Northern Health **Research Project Consent**	AFFIX PATIENT IDENTIFICATION LABEL HERE U.R. NUMBER: _____ SURNAME: _____ GIVEN NAME: _____ DATE OF BIRTH: _____/_____/_____ SEX: _____

PARTICIPANT INFORMATION SHEET/CONSENT FORM

Title	*Ivabradine in the prevention of Peri-operative Myocardial Injury*
Short Title	*IPMI Trial*
HREC No.	
Protocol Number	
Project Sponsor	*Department of Cardiology, The Northern Hospital*
Coordinating Principal Investigator/ Principal Investigator	*A/ Prof William van Gaal*
Associate Investigator(s) *(if required by institution)*	*Dr Dominic Chow, Prof Raphael Hau, Dr Carol Chong*
Location *(where CPI/PI will recruit)*	*Northern Health*

Participant Involvement In Research Project: *(to be completed when enrolling participants)*

Start Date:____/_____/_____ **Finish Date:** _____/_____/_____

Part 1 What does my participation involve?

1. Introduction

You are invited to take part in this project because you are about to undergo an orthopaedic surgery (surgery of the bones or joints).

This Participant Information Sheet/ Consent Form tells you about the research project. It explained the tests and treatments invovled. This information will allow you to decide if you wish to participate in this research.

Please read this information carefully. Ask questions about anything you do not understand. Before undertaking this research, you might want to discuss with a relative or a friend.

Participation in this research is voluntary. If you do not wish to take part, you do not have to. You will receive the best possible care regardless.

If you decide to participate in this research, 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?

Undergoing any kind of surgery imposes stress on the body. During and after a major operation (such as bones or joint operations, also known as orthopaedic operations), our body increases its heart rate as a response to the stress of the surgery. As the heart pumps faster to manage the stress, it can sometimes damage itself in the process. A previous study observed that up to 52% of patients undergoing major orthopaedic demonstrated some evidence of injury to the heart, and these patients have poorer clinical outcomes.

This has led to previous studies examining the benefits of heart rate lowering agents to prevent damage to the heart after surgery, to improve clinical outcomes. Unfortunately, many heart rate loweing agents have a common side effect of lowering the blood pressure as well. Hence, whilst these trials demonstrated promising benefit in reducing damage to the heart, they caused significant problems with low blood pressure.

Ivabradine (Brand Name: Coralan) is a relatively new agent that reduces heart rate, but does not drop blood pressure. It is currently approved for use in Australia for another condition called chronic heart failure. But given its unique properties, we postulate that it can reduce damage to the heart after a major operation as well, without the negative effect of causing low blood pressure. As a result, this trial was conceived to examine this effect.

3. What does participation in this research involve?

Before you begin the study, detailed information about the study medicine, procedures, and other relevant information will be given by research staff. You are encouraged to ask questions until you fully understand the nature and requirements of the study.

If you wished to be assessed for elligibility of this study, before any procedures are undertaken, you will be asked to sign a consent form. Then, your clinical information will be assessed for elligibility.

Although postulating that Ivabradine (the study medicine) will reduce heart rate and injury is theoretically logical, the effect needs to be proven in a trial. Therefore, in this study, all participants will be randomly allocated into two groups: one will receive standard medical care, and the other will receive ivabradine in addition standard medical care. The results will then be compared. The allocation is random (by chance, like flipping a coin).

The total period of this study involvement will be approximately 1 year. After providing informed consent, if you meet elligibility for this study, study activities will be undertaken as detailed below:

<u>Before your operation: Screening & Randomisation</u>

- Basic information will be recorded, including age, demographics, type of planned surgery, pre-existing medical conditions, pre-existing medications, height and weight, blood pressure, heart rate, breathing rate, temperature, and a tracing of your heart (electrocardiogram).
- A blood sample will need to be collected from you before you undergo the operation.
- You will then be randomly allocated to either receive Ivabradine (study drug) or not.
- All patients, regardless of allocated group, will be monitored and given best standard of care.
- For participants receiving Ivabradine, medication will commence between 2 and 48 hours before surgery.

This process will take about an hour.

During your operation: Day 0 (could be the same day as screening and randomisation)

- Your blood pressure, heart rate, and a tracing of your heart will be recorded.
- Study medication doses will be adjusted for you during this time.

This process will take about 10 minutes.

After your operation: Day 1

- Your blood pressure, heart rate, and a tracing of your heart will be recorded.
- A blood test to measure heart damage will be collected from you.
- Study medication dose adjustments might be necessary.

This process will take about 10 minutes.

After your operation: Day 2

- Your blood pressure, heart rate, and a tracing of your heart will be recorded.
- A blood test to measure heart damage will be collected from you.
- Study medication dose adjustments might be necessary.

This process will take about 10 minutes.

After your operation: Day 3

- Your blood pressure, heart rate, and a tracing of your heart will be recorded.
- A blood test to measure heart damage will be collected from you.
- Study medication dose adjustments might be necessary.
- Participants receiving study drug will continue on medication for another 4 days.

This process will take about 10 minutes.

Subsequent follow-ups:

- All participants will receive a phone call at 30-day, 6-month, and 1-year timepoints, in the form of a short telephone interview, to ensure the safety of all participants.

Each telephone interview will take approximately 10 minutes.

4. What do I have to do?

It is important for your safety to inform us of your complete medical history and all medications/ suplpements/ herbal preparations that you are taking. If you notice any health problems, please notify the study team immediately.

You must take the study medication as instructed by the study team. All other regular medications should be continued as usual. If you need to start a new medication, please consult your doctor first.

5. Other relevant information about the research project

Overall, approximately 200 patients will take part in this study.

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

Participation in any research project is voluntary. If you do not wish to participate, you do not have to. If you decide to withdraw from the study at any stage, you may do so as well.

If you decide to participate, a copy of this Participant Information and Consent Form (signed by yourself) will be given to you to keep.

Your decision to participate or not will not affect your routine treatment, or your relationship with your treating doctor or Northern Health.

7. What are the alternatives to participation?

You do not have to participate in this research project to receive treatment at this hospital. You will still receive standard medications and treatment, as the study medication is given in addition to these. Your study doctor will discuss these options with you before you decide whether or not to participate 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, possible benefits include prevention of heart injury or stress of surgery on the heart, and more frequent follow-up than other patients. If addition of Ivabradine to existing medical therapy is proven to be beneficial, members of the society in the future will benefit from this treatment regime as well.

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

Medical treatments often cause side effects. If you are allocated to receive study medication, you may have none, some or all of the side effects listed below, and they may be mild, moderate or severe. If you experience any of these side effects, or are worried about them, discuss with your study doctor. Your study doctor will also be looking out for these side effects. They include:

- Bright vision/ seeing lights (Frequency 14.5%)
- Low heart rate (Frequency 3.3%)
- Headache (Frequency 2.2%)

Several medications should also not be started with the study medication. They include:

- Cyclosporin: This is a medicine used to suppress the immune system
- Erythromycin or Clarithromycin: These are antibiotics used to treat bacterial infection
- Anti-retroviral drugs used for the treatment of HIV
- Anti-fungal treatments such as ketoconazole

Risk of procedures/ study medication

Having a blood sample taken may cause discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

There is no adequate data on the effect on ivabradine in pregnant women. However, in animal studies, it appeared to cause birth deformities. As such, all male participants are not allowed to

father a child or donate sperm for the at least 3 months after the last dose of study medication. All sexual activity must comply with highly effect contraception streategies (for example, condom AND intra-uterine device). All female participants are not alllowed to get pregnant, try to become pregnant, or breastfeed, until at least 3 months after the last dose of study medication. A breach in any of these conditions should be discussed immediately with your study doctor.

10. What will happen to my test samples?

By consenting to take part in this study, you also consent to the collection and testing of your blood samples for this research only.

The total volume of blood taken will be approximately 35mL. For comparison, a standard blood donation is 470mL. Blood samples collected for the assessment of your health status (such as liver and kidney function tests) will be processed by the laboratory at the study site. These samples will be labelled with your personal details, and destroyed once the analysis is complete.

Blood samples taken for testing of your heart function, will be sent to Covance® Singapore for testing. These samples will not contain any personal information that can directly identify you, but will be labelled with your unique study number. This means that the samples are considered re-identifiable. Only authorised laboratory staff will have access to your samples. The testing will use up most of the sample. If there is any left, they will be stored for up to 5 years, in case any of the original analysis has to be repeated. Any remaining samples will be destroyed after 5 years. No genetic testing will be done on any of your blood samples.

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 your 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 interest 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 should continue to take all usual medications. 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, 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.

13. What if I withdraw from this research project?

If you decide to withdraw from the study, 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 trtained to ensure that the results of the research project can be measured properly and to comply with the law. You should be aware that data collected 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. They include:

- Unacceptable side effects
- The drug is shown to be not effective
- The drug is shown to work, and no further study is required
- Decisions made by local regulatory authorities

15. What hppens when the research project ends?

A final report will be generated, and the Principal Investigator will share the results with you if requested. The disclosure and/ or any published results will be available to all participants when requested. It is usual for a number of months to elapse before definitive results of this type of study are available. These may be published in medical journals that are available to the public.

Part 2 How is the research project being conducted?

16. What will happen to information about me?

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 that can identify you will remain confidential. Personal data, which may be sensitive, will be collected and processed, but only for research purposes related to this study. All data collected about you will be coded with your study number. All records pertaining to this study will be stored in a secure location for at least 15 years, after which they may be destroyed.

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 help at this and other health services for the purposes 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. This is important to ensure that all safety procedures related to this study can be carried out appropriately, and safety standards met.

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 relevant authorities, including the institution relevant to this Participants Information Sheet, Northern Health or as required by law. By signing the consent form, you authorise release of, and 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, except with your permission.

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

You have the right to rquest 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. Complains and complications

Complaints

If you are not satisfied with how your personal information has been handled (as laid out in the Privacy Act, 1988), then you can make a complaint to the Office of the Australian Information Commissioner (OAIC). It is free to lodge a complaint and you do not need a lawyer, however if you do decide to hire a lawyer, you must pay the lawyer yourself. You can choose to withdraw your complaint at any time. Please refer to http://www.oaic.gov.au/privacy/privacy-complaints for more information.

Complications

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 asisted 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 and funded by the Cardiology Department of the Northern Hospital.

You will not benefit financially from your involvement in this research project.

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 Northern Hospital, Victoria.

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 want 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 may contact the principal study doctors at any time.

Northern Health Cardiovascular Research Team
Name: Dr Dominic Chow
Position: Cardiology Research Fellow
Telephone: (03) 8405 8996/ (03) 8405 8169
Email: dominic.chow2@nh.org.au

For complaints: *(for projects approved by NH HREC include this statement only)*

If you wish to contact someone, independent of the study, about ethical issues or your rights or to make a complaint, you may contact:

Name	Rita Wong
Position	Ethics & Research Governance Officer
Telephone	8405 2918
Email	ethics@nh.org.au

FNH010619

Northern Health **Research Project Consent**	AFFIX PATIENT IDENTIFICATION LABEL HERE U.R. NUMBER: _____ SURNAME: _____ GIVEN NAME: _____ DATE OF BIRTH: _____/_____/_____ SEX: _____

Consent Form - Adult providing own consent

Title	Ivabradine in the prevention of Peri-operative Myocardial Infarction
Short Title	The IPMI Trial
Principal Investigator	A/ Prof William van Gaal

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 Northern Hospital and the study team 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, 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. Alternatively, a member of the research team may request my persmission to obtain access to my meical records for collection of follow-up information for the purposes of research and analysis.

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

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/ Senior Researcher¶

I have given 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 regarding the research project.

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

Northern Health

Research Project Consent

AFFIX PATIENT IDENTIFICATION LABEL HERE

U.R. NUMBER: _____

SURNAME: _____

GIVEN NAME: _____

DATE OF BIRTH: _____/_____/_____ SEX: _____

Form of Withdrawal of Participation - Adult providing own consent

Title	Ivabradine in the prevention of Peri-operative Myocardial Infarction
Short Title	The IPMI Trial
Principal Investigator	A/ Prof William van Gaal

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 The Northern Hospital.

Name of Participant (please print) _____

Signature _____ Date _____

Please provide a description of the circumstances if the participant's decision to withdraw is communicated verbally.

Declaration by Study Doctor/ Senior Researcher¶

I have given 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 regarding the research project.

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