Participant Information Sheet

Title	Efficacy and safety of intra-articular botulinum toxin A versus corticosteroid injections in knee osteoarthritis: a randomised control trial
Short Title	Intra-articular botulinum toxin A in knee osteoarthritis
Coordinating Principal Investigator	Dr Stephanie Babic
Associate Investigator(s)	Dr Arnout Faveere Mr William Blakeney Mr James Plant
Location	***(<Insert Site>)***

1 Introduction

You are being invited to participate in a research project because you have knee osteoarthritis and you are attending ***[insert site name]*** for treatment of this condition. This Participant Information Sheet explains what will be involved should you decide to participate. Participation in this research is entirely voluntary. You will receive the best care whether or not you choose to participate. Please read the information carefully and ask any questions you might have. You may also wish to discuss the project with your GP, a relative or a friend. You will be given a copy of the Participant Information Sheet and Consent Form to keep.

If you decide you would like to participate in this research, you will be asked to sign the consent section to show that you:

- Understand what you have read;
- Consent to take part in the research project;
- Consent to the treatment options described; and
- Consent to the use of your personal and health information as described.

2 What is the purpose of this research?

The aim of this research is to investigate the effectiveness and safety of knee joint injections with botulinum toxin A (a medication commonly known as ‘Botox’) compared with knee joint injections with triamcinolone (a corticosteroid medication).

The use of corticosteroid knee joint injections in knee osteoarthritis is common in Australia. However, there is current research evidence showing that Botox injections may also be a good treatment option for knee osteoarthritis. The evidence so far is promising but limited and so the main aim of this project is to conduct an Australian trial to see if Botox injections are better at relieving pain and improving function in knee osteoarthritis than corticosteroid injections. A secondary aim is to compare the safety profiles of Botox versus corticosteroid injections for knee osteoarthritis and see which has fewer side effects.

Botox A is currently approved in Australia for use in multiple conditions including the treatment of chronic migraines, limb spasticity, excessive sweating from the armpit and certain eye

conditions. It is also used routinely for cosmetic treatment including for the improvement in the appearance of facial wrinkles or lines. **It is not currently approved for use as a knee joint injection for osteoarthritis.** Therefore, it is an experimental treatment for knee osteoarthritis and this means it must be tested to see if it is effective.

This research project has the potential to add a significant treatment option to the current Australian treatment guidelines for knee osteoarthritis.

3 What does participation in this research involve?

Participation is voluntary and requires signing a consent form prior to participating. If you choose to participate, you will be required to **complete several short questionnaires** prior to receiving an injection.

You will then be **randomly assigned to receive a knee joint injection** which will contain either:
(a) Botox A – botulinum toxin A (100 units) reconstituted with 5ml of 0.9% normal saline; or
(b) Corticosteroid – triamcinolone acetonide (40mg) and bupivacaine 0.25% (a local anaesthetic) (30ml).

You will receive the injection under ultrasound guidance by a trained radiologist in the Radiology Department of ***[insert site name]***. We do not know which treatment is better for knee osteoarthritis and so we must compare by putting participants into two separate groups. We assign participants randomly to each group to ensure that there is no selection bias in either group. This gives us the best chance of comparing both treatment options without introducing bias into the experiment.

You will be unaware of which injection you have received and the study doctors will also be unaware of which injection you have received. This is to make sure that results are interpreted in a fair and unbiased way. The only person who will know which medication you have received will be the radiologist performing the injection so that he or she is able to perform an appropriate medication check prior to injection.

You will then have **several follow-up appointments** after your injection and will need to complete several short questionnaires at each appointment. The follow-up appointments occur at **2 weeks, 6 weeks, 3 months, 6 months and 12 months after the injection.**

The questionnaire responses cover several areas relating to your knee osteoarthritis, including level of pain, physical function, medication use and quality of life. One of the questionnaires covers some aspects of mood/mental wellbeing as part of a quality of life measure. If your score on this dimension is of concern regarding your mental health, we will contact you and provide details for access to psychological support. With your permission, we will also contact your GP to let them know. In the unlikely circumstance that your life or wellbeing seems at imminent risk, we will advise you to attend your nearest emergency department for an urgent mental health review and may need to contact the relevant authorities if needed.

There will be no restrictions on the medication you can use after you have had the injection. Specifically, there will be no restrictions on the medication you can use for pain relief after the injection. However, **you will be required to record all pain medication used** so that we are able to assess the effectiveness of each type of injection at improving pain levels.

4 Cost of participation

There is no cost to you to participate in this research project. You will not be paid for participating. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

5 Voluntary participation and withdrawal

Participation in any research project is entirely 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. Your decision will not affect your routine treatment, your relationship with those treating you or your relationship with ***[insert site name]***.

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

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 doctor 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 up to the time you withdraw will form part of the research project results.

6 Possible benefits of participation

We cannot guarantee or promise that you will receive any benefits from this research. However, possible benefits may include a decrease in the pain you experience from your knee osteoarthritis and/or an improvement in your knee function.

Participation in this project may have no direct benefit for you but may help with better management of knee osteoarthritis for the Australian community in the future.

7 Possible risks of participation

Medical treatments often cause side effects. **You may have none, some, or all of the side effects listed below.** The side effects experienced 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 symptom you experience even if it is not listed on the side effects list below.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. Your study doctor will discuss the best way of managing any side effects with you.

Possible side effects

Injection:
Common (10%):

- Pain, swelling and/or bruising at injection site

Uncommon (less than 1%):

- Joint infection
- Bleeding into the joint

Triamcinolone:

Common (1 – 10%):

- Temporary flare of pain or inflammation in the joint
- Headache
- Palpitations (usually < 24 hours)
- Hot flushes (usually < 24 hours)
- Mood / sleep disturbances (usually < 24 hours)

Uncommon (0.1 – 10%):

- Temporary blood sugar elevation
- Temporary electrolyte imbalances
- Thinning of skin and soft tissue at injection site
- Whitening or lightening of skin at injection site
- Tendon weakening and/or rupture
- Cartilage damage
- Thinning of nearby bone (i.e. osteoporosis)
- Death of nearby bone (i.e. osteonecrosis)
- Severe allergic reaction (i.e. anaphylaxis)

Botox A:

Common (1 – 10%):

- Headache
- Flu-like symptoms, including fatigue and fever
- Temporary increase in blood pressure
- Constipation
- Nausea
- Anxiety

It is very unlikely but it is possible for the toxin to spread in your body and cause the following symptoms (less than 1%):

- Muscle pain / weakness / stiffness
- Visual changes / eye dryness or excessive tears
- Difficulty swallowing
- Difficulty speaking
- Difficulty breathing
- Cardiac arrhythmia
- Urinary incontinence
- Rash
- Severe allergic reaction (i.e. anaphylaxis)

8 Privacy and confidentiality

The information gathered about you by the investigator or obtained during this project will be held by the investigator in strict confidence as far as the law allows. All the people who handle your information will comply with the *Privacy Act 1988* (Cth). Your study data will be held securely at ***[insert site name]***. Where the data is electronic, it will be held on secure servers in a 're-identifiable' format. This means the research data is 'coded' with your data held against a unique study code, not your name. Once the data for the whole study is complete, the code

link that matches your name and study code will be deleted meaning it will be impossible from that point forward to match you to your data (i.e. the research data will be 'non-identifiable').

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

Information about your participation in this research project may be recorded in your health records.

In accordance with the *Privacy Act 1988* (Cth) and other relevant Australian 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.

9 Complaints and compensation

In the event that you suffer an expected or unexpected side effect or medical accident during this project that arises from your participation, you will be offered all full and necessary treatment by ***[insert site name]***. Participation in this project does not alter any right to compensation that you may have under statute or common law.

10 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 Royal Perth Hospital HREC.

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.

11 Contacts for further information

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

a) Clinical contact

If you have questions about 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 study doctor on [*phone number*] or Department of Orthopaedics Research Assistant at ***[insert site name]*** on XXXX XXXX.

b) HREC

This project has been granted ethical approval by the Royal Perth Hospital (RPH) Human Research Ethics Committee (HREC). If you have any concerns about the conduct of the project or your rights as a research participant, phone (08) 9224 2292 or email: EMHS.REG@health.wa.gov.au and quote the ethics approval number RGS0000004752.

c) Research Governance

For matters/complaints related to research at the site where you are participating please contact: Research Governance - phone XXXX XXXX or email: ……

Consent Form

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I have read the Participant Information Sheet and 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 ***[insert site name]*** concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential as far as the law allows.

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.

Name of Participant (please print) _____

Signature _____ Date _____

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.

Form for Withdrawal of Participation

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Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with ***[insert site name]***. I understand that data collected up until the time of withdrawal will continue to be used in the study.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project 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 withdrawal from the research project.