Participant Information Sheet/Consent Form

Monash University

Title	METHODS-Extend – An open label pragmatic trial to determine the efficacy and patient acceptability of methotrexate in hand osteoarthritis over 2 years.
Short Title	METHODS-Extend
Project Number	714/23
Project Sponsor	Monash University
Principal Investigator	Professor Flavia Cicuttini
Associate Investigators	Dr Yuan Lim, Dr Andrew Teichtahl, Dr Jo Hall, Dr Yuanyuan Wang, Professor Stephane Heritier, Professor Jenny Doust
Location	Melbourne

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 how effective and acceptable a new treatment for hand osteoarthritis is. The new treatment is called methotrexate, which is a drug widely used to treat rheumatoid arthritis.

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.

We have previously conducted the METHODS study, which was a randomised clinical trial to determine the effect of methotrexate, comparing with an inactive dummy tablet (that is called a placebo) on reducing pain in people with symptomatic hand osteoarthritis and synovitis. The trial was concluded in 2022. It showed that Methotrexate at 20mg weekly over 6 months had a moderate but potentially clinically meaningful effect in reducing pain and stiffness in people with symptomatic hand osteoarthritis.

This METHODS-extend study (this study) aims to establish:

- whether the effect of methotrexate extends beyond 6 months,
- who is more likely to respond and
- whether it reduces joint damage in individuals with hand osteoarthritis and associated inflammation.

A total of 150 participants will participate in this project. It is an open label study, so everyone will be given methotrexate.

Medications, drugs and devices have to be approved for use by the Australian Federal Government, through the Therapeutic Goods Administration (TGA). Methotrexate is approved in Australia to treat rheumatoid arthritis, as well as other rheumatic conditions such as juvenile arthritis, lupus, psoriatic arthritis and polymyositis; methotrexate has been approved for these purposes for more than 25 years. However, methotrexate is not approved to treat osteoarthritis and joint swelling of the hands. Therefore, it is an experimental treatment for hand osteoarthritis with synovitis and must be tested to see if it is an effective treatment for this.

The research team conducting this study are specialist rheumatologists extensively experienced in the clinical use of methotrexate.

This research is being conducted by Monash University and Alfred Hospital. This research has been initiated by the study investigators, Professor Flavia Cicuttini, Dr Yuan Lim, Dr Andrew Teichtahl, Dr Jo Hall, Dr Yuanyuan Wang, Professor Stephane Heritier, Professor Jenny Doust,

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

The results of this research will be used by student investigators to obtain their Honours, Masters or PhD degree.

3 What does participation in this research involve?

Your participation in the study will last 12 months to examine the effect of methotrexate on reducing pain and reducing joint damage.

During the trial you will have 7 study visits (either through telehealth or face-to-face): at screening/baseline, 4 weeks, 8 weeks, 3 months, and then every 3 months thereafter until 12 months; and have 1 telephone interview at 2 weeks. Each study visit will take up to 60 minutes, and each telephone interview will take about 10 minutes.

Participation in this trial will have initially involved a screening process. You will have been screened for your suitability for the study over the phone by answering questions about your health. If you met the inclusion criteria, this Participant Information Sheet would have been mailed or emailed out to you.

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

Screening

1. You will have an interview with a research assistant and a study doctor, during which the study will be explained to you in detail and any question you have about the study can be answered.
If you agree to participate in the study, you will be asked to provide consent, by signing the consent form at the end of this document.

eConsent via telehealth
If you have this interview with a research assistant and a study doctor over telehealth, we will explain the PICF to you while you look at the copy that has been previously posted or emailed to you. We will provide opportunities to ask questions and if you would like to participate, then we will ask you to sign the consent form electronically in REDCap (i.e. Research Electronic Data Capture, a secure web platform to capture data for clinical research) which can be accessed on a computer, mobile phone, or tablet.

- You will open the survey and read through the consent form (which you have already received).
- When you get to the bottom of the consent form, you will have the opportunity to fill in your information and 'sign' your consent by typing in your name or by utilizing REDCap's 'Signature' field type on the survey.
- You will select "Next Page" and a read only copy of the consent will be generated that you can review, download, and print.
- At the bottom of the page, you will need to select "I certify that all the information in the document above is correct. I understand that clicking "Submit" will electronically sign the form and that signing this form electronically is the equivalent of signing a physical document".
- Submit the form.

Following the baseline screening (conducted via telehealth appointment), the research assistant will post a hard copy of the signed eConsent pdf form to you to ensure you have a copy.

2. You will undergo clinical assessments
    a. You will have blood tests at the Melbourne Pathology Laboratory
        (i) Full blood count, kidney function, liver function are required to assess your suitability for the study and monitor the safety of the treatment.
        (ii) Inflammatory markers, rheumatoid factor and anti-citrullinated peptide antibody are required to ensure you do not have inflammatory arthritis (e.g. rheumatoid arthritis) as this is part of the exclusion criteria for the study.
        (iii) HIV (also called the 'AIDS' virus), hepatitis B, hepatitis C and tuberculosis will be screened 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.

        The total amount of blood required for the above mentioned tests would not be more than 60ml.

b. You will have X-rays:
   (i) a chest X-ray (unless you have had a chest X-ray within the last 12 months) and
   (ii) hand X-rays (both hands) at the I-Med radiology.

3. You will complete questionnaires (take about 30 minutes of your time):
   a. information about yourself (employment, education, smoking history, marital status, menopausal status and whether you have had child(ren) (if relevant);
   b. your medical history including vaccination, medications, allergies, and alcohol history
   c. your quality of life
   d. hand pain and function

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.

Treatment Period

If you are eligible to participate, you will proceed to commencing the treatment period.

The study treatment is
- methotrexate 10 mg once a week for 4 weeks,
- followed by methotrexate 20 mg once a week for 4 weeks,
- then methotrexate 25 mg once a week for the rest of the study

as long as you are not experiencing any toxicity from the drug, as determined by the study doctor.

All study particpants will also take a folic acid 5 mg on days other than when study medication is taken (i.e. 6 times per week). Folic acid is one of the B vitamins (also known as vitamin B9) that pregnant women take. Folic acid supplementation has been shown to reduce the potential side effects of methotrexate (see Section 9 for more information).

During the Treatment Period you will have 6 study visits (either through telehealth or face-to-face): at 4 weeks, 8 weeks, 3 months, and then every 3 months thereafter until 12 months; and have 1 telephone interview: at 2 weeks. Each study visit will take up to 60 minutes, and each telephone interview will take about 10 minutes.

You will have the following assessments during the Treatment Period.
- A blood test will occur at 2, 4, and 8 weeks, and 3 months, and 3 monthly thereafter until 12 months. This blood test will include checking your full blood count, kidney function and liver function to ensure that it is safe to continue methotrexate, and the total amount of blood required for this safety monitoring would not be more than 10ml.
- Hand X-rays of both hands will occur at 12 months
- Questionnaires will be completed:
  - quality of life (at 6 months and 12 months);
  - medical history including vaccination, medications, allergies, and alcohol history (at 3 months and 3 monthly thereafter until 12 months);
  - hand pain and function (at screening, 6 months and 12 months)
- Self-reported height and weight
- Safety and adverse events (AEs) will be recorded at 2, 4, 8 weeks, 3 months and then 3 monthly thereafter until 12 months; pill counts will occur at 4 weeks, 3 months and 3 monthly thereafter until 12 months.
- The total volume of blood to be collected during the study will not exceed 130ml. For comparison, a standard blood donation is approximately 470ml (approximately 2 cups).

At the 6-month study assessment, methotrexate may be stopped by your study doctor if you have not had any pain improvement.

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

	Screening		**Treatment Period**						
	Screening / baseline assessment	**Post-screening**	**Week 2**	**Week 4**	**Week 8**	**Months 3**	**Months 6**	**Months 9**	**1 year**
Visit/phone contact	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Informed consent	X								
Blood tests		X							
Safety blood tests			X	X	*X*	X	X	X	X
Clinical visit	X		*X**	X	X	X	X	X	X
Hand x-ray		X							X
Chest x-ray		X							
Medical history incl vaccination	X								
Medications and allergies	X			X	X		X		X
Employment and education history	X								
Smoking history	X								
Alcohol history	X		*X*	X	*X*	X	X	*X*	X
Marital status and parity	X								
Menopausal status	X								X
Questionnaires									
Hand VAS	X			X		X	X	X	X
AUSCAN, FIHOA	X						X		X
HAQ	X						X		X
MHQ, SF-36	X						X		X
PainDETECT	X						X		X
Compliance and safety (AEs)			*X*	X	*X*	X	X	X	X
Dispense medication		X			X		X		
Pill count				X		X	X	X	X

* telephone follow up

If you choose to withdraw from this study after 6 months, you will be requested to have an early hand x-ray. You may also be asked to attend a follow-up visit to allow collection of information regarding your health status (questionnaires).

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.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way.

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.

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 and your progress every 3 months.

4 What do I have to do?

- You will need to attend all the study visits.
- You will need to commit to taking the drug regularly.
    - 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 from week 5 to week 8, and then 2½ 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 everyday, except on the day when study medication (methotrexate) is taken.

- Whilst involved in this study, you should avoid drinking too much alcohol as 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 per day.
- 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 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.
- You may not be able to donate blood while you are in the study.

5 Other relevant information about the research project

A total of 150 participants with symptomatic hand osteoarthritis, aged 40-75 years will be recruited from the community. All participants will receive methotrexate. There is no placebo (dummy pill) group. All participants will be followed up over 12 months to examine whether methotrexate affects symptoms and progression of hand osteoarthritis.

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 Alfred Hospital or Monash University.

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, 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.

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.

Side effects of methotrexate
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.

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)
- inflammation of the lungs,
- hair thinning, and
- nodule formations in skin or lungs (very rarely).

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).

Reproductive risks of methotrexate
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.

Side effects of folic acid
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)
    - If you develop any severe allergic reaction e.g. swelling of the face, throat, difficlty breathing or swallowing or shock, this is a medical emergency and please contact your nearest hospital emergency or call 000 immediately.

- stomach and intestinal 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.

Risks of ionising radiation
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.

Risks of study procedures
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. The collection and test of your blood sample are a mandatory component of the research.

Use of samples for future related and unspecified research
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 (blood tests that can be used to either predict, diagnose or prognosticate a disease) 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.

Blood samples will be labelled with a code assigned specifically for the participant, stored securely at Monash University for 15 years and will only be accessible by senior researchers.

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 caused by participation in the study 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
- Decisions made by the sponsor or by local regulatory/health authorities.

15 What happens when the research project ends?

At the completion of the trial, we will send you a follow-up letter to inform you of the findings of the study.

Methotrexate and folic acid will be provided to you during the trial for a 12 months 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 participants will be assigned a study code that will be used in this study. 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 Department of Public Health and Preventive Medicine, Monash University. Access to data will be limited to the chief investigators and support staff only. Coded (re-identifiable) data will be extracted from the database for analysis, and will be securely and strictly kept within Monash University network and only accessed by chief investigators of the study.

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 and for extended (related research) or unspecified (any future research) use**. Please refer to section 10 (page 9) for information about the potential future use of your blood sample.

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.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Sponsor, Monash University, the institution relevant to this Participant Information Sheet, Alfred Health, the Therapeutic Goods Administration, the Human Research Ethics Committee that reviewed this project, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

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 Monash University, Melbourne, Victoria. The project is being funded though 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 Monash University 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 Monash University.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Monash University, 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 have been approved by the Alfred Hospital Ethics Committee.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research 2007 (updated 2018)*. 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 Flavia Cicuttini (Monash University): 9903 0158, flavia.cicuttini@monash.edu

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 project officers on 9903 0553 or email us at jointstudy@monash.edu.

If you have medical concerns outside office hours, please contact Rheumatology Registrar at the Alfred Hospital. Telephone: 9076 2000 (Ask to speak to Rheumatology Registrar)

Clinical contact person

Name	Prof Flavia Cicuttini
Position	Head of Musculoskeletal Unit, School of Public Health and Preventive Medicine, Monash University and Head of Rheumatology, Alfred Hospital
Telephone	9903 0158
Email	flavia.cicuttini@monash.edu

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Cassandra Humble
Position	Research Governance Officer
Telephone	9076 3619
Email	research@alfred.org.au

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, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Alfred Hospital Ethics Committee
Position	HREC Executive Officer
Telephone	03 9076 3619
Email	research@alfred.org.au

Please quote the following Alfred Health project number: 714/23

Consent Form

Title	METHODS-Extend – An open label pragmatic trial to determine the efficacy and patient acceptability of methotrexate in hand osteoarthritis over 2 years.
Short Title	METHODS-Extend
Project Number	714/23
Project Sponsor	Monash University
Principal Investigator	Professor Flavia Cicuttini
Associate Investigators	Professor Stephane Heritier, Professor Jenny Doust, Dr Yuanyuan Wang, Dr Yuan Lim, Dr Andrew Teichtahl, Dr Jo Hall
Location	Melbourne

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 Monash University 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 all of the below:**

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

Declaration by Participant – for participants who have read the information

Name of Participant (please print) _____

Signature _____ Date _____

Declaration - for participants unable to read the information and consent form
See Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 Section 4.8.9. A legally acceptable representative may be a witness*.
Witness to the informed consent process
Name (please print) _____

Signature _____ Date _____
* Witness is not to be the Investigator, a member of the study team or their delegate. Witness must be 18 years or older.

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 Study Doctor/
Senior 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.

Form for Withdrawal of Participation – Person Responsible

Title	METHODS-Extend – An open label pragmatic trial to determine the efficacy and patient acceptability of methotrexate in hand osteoarthritis over 2 years.
Short Title	METHODS-Extend
Project Number	714/23
Project Sponsor	Monash University
Principal Investigator	Professor Flavia Cicuttini
Associate Investigators	Professor Stephane Heritier, Professor Jenny Doust, Dr Yuanyuan Wang, Dr Yuan Lim, Dr Andrew Teichtahl, Dr Jo Hall
Location	Melbourne

Declaration by Person Responsible

I wish to withdraw the participant from taking part in the above research project and understand that such withdrawal will not affect the participant's routine treatment, relationship with those treating them or their relationship with Monash University and Alfred Health.

Name of Participant (please print)

Name of Person Responsible (please print)

Relationship of Person Responsible to Participant

Signature of Person Responsible _____ Date _____

Name of Study Doctor/
Senior Researcher (please print) _____

Signature _____ Date _____

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