Follow on study of two swine 'flu vaccines in children

INFORMATION BOOKLET

You and your child are being invited to take part in a follow-on study to the Influenza A H1N1 (swine 'flu) vaccine trial of last year. The study is being run by the Oxford Vaccine Group, part of the University of Oxford.

Before you decide whether to take part, 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 anything is unclear or you would like further information please contact the study team – details below.

Thank you for taking the time to consider participating in this study.

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Dear Parent/Legal Guardian,

Last year your child took part in a study comparing two different vaccines against Influenza A H1N1 (swine 'flu). We would like to thank you once again for taking part in this important study.

The Oxford Vaccine Group would now like to invite you and your child to participate in a follow-on study. This new study aims to find out how well the antibodies in your child's blood to the swine 'flu vaccine given last year have lasted. We would also like to assess your child's response to this year's "seasonal" 'flu vaccine, however you could still take part in the study even if you did not want your child to receive this. Just like last year, we will also monitor the side effects of the vaccine given. We would also like to ask you some questions about your child's health since we saw you last.

This booklet provides information about the follow-on study and what it would involve if your child were to take part. The study is being sponsored by the University of Oxford and is being conducted by a network of vaccine study centres in collaboration with the Health Protection Agency (HPA). This study has been approved by the Oxfordshire Research Ethics Committee and the Medicines and Healthcare products Regulatory Agency (MHRA) and is funded by the Department of Health.

What is this study about?

In 2009 the World Health Organization (WHO) declared the Influenza A H1N1 (swine 'flu) outbreak the first global pandemic of this century. It is thought to have been responsible for 16,226 deaths globally as of 21st February 2010. We know from previous influenza outbreaks that the number of cases also tends to increase during the winter season of the years after a pandemic. There is concern that last year's pandemic influenza strain will return this winter and it has, therefore, been included in WHO's recommendations for seasonal influenza vaccine combinations. This study will assess the duration of the immune response to the H1N1 influenza vaccines given last year, and how children will respond to this year's seasonal trivalent influenza vaccine (which includes the H1N1 strain). Participating children would receive one dose of a licensed seasonal influenza vaccine and blood tests would be taken before and after vaccination. As in the original study, we would also ask you to complete a diary card to monitor any side-effects of the vaccine.

Taking part in this study is voluntary and, if you do not want your child to participate, you do not have to do anything.

What does the study involve?

The study consists of 2 visits occurring 3 weeks apart and involves 1 vaccination and 2 blood tests. These visits would be conducted at the Children's Hospital (John Radcliffe Hospital) in Oxford.

At the first visit, the study would be explained and you would be given the chance to ask any questions you may have. Before enrolment into the study, a doctor would examine your child and ask you some questions to ensure s/he was able to be included. Reasons that children would <u>not</u> be able to take part in the study include:

- Having already received the seasonal influenza vaccine this autumn/winter
- History of egg allergy or allergic reaction after receiving the Influenza A H1N1 vaccine

- Problems with the immune system
- Bleeding disorders
- Receiving steroid tablets or syrup (e.g. for asthma) for more than 1 week within the previous 3 months (steroid inhalers or creams are allowed)
- Recent transfusion of blood or blood products within the previous 3 months
- Recent or current participation in another clinical trial
- Not being available for the study visits
- If they did not receive two doses of swine 'flu vaccine in last year's study
- If a third dose of the swine 'flu vaccine had been given (due to an inadequate response to the first two doses) in last year's study.

If your child was enrolled we would ask about any health problems since we saw them last and take a blood test to assess how well the immune response to the previous Influenza A H1N1 vaccine has lasted. If you were happy for your child to receive the seasonal influenza vaccine, we would give this, and a second blood test would be taken around 3 weeks later. For each blood test we would take 7 to 10 mls of blood (approximately 1½ to 2 teaspoonfuls, depending on the age of your child). Local anaesthetic cream or cold spray would be used to minimise the discomfort of the blood test.

After the first visit, a diary card would be given to you to record daily temperatures and any reactions, such as redness or swelling at the injection site for 7 days. We would also ask you to record any visits to a doctor or the hospital from the time of vaccination until the second visit. We will collect the diary card at the second visit.

If you do not wish your child to receive the seasonal influenza vaccine, then it is still possible to take part in the study. In this case, we would take one blood test (to assess how well immunity from last year's vaccination has lasted).

How many participants are there in the study?

937 children in Oxford, Bristol, Exeter, Southampton and South London completed the original study and we hope that as many as possible would be able to take part in this follow-on study.

Which vaccine is going to be used in this study?

The study will use a licensed seasonal influenza vaccine, Fluarix® (produced by GlaxoSmithKline Biologicals, Dresden, Germany), which is designed to provide protection against three influenza strains: A H1N1, A H3N2 and B.

The table below summarises the study design; it is possible for participants to just have the blood test at Day 0 if that was preferred:

Day 0	Day 21 (3 weeks)
- Blood test - Seasonal influenza vaccine	- Blood test

What are the advantages of taking part in the study?

The study provides the opportunity for your child to receive the seasonal 'flu vaccine. This is not routinely given to healthy children in this country, although it is routine in some other countries and it may help provide protection against the strains of flu most likely to be circulating this winter, including swine 'flu. At the end of the study we will also be able to tell you whether your child is protected against influenza A H1N1 and will contact the families of those children who have not mounted a full response to the Influenza A H1N1 component of the vaccine. We will offer to arrange an additional dose of the seasonal 'flu vaccine for these children.

What are the risks and side-effects of taking part in the study?

The trivalent seasonal influenza vaccine (Fluarix) is approved by the European Medicines Agency for prevention of influenza in all ages and has been available for use since 1987. It has consistently been shown to provide satisfactory immune responses against the influenza strains included in the vaccine, and has been shown to be safe. This vaccine does not contain live influenza virus and therefore cannot cause an influenza infection. Like all medicines, this vaccine may cause side effects in some individuals. More common side-effects (1-10% of those vaccinated) include headaches, sweating, muscle and joint pain, fever, feeling generally unwell, shivering, fatigue and local reactions (e.g. redness, swelling, pain, bruising and hardness). These events are generally mild and resolve within a few days. Very rare side-effects include an itchy rash (urticaria), blood vessel inflammation (vasculitis) which may result in skin rashes and in very rare cases temporary kidney problems, neurological disorders (e.g. Guillain-Barre syndrome), temporary reduction in the number of blood components (platelets) which can result in excessive bruising or bleeding (transient thrombocytopenia) and temporary swelling of the lymph nodes (glands) in the neck, armpits or groin. An increased risk of fever fits (febrile convulsions) following seasonal 'flu vaccine in children who had previously received a swine flu vaccine, has recently been described in Australia. This occurred in up to 9 in 1000 recipients (0.9%) of a particular influenza vaccine compared with a rate of less than 1 in 1000 (0.1%) with other seasonal 'flu vaccines. The vaccines used in Australia were different vaccines from those used in this study or the one your child took part in last year.

Finally, as with all vaccines there is the very small possibility of a severe allergic reaction (anaphylaxis). Your child would, therefore, be observed for at least 20 minutes after the vaccine is given; all staff are trained and specifically equipped to respond to this unlikely event.

What happens to the blood samples?

Blood samples obtained in the study would be labelled with your child's study code and study number, but not their name, and would be tested for the immune response to the swine 'flu virus. We would also ask your permission to use any remaining blood samples anonymously for future studies of immunity to infection. The stored blood samples will be anonymised before any further tests are performed so that it will not be possible to link the results of these extra tests back to your child. You will be asked to consent specifically for the storage of blood samples; if you are not happy for the samples to be stored and used for any other tests then you do not have to check this box on the consent form and it will not prevent you from taking part in the study. In this case your samples will be destroyed after testing for the influenza vaccine responses. Your

decision regarding the blood sample will not affect your child's participation in the influenza vaccine aspect of the study.

Also, for approximately 40 participants we will be asking for consent to use a small amount of the blood taken to study how your child's genetic code is 'read' when your child's immune system is responding to the influenza vaccine. As with the stored blood these genetic samples will be anonymised prior to testing, and if you did not want your child's blood to be tested in this way then you do not have to consent for this and can still take part in the main study. It is possible that blood samples or anonymised data may be sent outside the European Union for analysis.

Is there someone I can contact during the study? If your child were to take part in this study, we would provide you with a 24-hour telephone number to enable you to contact one of our study team should you have any concerns.

Who else would be told about my child's involvement in the study?

Your child's participation would remain confidential. With your permission we would inform your GP and child health department that your child was enrolled in this study and that we had administered the trivalent seasonal influenza vaccine. Any study records with your child's name and address would be held by the Oxford Vaccine Group only. Your child's first name will also be on the front of the diary card. We also plan to publish the results in a medical journal which will be accessible to the public, but will not contain any information that might allow children who took part to be identified by those reading it. At the end of the study, we will also write to all participating families to summarise the overall findings

In order to ensure that the study is being conducted correctly, the following groups may inspect the study records and your child's medical records, without violating your child's confidentiality:

- Monitors hired to check that the study is being conducted to a high standard
- The Clinical Trials and Research Governance Office, University of Oxford, who are responsible for ensuring the appropriate conduct of the research on behalf of the research sponsor (the University of Oxford)
- The Medicines and Healthcare products Regulatory Agency (MHRA), who regulate all medicines and vaccines in the United Kingdom.

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

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

What happens if I say '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 also free to change your mind at any time without giving any reason. If you decide not to take part, you should follow any advice from your GP or the government regarding influenza vaccines.

What if I wish to complain?

If you have any cause to complain about any aspect of the way in which you have been approached or treated during the course of this study we suggest that you contact us on 01865 857420 (*ovg@paediatrics.ox.ac.uk)* or, alternatively, the University of Oxford Clinical Trials and Research Governance Office on 01865 743005.

What else do I need to know?

In the highly improbable event that your child would suffer any harm during the study, compensation for harm arising from the vaccine would be provided by the vaccine manufacturers. The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment with which you are provided.

Should any information become available during the course of the study that may affect your child's participation, you would be informed as soon as possible.

At the end of the study, we will give you a "Feedback form", which you can fill in and return to us in a prepaid envelope. This is to give you the chance to tell us what you think we did well and whether you think there was anything we could do better in future. You will not be asked to write your name on this form, so we will not know who returned it.

At the end of the study we would pay you a fee of £10 per visit to compensate you for any travel costs incurred as a result of taking part in the study.

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

We would take a blood sample and collect relevant medical information.

If you are happy for your child to receive the seasonal influenza vaccine, we would also:

- Give one dose of this vaccine
- Collect a second blood sample, three weeks later
- Give you a diary card to record any possible side-effects after the vaccine
- Provide 24 hour telephone access to our study team, to discuss any concerns you may have following the vaccination.

What do I do now?

Participation in this study is voluntary. Please remember that you can withdraw your child from the study at any time without giving a reason. If you are interested in taking part, please visit the study website

http://www.paediatrics.ox.ac.uk/ovg/swineflu/, email us on (*ovg@paediatrics.ox.ac.uk*) or phone our appointment line on 01865 857420 to arrange a time to attend the Oxford Children's Hospital. Please remember to bring your child's health record (the 'red book') to your first visit. If you wish to discuss any element of the study further, then please contact us by e-mail (*ovg@paediatrics.ox.ac.uk*) or telephone 01865 857420.

Yours sincerely

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Professor of Paediatric Infection and Immunity

Honorary Consultant Paediatrician

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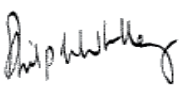

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