PARTICIPANT INFORMATION SHEET
A randomised trial of krill oil for osteoarthritis of the knee

1. Invitation
You are invited to participate in a research study investigating an experimental treatment for knee pain. The study is being conducted at the Menzies Institute for Medical Research (Hobart), Alfred Hospital (Melbourne), Royal North Shore Hospital (Sydney), The Queen Elizabeth Hospital (Adelaide) and the Fiona Stanley Hospital (Perth), by Professor Graeme Jones, Associate Professor Anita Wluka, Associate Professor Catherine Hill, Professor Lyn March, Dr Helen Keen, Dr Laura Laslett and Professor Flavia Cicuttini.

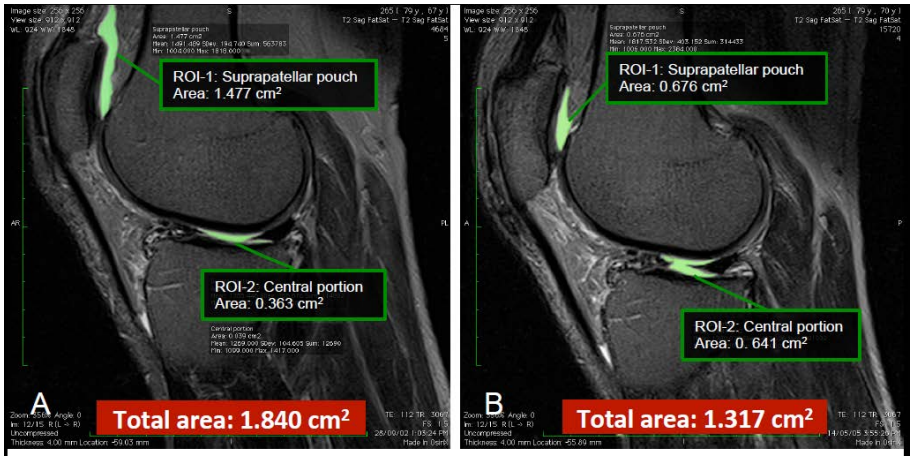
Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

2. What is the purpose of this study?
This study will examine a new treatment for knee pain. The treatment is called krill oil. This study will determine whether treating people with krill oil will improve knee pain and slow down the progression of knee osteoarthritis.

3. Why have I been invited to participate?
We will be studying up to 260 people. People can be included in the study if they:

- ✓ Are ≥ 40 years;
- ✓ Have significant knee pain on most days for more than 6 months;
- ✓ Have an abnormality present on a MRI (magnetic resonance imaging) scan; and
- ✓ Have clinically defined knee osteoarthritis

4. What knee abnormality do I need to be eligible to participate?
We are interested in people with fluid levels inside their knee joint that are higher than normal (effusion), or swelling of the lining of the cartilage (synovitis). This is known to be related to inflammation and to be a significant contributor to knee pain. This is commonly seen in people with knee pain.



Baseline **2.6 years later**

Figure 1: Example of changes in effusion-synovitis area (cm^2). Effusion-synovitis size decreased from baseline to follow-up 2.6 years later (A-B)
Overall, effusion size is smaller at follow–up MRI.

5. What type of drug is krill oil?

Krill oil is extracted from Antarctic Krill (*Ephausia Superba*, a zooplankton crustacean). Like fish oil, it is high in certain types of fatty acids, although the chemical structures of the fatty acids differ (phospholipids, rather than triacylglycerol or fatty acid ethyl esters); but unlike fish oil, it also naturally contains antioxidants (predominantly astaxanthin). Additionally, bioavailability of krill oil is better than fish oil, as comparable amounts of fatty acids are obtained from lower doses of krill oil compared to fish oil.

In animal studies, krill oil is more effective than fish oil in reducing the severity of arthritis.

Krill oil is an oily liquid, sealed inside a glycerin softgel. This is swallowed daily with liquid (water, juice) by mouth.

6. What if I don't want to take part in this study, or if I want to withdraw later?'

Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

New information about the treatment being studied may become available during the course of the study. Should any significant new findings that may affect your willingness to continue in the study, you will be kept informed.

If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason.

7. What does this study involve?

If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

Screening visit

All patients will be asked about their previous medical history and a medical examination will be performed, and they will be asked to provide a blood sample. All patients will be asked to complete a survey relating to knee pain. This survey has questions on symptoms, the degree of knee stiffness and pain and the effect the condition has on a patient's daily activities and quality of life. Patients will also be asked a separate question to assess the amount of knee pain they have. Those with a pain score in the moderate range will be booked in for a knee MRI scan and a knee X-ray, and will be given a date for a baseline visit.

If you have a normal MRI scan you will not be asked to continue in the study.

Continuing in the study

This study will go for 6 months. We will need to see you at the start of the study (month 0), and at 3 and 6 months. Measures will be done at the Menzies Institute for Medical Research, Alfred Hospital, Royal North Shore Hospital, The Queen Elizabeth Hospital and/or the Fiona Stanley Hospital.

The following procedures/measures will be performed:

- A blood test will occur at screening, 3 and 6 months;
- A knee x-ray will occur at screening;
- An MRI scan will occur at screening and 6 months;
- Patients will receive krill oil softgels (tablets) or a matching placebo treatment at baseline and the 3 month visit;
- Questionnaires about knee pain, knee function, your views on overall improvement in pain, and pain at other sites will be asked in clinic (baseline, 3 and 6 months) or posted to you monthly (1, 2, 4, 5 months); Clinic visits will occur at baseline, 3 and 6 months. At this time we will assess your leg strength, and measure height and weight, and ask about pain elsewhere. We will also send you questionnaires about your use of medications, any side effects, use of services, wellbeing, joint replacement and quality of life and may ask you to take part in

assessment of the point at which sensations become painful (selected sites only);

If you choose to withdraw from this study before 6 months you will be requested to have an early MRI scan.

Study participants will also be asked to allow study researchers to access health information from Medicare and Pharmaceutical Benefits Scheme (PBS) datasets, the National Death Index, the national joint replacement register, and state-based hospital emergency databases and hospital inpatient databases. The purpose of this is to allow study researchers to access health information on use of medical services, prescription medicines, whether participants have had joint replacements and if they have required admission to emergency departments or hospitals as inpatients.
This will be for the period 01 Jan 2016 to 31 December 2020.

'Randomised trial': Sometimes doctors don't know the best way of treating patients with a particular condition so comparisons need to be made between different treatments. To do this, study participants are put into groups and given different treatments, and the results are compared to see whether one treatment is better. To ensure the groups are similar to start with, a computer allocates each study participant into a group randomly, like the flip of a coin. Neither the study investigators nor the study participant can decide which treatment the participant receives.

All study participants will receive bottles of identical softgels to take daily. These softgels will contain either krill oil or placebo.

As this is a 'blind trial' all study patients will be unaware whether the softgels they receive will contain krill oil or inactive ingredients (placebo) until we have completed all data collection for the entire study.

Therefore, there are a total of 4 visits to your local medical research institute required as part of this study, and we will ask you to do monthly surveys during the study.

8. How is this study being paid for?

The study is funded by National Health and Medical Research Council (NHMRC) of Australia (Grant #1102732).

All of the money being paid by the NHMRC to run the trial will be deposited into an account managed by the University of Tasmania, Alfred Hospital, Royal North Shore Hospital, The Queen Elizabeth Hospital and/or the Fiona Stanley Hospital. No money is paid directly to individual researchers.

9. Are there risks to me in taking part in this study?

Krill oil is a very safe medication, with few known side effects. Krill oil may reduce insulin sensitivity by a small amount, although whether this would be large enough to make a difference to blood sugar control in people with diabetes is not clear. However, if you have diabetes, you may want to discuss this with the study doctor and your GP before starting the study.

Krill oil is not suitable for people who already use anticoagulants (eg warfarin), high dose aspirin or non-steroidal anti–inflammatory drugs (NSAIDs). If you are already using these medications, you will not be able to take part in this study.

Krill oil is not suitable for people who have allergies to seafood; if this applies to you, you will not be able to take part in this study.

There is a small amount of radiation exposure associated with a knee x-ray. This amount of radiation is unlikely to be associated with increased risk of disease and is less than the current National Health and Medical Research Council guidelines. Having blood taken causes minimal risk, but there may be a chance of discomfort, feeling faint and bruising. MRI scans may be claustrophobic, but are otherwise considered safe.

The effect of the study medication on an unborn baby is unknown. If you are a woman of childbearing age and there is any possibility that you are pregnant, the researchers will need to perform a urine pregnancy test before you start in the study.

We are asking questions about health and wellbeing in this study. Some people find that focusing on aspects of ill health raises concerns for them. If you have any concerns about health issues which arise, please contact your GP.

In addition, there may be risks associated with this study that are presently unknown or unforeseeable. In spite of all reasonable precautions, you might develop medical complications from participating in this study.

10. What happens if I suffer injury or complications as a result of the study?

If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment.

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies. You do not give up any legal rights to compensation by participating in this study.

If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital.

11. Will I benefit from the study?

This study aims to further medical knowledge and may improve future treatment of knee osteoarthritis, however it may not directly benefit you.

12. Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything, and we do not pay study participants to take part in the study.

13. How will my confidentiality be protected?

Of the people treating you, only study staff will know whether or not you are participating in this study. Any identifiable information that is collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law. Only the study researchers will have access to your details and results that will be held securely on confidential password protected databases and access will be limited to the researchers and support staff only. No biological specimens taken from patients will be kept or analysed except as listed.

14. What happens with the results?

If you give us your permission by signing the consent document, we plan to discuss/publish the results with the ethics committee for monitoring purposes, peer-reviewed journals, presentations at conferences and/or other professional forums.

In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you, if you wish.

15. What happens to my treatment when the study is finished?

Krill oil is available commercially. If you wish to continue krill oil, you will need to purchase it.

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

When you have read this information, study research assistants will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact XX on 6226 xxxx.

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

This study has been approved by the Tasmanian Health and Medical Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study should 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 [HREC project number].

Thank you for taking the time to consider this study.

This information sheet is for you to keep.