 2 groups, with one group receiving methotrexate and the other group receiving a placebo. All participants will be followed up over 2 years to examine whether methotrexate affects the progression of hand osteoarthritis and symptoms. The project involves researchers from multiple institutes including Monash University, University of Tasmania, University of Adelaide, and University of Western Australia.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with the Menzies Institute for Medical Research or the University of Tasmania.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment. You can see your doctor or health care professional to discuss different treatment options for your hand osteoarthritis, such as physiotherapy and medications for pain relief. Please feel free to discuss these with your healthcare worker before deciding whether or not to take part in this research project. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research. However, some participants may experience possible benefits, such as an improvement in their hand symptoms or a reduction in disease progression and joint swelling. If this study shows that methotrexate is effective in slowing the progression of hand osteoarthritis and improving hand pain, it may enable this treatment to be available to more people in the future. We will inform you of any abnormal findings from hand and chest X-ray, MRI, and other tests, so that you can then consult with your doctor.

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

Medical treatments often 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 study doctor. Your study doctor will also be looking out for side effects.

The most common side effects of methotrexate are nausea, vomiting and diarrhoea. These can be reduced if methotrexate is taken with food or in the evening. Mouth ulcers can occur, but the use of folic acid or folinic acid supplements makes this less likely. Skin dryness, a variety of skin rashes and increased sensitivity to the sun may also occur. You should wear sunscreen and a hat when out in the sun. Some people report mild tiredness, headache and mental clouding. Some also experience a temporary increase in muscle and joint pain after taking the weekly dose. There are some rare but potentially serious side effects with methotrexate, including a drop in the number of white blood cells and platelets, inflammation of the liver (hepatitis) or the lungs, hair thinning, and nodule formations. The development of some of these side effects (e.g. blood abnormalities) will be monitored closely and you will be required to have serial blood test monitoring (every 3 months after more regular monitoring when initiating therapy).

Methotrexate should not be taken during pregnancy as it can cause miscarriage or foetal deformity. It should also not be taken when breastfeeding. It is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. You must not get pregnant or father a child and, if necessary you must use effective contraception during the course of the research. Women planning to become pregnant should stop taking methotrexate 3 months before attempting to conceive. The best time for a male partner to stop taking methotrexate before trying to conceive is not known. You should discuss methods of effective contraception with your study doctor. Methotrexate does not affect a person's ability to have children in the long term. For female participants, if you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant. For male participants, you should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Tell the study doctor if you have any problems. Your study doctor will monitor for and discuss the best way of managing any side effects with you, should they occur. Use of methotrexate is an established safe and well-tolerated treatment for rheumatoid arthritis. The doses of methotrexate we use in the study are commonly used for rheumatoid arthritis.

Folic acid belongs to the vitamin B group. Rare side effects (affecting more than 1 in 10,000 but less than 1 in 1,000 patients) include allergic reaction, e.g. itchy/red skin, rash, swelling of the face, lips, tongue or throat or difficulty breathing or swallowing, shock (cold sweaty skin, weak pulse, dry mouth, dilated pupils), and stomach and intestines reactions, e.g. loss of appetite, feeling sick, a bloated feeling, wind.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is less than 0.05 mSv. At this dose level, no harmful effects of radiation have been demonstrated, as any effect is too small to measure. The risk is believed to be minimal.

Have you been involved in any other research studies that involve radiation? If so, please tell us. Please keep information contained within the Patient Information and Consent Form about

your exposure to radiation in this study, including the radiation dose, for at least five years. You will be required to provide this information to researchers of any future research projects involving exposure to radiation.

There are no proven long-term risks related to MRI scans as used in this research project. MRI is considered to be safe when performed at a centre with appropriate procedures. However, the magnetic attraction for some metal objects can pose a safety risk, so it is important that metal objects are not taken into the scanner room. We will thoroughly examine you to make sure there is no reason for you not to have the scan. You must tell us if you have metal implanted in your body, such as a pacemaker or metal pins.

The scans we are taking are for research purposes. They are not intended to be used like scans taken for a full clinical examination. The scans will not be used to help diagnose, treat or manage a particular condition. A specialist will look at your MRI scans for features relevant to the research project. On rare occasions, the specialist may find an unusual feature that could have a significant risk to your health. If this happens, we will contact you to talk about the findings. We cannot guarantee that we will find any/all unusual features.

Having blood taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated. Blood samples are collected by a qualified venipuncturist. We endeavour to make the collection process as simple and as stress free as possible.

10 What will happen to my test samples?

This research project involves the collection, storage, test and analysis of your blood samples. By signing the consent form you agree to the study investigator using your blood collected for this project and storing your samples for extended related research and any future research. If future funding is secured, we will be able to measure the stored blood samples for cartilage, bone, inflammatory, and other biomarkers and investigate the relationship between these biomarkers and pain and structural progression of hand osteoarthritis. For any future use of your blood samples, we will seek the approval from the relevant ethics committees. This research project does not involve the establishment of a tissue bank.

The collection and test of your blood sample are a mandatory component of the research. This is done to examine your liver function, kidney function, and haematological condition, in order to assess your suitability for the study and monitor the safety of the treatment.

Your blood samples will be re-identifiable (i.e. coded, without your name on them), and will be sent to Hobart Pathology for proposed blood tests. Some samples of your blood collected at screening and end of study will be stored securely at the Menzies Institute for Medical Research and will only be accessible by senior researchers. The samples will be retained for at least 15 years upon completion of the trial. However, there is the possibility for indefinite storage of the samples. Blood samples sent to Hobart Pathology will be destroyed after testing.

The proposed blood tests include a screening test for Hepatitis B and C, HIV (also called the ‘AIDS’ virus), and tuberculosis. This is because the study doctors need to know whether it is safe for you to take methotrexate. You will receive information and counselling before the test. If a test shows you have HIV, Hepatitis, or tuberculosis, you will have follow-up counselling and medical advice. If your test results are positive, the study doctors are required by law to notify government health authorities. Signing the consent form means that you agree to have this testing; it will not be done without your consent.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your

study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor will also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

It may also be necessary for you to take medication during or after the research project to address side effects or symptoms that you may have. This will be paid for by the sponsor of the study.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study investigator and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the study investigator up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
• Unacceptable side effects
• The drug/treatment being shown not to be effective
• The drug/treatment being shown to work and not requiring further testing

15 What happens when the research project ends?

At the completion of the trial, if you wish to know whether you received methotrexate or the placebo, please contact the research personnel for further information. We will send you a follow-up letter to inform you of the findings of the study.

Methotrexate or placebo and folic acid will be provided to you during the trial for a 2 year period at no cost. Once the trial has finished we will not be able to continue to provide this treatment to you. However, if your doctor is in agreement with continuing the treatment after the trial, he/she can provide you with a prescription for methotrexate and folic acid. From this point you will need to cover the cost of your medication.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form you agree to the study investigator and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential.

The data we collect or use will be individually identifiable or re-identifiable (i.e. coded). All electronic data will be kept in password protected databases, separate from identifying information. Hard copies of data will be kept in locked filing cabinets with restricted key access, at the Menzies Institute for Medical Research. The MRI scans will be name-identified in accordance with standard clinical practice, and will be stored securely on the Royal Hobart Hospital database and password protected databases at the Menzies Institute for Medical Research. Access to data will be limited to the chief investigators and support staff only. Data transfer will occur so that the final dataset with re-identifiable (i.e. coded) data can be accessed by all the chief investigators of the study. Re-identified blood samples will be stored securely at the Menzies Institute for Medical Research and will only be accessible by senior researchers. Identifiable information will not be released to anyone outside the research team. Your information will only be disclosed with your permission, except as required by law.

By signing the consent form you consent to the study investigator using your data collected for this project for extended (related research) or unspecified (any future research) use. Please refer to section 10 (page 8) for information about the potential future use of your data.

Blood samples, information from questionnaires and examinations will be retained for at least 15 years upon completion of the study. This research project does not involve the establishment of a databank.

It is necessary that your local doctor be advised of your decision to participate in this research project. By signing the consent section, you agree to your local doctor being notified of your decision to participate in this research project.

It is anticipated that the results of this research project will be published and presented in a variety of forums. In any publication, report, or presentation, information will be provided in such a way that you cannot be identified, except with your permission. This confidentiality will be maintained by presenting aggregate data. Should any sharing of data be considered (e.g. for combining data with other studies), then data sharing will strictly occur in a re-identified (i.e. coded) manner. In the event where personal information may need to be shared (e.g. data linkage), we will contact you or your guardian for consent for data sharing.

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

17 Injury

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

This research project is being conducted at Melbourne (Professor Flavia Cicuttini, Dr Andrew Teichtahl, Dr Yuanyuan Wang, Dr Jessica Kasza), Hobart (Professor Graeme Jones), Adelaide (Professor Catherine Hill), and Perth (Dr Helen Keen), funded by the National Health and Medical Research Council.

By taking part in this research project you agree that samples of your blood or knowledge acquired through analysis of your samples may directly or indirectly benefit the University of Tasmania and the Menzies Institute for Medical Research financially.

You will not benefit financially from your involvement in this research project even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to the University of Tasmania and the Menzies Institute for Medical Research.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to the University of Tasmania and the Menzies Institute for Medical Research, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

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 research project will be reviewed and approved by the Tasmanian Health & Medical Human Research Ethics Committee.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

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

If you would like any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), please contact the principal investigators.

Professor Graeme Jones (Menzies): 03 6226 7705, Graeme.Jones@utas.edu.au

If you have any other questions you wish to be answered before consenting or during the course of the study, you can also contact the Clinical Trial Coordinator, Ms Kathy Buttigieg on 03 6226 6909 or email Kathy.Buttigieg@utas.edu.au

If you have medical concerns outside office hours, please contact Rheumatology Registrar at the Royal Hobart Hospital.

For matters relating to research at the site at which you are participating, or if you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, you may contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The executive officer is the person nominated to receive complaints from research participants. You will need to quote **Reference # H0016794.**

Consent Form

Title	METHODS - A randomised controlled trial of methotrexate to treat hand osteoarthritis with synovitis
Short Title	METHODS study
Project Number	290/17
Project Sponsor	Monash University
Principal Investigators	Professor Flavia Cicuttini, Dr Andrew Teichtahl, Professor Graeme Jones, Dr Helen Keen, Dr Jessica Kasza, Dr Yuanyuan Wang, Professor Catherine Hill
Associate Investigators	Dr Benny Antony Dr Matthew Jiang
Location	Hobart

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to the Menzies Institute of Medical Research and the University of Tasmania concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

I understand that, if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status.

I consent to the storage and use of blood samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

- This specific research project
- Other research that is closely related to this research project
- Any future research

Name of participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.