**Parent/Guardian Information Sheet**

*Telethon Kids Institute/Perth Children’s Hospital*

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| **Title** | ***P****reterm Paediatric* ***I****nhaled* ***C****ortico****s****teroid* ***I****ntervention* |
| **Short Title** | *PICSI* |
| **Project Sponsor** | *Telethon Kids Institute* |
| **Coordinating Principal Investigator** | *Dr Shannon Simpson* |
| **Location** | *Telethon Kids Institute/Perth Children’s Hospital* |

**Introduction**

This is an invitation for the child in your care to take part in this research project because they were born premature. The research project is aiming to understand how inflammation in the lungs contributes to ongoing breathing problems in children who were born preterm. This research is also testing a treatment for these ongoing breathing problems. The treatment is called fluticasone propionate, or ‘Flixotide’.

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 the child to take part in the research.

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 the 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 the child to take part, they do not have to. The child will receive the best possible care whether or not they take part.

If you decide you want the 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 the child taking part in the research project

• Consent for the child to have the tests and treatments that are described

• Consent to the use of the child’s personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

**Why are we doing the study?**

Babies born before full term usually have underdeveloped lungs, which can result in breathing problems. These breathing problems may continue for years, and some children may have lung function that worsens through childhood. Some researchers have suggested that ongoing inflammation in the lungs might contribute to worsening lung function.

Our study aims to understand how inflammation in the lungs contributes to these ongoing breathing problems during childhood. We will also look at how the exhaled breath of preterm children is different to term children and test how treatment with an inhaled anti-inflammatory medicine changes the lung disease in preterm children.

The anti-inflammatory medicine is called fluticasone propionate, which is inside a ‘Flixotide’ inhaler, or puffer, which is commonly given to children with asthma. This medicine belongs to a group of medicines known as corticosteroids, frequently called 'steroids'. They are not 'anabolic steroids' which are the steroids sometimes misused by athletes. A Flixotide puffer provides a measured amount of steroid to breathe into the lungs. By using a Flixotide puffer regularly every day, the medicine reduces the inflammation, swelling and irritation in the walls of the small air passages in the lungs. This can help to ease breathing problems.

This study will help us understand more about why some children who were born premature have ongoing breathing problems. This study will also help us know if the anti-inflammatory medicine Flixotide is useful for treating the underlying lung disease and improving lung function in these children.

Medications, drugs and devices have to be approved for use by the Australian Federal Government. Flixotide is approved in Australia to treat breathing problems like asthma. We do not know whether it is an effective treatment for breathing problems in children born preterm.

**How is the study designed?**

This is a randomised, double-blind and placebo-controlled study.

Randomised means that whether your child received Flixotide or placebo will be assigned by a computer. Your child will have a one in two (50:50) chance of receiving Flixotide.

Double-blind means that no one at the study site will know if your child is taking Flixotide or the placebo. The doctor can find out if it is necessary for the medical care of your child.

Placebo controlled means an inhaler that looks like Flixotide but doesn’t contain any medicine will be taken by some children in the study. This is so we can look at the study findings fairly.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

**Who is carrying out the study?**

A total of 250 children from Western Australia will be taking part in this study.

This research has been initiated by the Senior Researcher, Dr Shannon Simpson and will be conducted by staff at the Telethon Kids Institute. Part of the analysis will take place in collaboration with researchers at a West Australian-based Metabolomics Laboratory. This research has been funded by National Health and Medical Research Council (NHMRC). The results of this research will be used by a member of the study teamto obtain a Doctor of Philosophy (PhD) degree.

No member of the research team will receive a personal financial benefit from the child’s involvement in this research project (other than their ordinary wages).

**What is involved in this study?**

If your child participates in this research project, we will ask you to sign the consent form before any study procedures are carried out.

If you choose for your child to participate in this study we will ask you to complete a diary that asks about your child’s respiratory symptoms every day for 2 weeks. We will then ask you and your child to visit Perth Children’s Hospital (PCH). This visit will take about 2 hours in total. At this visit, your child will have a physical exam, and we will ask your child to perform simple breathing tests (spirometry, respiratory mechanics, measurement of exhaled nitric oxide and exhaled breath condensate) and an allergy test. We will also ask you to complete a questionnaire and we will collect some biological samples from your child.

At the end of you and your child’s visit to PCH, your child will be randomised to receive the study treatment or placebo, which you will be given to take home.

The treatment is the anti-inflammatory medicine, Flixotide. Your child will be required to inhale 1 puff (125 micrograms) of Flixotide (or placebo) twice a day for 12 weeks. During the 12 weeks of treatment we will call you every fortnight to check on your child’s respiratory symptoms. Diary cards will be given to you so that you can record any of your child’s medications as well as any medical problems such as illnesses, hospitalisations or accidents; even if you think they are not related to your child’s participation in the study.

After 12 weeks of treatment, we will ask you and your child to visit PCH again. At this second visit, we will ask your child to perform all the same tests and procedures as the first visit, except for the allergy test. These tests and procedures are described in more detail below.

**Physical exam**

The study doctor will perform a physical exam, including chest sounds, height and weight. The study doctor will be happy to tell you and your family doctor of any findings that may need further medical assessment.

**Lung function tests**

**Spirometry:**

This test measures any airway obstruction your child may have. This test involves your child taking big breaths in and out. If your child finds it difficult or a little uncomfortable to breathe deeply, your child can take their time and have a break if needed. This test takes about 10 minutes to perform.

**Exhaled nitric oxide:** this test involves your child breathing normally into a machine which measures the level of nitric oxide that your child breathes out. This gives us information about inflammation in your child’s lungs. This takes about 5 minutes.

**Respiratory mechanics:**

This test will involve your child breathing normally into a machine. The machine uses a sound wave to measure the stiffness or elasticity of your child’s lungs. This works in a similar way to the way fishermen use sonar to find fish. We measure the sound waves that bounce back from your child’s lungs. The way they are changed by the lungs gives us information about lung function. This test takes about 5 minutes.

**Bronchodilator response:** We will give your child 4 puffs of salbutamol (also known as Ventolin) using a puffer. This is a ‘bronchodilator’ which relaxes the airways of people who have asthma. We will repeat the spirometry and respiratory mechanics test to see if the salbutamol makes a difference to your child’s lung function.

**Exhaled breath condensate:**

This tests allows us to measure the level of inflammation in your child’s lungs using a simple breathing test. Your child will breathe room air through a mouthpiece for 10-15 minutes. The air your child breathes out will be collected into a chilled collection tube. As the exhaled breath is cooled it will form droplets that we will collect for analysis.

**Allergy test:** We will also perform a skin prick test to see if your child has any allergies to 10 common allergic substances. This will involve placing small drops of different substances on the skin of the forearm, then giving the skin a light scratch. Some children may find this uncomfortable but recover very quickly. It is not painful and will not result in bleeding. Results of the test will be available within 10-15 minutes of the substance being applied. If your child has a positive reaction to a substance, a small wheal (lump) will appear on the skin, which is not painful but may feel itchy.

**Questionnaire:** We will give you a questionnaire which asks whether your child has symptoms that relate to breathing problems. This questionnaire may take up to 15 minutes to complete.

**Biological samples (optional):**

These samples will help us further understand the biological processes behind lung disease and treatment effectiveness in preterm-born children.

**Urine sample:** we will collect 2 urine samples from your child, 1 sample at the first visit and another at the second visit, to look for markers of inflammation and how these relate to lung health before and after treatment.

**Saliva sample:** At your child’s first visit, we will collect a sample of your child’s saliva to use for DNA analysis. We will ask your child to spit into a special tube with a funnel shaped opening. We require about 2 mL of saliva which takes approximately 2 – 5 minutes to collect.. We will like to look at whether genetics affect lung health in preterm-born children.

**Blood sample:** We will collect 1 blood sample from your child at their first visit. We will collect about 5-10 ml of blood from your child to look for markers of inflammation and immune function and how these relate to lung health.

**Nasal brushings:**

Studies on babies born preterm have suggested that the cells (epithelium) that line the inside of the airways (including the nose, windpipe and lungs) do not function the same as in babies born full term and may contribute to breathing problems. We would like to see if the functioning of these cells has changed in school-aged children who were born preterm. A small brush will be inserted into each of your child’s nostrils and rotated gently to collect a sample of cells from inside the nose. We will collect these cells at both the first and second visits.

There are no additional costs associated with participation in this research project, nor will you or the participant be paid. All medication, tests and medical care required as part of the research project will be provided to the child free of charge. We will reimburse you for parking at the Perth’s Children’s Hospital/Telethon Kids Institute at each visit.

If you decide that the child can participate in this research project, the study doctor will inform the child’s local doctor.

**What will my child have to do?**

This study runs for 12 weeks and will require 2 visits to Perth Children’s Hospital. Both visits will take about 2 hours. We will try to find appointment times that suit you and your child.

You will be given a supply of the study treatment to take home at the end of your first Visit to PCH. The study doctor will discuss how to take the study treatment with you. There are certain medications that your child cannot take and the study doctor will review these with you. During the 12 week treatment period your child will have no lifestyle or dietary restrictions and your child can still donate blood. As the parent/guardian of your child, you will have to ensure that your child takes the treatment regularly according to the instructions given.

**Does my child have to take part in this research project?**

Participation in any research project is voluntary. If you do not wish for the child to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw the child from the project at any stage.

If you do decide that the child can 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 that the 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, or their relationship with Perth Children’s Hospital or the Telethon Kids Institute. The child does not have to take part in this research project to receive treatment at this hospital. Other options are available which you can discuss with the child’s local doctor.

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

We cannot guarantee or promise that the child will receive any benefits from this research; however, possible benefits may include improvement of respiratory symptoms and/or lung function. If this study shows that Flixotide is useful in the treatment of lung disease in children who were born preterm, then other people who were born preterm may benefit in the future.

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

**Study Medication**

It is possible for any medicine to cause unwanted side effects. If they occur, most are likely to be minor and temporary. However, some may be serious. Check with your doctor as soon as possible if you think your child is experiencing any side effects or allergic reactions from this medicine that are troublesome or ongoing, even if the problem is not listed below. The following side-effects are unlikely to occur given the standard dose given in this trial and for a short duration (12 weeks). However it is important to tell your doctor immediately if you notice any of these signs:

The most commonly reported side effects are:

* A sore throat or tongue. This may be due to 'thrush' (candida infection)
* Hoarseness or throat irritation.

To avoid these, it may be helpful for your child to rinse their mouth with water and spit it out after using the Flixotide puffer. Check your child’s voice for signs of increased hoarseness.

It is possible that some people, particularly those taking higher doses of Flixotide puffer for a long time, may rarely (less than 1 in 1000) suffer from the following side effects:

* Rounded face
* Loss of bone density
* Eye problems (eg. cataract, glaucoma)
* Slowing of growth in children. It is unclear what, if any, difference this makes to their final height
* Soreness in the oesophagus.

Taking high doses of steroids for a long time could affect the adrenal glands, which make the body's own steroid. Your doctor may do tests to check how the adrenal glands are working. Your doctor will be able to answer any questions you may have. It is important that:

* Treatment with your child’s Flixotide puffer should not be stopped suddenly
* All doctors treating your child are aware that they are on inhaled steroids.

Very rarely (less than 1 in 10,000) the person taking the medicine may feel anxious, have disturbed sleep or notice increased irritability (mainly in children).

There may be an increase in the amount of sugar (glucose) in your child’s blood. If your child feels unwell in any other way or has any symptoms that you do not understand, you should ask your child’s doctor immediately.

If you think your child is having an allergic reaction to their Flixotide puffer, tell your child’s doctor immediately or go to the emergency department at your nearest hospital. Symptoms usually include some or all of the following:

* Wheezing
* Swelling of the lips/mouth, tongue or throat
* Difficulty in breathing
* Hay fever
* Lumpy rash ("hives")
* Fainting

This is not a complete list of all possible side-effects. Others may occur in some people and there may be some side-effects not yet known. Tell your child’s doctor if you notice anything else that is making your child feel unwell, even if it is not on this list. Ask your child’s doctor or the study team if you don't understand anything in this list. Do not be alarmed by this list of possible side-effects. Your child may not experience any of them.

**Nasal brushings:**

Having a nasal brushing may cause some discomfort in the nasal passageway at the time, and potentially some minor bleeding. This is usually resolved very quickly and is easily treated.

**Blood sample:**

Having a blood sample taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated. Your child will be offered numbing cream to lessen any pain or discomfort. A maximum of 2 attempts will be made to draw blood and we will ask for your consent if a third attempt needs to be made.

**Pregnancy**

The effects of Flixotide on the unborn child and on the newborn baby are not known. If your child has reached puberty and there is a possibility that your child may become pregnant or father a child during the study or within 3 months after the last dose of study medication, it is important that you inform the study doctor. If you or your child require information on preventing pregnancy please ask us.

**Other risks**

Although we don’t anticipate any other risks, the treatment and procedures involved in this research study may involve unexpected risks that are impossible to predict. These unforeseen risks may affect your child during his/her participation in the study and/or some point in the future.

**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, the study doctor will tell you about it and discuss with you whether you want your child to continue in the research project. If you decide to withdraw your child, their study doctor will make arrangements for their regular health care to continue. If you decide that your child can continue in the research project, you will be asked to sign an updated consent form.

Also, on receiving new information, the study doctor might consider it to be in your child’s best interests to withdraw them from the research project. If this happens, the doctor will explain the reasons and arrange for your child’s regular health care to continue.

**Can the child have other treatments during this research project?**

It is important to tell the study doctor and the study staff about any treatments or medications your child may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell the study doctor about any changes to these during your child’s participation in the research project. If your child needs to take medications that may interfere with the study treatment, then your child may need to be withdrawn from the study.

**What if I withdraw the child from this research project?**

If you decide to withdraw your child from the project, please notify a member of the research team before you withdraw them. This notice will allow that person or the research supervisor to further discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your child during the research project, the study doctor and relevant study staff will not collect additional personal information, 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 of withdrawal will form part of the research project results. If you do not want them to do this, you must tell them before your child joins the research project.

**What are the reasons that my child may be withdrawn from the study?**

Your child may be removed from the study without your consent at any time. Reasons why he/she may be removed from the study include, but are not limited to, the following:

* The study doctor determines that it is in your child’s best interest not to continue;
* Your child is unable to complete required study treatments and examinations;
* The study is stopped by the Institution, the Sponsor(s), or by the Therapeutic Goods Administration (TGA) or other health authorities in Australia;
* The study is cancelled due to adverse events or in circumstances where the trial is halted because of safety concerns.

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

After the trial ends, the study doctor will give your child a clinical review, and then provide your local doctor with a report to recommend you child continuing or discontinuing the study treatment. We will provide you with your child’s lung function results after each visit.

Once the research study is complete, the study staff will send you a letter with a summary of the results. Because of the length of the study, it may be some time before we are able to this.

**What about my child’s privacy?**

**Study Data**

By signing the consent form you consent to the study doctor and study 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. Data collected will be re-identifiable, meaning that it will be coded, and only the study staff will have access to the information which identifies your child. Data will be kept at the Telethon Kids Institute in a secure location with access restricted to only specific study staff, investigators and a representative of the Ethics office. According to policy, this data will be retained at the Telethon Kids Institute for a minimum of 25 years after the study is completed. Your child’s 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 your child may be obtained from their 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 the child’s participation in this research project. Information about the child’s participation in this research project may be recorded in their health records.

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 the child cannot be identified.

In accordance with relevant Australian and West Australian privacy and other relevant laws, you have the right to request access to the participant’s information collected and stored by the study 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 the participant’s information.

According to Good Clinical Practice guidelines the accuracy of information recorded for a study must be checked against source data (wherever information is recorded originally, for example your medical records, laboratory test results etc.) in order to ensure the results of the study are reliable and that study procedures were conducted correctly. By signing the informed consent form, you are giving your permission for authorised representatives of the study sponsor monitor(s), auditor(s), the ethics committee and domestic and foreign health authorities to be granted direct access to your child’s original medical records and other source data to the extent permitted by the applicable laws and regulations.

**Biological samples**

In addition to collecting exhaled breath condensate, we will ask you to provide additional consent for the collection of your child’s blood, urine, saliva and nasal brushings at both their visits to PCH during the research project. Collection of the blood, urine, saliva and nasal brushing samples is an optional part of the project, and are for related research purposes only. All samples will be labelled only with your child’s unique study number and stored at the Telethon Kids Institute until analysis. All samples will be analysed as group data and will not relate to your child as an individual.

These samples will be anonymised and sent to an external laboratory for testing during the study. It will not be possible for the external laboratory to identify your child’s sample(s). By signing this informed consent form, you are allowing your study doctor and study staff to provide these samples to the external laboratory working with the study team. You are also allowing your study doctor, study staff, and external laboratory working with the study team to use the samples collected from your child to conduct the study.

With your permission any remaining samples, including DNA, may be stored for future research comparing children who were born prematurely and those born at term and to enable us to predict which children will have ongoing lung disease and which children will respond to treatment. The samples will be anonymised before use in future studies which may include but are not limited to studies of immune function, genetic and epigenetic analyses and may be accessed by researchers in Australia and abroad. If you do not give your permission, any leftover sample will be destroyed.

Any results from the DNA testing will not involve information about your child’s future health risk, or information that may be relevant to the health of family members who are not a part of the project. No information concerning genetic disease predisposition will be made available to you or your child. Your child’s genetic information will not be released for any reasons other than this research. If consent for future research use is declined, the genetic material and information will be disposed of after the completion of the current study.

**Complaints and Compensation**

If the participant suffers 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 for the participant. If the participant is eligible for Medicare, they can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

In the event of loss or injury, compensation will be provided in accordance with the Medicines Australia Indemnity. A copy of this indemnity is available to you from the research staff on request.

**Who has approved 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 Child and Adolescent Health Service of Western Australia.

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.

**Who do I contact if I have any questions?**

If you would like any further information about this study, please do not hesitate to contact one of the research team. They are very happy to answer your questions.

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| **Name** | **Contact Number** |
| PICSI Study Team | 0421 489 869 |
| Dr Shannon Simpson | 08 6319 1631 |
| Ms Rhea Urs | 08 6319 1628 |
| Ms Denby Evans | 08 6319 1620 |
| Ms Naomi Hemy | 08 6319 1625 |

If you have any concerns or complaints regarding this study, you can contact the Director of Medical Services at PCH by calling 08 6456 2222. Your concerns will be brought to the attention of the Ethics Committee who is monitoring the study