Participant Information Sheet

Study title:	**The PLUSS Trial: Preventing Lung Disease Using Surfactant + Steroid**		
Locality:	Liggins Institute	Ethics committee ref.:	17/CEN/203
Lead investigator:	Dr Chris McKinlay (New Zealand) Dr Omar Kamlin (Australia)	Contact phone number:	0274725099

You are invited to take part in a study aimed at preventing chronic lung disease in very preterm infants.

Whether your baby takes part is your choice. If you don't want your baby to take part, you don't have to give a reason, and it won't affect the care your baby receives. If you do want your baby to take part now, but change your mind later, you can take your baby out of the study at any time.

This Participant Information Sheet will help you decide if you'd like your baby to take part. It sets out why we are doing the study, what your baby's participation would involve, what the benefits and risks to your baby might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide now whether your baby will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree for your baby to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 5 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

This study has ethical approval from the Central Health and Disability Ethics Committee 17/CEN/203.

WHAT IS THE PURPOSE OF THE STUDY?

When a baby is born before 28 weeks of pregnancy, they are extremely preterm. Their lungs are immature or not fully developed. They often have low levels of surfactant in their lungs, a natural occurring substance we all have in our lungs. This can make their lungs more stiff and poorly expanded and this is called respiratory distress syndrome (RDS).

As a result, most babies born at less than 28 weeks will need breathing support from birth. This can be via a tube in their windpipe connected to a breathing machine (ventilator) or with prongs in their nose (called continuous positive airway pressure or CPAP). Most extremely preterm babies who are receiving ventilation are treated with surfactant given directly into the lungs via a tube in the windpipe.

Around half these babies will develop chronic lung disease. Babies with chronic lung disease need prolonged breathing support and oxygen in the NICU, sometimes for many weeks or months. They even be discharge home on oxygen. Babies with chronic lung disease are more susceptible to chest infections and wheezing illnesses in childhood and beyond.

Airway inflammation is thought to be responsible for the development of chronic lung disease. Some babies receive systemic steroids (given with feeds or intravenous drip) to reduce lung inflammation. However, giving steroids in this way can cause problems with how preterm babies grow and develop. Even though airway inflammation is present in the first week after birth, systemic steroids

are usually avoided. An alternative is to give steroids directly into the lungs to minimise the side effects of systemic treatment.

This study aims to investigate whether a steroid called budesonide, given with surfactant directly into the lungs, is better than treatment with surfactant alone (standard or usual treatment) to prevent chronic lung disease.

Budesonide is approved to treat asthma. Budesonide is not approved to prevent or treat chronic lung disease. Therefore, budesonide is a new treatment for chronic lung disease. This means it must be tested to see if it is effective and safe for chronic lung disease.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

Your baby is being considered for this study because they will be or were born at less than 28 weeks' gestation. Babies can enter the study if they are less than 48 hours old, are receiving breathing support and will be treated with surfactant as part of their standard care.

Your baby will be allocated to one of two treatment groups:

- Group A: **Surfactant and Budesonide Group**. In this group, babies will be given surfactant mixed with budesonide.
- Group B: **Surfactant only Group**. In this group, babies will be given surfactant alone.

This will be done by chance, similar to tossing a coin, so your baby has an equal chance of being in either group. Neither you, nor the team of doctors and nurses involved in your baby's care, will know which treatment has been given. A secure record will be kept of each baby's group allocation in the hospital pharmacy, so it is possible for the doctors to find out this information, if needed.

STUDY TREATMENT (First two days after birth)

We will prepare the study treatment away from the team looking after your baby to ensure they are unaware of the allocated treatment. This involves either mixing budesonide with surfactant or preparing the standard dose of surfactant alone, which will then be given in the normal manner.

We may give your baby a second dose of study treatment (budesonide mixed with surfactant or surfactant alone) 6-12 hours after the first dose, if they are still receiving breathing support and your baby's doctor decides another dose of surfactant is needed.

To assess baby's steroid levels, we would like to collect a small amount of blood immediately before and at 1, 5, 12 and 36 hours after the study treatment. The total amount of blood taken for all samples is very small (1.0 ml), less than half a teaspoon. Where possible these samples will be timed with other tests and will be taken from the baby's blood sampling line.

A brief ultrasound scan will be performed to assess heart function at 48-72 hours and at 6-7 days, which will take between 5-10 minutes. This is part of standard care for most preterm infants.

POST-INTERVENTION ASSESSMENT (Primary admission and follow up at 2 years)

We will collect health information from your baby's hospital admission until they are discharged, including data from other hospitals if your baby is transferred for ongoing care. We will seek your consent to access this information from your baby's medical record.

Your baby will have an assessment close to term (36 weeks equivalent) to check for chronic lung disease. This assessment is routinely performed for extremely preterm babies and may take around an hour to complete if your baby is receiving oxygen therapy or breathing support at the time.
These standard assessments include:

- Shift Test – documenting the average amount of oxygen your baby needs during a 15 minute observation.

- Modified Walsh Test – reducing the amount of oxygen your baby is receiving gradually so that we can determine the lowest oxygen amount needed to keep their oxygen levels in the standard range.

Your baby will have a medical and developmental assessment at two years of age (corrected for prematurity) as part of their standard care. We will use the information collected from this assessment to determine any long-term effects of the study intervention.

We would also like to ask for your permission to collect routine government data on your child's health and education. This information is available to approved researchers through the national Integrated Data Infrastructure (IDI) administered by Statistics New Zealand. A key purpose of the IDI is to answer important research and policy questions for the benefit of New Zealand children. The information that we may seek from the IDI could include hospital visits, medications, Before School Check measurements, and school curriculum level. Data in the IDI is strictly controlled by Statistics New Zealand to protect privacy and prevent individuals being identified. This part of the study is optional. Your baby can still participate in the study if you do not agree to this.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

BENFITS

We cannot promise that your baby will get any benefits from this study; however, possible benefits may include your baby being less likely to develop chronic lung disease if the budesonide helps. The results of this study will be used to improve the care of extremely premature babies in the future.

RISKS

Budesonide is used in children and adults for treatment of asthma and hayfever, and is generally well tolerated. However, all medical treatments can cause side effects. Your baby may have none, some or all of the effects listed below, and they may be mild, moderate or severe. There may be side effects that we do not expect or do not know about and that may be serious. Tell us immediately about any new or unusual symptoms that your baby gets. We will also be looking out for side effects.

Providing extremely premature infants with "systemic steroids" in the first week of birth (either by mouth or the bloodstream), is often restricted to the sickest of babies because of concerns about the following side effects:

- Immediate – elevated blood pressure, elevated blood sugar levels, and increased risk of bleeding in the intestine.
- Long term – delayed brain development.

We believe that giving budesonide mixed with surfactant directly into the lungs has fewer side effects. Research has shown that when budesonide is mixed with another surfactant and given directly into the lungs, only a small amount (less than 4%) of the dose is detected in the baby's blood. Two previous studies in over 300 extremely premature infants using budesonide with another surfactant did not find any side effects of this treatment. One study found no adverse effect on early childhood development when assessed at an average age of 2 ½ years.

If a severe side effect or reaction occurs, the study doctor may need to stop your baby's treatment. Your baby's study doctor will discuss the best way of managing any side effects with you.

WHO PAYS FOR THE STUDY?

This research is being conducted by a collaborative group of clinical researchers in Australia, New Zealand and Canada. Funding is being sought from the National Health and Medical Research Council (NHMRC), Australia. The surfactant used in the study has been sponsored by Chiesi Farmaceutici (Parma, Italy), but this company has no role in the design or running of the study.

There are no additional costs associated with participation in this study, nor will you or your baby be paid. All medication, tests and medical care required as part of the study will be provided to your baby free of charge.

WHAT IF SOMETHING GOES WRONG?

If your baby were injured in this study, which is unlikely, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that if your baby takes part in this study, his or her cover won't be affected.

WHAT ARE MY RIGHTS?

Participation in this study is voluntary. If you join the study but change your mind you can withdraw your baby at any time and your baby's usual medical care will not be affected. With your consent, data collected prior to your withdrawal will be used in study analysis.

You and your baby's privacy will be protected. Study data will be de-identified and any identifiable data, such as name and address, will be held securely, accessible only to the immediate research team. Project reports will not identify any individual participants. You may request to view your baby's study data at any time.

WHAT HAPPENS AFTER THE STUDY?

When the study is completed, we will write to you outlining the main findings of the study. You will be able to find out which study group your baby was in after they have completed 2 years follow up. If your child had blood collected during the study, any leftover blood will be destroyed at the end of the study. Records will be kept securely for 25 years, and will be accessible only to the study investigators. We may contact you in the future about enrolling your child in later follow-up studies to investigate the longer-term effects of the study treatment into childhood.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr Chris McKinlay, Lead Investigator, NZ
Phone: +64 274725099
Email: c.mckinlay@auckland.ac.nz

Dr Omar Kamlin, Principal Investigator, Australia
Phone: +61 3 83453763
Email: omar.kamlin@thewomens.org.au

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

If there is a specific Māori issue/concern please contact: Leigh Henderson, Chair CMDHB Māori Research Review Committee, +64 9 2629562, x3162

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Consent Form - *The PLUSS Trial: Preventing Lung Disease Using Surfactant + Steroid*

PARENT / CAREGIVER STATEMENT

I have read and I understand the Participant Information Sheet.		
I have had time to consider whether to allow my child to take part.		
I have had the opportunity to discuss this study and I am satisfied with the answers I have been given.		
I have had the opportunity to use whānau/ family support or a friend to help me ask questions and understand the study.		
I understand that the participation of my child in this study is my choice and that he/she may withdraw from the study at any time and this will not affect his/her continuing health care.		
I understand that his/her participation in this study is confidential and that no material that could identify him/her will be used in any reports on this study.		
I know who to contact if I have any questions about the study in general.		
I understand the compensation provisions for the study.		
I understand that my child's blood samples may be sent overseas for analysis and I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste. I understand that I can request that my child's samples be destroyed but I will not be able to have them returned.		
I consent to investigators collecting blood to measure my child's steroid levels.	Yes ☐	No ☐
I wish to be notified of the results of this research when they are available	Yes ☐	No ☐
If I decide to withdraw my child from the study, I agree that the information collected up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to the investigators accessing my child's medical records, including from the Well Child Provider, Family Doctor or Ministry of Health up to 2 years of age, for study purposes only.	Yes ☐	No ☐
I consent to the investigators accessing my child's future de-identified health and school records up to 16 years of age, for study purposes only, subject to Ethics Committee approval.	Yes ☐	No ☐
You may contact me in the future to ask about my child participating in further aspects of the study.	Yes ☐	No ☐

Declaration by participant:
I hereby consent to my child taking take part in this study.

Participant's name: _____

Signature: _____ Date: _____

Declaration by member of research team:
I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it. I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: _____

Signature: _____ Date: _____