OXFORD VACCINE GROUP

Meningococcal B Booster Vaccine in Young People

Parent/Legal Guardian Information Booklet

Children are at risk of meningitis and septicaemia (blood poisoning) due to a bacteria called meningococcus. Understanding how young people respond to vaccination against this disease may help to protect them in the future**.**

Oxford Vaccine Group (OVG) are inviting your child to take part in a a study looking at the responses that young people make to a licensed vaccine (4CMenB) against meningococcus group B (MenB). We are recruiting 2 groups of childen: those who received the vaccine as an infant or toddler; and a group of children who did not.

Children who received the 4CMenB vaccine as an infant or toddler form a unique and special group. We want to assess how well the vaccine they received in the past is still protecting them from MenB , especially if we give them a booster vaccine, compared with children who have never receieved the vaccine.

Before you decide whether you would like your child to take part you should understand what the study is about and what participation would involve. Please read the information carefully and discuss with your child and others if you wish. There is an separate information leaflet available designed for your child to read. If anything is unclear, or you would like further information, please contact the study team.

Thank you for considering taking part in this study.

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Dear Parent/Legal Guardian,

The Oxford Vaccine Group (OVG) would like to invite your child to be involved in a study assessing how young people respond to a vaccine against meningococcus group B (MenB). Approval for this study has been gained from the East Midlands – Nottingham 2 Research Ethics Committee.

Who are the Oxford Vaccine Group?

The Oxford Vaccine Group, which is part of the University of Oxford, is an independent research team of Doctors, Nurses and Play Assistants. We carry out research studies on topics related to infectious diseases and vaccines for children and adults. In the past 5 years alone over 7,000 participants in the Thames Valley area have taken part in our research studies.

Why has my child been invited to take part?

We are inviting two groups of children who are aged about 11 years to be involved in the study:

1. A unique group of children who took part in an Oxford Vaccine Group study when they were an infant/toddler in which they received 4CMenB, the vaccination against meningococcus group B (MenB)
2. Healthy children who did not receive a MenB vaccine as an infant/toddler, who are within the age range for this study and living in an area where this study is being carried out

If your child previously took part in an Oxford Vaccine Group study and you agreed to hear about future research, we have used the contact details that you gave to us at that time, or asked your GP to send this invitation.

If your child did not did receive MenB vaccine as an infant/toddler, this invitation has either been posted to you by the National Health Applications and Infrastructure Services (NHAIS) who hold the central NHS patient database, via your child's school or your GP surgery. Please note that the Oxford Vaccine Group has not been given your child's name and address.

Why are vaccines important?

Vaccines stimulate our immune system to protect us from infectious diseases by making us produce something called antibodies in our blood. This is an immune response. If a child comes into contact with an infectious disease against which they have been vaccinated (or "immunised"), the antibodies will help their body to recognise and fight the disease. Without vaccines children are at increased risk of catching many serious diseases.

What is meningococcal infection?

Meningococcal infection is caused by a family/group of bacteria (or germs) called meningococcus. Meningococci are carried naturally in the back of the throat (or nasopharynx) and are most commonly found in adolescents. They don't usually cause any harm. However, in some situations the bacteria can overcome the body's defence and cause meningitis (infection around the surface of the brain) or septicaemia (blood poisoning). This is rare, but can be life-threatening, and mostly affects babies, young children and adolescents.

There are 5 main groups of the meningococcus family that cause disease: A, B, C, W and Y. In the UK, from the beginning of July 2015 to the end of June 2016 there were 805 confirmed cases of meningococcal disease; 15% occurred in 15-24 years olds. MenB accounted for 55% of all cases; or 444 out of the 805 cases.

What is this study about?

In this study we are seeking to understand the immune response of young people to the 4CMenB vaccine, the vaccine against MenB infection. We are trying to determine if children who received the vaccine as infants and toddlers are still protected from MenB infection as they enter adolescence, and if they have a stronger immune response with just a single booster ("top up") vaccine than those who have never received the vaccine.

4CMenB has been given to infants and toddlers as part of the routine immunisation schedule in the U.K. since September 2015. It has not been given to adolescents as part of the schedule due to concerns about cost-effectiveness. If the vaccine can be given as a one-off booster to those that received the vaccine as infants, rather than two doses that are currently required in adolescents who never previously received the vaccine, then this could be a cost-effective and acceptable way to protect adolescents from MenB infection.

What happens in this study?

Children will receive one or two doses of the licensed 4CMenB (Bexsero®) vaccine and have four blood tests taken over the course of a year.

Children who received a course of 4CMenB vaccine as an infant or toddler whilst taking part in an Oxford Vaccine Group research study (the same vaccine that is now used in the routine infant immunisation schedule) are being invited to take part if their parents agreed to hear about future research studies. All previously vaccinated children will receive one dose of 4CMenB.

In addition a group of about 30 children of the same age, around 11 years (born between 25/06/2006 and 17/12/2006), who have never received any 4CMenB vaccine are being recruited to this study (they will make up the control groups). These children will receive two doses of 4CMenB. The children in the control groups will be randomised, like flipping a coin, to receive two doses of 4CMenB vaccine either one month or one year apart. You or the study team would not be able to influence which vaccine schedule your child is randomised to receive.

To test the immune response to the 4CMenB vaccine, all children who take part in the study will have four blood tests performed, spaced out over a year, as shown in the table below. The blood samples taken before receiving a 4CMenB vaccine in this study will allow us to see if there is an immune response still present after being vaccinated as a baby or toddler. Samples collected from the control groups will provide a comparison.

Blood samples collected at visits 2, 3 and 4 are taken after all children have received one dose of 4CMenB vaccine in this study. This will allow us to compare the immune response between one dose of 4CMenB in those vaccinated as an infant or toddler and those who were not.

Where will the study visits happen?

There will be a total of 4 visits for all children. All visits and study procedures would be conducted at your home or within a central location such a hospital outpatients clinic. Study visits would take place before or after school, at weekends or during school holidays and all but the first would take around 30 minutes. The total duration of the study for each child will be 12 months.

At the first visit you and your child would be given the chance to discuss the study in more detail, including the risks and benefits of participation. If you were happy

for your child to take part we would ask you to sign the consent form and you would be given a copy of this to keep. We would ask your child to sign an assent form. One of our study doctors or nurses would ask you some questions about your child's medical history to ensure he/she was able to be included. This visit may take longer than the others, approximately 1 hour.

How will the blood test be taken?

The amount of blood taken at each visit will be 20ml, approximately four teaspoons. This will be taken from the inner arm in the elbow crease or the back of the hand. In order to minimise discomfort from these blood tests we would use an anaesthetic cream or cold spray to help numb the skin. At the first visit the OVG staff would put it on and for all the other blood test visits, we would give you the cream and instructions to put it on before study visits.

How will the 4CMenB vaccines be given?

The 4CMenB vaccine would be given by injection into the top of your child's non-dominant arm.

What will we ask you to do after each vaccine?

After the vaccination visits, you would need to measure and record your child's temperature as well as any side effects from the vaccine that he/she may have.

We would ask you to record within an electronic diary (e-Diary) how your child was feeling in the seven days after receiving the vaccine. In addition, we would require you to record details of any illnesses requiring a medical visit and any medicines given to treat these for the 28 days following vaccination.

Children in groups 1-6, which differ depending on their previous vaccination schedule, will only need to complete the e-Diary once because they are only receiving one dose of vaccine. Children in group 8 will have a second dose of vaccine at visit 2 (four weeks after the first dose) and will be asked to complete the e-Diary for 28 days for a second time. Children in group 7 who receive their second vaccine at the final study visit (visit four, one year after the first dose) are only required to complete the e-Diary for seven days after this final study visit.

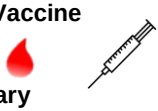
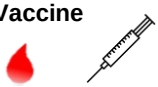
Recording any vaccine side effects is a very important part of the study. As this will be done by using an electronic diary (e-Diary), having access to the internet during the study period is crucial. The e-Diary will allow us to capture both expected side-effects (e.g. fever, redness, swelling and pain around the injection

site) and non-expected side effects from the vaccines. Completing the e-Diary is usually quick and you will be shown how to use it by a Doctor or Nurse.

After each 4CMenB vaccine we may also ask you to monitor your child's temperature continuously for 24 hours. We would issue you with a special temperature monitoring device for this as well as instructions on how to fit it, and what to do with it at the end of the monitoring period. It would be about the size of a small watch and would be worn around the wrist. It needs to be removed for activities like bathing, showering and swimming and then put on again afterwards.

You will be provided with a telephone number to enable you to have 24-hour access to one of our paediatric doctors for telephone advice should you have any concerns about your child's health following vaccination.

Table summaring what happens in this study

Study Group	**Visit 1** Day 0	**Visit 2** Day 28 (one month)	**Visit** 3 Day 180 (six months)	**Visit 4** Day 365 (one year)
1- 6	**Blood sample + Vaccine**  **Diary Temperature monitoring**	**Blood sample** 	**Blood sample** 	**Blood sample** 
7	**Blood sample + Vaccine**  **Diary Temperature monitoring**	**Blood sample** 	**Blood sample** 	**Blood sample + Vaccine**  **Diary Temperature monitoring**
8	**Blood sample + Vaccine**  **Diary Temperature monitoring**	**Blood sample + Vaccine**  **Diary Temperature monitoring**	**Blood sample** 	**Blood sample** 

What are the possible side-effects of the vaccines?

The 4CMenB vaccine is a licensed vaccine, meaning that it has met the rigorous safety standards required by European medicine safety organisations.

Your child may have some side effects from immunisation with the 4CMenB vaccine. 4CMenB is not a live vaccine and therefore cannot cause a meningitis infection. Side effects that we would expect to see after immunisation generally are pain, swelling or redness at the site of the injection and more general effects such as fever, malaise (general feeling of being unwell), muscle pain, irritability and headache. With 4CMenB vaccine, the most common side effects in young people (from 11 years of age) and adults were pain at the injection site, malaise and headache. Paracetamol or Ibuprofen can be given to relieve these reactions if they occur.

In addition to the reactions listed above, there may be reactions to the 4CMenB vaccine that are not yet known because it has never been given as a booster dose to those that have been immunised as infants or toddlers. However, as the 4CMenB vaccine is part of the UK national infant immunisation schedule, and recommended for all individauls with increased risk factors due to certain medical conditions, its safety is continually being monitored through the routine safety surveillance systems.

As with all vaccines, there is a small chance of an allergic reaction to the 4CMenB vaccine so we would monitor your child for 15 minutes following vaccination. The study nurses/doctors are specifically trained and equipped to deal with this unlikely event.

What are the possible side-effects of blood sampling?

There may be some pain at the blood sampling site, as well as possible bleeding and/or bruising following the blood sample.

Does my child have to take part in the study?

No, taking part in research is voluntary. If you decided not to participate this would not affect your child's routine care in any way. You are free to change your mind at any point in the study. Whatever you choose it is important that you and your child are happy with your decision and it is not the role of the study team to help decide for you.

What are the benefits of taking part?

We anticipate that the 4CMenB vaccine will protect against most types of MenB disease. Although it is already licensed, 4CMenB is not currently routinely given to young people in the UK. Information from this study will help us learn more about

how the vaccine could been used in the future as a booster (topping up) to extend protection against meningococcal group B disease.
Please note that if your child is randomly allocated to group 7 then the final vaccine at Visit 4 is to complete the recommended vaccination schedule for adolescents.

What will happen to the samples obtained in the study?

Blood samples obtained in the study would be labelled with your child's study code and number but not his/her name. They will be stored in a freezer at the Oxford Vaccine Group until the analysis takes place. The samples may be shipped to collaborators outside of the UK and the European Union, for analysis.

Separately, we will ask you for permission to store left over components of your child's blood, including DNA (genetic material), in a collection of samples called a 'BioBank'. Details of this will be provided to you before you are enrolled into this 4CMenB vaccine study. You are free to say no to the BioBank study and continue to take part in this 4CMenB study.

At the completion of the study any remaining blood samples will be destroyed if you have not given consent for these to be retained in the Oxford Vaccine Centre Biobank.

Would my child's taking part in this study be kept confidential?

We inform your child's GP after you and your child have consented to taking part in the this study. We will also let them know when we have given the 4CMenB vaccine.

The University of Oxford is the data controller for this study, and is therefore responsible for looking after your information and using it properly. All personal information and samples collected from your child will be coded with a study number and kept strictly confidential. Your child's information would be stored on a secure server hosted by the University of Oxford and paper notes would be held by the Oxford Vaccine Group in a locked filing cabinet. Only authorised study staff can access your child's data and samples. Your child's personal information (name, date of birth, and contact information) is kept separately to their study results and will only be used to contact you about the study or for medical reasons. Following completion of the study all study records (which includes some personal data such as name, date of birth and contact details) will be retained up to 3 years after the youngest participant reaches 18 years of age. We would also seek your permission to use the data in future related research. Files will be confidentially destroyed when no longer required. Your

rights to access, change or move your information are limited as we need to manage your information in specific ways in order for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally identifiable information possible. You can find out more about how we use your information by contacting the study team.**Who else can see my child's study records?**

In order to ensure that the study is being conducted correctly the study records can be inspected by the Clinical Trials and Research Governance Office (CTRG), University of Oxford, without violating yours child's confidentiality. This group is responsible for ensuring the appropriate conduct and accuracy of the research on behalf of the research sponsor (University of Oxford).

By signing the consent form for this study you would be giving permission for CTRG to look at your child's medical records, however they would not be able to remove information that identified your child from the Oxford Vaccine Group premises.

Your child's study information, removed of any identifying information, might also be used for additional medical and/or scientific research projects in the future. If you do not want the information used in this way, or have any questions about the use of your child's information in the study, please inform the study team.

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

You can change your mind and withdraw your child from the study at any time without giving any reason. If you change your mind and withdraw your child from the study we would use the samples and data we have collected up until the point you informed us that you wanted to withdraw, unless you inform us in writing that you wish for your child's data and samples to be destroyed.

What will happen at the end of the research study?

The results of the research will be published in a scientific medical journal; this potentially can take up to 2 years. All Oxford Vaccine Group publications will appear on the Oxford Vaccine Group website and you will receive a letter containing these results. Your child would not be identified in any report or publication and we will not provide individual results.

If you are interested in hearing about other research studies that we may be running in the future then there is an option to sign up to an Oxford Vacine Group Children

and Young People's Database through which we can get in touch. This does not oblige you in any way to take part in the future research.

What if I wish to complain?

If you wish to complain about any aspect of the way 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 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 http://trials.ovg.ox.ac.uk/trials/opt-out/.

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that your child suffers any harm as a direct consequence of participating in this study. Similarly, the venues where the study may be conducted will also have appropriate insurance; more information can be provided as required.

What else do I need to know?

All research is looked at by an independent group of people, called a Research Ethics Committee, to protect participant's interests. This study has been reviewed and given favourable opinion by East Midlands - Nottingham 2 Research Ethics Committee.

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

- Your child would receive one dose of 4CMenB vaccine if they were vaccinated as an infant or toddler
- Your child would receive two doses of 4CMenB, one month or one year apart, if they have never received this vaccine before
- A member of the research team would give the vaccines at your home or appriopriate venue before or after school, at weekends or in the school holidays.

- Your child will have four blood samples taken during the study spaced out over one year
- You will need to complete an electronic diary online for 7 days after each vaccine

- You will be given and shown how to use a 24 hour temperature monitoring device after each vaccine to be worn around your child's wrist.
- You would have 24-hour telephone access to a study doctor in case you had any concerns following vaccinations

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, the next step would be to proceed to www.menbb.org.uk to complete the online eligibility and then we will contact you to arrange the first study visit if appropriate. Alternatively, you can contact the research team, who will be happy to discuss the study with you, answer any questions you have, screen your child and book the study visit over the phone. If your response reaches us after recruitment is closed we will contact you to let you know.

For those we are re-contacting, if we have not heard from you within 2 weeks we may send you a recruitment pack either through your GP or through Child Health Information Services. We may also contact you through other methods such as an email or phone call to invite your child to participate in this study.

Contact Details:

Oxford Vaccine Group
Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)
Churchill Hospital
Oxford,
OX3 7LE
Tel: 01865 611400 **Email:** info@ovg.ox.ac.uk

Thank you for considering taking part in this study.

Yours sincerely,

Professor Andrew Pollard
Study Chief Investigator
Professor of Paediatric Infection and Immunity
Honorary Consultant Paediatrician