Centre Name: Royal London Hospital ☐

Centre Number: _____ (as appropriate)

The "WAIT" Study; Wheeze And Intermittent Treatment

We are inviting parents[1] and their children to take part in a research study. Before you decide if you would like to take part it is important that you understand why the research is being done and what it will mean for you and your child. This information sheet gives all of the important information about our trial. We have divided this information sheet 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.

Part 1

What is the purpose of the study?

Attacks of wheeze (the noise we make when our airways become narrowed) are very common in children under 6 years of age (we call this preschool wheeze). Most of these attacks happen during colds, but in some children wheeze can happen between colds as well. We know that most young children grow out of their wheeze after the age of 6 years. At the moment we don't know the best way to stop these attacks of wheeze but we think that a medicine called "Montelukast" will make the attacks of wheeze less severe. Montelukast stops a substance in the body called "leukotriene" from narrowing the airways and causing wheeze. It is already licensed as safe for young children – but at the moment is used only as an "add on" to regular inhaled steroids and it has to be given every day.

We think that Montelukast may be helpful in preschool wheeze on its own, and that regular daily use may not be necessary. We have designed this study to see if Montelukast, if started by parents at the first sign of a cold and stopped when children are better, may prevent wheeze becoming so bad that your child needs to

[1] Where we use the word 'Parent' we mean people who have parental responsibility, which may include a legal representative (guardian).

see your GP or emergency doctor. To see if montelukast really works in the way we think we have to give some children the active medicine – montelukast coated onto granules of sugar taken by mouth once a day - and some children the sugar granules only (with no montelukast). No one knows in advance which one your child will get. This sort of study is called a "randomised controlled trial".

Studies of montelukast in adults with asthma have shown that genetic make-up affects whether someone responds very well, or not so well to montelukast. Another aim of our trial is to measure the amount of leukotriene produced by the body and the genes that control it to see if we can identify children who may respond very well to montelukast.

What is the drug, device or procedure that is being tested?

The medicine that we are testing is called montelukast. Its "trade name" is "Singulair". Montelukast is not a new medicine and has been licensed as safe for use in young children for several years. It comes as granules in individually packaged sachets and can be given either directly into the mouth, or mixed with a spoonful of cold or room temperature soft food (e.g. apple sauce, ice cream, carrots or rice). The granules consist of a sugar core with a fine coating of the drug. Each dose of montelukast granules stops the airway narrowing effect of leukotriene for 24 hours – so you only need to give it once a day. Some children will be given the core sugar granules, but without the coating of montelukast, this is called a placebo medicine and has no effect. These are packed so they look and taste exactly the same as montelukast granules.

Why has my child been chosen?

Your child has been asked to take part in this study because he/she has had at least 2 episodes of wheeze. Your General Practitioner (GP), specialist asthma nurse or hospital doctor thinks your child might be suitable to take part in this study and wants to refer them to the research team to assess this. We will be recruiting 1300 children for this study from a number of children's hospitals across the UK as well as from GP practices.

Does my child have to take part?

No, taking part is completely voluntary. It is up to you to decide whether or not to take part. Even if you do agree to join, you can drop out at any time without giving a reason. A decision to leave the study, or a decision not to take part, will not in any way affect the standard of care you and your child receive now or in the future. If you

change your mind about staying in the study we would appreciate it if you would let us know. 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.

What will happen to my child if we agree to take part and how long will it take?
If you do take part, you will be given this information sheet to keep and be asked to sign a consent form. We would like your child to remain in the study for a year. If you agree to take part, you will have another visit to receive the medication. After that we will be contacting you by phone or email only. We may ask some of you to allow us a more extended interview about parents' views on the study and if so we will visit your home at the end of the study. Each visit will last under an hour. We will now explain what will happen at each of the visits.

Visit 1[2].
If you are interested in taking part, and are satisfied with the explanations from your research team, you will be asked to sign a consent form at your first clinic visit. You will be given a copy of this information sheet and your signed consent forms to keep. Once consent has been given, you and your child will be asked some questions to make sure that they are suitable to join. The research doctor or nurse will want to know about your child's wheezing symptoms. They will ask some questions about your child's medical history and what other medicines they are taking. We will check that you can use the salbutamol (blue) inhaler properly so that they are getting the right amount of medication each time they use it. The doctor or nurse will also collect a saliva sample from your child using a specially designed mini-sponge which is entirely painless. The saliva will be analysed for genes (DNA) for leukotrienes. We will give you a container to collect some urine on the day of visit number 2. We will measure the amount of leukotrienes in your child's urine.

The amount of leukotriene in our urine can be affected by exposure to tobacco smoke (this can come from the air breathed out by smokers nearby – it does not mean that you or your child is a smoker) and so we will also measure levels of cotinine (produced if we are exposed to tobacco smoke) in the urine samples. This will make it easier for us to understand the results of the urinary leukotriene measurement. If you like we will tell you the cotinine result at the end of the study. The amount of leukotriene in the urine may also vary with time or illness, so we will

[2] The study group will pay a £10 contribution to clinic visit travel expenses for you and your child.

collect a repeat sample if you come into hospital with wheeze, and also at the end of your year in the study at a time when your child is well. We will only do this if it is convenient to you.

Visit 2.

If you are happy to, and the doctor or nurse says you are suitable to take part, we will invite you to come for a second visit at a convenient time for you – normally within 2 weeks of the first visit. We may be able to visit your home, if you agree. We will then give you a box of sachets and instruction on how to use them. We will also give you a simple diary card to fill out when/if you have to use the medicine. The doctor or nurse will talk to you about it and answer any questions you have. There is space to write down anything you think is important for the nurse to know next time you see them. If you agree, we will let your GP know that your child has been enrolled into a study.

Your study doctor and/or nurse may ask your permission to make a sound recording of the interview when we give you the trial medicine and at the end of the study. This is because in a small number of parents we would like to find out their views on parent-guided medicines and whether we can improve the experience of parent and children in future studies. This is an "add on" study; you can take part in the main study without agreeing to this.

Phone Calls

You will be contacted once every two months by the research nurse. She will check whether you have used the trial medicine, and whether you have visited your GP or the Hospital. If you child has had an attack of wheeze she will ask you about the effect on the family, including things such as additional child care and days off work. If you have to use the trial mediation we will ask you to post to us the completed diary card (and empty sachets) using a provided freepost envelope.

Replacement Medicines

If your child uses all their medicines, or the medicines reach their use-by date, we will contact you to provide you with a replacement box. If we do not contact you (or the medicines are lost or damaged) please contact us on the number provided. Do not attempt to get replacement medications from your GP or hospital doctor.

Extended Interview

If you have agreed to the optional extended interview a researcher will contact you and arrange a time that is convenient to you.

At 12 months

The study finishes for your child. We will ask you to send back all the used and unused medicine sachets.

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

- Your child will need to provide a saliva sample and urine sample(s).
- You should give your child the study medicine if they get a cold or wheeze attack
- There is nothing unpleasant or painful involved in the study.
- You will need to complete a symptom diary during attacks of wheeze.

You should 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. Names and contact telephone numbers of the people running this study 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 the research study.

What will happen when I start treatment?

- You will give your child 1 sachet of medication either directly into the mouth or mixed with cold or room temperature food from the start of every cold or wheezing attack.
- You will continue to give this every day for 10 days, even if your child gets better.
- You will complete a simple 10-day diary card for every course of medicine.
- If your child vomits after taking the medicine no additional dose should be given, and the vomit should be recorded on the diary chart.
- You should give all other medicines to your child as normal.
- You will inform the research team (see contact details) that you have commenced the study medicine by sending back the completed diary card at the end of the 10 days.

What are the alternatives for treatment?

Your child will receive the standard (normal) treatment for preschool wheeze of “as needed” inhaled salbutamol (the blue inhaler). If a doctor thinks that your child

needs to have regular inhaled steroids, these may be given without affecting the trial. If a doctor thinks that you child also need daily montelukast, this can also be given, but in this case we will stop the trial medicine and, with your permission continue to collect information about the number of wheeze episodes.

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

- There are very few side effects reported with continuous montelukast. A possible side effect is a mild tummy upset and increased thirst. Some older children have had mild headaches.
- If your child accidentally takes too much montelukast the symptoms are similar to those already described. There may also be some increased sleepiness or agitation in some children. If your child takes an overdose of any medication you should seek medical advice. There is no evidence of longterm harm from montelukast overdose.

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

Some parents might worry that if their child is given the placebo (inactive) medicine they won't be getting enough medicine to manage their wheeze. However, every child in the study will get the normal standard care of inhaled salbutamol as well as other medicines that their doctor prescribes. Only children enrolled in the study are eligible to have "as required" montelukast.

What are the possible benefits of taking part?

During the study we will check that all of the children are well at every visit/phonecall. At any time during the study your GP or hospital doctor may decide to change your child's medicine or stop the study medicine. We are conducting this research so that we can know how best to treat children with preschool wheeze. We cannot promise that taking part will help your child personally, but your child will not be disadvantaged in any way. The information we get might help to improve the treatment of other children with preschool wheeze in the future.

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. We have to wait until the end of the whole study before we can analyse the results. Once the results are known we will write to you personally and tell your GP.

What if there is a problem?

Any complaint about the way you or your child have been dealt with during the study or any possible harm you might suffer will be addressed appropriately. Information relating to this is detailed in Part Two. If you have any complaints about this research study, please contact the appropriate Patient Advice and Liaison Service (PALS) office.

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:

You will be able to contact a member of the research team to discuss any questions or concerns you may have and/or to get help.
Please call:

Research Nurse:	****** *****/*** ******
Tel:	**********/**********
Email:	**********/**********
Research Doctor:	********* *****/** ******
Tel:	**********
Email:	**********
Patient Advice and Liaison Service:	****
	****** ****** ***** ******
	*** ***** ****** *********
	********** *****
	******* ** ***
Fax:	*** **** ****
Minicom:	*** **** ****
E-mail:	**********

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 treatment/s 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 doctor decides that you should not carry on, your research doctor will discuss the reasons with you and make arrangements for your child's medical care to continue outside the study. If you decide to continue in the study you (and your child if appropriate) will be asked to sign updated consent forms. 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?

If at any point you decide to withdraw from the study, we will ask that you return all of the unused study medications to us. You can withdraw from treatment but continue to be followed up and have information collected.

Following withdrawal from the study, the research doctor will talk to you about whether they need to find out what medications your child was taking during the study to enable appropriate follow-on treatment. Your child will then be treated as per standard local clinical procedures. All data collected up until the time of withdrawal will be anonymised[3] and included in the study analysis, unless you specifically state otherwise.

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.
- If you have a complaint about a study doctor or nurse you have seen at the hospital, you can contact the Patient Advice and Liaison Service (PALS) department at the hospital for help.
- If you wish to complain about a General Practitioner you have seen as part of this study, then you should contact the Primary Care Trust they belong to. Your study nurse will be able to help you with this if you want.

[3] Anonymised means that a number will be used instead of your child's name so that no one will know that the information is about them.

- In the event that something goes wrong and your child is harmed during the research study the normal NHS complaints mechanism will be available to you. Additionally, if harm arises as a result of the design or management of this study, even if no one is at fault, you may have grounds for legal action against, or compensation from, the study sponsor: Queen Mary University of London. Please ask your doctor or research nurse for more information on this if you have any questions.
- If your child is harmed due to hospital staff negligence then you may have grounds for a legal action against the hospital where those staff are employed. However, you may have to pay your own legal costs.

Will my child's participation in this study be kept confidential?

- All information that is collected about you and your child during this study is considered to be confidential and giving this information to someone else ('a third party') is not allowed with the exceptions noted below.
- The paper files used to record information in this study will be labelled with a unique study number.
- Medical information may be given to your child's doctor or appropriate medical personnel responsible for their welfare.
- The paper files used to record information in this study will also be stored securely in a locked cabinet and the information will then be entered into a secure computer database file. This file will be labelled with your child's number but NOT their name. A copy of the information in the paper files will be stored securely by the research team at the coordinating study centre at Queen Mary University London. This is to ensure that all the information regarding the study remains accessible and secure for later analysis of the study results, and to check accuracy of information.
- When your child finishes taking part in the study we will need to find out what treatment they were taking so that they can inform your GP. To do this, we will have to link your child's trial number to their name but this link will still be kept separate to all of the other information collected about them in the study. The trial team will ensure that confidentiality is preserved.
- If you join the study, some parts of your child's medical records and the data collected for the study will be looked at by representatives of regulatory authorities and by authorised people from other NHS bodies to check that the study is being carried out correctly. Your child's medical records will be checked at the hospital and will not be removed. All authorised individuals have a duty of confidentiality to you and your child as research participants and nothing that could reveal your child's identity will be disclosed outside the research site. 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 hospital.
- All documents and files relating to the study will be stored confidentially either at your local study site or the main study site or both for a maximum period of 20 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. In some circumstances your GP will already know since he/she will have sent out your invitation letter. The study doctor may ask your child's GP for further medical information about them if necessary.
- All patients (children) who are registered in the study will have follow up data collected about them. The information requested will all be related to your child's wheezing control and the research team will ask your GP to give them access to this data. By signing the attached consent form, you are agreeing for your GP to share this information with the research team.

I have private health insurance – does this make a difference?

You should inform your health insurance provider that your child has been enrolled into the study. They may wish to speak with the study group, in which case they can be provided with our contact details. Study involvement should not affect your insurance cover.

What will happen to any samples my child gives?

Your child's DNA and urine sample will be transferred to Queen Mary University London for testing and will be identified only by a special number to maintain your child's anonymity.

Will any genetic tests be done?

We will measure only the genes that affect how leukotrienes work in the body. Your child's sample will be collected by a researcher and sent directly to the laboratory at Queen Mary University London where it will be stored. Within 2 weeks we will measure the ALOX5 gene (a leukotriene gene). A DNA sample will be securely stored with a label that gives a subject number only (so that it cannot be directly linked to your child) and within 2 years sent to an external laboratory (KB Bio Science) for analysis of all the other genes that are associated with leukotrienes. Your child's sample will always be labelled with a special number, instead of their name, so no-one will know that it belongs to them. Once we have analysed it for leukotriene genes, the DNA sample will be disposed of and not kept.

What will happen to the results of the research study?

The results are likely to be published in the year following the end of the study. 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 group results will be made available to you and/or your GP (should you wish). They will also be published on the National Institute of Health Research (NIHR) website.

Who is organising and funding the research?

The study is sponsored by Queen Mary University of London. This study is funded by the Efficacy and Mechanism Evaluation Programme of the Department of Health. Each participating research site has been allocated funds to pay for a researcher for this study, for the provision of general office supplies and to support pharmacy costs.

Who has reviewed the study?

The trial protocol has received the favourable opinion of the South East Research Ethics Committee

THANK YOU FOR READING THIS INFORMATION SHEET. WE HOPE YOU HAVE FOUND THE INFORMATION HELPFUL.