(To be presented on local headed paper)

Centre Name:

Centre Number:

MASCOT – Management of Asthma in School-age Children On Therapy

Parent/Guardian Information Sheet and Consent Form (v4.1, 26.03.2010)

Where the word 'Parent' is used please read parent/guardian i.e. those who have parental responsibility, which may include a legal representative.

Parents and children are being invited to take part in a research study. Before you decide if you want 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. Please take time to read the following information carefully. You are free to talk to others about the study if you wish.

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?
At the moment, doctors do not know for definite which treatments work best for children with asthma whose symptoms are not controlled very well on medications called 'inhaled corticosteroids' (ICS). They believe that adding in other treatments (called 'long acting beta$_2$ agonists' and 'leukotriene receptor antagonists'), rather than just increasing the amount of their current medication, works better and is safer but no research studies have tested this adequately in children. As a result, we do not know whether adding in either of these medicines is actually better than just taking an inhaled corticosteroid on its own.

The purpose of this study is to try to examine how effective these 'add-on medicines' are for children with asthma. The only way of doing this is to compare children who receive

one type of add-on medicine with those who receive the other, and then comparing both of these with children who stay on the same low dose of inhaled corticosteroid and do not take any extra add-on medicine. To do this fairly, we need to allocate the different treatments at random, which is a bit like throwing a dice to decide. No one knows in advance which one your child will get and the chance that they'll get any one is exactly the same for all of the options. This sort of study is called a randomised controlled trial or RCT. So, in this study, one third of the children will receive inhaled corticosteroids plus one type of add-on medicine, one third will receive inhaled corticosteroids plus the other type of add-on medicine and one third will just receive inhaled corticosteroids alone. Your child has a one in three chance of being given any one of the three different treatment regimes.

What is the drug, device or procedure that is being tested?
The add-on medicines we are testing are called 'salmeterol' (known as a 'long acting beta$_2$ agonist') and 'montelukast' (known as a 'leukotriene receptor antagonist'). All of the children taking part in the study will also be given a medicine called fluticasone, which is an inhaled corticosteroid. These medicines all work to help your child to breathe normally and try to prevent them from having asthma attacks. They do this in different ways:

- Fluticasone is used in an inhaler and makes it easier to breathe by **reducing any swelling in the airways**
- Salmeterol is also used in an inhaler and **relaxes muscles in the chest to widen the airways (tubes that** let air into the lungs)
- Montelukast is a **tablet that reduces tightness in the lungs**

Some children will be given a placebo tablet, which is a dummy tablet that looks the same as the montelukast but contains no medicine. Apart from the placebo, the medicines are all already used by doctors to treat children with asthma but we want to see if any of them work better when used together. There will be three different combinations of medicines we are looking at:

1. fluticasone and salmeterol
2. fluticasone and montelukast
3. fluticasone and placebo

You and your child will not be able to choose which combination you are given and you will not know which medicines they are taking. The study doctor and nurse will not know which medicines you are given either but they can find out if they need to.

During the study, your child will not be allowed to take any of the following medications (inhalers or tablets):

- Inhaled corticosteroids (other than the trial treatment)
- Long-acting beta$_2$ agonists (other than trial treatment)
- Leukotriene receptor antagonists (other than trial treatment)
- Beta-blockers
- Theophylline

You can ask your study doctor or nurse if you are unsure about any of these.

<u>Please inform your study doctor or nurse if your child is prescribed any new medications or if any changes are made to their current medications.</u>

Why has my child been chosen?
Your child has been asked to take part in this study because they have asthma which is not controlled well enough on their current medication. 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 around 900 children for this study from at least twelve 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 and your child (if they can) 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 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 is OK.

Your study doctor and/or nurse may ask your permission to make an audio recording of the interview when they are inviting you to take part in the MASCOT trial. This is because another study, called RECRUIT, is being carried out to find out what it is like for parents when their child is invited to take part in a clinical trial. With your permission, your study doctor will also pass your contact details to the researchers carrying out the RECRUIT study who will make direct contact with you at a later date.

You do not have to agree to the interview being recorded and the recordings will only be given to the RECRUIT researchers if you consent to take part in that study, otherwise it will be deleted. If you say yes to taking part at first and then change your mind, that's fine and the RECRUIT researchers will then erase your recording.

What will happen to my child if we agree to take part and how long will it take?
We would like your child to remain in the study for a year. If they agree to take part, they will have a maximum of five study visits over the course of the year. Each visit could last for about an hour though the first two will might take a little bit longer than that.

Screening
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. 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, if they can. 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 suitable to join. The research doctor or nurse will want to know about your child's asthma symptoms and how they affect day to day activities (if they do). They will ask some questions about your child's medical history, what other medicines they are taking and might do a quick examination to make sure they are well enough to take part.

The doctor or nurse will also talk to you about doing another optional test, which will involve them collecting a genetic (DNA) sample, using saliva, from your child (see questions below and separate information sheet). They will give you a special information sheet at this visit so you can read about it when you go home and discuss it with anyone you want. You do not have to say whether you want to give this sample or not until your next visit.

Four week run-in period

If you are happy to, and the doctor or nurse says you are suitable to take part, then you will be given some advice and information about how to help manage your child's asthma. They will also talk to you about how to make sure your child, and you, are using their inhaler properly so that they are getting the right amount of medication each time they use it. They will ask you both to show them how you use the inhaler to make sure that it's OK. These techniques have helped other children with asthma like your child so it's important that you try to use them for the next few weeks.

The doctor or nurse will give you a new inhaler to use until the next study visit in four weeks time. The inhaler has a low dose of a medicine called fluticasone in it, which is an inhaled corticosteroid. This might be the same treatment your child is taking before they enter the study or it might be a different one but you need to make sure they use it twice every day (once in the morning and once in the evening) and try not to miss any doses. All of the children registered in the study will get the same treatment for the first four weeks.

You will also be given a special diary that you and your child will be able to use to record any times that their asthma interferes with the things they want to do, like playing sport. 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.

Treatment allocation

After four weeks your child will be seen by the research doctor or nurse again. If their symptoms have improved and the doctor thinks your child's asthma is now well controlled, they will not go on to the next part of the study. However, if they still have troublesome asthma symptoms and are still suitable, then they will carry on into the main part of the study if you and your child are happy to do so.

All of the children in the study will be taking a medicine called **fluticasone propionate** (an inhaled corticosteroid), to make sure their asthma is being treated. This is the same treatment they will have received during the four week run-in phase. In addition to this one third of the children will receive add-on treatment with a medicine called **salmeterol** (a 'long acting beta$_2$ agonist') and one third with **montelukast** (a 'leukotriene receptor antagonist'). The other third will just take the fluticasone on its own. At the end of the trial we will compare the improvement in the children who have received the two add-on treatments with each other and then compare both of those groups against the other third of the children, who did not take either add-on medicine, to see if taking either salmeterol or montelukast as well as the inhaled corticosteroid is better than just taking it on its own.

This trial is called a 'double blind' trial as neither you (nor your child), your child's doctor, research nurse or pharmacist will know which of the treatment groups your child has been put into. However, your doctor can find out if they need to. We need to make sure that we are being fair when we compare the different medicines against each other and we do this by disguising the medications so they look the same. Fluticasone and salmeterol are both administered through an inhaler so the inhalers they come in will be the same shape, size and colour to make sure that no-one will know which medicine is in it apart from the pharmacist. The montelukast comes as a tablet so we have had another tablet made that looks exactly the same but contains no medicine (called a '**placebo**'). This is so no-one will know what treatment they are on. All of the children in the study will take medicines from both an inhaler and in tablet form.

We do all of this so we can be sure the information provided about all of the groups is fair and has not been swayed by knowledge of what medicine is being given. These measures help us to make a proper judgement about the effects of the medicines being tested when the results from children in the different groups are compared at the end of the study.

If you agree, and are able to continue into the main study, there are a few things you will need to do at this clinic visit. The doctor or nurse will look over the symptom record you have been keeping and will ask about how your child's asthma has been since your last visit. The doctor will examine your child to make sure they are well enough to take part and will measure their height and weight. They will measure how well your child's lungs are functioning using something called a spirometer, which your child will have to blow into as fast and as hard as they can.

You will both be asked to complete a questionnaire at the visit that will ask about how your child's asthma affects their quality of life and how it affects you and the rest of your family. In the asthma diary, there will also be a different questionnaire that the nurse will ask you to fill in during the times between your study visits. The form asks you to record all of the things you have to do because of your child's asthma such as taking time off work, visiting the hospital and buying extra medicines or treatments. This is so that when look at the different groups at the end of the study, we can see what the overall benefits were (if any) of each of the different medicines. This is called 'health economics'.

48 week treatment period

Your child will be checked by the research team four more times after they start taking the study treatment. These checks will usually be carried out by the research nurse either at the clinic or by making a telephone call to you. During this period you will be asked about your child's health and about any asthma symptoms or exacerbations they have had. You will be reminded to fill in the asthma diary between visits and bring it for the nurse to look at with you. You and your child will also each be asked at every visit to complete the same questionnaire you did at the start of the study.

We have drawn up a table ('Table 1', below) to show what will happen at each of the clinic visits and during the telephone call. The left hand column shows the study procedures and the top row is the time in weeks. An 'X' is used in the boxes to mark when a procedure will be carried out.

Week 52

Week 52 is when the study finishes for your child. At the end of this week you and your child will return to the clinic where you will both repeat the questionnaire that you have been doing at each study visit. Your child's lung function will be measured again and the study doctor or nurse will physically examine them. They will review the asthma diary with you both and talk about how your child's asthma will be looked after now the study has ended.

Table of study procedures (Table 1)

			Follow-Up Schedule (weeks)				
Procedures		Screening (T-4)	Baseline (T0 [clinic])	T+ 8 Weeks (clinic)	T+ 24 Weeks (clinic)	T + 36 Weeks (telephone)	T + 48 Weeks (clinic) Study Completion	Premature Discontinuation
Signed Consent Form		X						
Assessment of Eligibility Criteria		X	X					
Quality of Life Questionnaires			X	X	X		X	(X)
Health economics questionnaire				X	X	X	X	X
Lung Function Test			X				X	(X)
Review patient held record		X	X	X	X	X	X	X
Review of Medical History		X	X					
Review of Additional Medications		X	X	X	X	X	X	X
Randomised medications dispensed			X	X	X	X		
Physical Exam	Complete		X					X
	Symptom-Directed			(X)	(X)	(X)	(X)	
	Vital Signs		X	(X)	(X)	(X)	(X)	(X)
Assessment of Adverse Events			X	X	X	X	X	X
Special Assay or Procedure	Consent and obtain saliva sample for later DNA analysis		X					

(X) – As needed.

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 asthma seems 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 study visit, you should also tell the research doctor or nurse about any other medicines your child is taking.

You will need to return all of the study medication packaging and unused medication to your study nurse at every visit. 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 the research study.

If the results of the second visit mean that your child is suitable to take part in the randomised part of the research, they may start taking study medication on that day. You will need to make sure that your child takes:

- one suck from the inhaler twice a day, once in the morning and once at night-time
- one tablet a day, ideally in the evening before they go to bed

They will need to stay on both of these treatments for the next 48 weeks. It is important that the treatments are stored safely and kept out of reach of younger children.

What are the alternatives for treatment?

There are a few different medicines used for children with asthma. If you were not taking part in the study, your child would have been given the medicine your doctor thought would work best for them. The study medications we are looking at are used to treat children with asthma 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 treatments might have some side effects, though these are not very common and are usually quite mild when they do occur.

Please look out for the presence of 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 (called palpitations)
- mild throat infections

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

Some people might worry that if their child is given the placebo medicine they won't be getting enough medicine to manage their asthma. However, everyone in the study will be taking inhaled corticosteroids, which can be enough to manage asthma on its own. We know from previous research that patients taking this medicine 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. Throughout the study we check that all of the children are well at every study visit. If a child's asthma gets worse at any time then the doctor will decide if they need to stop taking the trial medications and might put them 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 asthma has got any worse or if you are worried that it still isn't getting any better.

We think the trial medications are safe for unborn children but not enough is known about this for us to be sure. If your child does become pregnant during the course of the study, you and/or your child must tell the study doctor or nurse immediately so appropriate action can be discussed. Arrangements will be offered to monitor the health of both your child and their unborn baby.

What are the possible benefits of taking part?
We are conducting this research so that we know how best to treat children with asthma who are not currently well controlled on inhaled corticosteroid therapy. We expect that your child's asthma will 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 asthma 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 tell them what treatment/s your child was receiving. 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 help decide what treatment is best for your child's asthma.

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 hospital's Patient Advice and Liaison Service (PALS) office on: ??

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: ?
Research Doctor: ?

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 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?
If at any point you or your child decide to withdraw from the study, we will ask that you return all of their unused study medications back to us. You can withdraw from treatment but continue to be followed up and have information collected as outlined in Table 1.

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 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.

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.

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 a legal action against (name of Trust). 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 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.

In order to ensure that appropriate informed consent has been taken, copies of you and your child's signed consent/assent forms will be sent to the Medicines for Children Research Network Clinical Trials Unit (MCRN CTU), who are coordinating the study. The paper files used to record information in this study will also be sent to the MCRN CTU so the information can be entered into a secure database. These files will not have your child's name on though, they will just be labelled with their trial number. When your child finishes taking part in the study, the MCRN CTU will need to find out what treatment they were taking so that they can inform your GP. To do this, they 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 MCRN CTU is part of the University of Liverpool which is in turn registered as a data controller with the Information Commissioners Office. The MCRN CTU will ensure that you and your child's confidentiality are preserved.

If you and your child 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, at the MCRN CTU or both for a maximum period of 15 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.

All patients who are registered in the study will have follow up data collected about them at the end of a year, regardless of whether they enter the randomised part of the study or not. The information requested will all be related to your child's asthma and their control of it 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.

What will happen to any samples my child gives?
If you and your child consent to the additional genetic testing a DNA sample will be obtained by asking your child to spit directly into a collection kit (see question below and separate information sheet). These samples will be transferred to an external laboratory facility at the University of Liverpool and will be identified by special numbers to maintain your child's anonymity.

Will any genetic tests be done?
In addition to the main study we would also like to collect a genetic (DNA) sample from all of the children participating in the study. We want to use these samples to look at how people's individual genes affect things such as how severe their asthma is, how it develops over time and how it responds to different medicines. Asthma behaves in different ways in different people and we think this might be linked to their genes. This is an optional test, with a separate information sheet and consent form, which will be provided to you at your first clinic visit. You and your child can still participate in the main study (outlined in this information sheet) without taking part in the additional genetic study.

If you agree to take part, your child's sample will be collected by a researcher and sent directly to the University of Liverpool where it will be stored for future use. We do not know what tests we will do on the sample yet but they will definitely be related to asthma and the treatment of it. Approval will be sought from an ethics committee before any research is done on your child's sample. Your child's sample will be labelled with a special number, instead of their name, so no-one will know that it belongs to them.

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 results can 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 co-sponsored by University Hospital of North Staffordshire NHS Trust and Keele University. They have assigned the day to day running of the study to the Medicines for Children Research Network Clinical Trials Unit (MCRN CTU). If you take part it will be necessary for members of the MCRN CTU, and possibly regulatory authorities, to have access to your child's medical records to ensure that the information from the study has been recorded accurately. The medical records will be checked in the hospital and will not be removed. By signing the consent form you are giving permission for this to happen. In the event of the study results being sent to Health Authorities or published, all of your child's records will be kept confidential and their name will not be given to anyone outside the hospital.

This study is funded by the Health Technology Assessment (HTA) Programme of the Department of Health. Each participating hospital site has been allocated funds to pay for a specialist research nurse 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 North West Research Ethics Committee.

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

Centre Name:

Centre Number:

MASCOT – Management of Asthma in School-age Children On Therapy

Parent/Guardian Consent Form (v4.1, 26.03.2010)

	Please initial box
1. I confirm that I have read and understand the information sheet dated 24.07.08 (v4.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my child's participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my care/my child's care or legal rights being affected.	
3. I understand that relevant sections of my child's medical notes and data collected during the study may be looked at by responsible individuals from the Medicines for Children Research Network Clinical Trials Unit, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my child's records.	
4. I agree to my child's GP being informed of my child's participation in the study.	
5. I agree to this consent discussion being audio-recorded and for my contact details to be disclosed to RECRUIT* researchers.	
6. I agree for my child to take part in this study.	

*delete if not applicable to this centre

Name of patient		
Name of parent	Signature	Date
Researcher	Signature	Date
Translator (if applicable) †	Signature	Date

†*I can confirm that the information I have translated to the family was a full and accurate representation of the statements made by the researcher.*

1 copy for patient, 1 for researcher site file, 1 for MCRN CTU, 1 (original) to be kept in patient notes