Oxford Vaccine Group
University of Oxford
Centre for Clinical Vaccinology and Tropical Medicine,
Churchill Hospital, Headington, Oxford OX3 7LE
Tel: 01865 611400 info@ovg.ox.ac.uk www.ovg.ox.ac.uk

PARENT INFORMATION SHEET

"A Study to see if a new experimental medicine (MEDI8897) is safe and effective in preventing Respiratory Syncytial Virus in healthy preterm infants"

INTRODUCTION

You and your child are being invited to take part in this research study of an experimental drug called MEDI8897. MEDI8897 is being developed to evaluate how effective it is at preventing serious Respiratory Syncytial Virus (RSV) disease in preterm infants. "Experimental" means the drug is not yet licensed for use by any Authority that regulates new medicines. The study is being sponsored by MedImmune ("the Sponsor"), a member of the Astra Zeneca group, which is a pharmaceutical company.

Additional information about MEDI8897 and the purpose of this study is provided below.

Please take some time to read this information and ask any questions you may have before you make a decision about whether or not to participate.

Your child's study doctor is a researcher for this study. As a researcher, he/she is interested both in your child's health and how this study is carried out.

WHY IS THIS STUDY BEING DONE?

MedImmune is developing a new medicine to protect infants from getting serious lower respiratory tract infection caused by RSV. RSV is a virus that is present in the general population from late Autumn to early spring. Infection with RSV is very common in children. In the first year of life, about half of all infants become infected with RSV. RSV typically causes a cold-like illness in older children and adults, but can cause serious lung disease in infants and young children which may require medical attention such as outpatient and emergency department visits or hospitalisation. Preterm infants are at high risk for having serious illness from RSV infection.

MEDI8897 is a type of drug called a monoclonal antibody. This is a man-made drug that works in the same way as antibodies produced by the body's own immune system to infections or vaccines. MEDI8897 is not manufactured from blood but is artificially manufactured.

This study is being done in healthy preterm infants born between 29 weeks and 35 weeks' gestational age who are up to 8 months old and entering their first full RSV season.

The purpose of this study is to evaluate how effective MEDI8897 is at preventing lung disease caused by RSV and to evaluate the safety and tolerability of MEDI8897 in healthy preterm infants compared with placebo (a saline solution that looks like the study drug but does not contain any active ingredient). The study will also measure drug levels of MEDI8897 in the blood, as well as looking at days missed from work and daycare.

Does my child have to take part?

Your participation in this study is completely voluntary. You can change your mind at any time, even after your child is enrolled. Your child's medical care will not be affected in any way if you decide not to allow them to take part.

If you agree, your child's GP will be informed about their participation in this study.

Why has my child been invited?

Your child has been invited to participate in this study because they are a healthy infant born between 29 weeks 0 days and 34 weeks 6 days gestational age, are no more than 8 months old and are approaching their first full RSV season.

There will be approximately 1,500 infants participating in this study. Enrollment is planned at approximately 197 sites globally.

How long will my child be in the study?

The planned length of time that your child will be in the study for is approximately 1 year. This includes Visit 1 which is a screening visit, Visit 2 when the study drug will be given and a follow up period of approximately 360 days (including 5 face-to-face visits, as well as telephone calls).

WHAT WILL HAPPEN TO MY CHILD IF HE/SHE TAKES PART?

Before any study related procedures are performed, you will be asked to read this information sheet and sign and date a consent form.

If your child can take part, he/she will receive either 50mg of the study drug or placebo. Your child will be assigned by chance to receive either study drug or placebo (for every 3 children taking part, 2 will receive the study drug, and one the placebo). Neither you nor your study doctor will know which study group your child is assigned to until the study is completely finished and all results have been analysed.

Study Visit	**What happens?**
Screening	• questions about your child's general health, medical history and current medications • A physical examination and weight measurement • Vital signs (temperature, blood pressure, breathing rate and heart rate) • A blood sample of about 1.5 mL (about 1/3 teaspoon)
Day 1 (may occur on same day as screening)	• Questions about your child's general health and current medications • A dose of study drug or placebo will be given as an injection into your child's thigh muscle • A physical examination and weight measurement • Vital signs will be taken in the 60 minutes before dosing, and at 30 and 60 minutes after dosing
Day 8 and Day 31 – (these visits can be completed at the research facility or at your home)	• Questions about any problems, illnesses, doctor visits or hospitalisations since the last visit and any medication your child is currently taking • Questions about any missed work days that you may have had and/or child absences from day care due to a respiratory illness • A physical examination and weight measurement • Vital signs
Day 91, Day 151 and Day 361 – (these visits can be completed at the research	• Questions about any problems, illnesses, doctor visits or hospitalisations since the last visit and any medication your child is currently taking

facility or at your home)	• Questions about any missed work days that you may have had and/or child absences from day care due to a respiratory illness • A physical examination and weight measurement • Vital signs • A blood sample of about 1.5 mL (about 1/3 teaspoon)
Unscheduled Illness Visits - if you take your child to any health care provider for a respiratory illness, we will ask you to bring your child to the research facility within 2 days or as soon as possible. Or if you wish, we can arrange to visit you at home.	• Questions about any missed work days that you may have had and/or child absences from day care due to a respiratory illness (e.g. cough, cold etc.) • A nasal swab to collect a nasal mucus sample • A blood sample of about 1.5 mL (about 1/3 teaspoon) if your child has been admitted to hospital for a respiratory illness
Follow-up Telephone Calls - every two weeks from the time your child receives the study medication until the Day 151 visit and then monthly after that until the final visit (Day 361)	• Questions about your child's general health and to confirm if they have had a respiratory illness requiring medical attention

The total amount of blood that will be collected over the course of this one-year study is about 6 mL (a little more than 1 teaspoon).

WHAT ARE THE POSSIBLE SIDE EFFECTS, RISKS AND DISCOMFORTS OF TAKING PART?

What is known about the safety of MEDI8897?

One clinical study of MEDI8897 was conducted in healthy adult volunteers before giving the drug to infants. Participants in this study were randomised to receive a single dose of MEDI8897 or placebo in 1 of 5 groups (300, 1000, or 3000 mg given into their vein, or 100 or 300 mg given in their muscle). A total of 136 participants were enrolled. Participants were

followed for about 1 year and the study was completed in June 2015. The drug was well tolerated and there were no safety concerns.

Another clinical study of MEDI8897 is being conducted in healthy preterm infants. Participants in this study were randomised to receive a single dose of MEDI8897 or placebo in 1 of 3 groups (10, 25 or 50 mg given in their muscle). A total of 89 infants were enrolled and dosed; follow up is ongoing. Nine children have completed the 1 year follow up visit, and 77 have been followed for at least 6 months. So far, the drug has been well tolerated and there have been no safety concerns.

What are the possible side effects, risks, and discomforts of taking part?

Sometimes people have allergic reactions to vaccines. These are rare but can be serious or even life threatening if not treated promptly. A serious allergic reaction (anaphylaxis) can lead to difficulty in breathing, wheezing, a sudden drop in blood pressure (dizziness, paleness), and swelling around the mouth, throat, or eyes. These kinds of reactions usually happen within a few minutes to a few hours after getting the injection. Your child will therefore be observed by our study staff for 60 minutes after vaccination. If an allergic reaction happens, treatment will be available and started promptly by our team.

You will be given a card with instructions to contact the site immediately if your child experiences symptoms such as hives, itching skin, rash, difficulty breathing, swelling of the lips, tongue or face, or wheezing. If your child experiences any breathing difficulty or symptoms of a serious allergic reaction, it is important that you seek emergency care.

Your child's body may make an immune reaction (antibody) to this study drug. This is the case even though the study drug is an antibody itself. We will be testing for such antibodies during the study. Rarely this immune response can cause symptoms such as joint pain and swelling, rash, fever or inflammation of your child's heart, blood vessels, nerves, and/or kidneys or a drop in platelets. Platelets are cells which help the blood to clot so low platelets can lead to bleeding in the mouth, gums, bruising, nose bleeds, and pinpoint red spots on the skin. Participants that develop these types of reactions during the course of the trial are advised to seek immediate medical help in managing their medical condition.

No risks associated with MEDI8897 have been identified in clinical trials conducted so far. However, there may be risks involved in taking this medication that have not yet been identified. There is always a risk involved in taking a new medication but your child will be closely monitored and you are encouraged to report anything that is troubling your child.

Risks from placebo

There are no specific risks of receiving placebo but your child will not be protected from RSV infection and will have the same risk as other preterm infants who do not receive prophylaxis (preventative treatment) for RSV.

Risks from study procedures

As with any injection, the study drug injection in the muscle may cause the area to become sore or tender, red, bruised, or swollen.

The taking of a blood sample by a needle may cause some discomfort. Problems with blood collection can include pain, tenderness, swelling, or bruising at the site of needle entry. **We will offer you local anaesthetic cream or cold spray before any procedures involving needles for your child.**

What if new information becomes available?

You will be told if any new information about the study medication is discovered that might affect your decision to have your child continue in the study.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

You will receive a summary of the study results when the study ends. To allow for full analysis of all participants' data, this information will be disseminated about 12 months after the last child finishes participating in the study.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

For the children who receive MEDI8897 it is possible that the drug may provide protection against serious RSV disease. However, this has not yet been proven. There is no medical benefit to your child as an individual if he/she receives placebo.

Even if there is no benefit to your child, other children may benefit in the future from what is learned in this study.

WHAT OTHER TREATMENTS ARE AVAILABLE?

A medicine called palivizumab (Synagis®) is approved for the prevention of serious illness caused by RSV in premature infants and children with lung disease or congenital heart

disease. However, based on analysis of the cost and effectiveness of palivizumab, national guidelines in the UK and the US limit the use of palivizumab to specific groups of high risk infants such as very premature infants with ongoing lung disease. We will not enrol your child in this study if they are eligible for palivizumab.

There is no currently no treatment for RSV infection. Children who get RSV infection receive supportive care to manage their symptoms while their body fights the infection.

WHAT HAPPENS IF YOUR CHILD HAS AN INJURY RESULTING FROM THIS STUDY?

If your child has any side effects after taking the study drug or are injured during the study, then tell the study doctor straight away. The study doctor will make sure your child receives medical treatment.

The Sponsor will follow local compensation laws in line with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). This means that if side effects or other physical injuries are caused by the study drug, the study sponsor will pay for the reasonable costs of medical treatment if:

Your child received the study drug and you followed the study doctor's instructions after receipt of the study drug

Your child's injury was not caused by you or your child

You (on behalf of your child) told the study doctor straight away; and

You (on behalf of your child) followed the study doctor's medical advice.

The Sponsor has adequate liability insurance to cover compensation as a direct result of taking part in this study.

If you have medical insurance please check with your insurance company that taking part in this study will not affect your policy.

COSTS AND EXPENSES:

You will be reimbursed for any reasonable travel expenses incurred for attending clinic visits with your child and also the cost of a meal during clinic visits. Please retain your receipts and provide these to a member of the research staff so that you can be refunded

DOES MY CHILD HAVE TO TAKE PART?

It is up to you whether to allow your child to take part in this study or not. Your child's medical care will not be affected in any way if you decide not to allow them to take part.

CAN I WITHDRAW MY CHILD FROM THE STUDY?

At any time after joining the study and for any reason, you can withdraw your child from the study; your decision t will have not affect your child's medical care. If you, on behalf of your child, withdraw your permission, your child cannot be in the study anymore. If you choose to end your child's participation in the study, the study doctor may ask you if you would be happy for your child to continue with any of the following:

- Attend study visits to take part in specific study assessments (including biological sampling, e.g., blood and/or nasal samples)
- Agree to be contacted by telephone when needed for safety follow ups
- Agree to allow the study doctor to collect information regarding study related health from available sources, such as medical records.

If your child continues to participate in some portions of the study, the information that was shared with the study sponsor or obtained from these portions of the study may continue to be used or disclosed as described in this information sheet.

If your child has any ongoing health problems at the time they withdraw then the study team may wish to contact you and ask you about this, until it has completely resolved. The sponsoring company may also ask the study team for this information.

The study doctor may choose to end your child's participation in this study without your consent for any of the following reasons:

The instructions of the study team are not followed

Your child experiences an injury related to the study; or

For any other reason.

The study may also be ended early by the Sponsor for any reason.

HOW WILL PERSONAL DATA ABOUT MY CHILD BE USED?/ HOW WILL MY CHILD'S PARTICIPATION BE KEPT CONFIDENTIAL?

By signing the consent form you agree to the Study Team collecting and using personal data about your child for the study ("Study Data"). This includes: your child's date of birth or age as permitted by local laws, your child's sex, your child's ethnic origin, and personal data on your child's physical or mental health or condition. The Study Team will keep this information confidential and will only use it to conduct the Study.

You may withdraw your consent at any time by notifying the Study Team; any Study Data collected prior to that time may still be given to and used by the Sponsor but the Study Team will not collect any new Study Data.

The Study Doctor's institution and the Sponsor are each responsible for handling Study Data in accordance with the UK Data Protection Act 1998. Study Data given to the Sponsor will not include identifying information like your child's name, only a code number. A person appointed by the Sponsor, regulatory authorities, or other supervisory bodies may review the Study Data held by the Study Team to make sure the Study has been done the right way and that the Study Data are accurate.

The Sponsor may use Study Data to conduct the Study, to support research and development of pharmaceutical products, diagnostics or medical aids, or to apply for approval to sell their product. This may involve sharing the coded Study Data with other companies, service providers, contractors, research institutions and research-based commercial organizations who may be located outside of the United States of America (US) and European Union (EU). The laws in such countries may not provide the same level of data protection as in the US or EU, but the Sponsor will take all reasonable steps necessary to ensure that any Study Data transferred is treated securely and in accordance with this form to the extent permitted by law.

Information about the study, including the results, may be published for scientific purposes or posted electronically (on http://www.ClinicalTrials.gov) or presented to scientific groups, but your child's identity will not be revealed.

You have the right to ask to see your child's Study Data and to have any inaccuracies corrected. To do so, please contact the Study Team who can help you contact the Sponsor, if necessary.

WHAT WILL HAPPEN TO ANY SAMPLES MY CHILD GIVES DURING THE STUDY?

Your child's samples will not be labelled with any information that could identify your child. The samples will be stored in a secure central laboratory where only authorised staff will have access for the period the samples are stored. If you consent to optional biological sample research (see the section below), the samples which are taken during this study will be stored for up to 25 years after the study ends. After this period, they will be destroyed. If you do not wish to consent to optional biological sample research, the samples will be destroyed at the end of the study (when your child has completed all tests).

OPTIONAL BIOLOGICAL SAMPLE RESEARCH

With your permission, the Sponsor would also like to perform additional research, either now or in the future, on blood or nasal samples that your child would have already provided as part of the study. The Sponsor would also like your permission to contact you after study completion to answer questions related to your child's health regarding respiratory illness and wheezing. The Study Doctor or a member of the study team will contact you for this information several years after study completion.

You do not have to agree for your child to take part in any of this additional research in order to take part in the main study.

All the testing done on your child's blood or nasal samples, outside of the protocol required tests, will be performed for research and development purposes only and may lead to the development of new patents, drugs, or biological products. No human genetic research (DNA testing) will be done on these samples.

The information you may provide regarding your child's health after study completion will help the Sponsor to understand respiratory illnesses and wheezing in children. Questions will be specific to respiratory illnesses and any experiences of wheezing your child may have had.

You may withdraw your consent to the use of donated sample(s) or to be contacted to answer respiratory illness and/or wheezing questions at any time by contacting your study team. If you withdraw your consent to the use of the samples, the study doctor or the sponsoring company will arrange to have them destroyed and you will be notified of the action.

However, if any analysis has already been performed the Sponsor is not obliged to destroy the results of this research.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The study is being sponsored by MedImmune ("the sponsor") a member of the Astra Zeneca group and may involve other companies in the AstraZeneca group as well as service providers, contractors and research institutions that support this study. The study doctor's research centre/hospital is being paid by the Sponsor to carry out this study.

WHO HAS REVIEWED THE STUDY?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by the South Central - Hampshire A Research Ethics Committee.

WHO SHOULD I CONTACT IF I WANT MORE INFORMATION?

You have the right to ask questions about this study at any time and are encouraged to do so. In case of a study-related injury or if you have questions about the study or the study medication, please contact:

Sophie Janet (Research Fellow to Dr Matthew Snape)

Day time telephone number: 01865 611400

Out of office hours telephone number: 07699785400

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the Oxford Vaccine Group on 01865 611400 or email info@ovg.ox.ac.uk. You can also contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224 or email the head of CTRG, Heather House ctrg@admin.ox.ac.uk.

If you have questions about your child's rights as a research participant, you may contact:

Our independent contact for queries (patients' rights, PALS) - The Patient Advice and Liaison Service is part of the Patient Services Team here at the Oxford University Hospitals NHS Trust. They can be contacted via switchboard (01865 741166) or on ext 21473 or 40868. Their email address is PALSJR@ouh.nhs.uk.