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## Parent Information Sheet and Consent Form

# Invitation to lung testing and inhaler study

FULL STUDY TITLE: **Respiratory Health Outcomes in Neonates** (RHiNO)

CHIEF INVESTIGATOR: **Professor Sailesh Kotecha** (University Hospital of Wales, Heath Park, Cardiff)

This information sheet is divided into two parts:

**PART ONE** – tells you the purpose of the research and what will happen if you decide to take part.

**PART TWO** – gives you more detailed information about how the study will be organised.
Please ask us if there is anything that is not clear or if you would like any more information.

## PART ONE

### What is the purpose of the study?

You and your child kindly took part in the first part of the study and as we noticed that your child had lower values in their lung function (blowing tests), we would like to find out why this might be. We would also like to assess if these lower values respond to medicines commonly used for treating asthma. By studying the possible mechanism (reasons) for the low values and by using different treatments for breathing problems in premature children, our aim is to find the best treatment to use.

### Does my child have to take part?

No, taking part is completely voluntary. It is up to you and your child (if they can) to decide whether or not to take part. Even if you do agree to join, you can stop at any time without giving a reason. A decision to leave the study, or a decision not to take part, will not change the standard of care you and your child receive now or in the future.
If you do take part, you will be given this information sheet to keep and be asked to sign a consent form. The study doctor may also stop your child from taking the study treatments at any time if they feel it is best for them to do so. However, if this happens, they will still want to carry on collecting information from your child if you both agree this.

### What will happen to my child if we agree to take part and how long will it take?

Because your child is already on a steroid inhaler, we want to get expert advice to see if it is okay for your child to come off their treatment so we can do the tests before we place him/her back on to trial drugs which will contain a steroid. You and your child will be invited to a clinic appointment at the Children's Hospital for Wales with a consultant who is an expert in children's lung diseases. They will assess if it is okay for your child to stop taking their inhalers for 4 weeks before taking part.

We will then arrange for you to visit the RHiNO study clinic at the Paediatric Clinical Research Facility (CRF), Children's Hospital for Wales on two occasions. Each visit will take most of the morning or afternoon (3-4 hours). We will ensure your car parking (if necessary) is paid for and that you are provided with a voucher for a meal after the testing is finished for you and your child.
We would like your child to remain in this part of the study for about 3 months.

### VISIT 1

When you arrive, the nurse or doctor will explain this part of the research in detail. If you are satisfied with the explanations, you will be asked to sign a consent form. If your child is able to understand the research and is happy to take part, they will be asked to sign an assent form with you. You will be given a copy of this information sheet and your signed consent/assent forms to keep.

Once consent has been given, you and your child will be asked some questions to make sure that they are OK to join. They will ask some questions about your child's medical history (including any allergies), what other medicines they may be taking and do a quick examination, including taking their temperature, to make sure they are well enough to take part. A cardiovascular assessment will also be performed which is very similar to taking a blood pressure but also needs an extra cuff to go around your child's thigh as well as their upper arm - this will only take a few minutes. The nurse will then measure their height, weight and body composition (how much muscle and fat they have). We will also perform an allergy 'skin prick' test. For this test your child's skin is lightly pricked with substances to which they might be allergic. This is relatively painless – the skin is gently pricked but it is not punctured. If they are allergic to a given substance, the skin reacts with a small 'hives-like' reaction, and we will measure the size of the reaction.

Next, the nurse or doctor will ask your child to do some breathing and blowing tests and pedalling on an exercise bike to see if they have any signs of narrowing or 'redness' (inflammation) in their breathing tubes. We will demonstrate the tests to your child and let them practise until they are happy to do the tests. Some of the breathing tests will also involve collecting samples of water vapour from their breath and some of their sputum (phlegm). Collecting the water vapour involves simple breathing in and out of a cooled collection tube. To collect the sputum, we will ask your child to breathe in vaporised (nebulised) salty water (saline) then cough to bring up the secretions. We would like to collect a urine sample during the visit to check your child's exposure to other peoples cigarette smoke and to measure substances that are increased in other lung diseases. All of these samples can be tested to tell us more about the health of the lungs and airways.

We would also like to collect a sample of your child's saliva (spit) so we can look at some of their genes (DNA) which we think are important for breathing problems and how they respond to different medicines. The saliva sample is optional and it is OK if you would prefer your child not to provide it - you can still take part in the rest of the study. More information about what will happen to the samples your child provides is given in part 2.

For some of the tests, your child will be asked to sit inside a cubicle with glass doors; the cubicle door will be closed for a few minutes but they will still be able to hear and see us. For the exercise test, your child will be asked to pedal a bike for as long as possible. We expect this to be around 15 minutes. We will closely monitor your child during the exercise test and will stop when your child is too tired to continue or if their heart rate goes too high. After the exercise test, the nurse will then give a small dose of a medicine called salbutamol using an inhaler, before repeating some of the breathing tests to see if the medicine has any effect. The most common side effects are an increased heart rate and headaches. We do not expect these to happen often, but we will check to make sure your child is OK.

We will ensure that your child is comfortable and that there is time for breaks; you will be able to stay with them throughout the tests. During a break period, we would like you to complete a short questionnaire about how your child's health affects their and your lifestyle (such as time taken off work and missing school) and how your child is feeling on the day of the visit.

If the doctor or nurse finds that your child has signs of narrowing of the airways, we would like you and your child to think about taking an inhaler for 3 months (12 weeks). We are testing the inhalers **fluticasone** (known as an 'inhaled corticosteroid' or 'ICS') and **salmeterol** (known as a 'long acting beta 2 agonist' or 'LABA') both work in asthma to help children breathe better and try to prevent them from having symptoms such as wheeze and tightness in the chest. They do this in different ways:

- **Fluticasone** makes it easier to breathe by reducing any inflammation (redness) in the airways
- **Salmeterol** relaxes muscles in the chest to widen the airways (tubes that let air into the lungs)

All the inhalers have been specially made to look the same. Every child will get two inhalers:

- Fluticasone inhaler and placebo inhaler
- Fluticasone inhaler and salmeterol inhaler

No one including the nurses or doctors will know which inhalers your child will get. The chance that they will get any one is exactly the same for all of the options. You, your child, the doctors or nurses will not be able to choose or know which combination your child is given, however the study doctors and nurses can find out if they need to.

During the study, your child should not take any of the following medicines (inhalers or tablets) unless prescribed by your doctor (for example if the medicine prescribed by us is not working) or in an emergency:

- Inhaled corticosteroids (other than the trial treatment)
- Long-acting beta 2 agonists (other than trial treatment)
- Leukotriene receptor antagonists (such as montelukast e.g. Singulair)
- Beta-blockers
- Theophylline

You can ask your study doctor or nurse if you are unsure about any of these. Please inform your study doctor or nurse if your child is prescribed any new medicines or if any changes are made to their current medicines.

You will need to make sure that your child takes:

- **Two puffs** from **each** inhaler **twice a day** (in the morning and at night time)
- Before taking the inhalers in the morning and in the evening, we would like to test your child's breathing using a 'peak flow meter'. This is a simple device your child blows in to as hard and as fast as they can to see how quickly they can breathe out.

We will make sure both you and your child understand the best way to take the inhaler and use the peak flow meter before you leave. You will be given a diary to record the peak flows, if your child missed any inhaler doses, or if they have any other symptoms or problems. It is important that the treatments are stored safely and kept out of reach of younger children. **Please telephone us if you have any questions (contact details below).**

Your child will also be given the "reliever" inhaler (salbutamol) which he or she should use if they are wheezy even when taking the drug we prescribe. You should record why and when this is used.

We will ensure that your child is comfortable before we allow them home. Your child will be checked by the research team after they start taking the study medicine, usually by the research nurse making a telephone call; you will be asked about your child's health and about any symptoms they have had and will be reminded to fill in the symptom diary between visits.

## VISIT TWO

When you return after 3 months of trying the inhaler, we will ask your child to repeat the test they did at the first visit to see if the medicine had an effect. We will not repeat the tests that the medicine will not change (allergy test and saliva samples).

You will need to return all of the study medicine packaging and unused medicine to your study nurse at the 2nd visit.

## What does my child have to do if we agree to take part?

If you and your child decide to take part in this study, it is important that you both follow the instructions and advice given to you by the study doctor and research nurse. If you are unsure about anything, please ask us. Before taking part and throughout the study it is important that you tell the study doctor (or any of the staff) about any changes in your child's health that you have noticed. You must tell them if your child's symptoms seem to be any worse or if you are worried that they are not getting any better. If you are concerned at any time you should seek medical advice as you usually would (e.g. by visiting your GP). At each visit or phone call, you should also tell the research doctor or nurse about any other medicines your child is taking.

It is important to make sure that any other doctor your child visits knows that they are taking part in this study. Details of the contact people for this study and their telephone numbers will be in the diary which is issued to you at your first visit. The study doctor will write to your GP and let them know that you are taking part in a research study.

## What are the alternatives for treatment?

There are a few different medicines used for children with breathing symptoms. If you were not taking part in the study, your child may have been given a medicine your doctor thought would work best for them. The medicines we are looking at are used to treat children with similar breathing symptoms anyway so your child may have received one or more of them even if they weren't taking part in the study.

## What are the side effects of any treatment received when taking part?

The trial medicine might have some side effects, though these are not very common and are usually quite mild when they do happen. Please look out for the following signs and symptoms in your child and report them to the study doctor or nurse when you next see or speak to them:

- throat irritations
- chest infections
- hoarseness
- headaches
- muscle cramps
- fluttery feelings in the chest (palpitations)
- mild throat infections

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

Although the breathing tests involved in the study are straightforward, it can be tiring to get through the whole set; we will make sure there are opportunities to take breaks and that water is available to drink. Some children may not like the taste of the salty water used to encourage the sputum (phlegm) production, and in some rare cases the salty water can cause the airways to narrow. However, we will only do this test after the exercise bike so that your child will have had a rest and received the 'reliever' (salbutamol) inhaler to open their airways. We will do some blowing tests during the sputum collection to make sure this is OK.

Sometimes, the allergy test liquids can make the skin red, itchy and a bit swollen if the test is positive (a reaction). This wears off quickly and we will have some relief (antihistamine) cream available to make things more comfortable.

Some people might worry that the study medicine is not enough to manage their child's symptoms. We know from previous research that people taking the study medicines tend to improve over time. Making sure that your child takes their medicines properly and does not miss any doses, wherever possible, should also really help to manage their symptoms.

We will also give everyone a 'reliever' inhaler (salbutamol), which your child can take 'on the spot' if you think they need to.

Throughout the study we will check that all of the children are well at each study visit. If a child's symptoms gets worse at any time then the doctor will decide if they need to stop taking the trial medicines and might recommend they are put on a different medicine. You will need to make sure that you contact the study doctor or nurse, or your GP, at any time between visits if you think your child's symptoms have got any worse or if you are worried that they are not getting any better.

## What are the possible benefits of taking part?

We are conducting this research so that we know how best to treat children born prematurely who have breathing problems and symptoms. Your child's symptoms may improve by taking the study treatments and with the extra help they receive from taking part in this research. However, we cannot promise that taking part will help your child personally. The information we get might help to improve the treatment of other children with similar symptoms in the future though.

## What happens when the research study stops?

It may be some time after your child has completed the study before the results from all of the children taking part are known. However, when your child completes their own participation in the study, the main research team will write to your General Practitioner (GP) to advise them about whether the study appeared to help your child. We will try to provide the information in writing within seven days of your child's last study visit.

You will be able to ask your GP for this information and they will use it to decide the best treatment for your child.

## What if there is a problem?

If you have a concern about any aspect of this study you should contact the researchers who will do their best to answer any questions. If you are still unhappy after you have spoken to them and wish to complain formally, you can do this through the NHS Complaints Procedure.

In the event that something goes wrong and your child is harmed during the research study, there are no special compensation arrangements. If your child is harmed due to someone's negligence then you may have grounds for legal action. However, you may have to pay your own legal costs. The normal NHS complaints mechanism will still be available to you.

## Will my child's taking part be kept confidential?

Yes. All of the information about your child's participation in this study will be kept confidential. The details are included in Part Two.

## Contact details:

Please do not hesitate to contact the RHiNO team on telephone 029 2074 4187 or by email (rhino@cardiff.ac.uk) if you have any questions. Further information is available at our website http://rhino-health.org.

This completes PART ONE of the Information Sheet.

If the information in PART ONE has interested you and you are considering participation, please continue to read the additional information in PART TWO before making any decisions.

# PART TWO

## What if relevant new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatments being studied. If this happens, your study doctor will tell you and your child about it and discuss whether you both want to, or should, continue in the study. If you or your child decides not to carry on, your research doctor will make arrangements for your child's care to continue. If you and your child decide to continue in the study you will be asked to sign a new consent form and your child (where appropriate) will be asked to sign an updated assent form. Alternatively, on receiving the new information your study doctor might consider it in your child's best interests to withdraw them from the study. They will explain their reasons and arrange for appropriate care for your child.

If the study is stopped for any other reason, you will be told why and your child's continuing care will be arranged.

## What will happen if my child or I don't want to carry on with the research?

You or your child can withdraw at any time, if you wish. Your child will then be treated as per local clinical practice and procedures. All data collected up until the time of withdrawal will be anonymised (this means that a number will be used instead of your child's name so that no-one will know the information is about them) and included in the study analysis, unless you specifically state otherwise. If at any point you or your child decides to withdraw from the study, we will ask that you return all of their unused study medicine back to us. You can withdraw from treatment but please consider permitting us to follow up your child so we can collect information.

## What if there is a problem?

If you have a concern about any aspect of this study you should contact the researchers who will do their best to answer any questions (contact numbers are in Part One). If you are still unhappy after you have spoken to them and wish to complain formally, you can do this through the NHS Complaints Procedure.

In the event that something goes wrong and your child is harmed during the research study, there are no special compensation arrangements. If your child is harmed due to someone's negligence then you may have grounds for legal action. However, you may have to pay your own legal costs. The normal NHS complaints mechanism will still be available to you.

## Will my child's taking part be kept confidential?

Yes. As in the first part of the study, all of the information about your child's participation will be kept confidential. The paper files used to record information in this study will be labelled with an anonymous study number only. Giving information to someone else ('a third party') is not allowed. However, it will be necessary for authorised people from regulatory authorities, the study sponsor, or NHS bodies to check the study is being carried out correctly. Medical information may be also given to your child's doctor or appropriate medical personnel responsible for their welfare. By signing the consent form you are giving permission for this to happen. In the event of the results of the study being sent to Health Authorities or published, all of your child's records will be kept confidential and your child's name will not be disclosed to anyone outside of the study. All documents and files relating to the study will be stored confidentially for a maximum period of 25 years.

## Involvement of the General Practitioner/ family doctor (GP)

With your consent, the study doctor will write to your child's GP to let them know that they are taking part in the study. The study doctor may ask your child's GP for further medical information about them if necessary.

## What will happen to any samples my child gives?

All samples (saliva, urine) will be sent to the Department of Child Health at Cardiff University for testing in our laboratory. Some tests may be conducted by commercial companies or other university laboratories which have expertise to analyse the samples. The samples will have a code which means they will not be linked to information about your child.

With your permission any remaining samples, including DNA, may be stored for future research into comparing children who were born prematurely and those who were born at term. The samples will be anonymised before use in future studies and may be accessed by researchers in the UK and abroad; the research may include genetic (e.g. DNA) and commercial research. You may withdraw your consent for the storage and future use of your child's samples at any point. If you do withdraw your consent your child's samples will not be used in any subsequent studies and will be destroyed according to locally approved practices of Cardiff University. Any samples already distributed for use in research prior to the withdrawal of consent will continue to be used in that study and any samples remaining at the end of the study will be destroyed.

## What will happen to the results of the research study?

The results will be published in medical journals and presented at medical conferences. Your child's confidentiality will be ensured at all times and they will not be identified in any publication. At the end of the study, the results can be made available to you (should you wish). They will also be published on the RHiNO website.

## Who is organising and funding the research?

The study is sponsored by Cardiff University and funded by the Medical Research Council (MRC). Cardiff University have assigned the management of the study to the North Wales Organisation for Randomised Trials in Health (NWORTH) at Bangor University.

## Who has reviewed the study?

The study was approved by the South West-Central Bristol Research Ethics Committee (Ref 15/SW/0289). It has been registered with the International Standard Randomised Controlled Trial Number ISRCTN14767962.

Thank you for reading this information sheet.

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# Parent/Guardian Consent Form

RHiNO: Respiratory Health Outcomes in Neonates (Part 2)

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|---|---|---|
| 1 I confirm that I have read and understood the information sheet dated 'Version 5 29/07/2016' for the above study. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. | | Initial: |
| 2 I understand that my child's participation is voluntary and that we are free to withdraw at any time, without giving a reason, and without my child's present or future medical care or legal rights being affected. | | Initial: |
| 3 I understand that relevant sections of any of my child's records and data collected during the study relating to my child may be looked at by responsible individuals from the sponsor, funder, regulatory authorities or hospital. I give permission for these individuals to have access to these records where it is relevant to taking part in this research. | | Initial: |
| 4 I agree that personal identifiable information will be collected, stored and used to enable follow-up of my child. This is on the understanding that all information will be treated confidentially. | | Initial: |
| 5 I agree to my family doctor being informed of my child's participation in the study. | | Initial: |
| 6 I agree to allow my child to take part in the RHiNO study (part 2). | | Initial: |
| 7 Optional: I agree to allow a sample of my child's saliva to be taken for use in this study, which will include genetic (DNA) research. | YES NO<br>Please circle | Initial: |
| 8 Optional: I agree for any remaining samples to be used in future for research into children who were born prematurely in the UK and abroad which may include genetic (DNA) and commercial research. I understand I am free to withdraw my consent to future research at any point and that all samples will be destroyed as detailed in the information sheet. | YES NO<br>Please circle | Initial: |

Name of Child:

| | | |
|---|---|---|
| Name of Parent: | Signature: | Date: |
| Researcher: | Signature: | Date: |

Original for case notes, 1 copy for parent/guardian, 1 copy for investigator site file