



(Affix patient identification label here)

URN:

Family Name:

Given Names:

Address:

Date of Birth:

Sex:  M  F  I

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## Parent/Guardian Information Sheet/Consent Form

Interventional Study - Parent/Guardian consenting on behalf of participant

**Title** Nitric oxide during Cardiopulmonary Bypass for infants undergoing arterial switch operation for repair of transposition of the great arteries.  
A blinded randomised controlled trial

**Short Title** NASO

**Project Sponsor** MCRI, Australia

**Protocol Number** HREC38017A

**Principal Investigator** XXXXXX

**Associate Investigator(s)** XXXXXX

**Location** XXXXXX

## **1 Introduction**

We are inviting your child to take part in this research project because they are going to have a heart operation called an arterial switch operation. As you know, the aim of this operation is to fix the position of your child's great arteries. This will require them to be placed on a cardiopulmonary bypass during surgery. The cardiopulmonary bypass is a machine that will work for the heart and lungs while the surgeon operates on your child's heart. Bypass will maintain the circulation of blood and oxygen in your child's body. This research project is looking at the effects of using nitric oxide during bypass on children who are have this type of surgery.

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 your child to take part in the research. Thank you for taking the time to read this Parent/Guardian Information Statement and Consent Form.

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 your child can take part, you might want to talk about it with a relative, friend or the child's local doctor.

Participation in this research is voluntary. If you do not wish your child to take part, they do not have to. Your child will receive the best possible care whether or not they take part. Before you decide,

you may want to ask questions or talk about the research with your family, friends or health care worker.

If you decide you want your child 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 your child taking part in the research project
- Consent for your child to have the tests and treatments that are described
- Consent to the use of your child's personal and health information as described.

You will be given a copy of this Parent/Guardian Information and Consent Form to keep.

## **2 What is the purpose of this research?**

Children undergoing this surgery often develop an inflammatory response to the bypass. The inflammatory response happens when the cells in your child's body does not recognise the bypass circuit. The cells start a normal response to try protect and repair the body from something that it does not recognise. We know this inflammatory response contributes to complications after surgery and can also delay recovery. Nitric oxide has been shown to reduce this inflammatory response. We believe that administering nitric oxide into the cardiopulmonary bypass circuit could result in fewer post-operative complications.

As part of this study we will look at what happens when nitric oxide is given with oxygen during cardiopulmonary bypass. We will compare this to what happens when we just give oxygen, which is

current practice. We want to find out whether adding nitric oxide means that children have less complications and leave hospital faster compared to when just oxygen is used during bypass. If adding nitric oxide means that children have less post-operative complications then this could change bypass during heart surgeries throughout the world. This could save lives and reduce the amount of time children need to stay in hospital after heart surgery.

### **Nitric oxide**

Nitric oxide is a safe gas. It is widely used throughout the world in paediatric and neonatal intensive care units. Nitric oxide is approved to treat newborn babies with pulmonary hypertension. It is often used for other severe diseases of the heart and lung in young children.

### **3 What does participation in this research involve?**

The study is a randomised trial. This means that your child will be randomly allocated to one of two groups. To try to make sure the groups are the same, participant is put into a group by chance, your child has a fifty per cent chance of getting in to either group. Your child will receive either standard cardiopulmonary bypass with oxygen or cardiopulmonary bypass with nitric oxide and oxygen. None of the treating team will know which treatment your child has been allocated to. Only the perfusionist will know whether your child received just oxygen or nitric oxide and oxygen as they are responsible for the running of the bypass circuit. Neither you nor the treating team will know if nitric oxide was given or not. We will compare results from both groups to see if one form of treatment is better.

#### **4 What does your child have to do?**

We will enter information about your child's heart surgery and their admission to intensive care into a secure database called REDCap. This will include results from blood tests done as part of standard of care. We will compare children in the two groups. Any information obtained in connection with this research project that can identify your child will remain confidential. Your child will receive all usual standard care as if they were not taking part in the study. We will follow up on your child's progress for the first month after their operation from your routine hospital visits here or at your local hospital.

#### **5 Other relevant information about the research project**

We did this study a few years ago in a small group of patients in Melbourne. We found that patients who got nitric oxide spent less time in intensive care after their operation and needed less medications to help their hearts after surgery. We are now doing the study on a bigger group of patients to compare both groups. The project will run for two years, we expect around 800 infants from all over the world to take part in the study. Half of the children will receive nitric oxide in addition to oxygen and half will receive oxygen alone into their cardiopulmonary bypass circuit.

## **6 Does your child have to take part in this research project?**

Your child's participation in this study is entirely voluntary. If you decide that you do not wish your child to take part in this study, your child will undergo their operation as planned, with standard care using only oxygen during cardiopulmonary bypass. If you do decide that your child can take part, you will be given this Parent/ Guardian Information and Consent Form to sign and you will be given a copy to keep. Your decision that your child can or cannot take part, or that they can take part and then be withdrawn, will not affect their routine treatment, relationship with those treating them.

## **7 What are the possible benefits of taking part?**

If your child receives nitric oxide during cardiopulmonary bypass it is possible that the usual inflammatory response may be lessened. This may mean the amount of support required post operatively is reduced. However, we cannot guarantee that your child will get any benefit from this project.

## **8 Are there any benefits for other people in the future?**

Thousands of children around the world every month undergo surgery for congenital heart disease requiring cardiopulmonary bypass. The inflammatory response caused by cardiopulmonary bypass often results in complications after surgery and a longer hospital stay. Reducing the inflammatory response could save many children from these complications.

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

Nitric oxide is already regularly used in paediatric intensive care unit. This is not a new medical gas. All medications/gases given to patients in and out of hospital have side effects. However, for most medications/gases the benefits outweigh the risks.

A possible side-effect is that your child might have a high methaemoglobin. Methaemoglobin is a temporary change in the red blood cells reducing their ability to carry oxygen. In the past, nitric oxide has been associated with higher than normal methaemoglobin. However, this was seen when delivering much higher doses of nitric oxide for much longer periods than in this study. As a part of standard care, we will regularly monitor your child's methaemoglobin levels. We will stop the nitric oxide therapy if we see higher levels of methaemoglobin than normal. This will decrease the methaemoglobin and we will continue to monitor your child's level of methaemoglobin. We have performed a pilot study on nitric in 198 children receiving heart surgery and no serious side effects due to nitric oxide were observed.

## **10 What are the possible discomforts and/or inconveniences for your child?**

Your child is being considered for this study as we know they are going to have an arterial switch operation. During surgery your child will have drips and lines put into their artery and veins. This is a normal part of medical practice. There will be no need for any extra drips, or any other painful procedures to allow your child to participate in this study.

### **11 What if I withdraw my child from this research project?**

If you decide not participate in this study, this will in no way affect your current or future relationship with the hospital. It will also have no effect on your child's treatment or your relationship with the people treating them. If you agree to your child participating in the study, you are free at any time to withdraw from the study without prejudice or reproach. You should be aware that data collected up to the time of withdrawal will form part of the research project results. If you do not want us to do this, you must tell us.

### **12 What happens when the research project ends?**

This study will take around four years to be finished. We will send you a copy of the overall results at the end of the study.

### **13 What will happen to information about my child?**

By signing this form you consent to the study doctor and our research staff collecting and using personal information about your child for the research project. Any information obtained in connection with this research project that can identify your child will remain confidential. We can only disclose the information with your permission, except as required by law.

We will store all data collected securely; hard copy data will be stored by the investigating site in a locked cupboard at a secure location. Electronic data will be stored on a secure database called Redcap, in Australia. The information will be re-identifiable. This means that we will remove your



child's name and give the information a special code number. Only the research team in your child's hospital can match your child's name to their code number, if it is necessary to do so.

The following people may access information collected as part of this research project:

- the research team involved with this project
- The Royal Children's Hospital Human Research Ethics Committee

As the participants in this project are under 18 years old, information will be kept until the youngest participant turns 25 years old. The research information may be destroyed or kept indefinitely in secure storage after this time. In accordance with relevant Australian and/or Victorian privacy and other relevant local laws, you have the right to access and correct the information we collect and store about your child. Please contact us if you would like to access this information.

We will send you a summary of the overall project results. The summary will be of the whole group of research study participants, not your child's individual results. We plan to publish the results of this research project and present them in a variety of forums. In any publication and/or presentation, information will be provided in such a way that your child cannot be identified.

#### **14 Who do I speak to if I have a complaint?**

If you have any concerns and/or complaints about the project, the way it is being conducted or your rights as a research participant, and would like to speak to someone independent of the project,

please contact: Director, Research Ethics & Governance, The Royal Children’s Hospital Melbourne on telephone: (03) 9345 5044 .

### **15 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 Royal Children’s Hospital.

This study has also been review by **xxxxxxx** ethics board.

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.

### **16 Further information and who to contact**

#### **Contact People**

**xxxxxxx**

**PARENT/GUARDIAN AND PATIENT CONSENT FORM**

**Title** Nitric oxide during Cardiopulmonary Bypass for infants undergoing arterial switch operation for repair of transposition of the great arteries: A blinded randomised controlled trial

**Short Title** NASO

**Protocol Number** HREC38017A

**Principal Investigator** XXXXXX

**Declaration by Parent/Guardian**

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 have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to my child participating in this research project as described and understand that I am free to withdraw them at any time during the research project without affecting their future health care.

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

I agree to my child receiving the treatment allocation for this immediate surgical intervention only.

I agree to the use of de-identified (coded) data obtained in this study to be used for further analyses

I have read the above information. I have asked all of my questions and I have received answers.  
I agree to enroll my child in this study.

\_\_\_\_\_  
Signature of Parent/Guardian

\_\_\_\_\_  
Date

**INVESTIGATOR**

I have fully explained to the parent/guardian ..... the nature and purpose of the program and the procedures to be employed as described above and such risks as are involved in their performance, and I have provided the parent/guardian with a copy of the Patient Information Sheet.

\_\_\_\_\_  
Signature of Investigator

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name

\_\_\_\_\_  
Title