OXFORD VACCINE GROUP

Swine Flu (Novel Influenza A H1N1) Vaccine Study

Information Booklet

You and your child are being invited to take part in a study of a vaccine against Influenza A H1N1 (swine flu). 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 taking part in this study.

Contact Details

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Dear Parent/Legal Guardian,

The Oxford Vaccine Group would like to invite your child to be in a study that will look at how well children respond to two new vaccines against H1N1 influenza (swine flu). This booklet outlines the study and what it would involve if your child were to take part. This 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). Approval for this study has been gained from the Oxfordshire Research Ethics Committee and the Medicines and Healthcare products Regulatory Agency (MHRA).

What is this study about?

In the first half of this year a new strain of Influenza A H1N1 virus (known as 'swine flu' or 'Mexican flu') began to cause infections in humans. As this virus is very different from previously circulating influenza strains, few people have immunity to it and a global influenza pandemic has occurred. Fortunately most people who catch swine flu have a relatively mild illness, but a few people become very unwell and may even die. Many of these people have other underlying health conditions, such as heart or lung disease that put them at increased risk of severe disease.

Two new vaccines have been made against swine flu in response to the pandemic. These vaccines have been tested in adults, but there is less information on how well they work in children. This study will assess these two new vaccines in children aged between six months and twelve years. Participating children would receive two doses of swine flu vaccine and blood tests would be taken before and after vaccination to see how well the immune system responds. We will also look at any side effects of the two vaccines.

Taking part in this study is voluntary and if you do not want your child to participate he/she would still be eligible to receive a swine flu vaccine if it were to become available as part of a government immunisation program.

What does the study involve?

This study would consist of 3 visits each occurring 3 weeks apart over a 6 week period and would involve 2 vaccinations 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 not be able to take part in the study include:

- Previous swine flu vaccination
- Previous swine flu infection (only if confirmed by laboratory testing or treated with oseltamivir ('Tamiflu') or zanamivir ('Relenza'))
- History of egg allergy or allergic reaction after previous vaccinations
- Problems with the immune system
- Coagulation 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)
- Concurrent participation in another clinical trial
- Not being available for all the study visits

If your child was able to be enrolled, s/he would be allocated to one of two groups to decide which vaccine s/he would receive. The group allocation would be determined by a computer programme so that this would be decided by chance (similar to tossing a coin). Neither you nor the study team would be able to influence which group your child was allocated to.The vaccines would be given at the 1st and 2nd visit.

In order to assess the response to the vaccine each child would have 2 blood tests, one before the first vaccination and the second 3 weeks after the 2nd dose of vaccine. For each blood test we would take 6 to 10 mls of blood (one to two 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.

A diary card would be given to you after each vaccine visit. In this diary we would ask you to record daily temperatures and any reactions, such as injection site redness or swelling for 7 days after each immunisation. After this, we would ask that you to send the completed diary card to the Health Protection Agency using a pre-paid envelope. A

member of the study team will phone you after 7 days to ensure that your child is well and to remind you to post the diary card. A memory card would also be given to you after each vaccine visit. In this card we would ask you to record any reactions recorded in the diary card that are ongoing after day 7 and any visits to a doctor or emergency department until your next study visit.

In order to conduct this study as quickly as possible we plan to see many children over a short space of time. We would therefore ask you to come prepared to wait at various points during the visits. We will try to see you and your child as quickly as possible.

How many participants are there in the study?

A total of 1000 children will take part in this study; 500 aged 6 months to 3 years and 500 aged 3 to 12 years. Children will be recruited in Oxford, Bristol, Exeter, Southampton and South London.

What vaccines are going to be used in this study?

The two vaccines being assessed in this study are those that the UK government has arranged to be supplied for use if routine immunisation is recommended. One of these vaccines is made from an inactivated form of the whole swine flu virus, and is produced by the pharmaceutical company Baxter Vaccines. The other vaccine is known as a 'split virion' vaccine, meaning that it is made from a few key components of the virus, and is produced by the pharmaceutical company GlaxoSmithKline. This vaccine also contains an adjuvant called AS03 (an adjuvant is a substance designed to stimulate the immune system) and the preservative thiomersal.

The table below summarises the study design:

	Day 0	Day 21 (3 weeks)	Day 42 (6 weeks)
Group A	Baxter swine flu vaccine Blood test	Baxter swine flu vaccine	Blood test
Group B	GSK swine flu vaccine Blood test	GSK swine flu vaccine	Blood test

(Each group will have 250 children aged 6 months to 3 years and 250 children aged 3 to 12 years)

What happens if my child receives the vaccine that is not used by the government in the future?

As a result of this research the government may choose to use the vaccine that your child DID NOT receive. There may be several reasons why one of the vaccines is chosen over the other including vaccine cost, side effect frequency, response of the immune system and vaccine availability. We are expecting both vaccines to give sufficient protection and therefore don't anticipate your child requiring a further vaccine in the future. However, if your child would be better protected by receiving the other vaccine at a later date then there is no medical reason why s/he could not receive it.

Why does my child need two doses of the vaccine?

The information that we have from previous research shows that children's immune systems do not respond sufficiently after just one vaccine dose. It is expected that giving 2 doses 3 weeks apart will give the best immune response in children. Having a good immune response will be especially important if the virus changes in the future.

What are the advantages of taking part in the study?

The study provides the opportunity for your child to receive a swine flu vaccine whilst helping us to assess the response to the vaccine.

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

Both of the vaccines to be used in this study have been adapted from vaccines originally designed to protect against 'bird flu' (influenza A H5N1), and most of the information that we have about the vaccines to be used in the study comes from trials of the 'bird flu' versions of the vaccines. Over 600 adults have received the 'bird flu' form of the Baxter vaccine in clinical trials, but this vaccine has not been tested in children or adolescents under 18 years of age. Over 5,000 adults and 300 children aged 3 to 9 years have received various doses of the 'bird flu' version of the GSK vaccine in clinical trials. Both companies have started, or are about to start, studies of their 'swine flu' vaccines in children.

From the studies of the GSK 'bird flu' vaccine in children it is possible that approximately one third of children receiving the GSK 'swine flu' vaccine will have a fever over 37.5 °C, and that this fever may be above 39°C in approximately 1 in 10

children. In the ‘bird flu’ vaccine studies these fevers are short lived and were not associated with any complications such as febrile convulsions (a seizure associated with fever that does not have long term effects), but it is possible that complications such as these could rarely be seen following the ‘swine flu’ vaccine. As no studies of the Baxter ‘bird flu’ vaccine have been completed in children we do not know what the fever rates following this vaccine will be, but it is to be expected that some children receiving this vaccine will also develop a fever. We would therefore suggest that you have a supply of medicine against fever (such as paracetamol or ibuprofen) available for the first few days after immunisation.

Other reactions that may be observed are tenderness, redness, bruising, swelling, hardness or warmth at the injection site. Uncommon reactions are a change in eating habits, sleepiness, persistent crying, irritability, swelling of lymph nodes (‘glands’), muscle pain or joint pain. Very rare (less than 1 in 1000) reactions seen in adults receiving the H5N1 vaccines include vomiting, diarrhoea, rash, cough and a congested nose. We expect these events to be generally mild and to resolve within a few days. Other very rare events that have been seen with routine flu vaccines include seizures and temporary bleeding disorders. In the past Guillian-Barré syndrome (a rare disorder of nerves) has been associated with flu vaccines but the relationship remains uncertain, with some studies suggesting a possible link but others not finding it. One large study in the UK found that influenza-like illness itself was associated with an increased risk of the Guillian-Barré syndrome but there was no link with the seasonal influenza vaccines, suggesting that vaccination might actually protect against the disorder by preventing flu.

Following the blood tests your child may experience temporary soreness and bruising. This discomfort will be minimised by the use of a local anaesthetic cream or cold spray.
In addition to the reactions listed above, there is a chance that an unexpected reaction may occur as these are new vaccines that are still being evaluated in children. We would therefore ask that you tell the study team about any changes in your child’s health.

As with all vaccines there is the very small possibility of an allergic reaction. Your child would be observed for at least 20 minutes following the vaccine to monitor for any such reaction; 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. The blood sample would be stored in a freezer until the tests looking at your child's immune response had been performed. Blood samples would be tested for markers of immunity to the swine flu virus. With your specific permission we would use a small amount of blood to look at your child's DNA as part of a project looking at the influence of genetic factors on the response to vaccines. This would help us understand the body's response to immunisation. We would also ask your permission to store your child's blood samples, including DNA, for future research into infection and the immune system. The blood samples would only be used for research and would not be sold or used directly for commercial purposes. The use of blood for the genetic study and the storing of blood for future research are voluntary; you could choose not to take part in these aspects of the study and still take part in the swine flu vaccine study.

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 and if the results of the study were published your child would not be identified. 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 swine flu vaccine. Any study records with your child's name and address would be held by the Oxford Vaccine Group. Your child's first name will also be on the front of the diary card and memory card that will be sent to the Health Protection Agency.

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 Ethics Committee (EC) - A group that oversees the conduct of human research and assures the protection of patient rights and welfare.
- 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 in the study, 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 in this study you should follow any advice from your GP or the government regarding swine flu or swine flu 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 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 vaccines would be provided by the vaccine manufacturers. The University has arrangements in place to provide for harm arising from participation in the study that is not due to the vaccines themselves. 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 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. The study has been funded by a grant from the NIHR Health Technology Assessment programme.

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

- We would administer 2 doses of the influenza A H1N1 (swine flu) vaccine and take two 6 to 10 ml blood samples from your child over 3 visits each occurring 3 weeks apart.
- You would have 24-hour telephone access to our study team should you have any concerns following vaccination.

What do I do now?

Participation in this study is voluntary. If you are interested in taking part, please phone our appointment line on 01865 857080 to arrange a time to come to the Oxford Children's Hospital. If you agree for your child to take part in the study it will still be possible to change your mind at any point and withdraw. If you wish to discuss any element of the study further, then please contact us by telephone (01865 857420) or e-mail (*ovg@paediatrics.ox.ac.uk*). If you do decide to take part we would be grateful if you could bring along your child's health record (the 'red book') to your first visit.

Yours sincerely,

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Honorary Consultant Paediatrician

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