Participant Information Sheet/Consent Form

Royal Perth Hospital

Title	***Long-term Outcomes of Lidocaine Infusions for PostOperative Pain (LOLIPOP) Pilot Study***
Short Title	***LOLIPOP Pilot Study***
Protocol Number	*Protocol Version 1.2*
Project Sponsor	*Royal Perth Hospital*
Coordinating Principal Investigator/ Principal Investigator	*Professor Tomas Corcoran*
Associate Investigator(s)	*Dr Andrew Toner*
Locations	*Royal Perth Hospital*

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project as you are due to undergo breast cancer surgery. This research project is testing a new treatment for the prevention of persistent pain at the site of surgery lasting for three months or more. The new treatment involves steady administration of lidocaine, a commonly used local anaesthetic drug, into your body over a period of hours – a lidocaine infusion. 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. 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.

2 What is the purpose of this research?

After breast cancer operations a quarter to a half of people will continue to have some degree of chronic pain at the site of surgery for 3 months or longer. For most of these people the pain will be mild, but in some it can be moderate or severe. We are therefore interested in finding

medications that can be administered around the time of surgery to prevent the development or reduce the severity of chronic pain.

Lidocaine infusions have already been tested in 4 small studies of patients undergoing breast cancer surgery, and appear to be safe and effective at reducing chronic pain rates. However, small studies can be misleading and larger studies conducted to a very high standard are required before lidocaine infusions can be recommended as routine for breast cancer or other types of surgery. This study will assess whether lidocaine is effective for breast cancer surgery. It will also assess how practical it will be to conduct a large international trial in patients having a wide variety of surgery.

This research has been initiated by the study doctor, Professor Tomás Corcoran in collaboration with Professor Cristobel Saunders, the lead breast surgeon for the trial.

3 What does participation in this research involve?

If you agree to participate in this study then you will be randomly allocated (much like the toss of coin), to receive a lidocaine or placebo (inactive salt water solution with no drug) infusion. You have a 50% chance of receiving lidocaine, and a 50 % chance of receiving the placebo. This will be administered into your veins from the start of your general anaesthetic until you arrive in the recovery area. At this point the infusion will be continued via a small plastic tube (cannula) placed under the skin of your tummy for 12 hours after your surgery (or earlier if you are ready for discharge). This infusion will be controlled by a small pump worn around the waist. Your mobility will not be restricted.

You will be participating in a double-blind study. This means that neither you nor your study doctor will know which treatment you are receiving. However, in certain rare circumstances your study doctor can find out which treatment you are receiving.

We will collect information relevant to pain, nausea and activity levels using brief questionnaires before the start of your surgery, in the postoperative recovery area and on the 1st and 2nd day after your surgery. During the lidocaine or placebo infusion you will be asked some simple ***Yes/No*** style questions at 4 hourly intervals to assess any side-effects. Routine observations (pulse rate, blood pressure, temperature and oxygen levels) are always taken every 4 hours in the early period after surgery, and so we will ask the side-effect questions at the same time.

We will take two additional blood tests (approximately a tablespoon each time), once in the postoperative recovery area and once 6 hours after your surgery ends. Where possible, these will be taken from a dedicated study cannula and will involve no further needle insertions.

Following discharge from hospital you will be followed up by phone at 30 days, three months and six months post-surgery. After 30 days we will ask you about the presence of surgical site infections and whether you have required further surgery or admissions to hospital. At both 3 and 6 months, we will ask about the presence or absence of pain, the characteristics of any pain that is present and about your use of pain killers. After 6 months, any involvement in the study will be over although the research staff will still be available to answer your questions should you have any.

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 desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that you inform them of your participation in this research project.

4 What do I have to do?

You will be required to wear a mobile syringe pump placed in a small pouch around the waist for 12 hours after your surgery, which will deliver the study drug via a cannula placed just under the skin.

5 Other relevant information about the research project

176 patients will be recruited at a number of hospitals including Royal Perth Hospital and Fiona Stanley Hospital.

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

No. 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 in any way affect your routine treatment, your relationship with those treating you or your relationship with Royal Perth Hospital.

7 What are the alternatives to participation?

You are free to decline to participate and receive your treatment as normal at this hospital. As lidocaine infusions are not currently part of routine practice it is unlikely you will be offered this option by your anaesthetist. There are no other treatments currently proven to reduce the development of chronic pain after breast surgery.

8 What are the possible benefits of taking part?

We cannot guarantee that you will receive any benefits from this research. However, benefits may include a reduction in acute and persistent pain after surgery and a reduction in side effects relating to the use of strong pain killers. It is also possible that lidocaine infusions could lead to a better quality of recovery and less wound infections. As a result of the follow up process, all patients may benefit from research staff paying close attention to detail during the recovery period.

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

The drug Lidocaine has been approved in Australia by the Therapeutic Goods Administration (TGA) branch of the federal government for several decades.

Lidocaine infusions under the skin, close to nerves and into veins are used commonly in everyday anaesthesia practice. In clinical trials targeting the reduction of acute pain only, lidocaine infusions into veins for up to 24 hours after surgery have been extensively investigated in over 2,500 patients. Although side-effects have not always been specifically screened for, very few significant problems have been reported with such infusions. However, if lidocaine reaches a high enough concentration in the blood it can cause the following side-effects.

- Tingling or numbness (most often experienced around the mouth)
- Ringing in the ears
- Mild changes in your vision
- Dizziness

- Strange taste in the mouth
- Being aware of your own heartbeat
- Feeling faint
- Twitching in the muscles
- Confusion
- Short Seizures
- Abnormal Heart Rhythms
- Significant drops in blood pressure

We have designed the dose of the lidocaine infusions in this study to make it extremely unlikely that such side-effects occur. In addition, an investigator or nurse will check with you every 4 hours that the study drug infusion is running to ensure no side-effects are developing. In the unlikely circumstance that they do occur, the infusion will be stopped and you will be closely monitored whilst the levels in your bloodstream fall over 1-2 hours. A specific antidote to lidocaine side-effects will also be readily available on the ward.

10 What will happen to my test samples?

We plan to collect two samples of blood for each patient enrolled in the study. This is to look at the concentration of the lidocaine and any other local anaesthetic drug in the blood stream following the operation to make sure it is at an appropriate level. The blood samples will be de-identified, frozen and stored. At the end of study enrolment, the frozen samples will be analysed by a single laboratory and then destroyed

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 that is 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?

Yes. This project has very few restrictions relating to other treatments. If any of these restrictions apply they will be explained by your study doctor.

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 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 by the sponsor 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. The study investigators always have your safety and wellbeing as their top priority and will always act in your best interests. Accordingly, we have designed this trial in such a way to maximise safety. The trial may be prematurely stopped for reasons such as:

- Unacceptable side effects
- The drug being shown not to be effective
- The drug being shown to work and not need further testing

15 What happens when the research project ends?

As the treatment involves only a therapy during your hospital stay and the follow up period will last for 6 months, there is no expectation that you should need to be involved afterwards. Results of the study will be published in a medical journal with international readership. These studies will be available to mainstream media who may wish to report them. A plain language summary will be available to study participants on request.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

All of the data collected will be non-identifiable. This means that anybody looking at the data will be unable to work out that it has come from you.

The data will be kept on an online database, to which only research staff will have access. In the future, the data collected could be used in other research but this will remain non-identifiable. The data will be kept for at least 15 years.

By signing the consent form you consent to the study doctor 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. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

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.

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, Royal Perth Hospital, the institution relevant to this Participant Information Sheet, *Royal Perth Hospital*, 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 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. At the outset of the study you will be assigned a specific study number which will be stored against your data in the database. When looking at the database, nobody will be able to identify that the specific study number is you thus maintaining confidentiality.

Information about your participation in this research project will be recorded in your health records. In accordance with relevant Western Australia 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.

Any information obtained for the purpose of this research project, and any future research, that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

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.

If your complaints relate to your treatment by members of staff (doctors, nurses etc) then you can speak to research staff who will advise you of your options or contact the patient advisory group in the hospital if you would prefer.

No provisions have been made in this trial to offer patients who suffer an adverse event monetary compensation, but the absence of such a provision does not remove your rights to seek compensation under common law.

18 Who is organising and funding the research?

This research project is being conducted by Professor Tomás Corcoran. Study costs will be covered locally with no external sources of funding or influence. No member of the research team will receive a personal financial benefit from your involvement in this research project.

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 HREC of the South Metropolitan Health Service.

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

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), you can contact the principal study doctor. Professor Tomás Corcoran, on (08) 9224 1036.

If you should have any complaints or concerns about the way in which the study is being conducted, you may contact the Chair of the South Metropolitan Health Service Human Research Ethics Committee on 6152 2064. Alternatively, you may also contact the Research Governance Officer - at East Metropolitan Health Service on 9224 2260.

Consent Form - *Adult providing own consent*

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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 *Royal Perth Hospital* 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.

Name of Participant (please print) _____

Signature _____ Date _____

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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.