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

The 6-in-1 vaccine study

Study Information Booklet

We are inviting infants aged 8-13 weeks of age to take part in a study comparing two licensed combination vaccines that can be given in the routine UK immunisation schedule. These vaccines protect against 6 different infections in the one injection.

Before you decide to take part in this study, it is important for you to understand what the study is about and what participation would involve. Please take time to read the information carefully, and discuss with others if you wish. If you have any questions please contact the study team. Thank you for taking the time to consider this study.

Contact the local study team at:

Oxford Vaccine Group

CCVTM, Churchill Hospital, Oxford, OX3 7LE

01865 611400 info@ovg.ox.ac.uk

www.ovg.ox.ac.uk/recruiting-studies

Summary

- This study will help us to better understand the interaction between '6-in-1' vaccines and the Meningococcal B vaccine in the routine UK immunisation schedule
- We will be enrolling 240 healthy babies aged 8 – 13 weeks into this study
- Babies will receive all their infant immunisations in their own home or in a convenient location until 12 months of age
- There will be six study visits including 4 vaccine visits and 2 visits for blood sampling (we will use a topical anaesthetic cream to numb the skin for blood sampling)

Why has my child been invited to take part?

You have been approached as your child is in the age range for this study and lives in the Thames Valley. If you have received this invitation through the mail it has been posted to you by the National Health Applications and Infrastructure Services (NHAIS) who hold the central NHS patient database and the Child Health Information Service, an equivalent NHS database. Please note that the Oxford Vaccine Group has not been given your child's name or address.

What is this study about?

In 2017, the hepatitis B vaccine was added to the UK routine immunisation programme. An infection with the hepatitis B virus can cause severe inflammation of the liver and can cause severe long term liver damage. So that the hepatitis B vaccine could be introduced into the UK's childhood immunisation schedule without increasing the number of vaccine injections, the previously used '5-in-1' vaccine was replaced by a '6-in-1' vaccine. The '6-in-1' vaccine protects against diphtheria, tetanus, poliovirus, whooping cough (pertussis), hepatitis B and *Haemophilus influenzae* b (Hib). There are two licensed '6-in-1' vaccines available and these are called Infanrix hexa (6 in 1(IH)) and Vaxelis (6 in 1(V)).

The Infanrix hexa vaccine is currently used routinely in the UK. We know from previous research studies that this vaccine works well with the other vaccines in the UK schedule, including the meningococcal B vaccine (MenB or Bexsero). At present we do not have this information for the Vaxelis vaccine, and it is important to check this as the components of Vaxelis are slightly different from Infanrix hexa.

If we can show that immunisation with Vaxelis creates a similar response from the immune system to Infanrix hexa and is just as safe when given in the immunisation schedule along with the MenB vaccine, the NHS will be able to use either vaccine for children in the UK. Having the option to use either of the 6 in 1 vaccines is important to ensure all children continue to be protected even if one vaccine becomes temporarily unavailable.

What happens in this study?

This study involves six study visits over approximately 11 months. All study visits will either be conducted in your own home or a convenient location.

The study includes:

- 4 visits to give your child's routine immunisations (at 2, 3, 4 and 12 months of age approximately) including either Infanrix hexa or Vaxelis
- 2 visits for blood sampling (at 5 and 13 months approximately)
- Completion of a symptom diary for 5 days after each vaccine visit

If you decide you would like to take part in the study, our study team are available to answer your questions and make an appointment to see you and your child. During the first visit, the study team will discuss the study with you and answer any questions.

If you decide to continue with the study, we would then ask you to complete a consent form.

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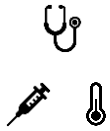
Study schedule

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Age	2 months	3 months	4 months	5 months	12 months	13 months
Visit reason						
Group 1	Infanrix hexa MenB Rotavirus	Infanrix hexa Rotavirus *PCV 13	Infanrix hexa MenB		Hib-MenC PCV13 MMR MenB	
Group 2	Vaxelis MenB Rotavirus	Vaxelis Rotavirus *PCV 13	Vaxelis MenB			

*PCV 13 will be administered at 3 and 12 months, instead of 2, 4 and 12 months as routinely given at the time of the study start date (May 2019). This reflects a change in the UK infant immunisation schedule planned for 2019.

6 in1 (IH) (Infanrix hexa)
6 in1(V) (Vaxelis)
PCV13 (Prevenar13)
MMR (MMR VaxPro or Priorix)
MenB (Bexsero)
Hib/MenC (Menitorix)

 Examination

 Vaccination/s

 Blood sample

 Temperature check

In order to be in this study, your child must be:

- born at 37 weeks gestation or more
- healthy with no major medical problems (including no problems with their immune system)

- not yet received their first routine immunisations (due at 2 months of age)
- aged 8 to 13 weeks (i.e. the day they turn 13 weeks of age)
- not known to be allergic to any of the vaccines in the UK schedule

If your infant has any of the below, we would have to delay the study visit:

- a fever in the 24 hours before the visit or on the day of the visit
- received any other vaccine in the 2 weeks beforehand
- planned elective surgery, admission to hospital or any other procedure that may require a general anaesthetic in the 7 days beforehand

We would ask you some questions about your child's medical history including medication use and any vaccinations. We would record demographic details such as date of birth, and the study doctor would examine your baby to check they are able to take part. If available, we would also like to consent mum separately to collect her pertussis vaccination history during pregnancy, which may involve access to her medical notes. Why do we wish to collect this information? The UK Department of Health pertussis immunisation programme offers all pregnant women in the UK a vaccine against pertussis during pregnancy and this could have a possible effect on an infant's immune response to the pertussis vaccine.

If your child is enrolled in the study, your child's temperature will be taken before vaccination. We will ask you to give your child paracetamol at the same time as the meningococcal B vaccine at visit 1 and 3 as per Public Health England recommendations.

After each vaccination visit, we will ask you to complete a diary of symptoms every day for 5 days and we would like to know if you have given your child any medications after vaccination. We would also ask you to contact the study team if your child is admitted to a hospital at any point during the study.

To check your child's immune response to the vaccines (ie how well the body is able to fight off the infection that they have been vaccinated for), we would take 2 blood samples during the study, at 5 months and 13 months of age. We would use an anaesthetic cream to numb the skin for this and play assistants to distract your child if needed. Taking blood from children can sometimes be difficult and we may ask you for a second attempt if needed.

We would take a maximum of 5 ml (approximately 1 teaspoon) at each blood sampling visit. The main infection for which we will be checking your child's immunity will be Hib, a cause of meningitis and epiglottitis (a life threatening throat infection), but we will also be testing immunity to other infections.

You will be able to speak to a study doctor or nurse on the phone throughout the duration of the study if you have concerns about any of the study procedures.

How do we decide which group your child is in?

Infants will receive either Infanrix hexa (Group 1) or Vaxelis (Group 2) alongside their other routine vaccines. The group your child is allocated to is decided by chance, like tossing a coin. In this study, we will be using a computer programme and there will be a 50% chance of allocation to either group. Neither you nor the study team will be able to influence which group your child is allocated to.

Do I have to take part?

No, taking part in research is voluntary. If you decide you would like your child to take part in the study and later you change your mind, you can withdraw from the study at any time. You don't have to give a reason. If you withdraw from the study, we will keep the information about you that we have already obtained and your samples unless you let us know you would prefer us to destroy them.

What are the risks and benefits of taking part?

The benefits for your child are that they will receive their routine vaccinations in your home or a convenient location. We will be testing the immune response to the vaccines received, and if any child were to have an inadequate immune response to the Hib component of the 6-in-1 vaccines we would arrange for a booster dose of the appropriate vaccine. It is important to note we may not have this information for 12 or more months after the blood test.

Giving two different vaccines together can result in differences in how well they stimulate an immune response. Sometimes this can result in better immune responses and sometimes it is worse, particularly for the Hib part of the Vaxelis vaccine. It is important to test these interactions because Vaxelis shares some components with the MenB vaccine. This may also result in differing rates of common side effects such as fever.

Vaccines (like any medicine) can sometimes cause side effects. The most common side effects reported from Vaxelis are irritability, crying, fatigue, fever, reduced appetite, vomiting and redness/swelling and pain at the site of injection (which is similar to the other study vaccines). It is possible that these side effects may be more likely to occur if Vaxelis is given at the same time as the MenB vaccine.

Severe allergic reactions (anaphylaxis) to vaccines are very rare (less than 1 in 1 million) however our research nurses and doctors are trained and have the equipment to treat this should it occur. We will also observe your child for 15 minutes after a vaccine in case they have a reaction to a vaccine.

It is possible that after a blood sample there may be temporary bruising or tenderness. This pain will be reduced by using anaesthetic cream.

Who is doing this study?

The study is sponsored by the University of Oxford. The study is being coordinated by the Oxford Vaccine Group. The Oxford Vaccine Group is a research team at the

University of Oxford that includes scientists, doctors, nurses and play assistants. We perform research studies on topics related to infectious diseases and vaccines for children and adults. In the past 5 years over 7000 participants from the Thames Valley area have taken part in our research studies.

Funding has been received from MCM, the vaccine manufacturer of Vaxelis. The funder will have no influence on the results of the study.

What will happen to the samples obtained in the study?

Samples will be processed and stored at the Oxford Vaccine Group laboratory and sent to other laboratories in the UK for analysis. It won't be possible for your child to be identified from their samples. We will ask you if you would like to have any left over samples stored in our library of samples called a biobank. If you are interested in this, we will provide you with a separate booklet and ask you to sign another consent form for this. To be able to answer the study questions we need to enrol at least 240 participants in this study.

What will happen to the information collected in the study?

Your child will be given a study number, which will be used on study paperwork and samples collected. Any paper notes will be held securely in the Oxford Vaccine Group. With your permission, we may need to obtain information from your child's medical records to confirm medical history or vaccinations received. We will inform your child's GP/health visitor that your infant is taking part in the study and that we will be giving them their routine vaccinations up to and including their 12 month vaccines.
GDPR Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest'.

We will use the minimum personally-identifiable information possible. We will store the anonymised research data and any research documents with personal information, such as consent forms, securely at the University of Oxford for 21 years after the end

of the study as per the University requirements for studies that include paediatric participants.

The University of Oxford will use your and your child's name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your child's care, and to oversee the quality of the study. Individuals from the University of Oxford and regulatory organisations may look at your child's or the child's mother's medical and research records to check the accuracy of the research study. The only people in the University of Oxford who will have access to information that identifies you will be people who need to contact you about the study or the care of your child or to audit the data collection process. The people who analyse the information collected and the samples will not be able to identify your child and will not be able to find out your child's name or contact details. If you withdraw from the study, we will keep the information about you that we have already obtained. We may contact you about future studies if you have indicated this on the consent form.

We will keep your contact details, confidentially, to inform you about the results of the research. Once the research has been published, we will no longer keep full contact details only your child's date of birth and name to allow us to identify your child should you make an enquiry about the study. Files will be confidentially destroyed if storage is no longer required.

The Oxford Vaccine Group will use your child's name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. You can find out more about how we use your information by contacting the Oxford

Vaccine Group either by telephone on 01865 611400 or by emailing info@ovg.ox.ac.uk.

Further information about your rights with respect to your personal data is available at http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights/*].*

What happens at the end of the study?

We will let you know if your child does not have adequate immunity to Hib and offer your child an additional booster vaccine if needed. We will provide a copy of the published data on our website and a summary of this will be sent to you with a link to enable you to access the full information.

Who has reviewed this research study?

Before any research goes ahead it is checked by a Research Ethics Committee. This project has received a favourable ethical opinion from the South Central- Oxford A Research Ethics Committee (REC reference: 19/SC/0052).

What if I wish to complain?

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 your local study team at the Oxford Vaccine Group office (who are the central site for this study) on 01865 611400 or email info@ovg.ox.ac.uk. You may also contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or the head of CTRG, email ctrg@admin.ox.ac.uk . The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this trial. If you do not wish to receive invitations of this kind in the future, please register your child on the Oxford Vaccine Group opt-out list at www.trials.ovg.ox.ac.uk/trials/opt-out.

So, in summary, what would happen if I decide to take part in the study?

- We would make an appointment to see you and your child at home or at a convenient location.
- At this visit we will discuss the study with you and answer any questions
- If you're happy to participate in the study, we will ask you to sign a consent form

What should I do now if I'm interested in taking part?

You do not need to make a final decision straight away. If you decide to take part in this study or have any questions, there are a few options;

- You can contact the research team by the phone number or email address in this booklet
- Complete the reply slip and post it to the study team using the pre-paid envelope provided.

If your response reaches us after recruitment is complete we will let you know. A postcard reminder may be posted to you by the National Health Applications and Infrastructure Services (NHAIS), the Child Health Information Service or an equivalent NHS database as described above. If we do not hear from you after this, we will assume that you do not want to take part.

Thank you for taking the time to read this information sheet.

Yours sincerely,

Professor Matthew Snape
Chief Investigator
Associate Professor in General Paediatrics and Vaccinology