



## *Patient Information Leaflet*

# HPV Vaccination Study

**Full title:** A Phase IV, randomised study to evaluate the immune responses of UK adolescent girls receiving Cervarix™ or Gardasil™ Human Papillomavirus vaccines

**Study code:** HPV CSP01

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Your doctors' surgery or school is taking part in a study with the Health Protection Agency of two licensed HPV vaccines, one of which is being used in the routine UK schedule. Before you decide if you would like to join this study you need to understand the reasons the research is being done and what it would involve. Ask us if there is anything that is not clear or if you would like more information. We encourage you to discuss this leaflet with your parents and others to help you with your decision. It is important to take time to decide whether or not you wish to take part.

*Part 1 tells you the purpose of the study and what it would involve*

*Part 2 gives you more detailed information about the conduct of the study*

## **PART 1**

### **What is the purpose of the study?**

HPV is a virus that can cause cervical cancer in some women. There are many strains of HPV. About 12 HPV strains can cause cervical cancer, two strains of HPV can cause genital warts and many other HPV strains cause no disease. Around 70% of cervical cancers are caused by just two strains (known as HPV 16 and HPV 18). Many of the other strains that can cause cervical cancer are very similar to these two strains.

Two vaccines against HPV, called Cervarix™ and Gardasil™, have recently been licensed in the UK. These vaccines protect against infection with HPV 16 and HPV 18 (the strains that cause 70% of cervical cancers). Gardasil™ also protects against the two strains (HPV 6 and HPV 11) that can cause genital warts. The study will assess both vaccines (Cervarix™ and Gardasil™).

We are interested in whether the HPV vaccines will protect against infection with other strains similar to those included in the vaccine. To do this, we will look at the antibodies produced by your body after vaccination and use these in laboratory experiments to see which strains of virus they work against. Antibodies are the substances in your blood that help you fight infections. Some antibodies, called mucosal antibodies, are found on the outside of the body (such as the genitals and mouth) and protect against infection at those sites. We will examine white blood cells after the third dose of vaccine: it is these cells which co-ordinate the production of antibodies in the body.

### **Is HPV vaccine routinely given in the UK?**

Since September 2008, HPV vaccine is being given routinely to 12-13 year old girls (school year 8). The vaccine being used is Cervarix™. Older girls aged up to 18 years will also be offered the vaccine in a catch-up programme. Both HPV vaccines are licensed for use in the UK. If you do not wish to take part in this study then you will still be able to have the Cervarix™ HPV vaccine in the

future. Most people will be offered the vaccine through their school. Your local primary care trust (PCT) will let you know when you are due to be given the vaccine.

### **How effective are the HPV vaccines?**

Both HPV vaccines are 99% effective in preventing pre-cancerous cervical abnormalities caused by the HPV types 16 and 18. Pre-cancerous abnormalities can lead to cervical cancer if left untreated. HPV 16 and 18 cause about 70% of cervical cancers. HPV vaccines work by preventing initial HPV infection. HPV is sexually transmitted and is extremely common: about 40% of 20-25 year old women have HPV infection.

The vaccines have been shown to provide high levels of protection for at least six years. It is likely that protection will last much longer than this however as antibody levels in vaccinated women in clinical trials have remained very high.

For further information please visit: [www.immunisation.nhs.uk/Vaccines/HPV](http://www.immunisation.nhs.uk/Vaccines/HPV)

### **Vaccine Safety**

Both HPV vaccines have been shown to be safe in clinical trials and are licensed for use in Europe. In clinical trials alone 60,000 women have received HPV vaccine and HPV vaccination is now recommended for girls in many developed countries.

As with most vaccines, the most common side effect is mild to moderate swelling, redness and pain at the site where the injection is given. Other mild side effects, such as slightly raised temperature, sickness, dizziness, diarrhoea and muscle aches have been reported. Very rarely, as with most vaccines, some people have an allergic reaction soon after immunisation. The Vaccine Research Nurse will know how to treat this.

For further information please visit: [www.immunisation.nhs.uk/Vaccines/HPV](http://www.immunisation.nhs.uk/Vaccines/HPV)

### **Can women take part if they are pregnant?**

You will be asked by the Vaccine Research Nurse (VRN) about the possibility that you may be pregnant. If you are pregnant or breast-feeding you cannot take part in this study. This is because HPV vaccination for pregnant women has not been well studied. Whilst you are in this study, if you are having sex, you must use an effective method of contraception to reduce the risk of pregnancy. If you would like, you can discuss this with a nurse/doctor at your GP practice.

### **Will I benefit from taking part in this study?**

You may not benefit from taking part in this study as you may be given the same vaccine as most other girls in the UK (Cervarix™). However you may benefit as you may be given Gardasil™. Gardasil™ is licensed in the UK but is not being used for most girls because it is more expensive. Both vaccines will protect you from infection with two types of HPV that cause 70% of cervical cancers. If you are given Gardasil™ you will also be protected against genital warts. By taking part in this study you will benefit girls and women in the future because the results from this study will help decide future vaccination policy from the Department of Health.

### **Are there any disadvantages if I take part?**

If you take part in this study you will have 4 blood samples taken. Having a blood sample taken may occasionally result in a bruise, which will usually disappear after a couple of days. You will also be asked for an entirely voluntary self-taken lower vaginal sample. You will be able to take this sample in private and it should not cause discomfort. If you do not wish to provide this sample you can still take part in the study.

### **Do I have to take part?**

No. You can choose whether you would like to take part in this study. If you decide to take part after discussion with your VRN, you and your parent/guardian will be asked to sign a consent form. Taking

part in this study is entirely voluntary, you can stop at any time without giving a reason, and your VRN will be happy to discuss any further vaccinations that should be given by your GP surgery or at school.

### Why have I been invited to take part?

We wish to examine the body's responses to the HPV vaccines Cervarix™ and Gardasil™ to determine the likelihood that the current vaccines will protect against other cancer-causing strains of HPV that are not present in the vaccines. We would like to invite you to take part in a study that will enrol 400 girls in Hertfordshire and Gloucestershire. Girls aged 13 to 15 years at your GP surgery or school will be invited to take part as these girls are closest in age to those who will usually be given the HPV vaccine in the UK.

### What will happen to me if I take part?

If you choose to take part you will receive the HPV vaccine and be asked to give 4 blood samples and, if you agree, provide one self-taken lower vaginal sample. The study will involve 6 visits to see the VRN at your GP surgery or school over 12 months (as shown in the table below). The first appointment will take about an hour and the rest about half an hour each. We will inform your GP that you are taking part in the study.

Activity	Month												
Vaccination (Cervarix™ or Gardasil™)	0	1	2	3	4	5	6	7	8	9	10	11	12
Blood taken by Vaccine Research Nurse	0	1	2	3	4	5	6	7	8	9	10	11	12
Voluntary self-taken lower vaginal sponge	0	1	2	3	4	5	6	7	8	9	10	11	12

#### 1. HPV vaccinations

All people taking part in the study will be given three doses of HPV vaccine at months 0, 1 and 6 of the study (highlighted in yellow in the table, above). All vaccines will be given at your GP surgery or school by your VRN. There are two groups in this study, girls in one group will be given Gardasil™ and girls in the other group will be given Cervarix™. A computer programme will decide randomly (like tossing a coin) which group you are in. This random draw helps us make sure the groups are similar when we are comparing the two HPV vaccines.

#### 2. Blood Samples

Blood samples will be taken at four visits (months 0, 2, 7 and 12 highlighted in blue on the table above). At each visit, your VRN will offer you some cream to numb the skin and will take one tube (5-10mls) of blood. At month 7, a larger tube (30ml) will also be filled with blood. The blood samples will be used to measure blood antibodies and cells and compare them between the two groups.

#### 3. Self-taken lower vaginal sample

We would like you to provide one self-taken lower vaginal sponge at month 7 (highlighted in green on the table above). If you do not wish to provide this sample you can still take part in the study. If you would like to decide nearer to the time (month 7), you can still take part in the study. If you do decide to provide this sample, the VRN will give you the self-taken sample kit and talk to you about the sample in months 6-7. You will be able to take the sample in private and it should not cause any discomfort. This sponge sample will be very useful because it will let us look at the mucosal antibodies. These are the antibodies that are outside the blood at the genital surface and will be the body's first defence against HPV infection.

The consent form includes consent to provide a lower vaginal sponge sample. If you agree to provide this sample please initial the box. If you initial the box and then change your mind and do not wish to provide the sample, please tell the VRN. If you do not initial the box and later change your mind and wish to provide a lower vaginal sponge sample, please talk to your VRN.

#### 4. Health diary and records

We will ask you to complete a health diary to record how well you have felt after each vaccination (e.g. any problems, reactions at injection site, temperature, if you have seen a doctor, etc). Your VRN will explain how to fill in the diary and will show you how to use the thermometer you will be

given. We will review your medical notes before each vaccination to collect information about any illnesses or medicines prescribed. We may then contact your doctor for further information. If you have a serious illness and see the GP or are admitted to hospital, please inform the doctor that you are taking part in this study. Regardless of the illness or reason for admission, please then let us know by telephoning your VRN.

The samples collected for this study and the health diary would not be part of your routine care if you do not take part in the study.

At the end of the study, we will inform you of the overall results of the study and which vaccine you received. We will not tell you or anyone else your individual results.

### **Expenses and payments**

If you incur any costs when seeing the VRN (to have the vaccine or give samples) which you wish to claim back, please ask your VRN for a claim form and we will reimburse you.

### **Will my taking part in the study be kept confidential?**

Yes, we will follow ethical and legal practice and all information will be handled in confidence. For further details on confidentiality, see **Part 2** of this information sheet.

### **What happens when the research study stops?**

When the study ends we will tell you which of the HPV vaccines you were given. If you completed the study, you will not need to have the HPV vaccine when you are offered it through the PCT (probably through your school). If you stop taking part in the study early then we will let your GP know as you will need to complete your vaccination under the national HPV immunisation programme.

After we have completed this study, there may be small amounts of your samples remaining. We would like to be able to use these samples for other studies that will help us understand better how vaccines work. Before we do this we will remove your name and any other information from which you could be identified. If you are happy for us to use your left-over samples for other studies, please consent to this on the consent form. If you do not wish your left-over samples to be kept for future studies, you can still take part in this study.

### **Part 1 summary:**

- **You will be given the usual course of three HPV vaccinations, have four sets of blood samples taken plus one optional self-taken lower vaginal sample**
- **The study will take a year and involve 6 visits to the Vaccine Research Nurse – either at your GP or School.**
- **The vaccines we are using are licensed for use in the UK and Europe**

**If the information in Part 1 has interested you and you are considering taking part please read the additional information in Part 2 before making any decision.**

**This is the end of Part 1**

## **PART 2**

### **What if relevant new information becomes available?**

If relevant new information becomes available or the study is to be stopped for any reason we will let you know, as well as give you and your GP information about your continuing care if appropriate.

### **What will happen if I do not want to carry on in the study?**

You can withdraw from the study at any time without affecting your routine care. We will let your GP know so you can complete your vaccination under the national HPV immunisation programme.

If you withdraw you would need to decide if you want samples collected from you to be destroyed. If you would like them to be destroyed you would need to inform us in writing. We would retain any information collected to that point in case we needed to reach you at some point in the future based on the outcome of the study.

### **What if there is a problem?**

- **Complaints**

If you have a concern about any aspect of this study, you can contact the study organiser, Prof Elizabeth Miller on 0208 327 7434, who will do her best to answer your questions. If you remain unhappy and wish to complain formally then you can do this through the NHS Complaints Procedure, details of which can be obtained at [www.nhs.uk](http://www.nhs.uk) or by phoning 0845 601 3012

- **Harm**

The vaccines that will be given in this study are licensed for use in the UK. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for legal action for compensation against the Health Protection Agency but you may have to pay your legal costs. The National Health Service complaints mechanism will still be available to you. Where justified, an *ex gratia* payment for any non-negligent harm may be made.

### **Will my participation in the study be kept confidential?**

Under the data protection laws, you have a right to know how your personal data from this trial will be used so you can understand what information will be collected and who will have access to it. We will collect only sufficient data to enable us to conduct the study and answer the study questions. The people who require data will only be given information about you that is necessary for their task, for example, people analysing samples and study results will not be told your name or address. The only people who may be given access to study information will be employees or agents of the Health Protection Agency, the Department of Health or regulatory authorities who may wish to check the study is being carried out within the appropriate guidelines.

The data will only be used for the purposes of this study and any data released outside the above group will be anonymised. This means that your name and address will be removed. Data will be stored in secure Health Protection Agency facilities and will be disposed of within clinical trial guidelines after the appropriate time period which may be a number of years.

### **Will my GP be involved in this study?**

We will write to your GP to let him/her know that you are taking part in the study. During the study, your GP will not be involved in giving the vaccine or taking samples – the VRN will do these tasks.

### **What will happen to any samples I give?**

The samples will be labelled with your study number and initials but not your name. The samples will be tested in laboratories and results sent to the Health Protection Agency, Centre for Infections where they will be linked with information about you.

### **Will any genetic tests be done?**

No genetic tests will be carried out on your samples.

**What will happen to the results of the research study?**

We plan to publish the results in a medical journal which will be accessible to the public. The results of the study will also be reported to the Department of Health to help with planning national vaccination programmes in the future. You will not be named in any report or publication and it will not be possible for anyone to work out that you took part in the study.

**Who is organising and funding the research?**

The study is funded by the UK Department of Health and is being organised by the Immunisation Department of the Health Protection Agency. The Health Protection Agency (HPA) is an independent body that protects the health and well-being of the population. The Agency plays a critical role in protecting people from infectious diseases and in preventing harm when hazards involving chemicals, poisons or radiation occur.

**Who reviewed the study?**

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect the safety, rights, well being and dignity of individuals. This study has been reviewed and given favourable opinion by the Royal Free Hospital and Medical School Research Ethics Committee (Tel No. 020 7794 0581). The Research Ethics Committee reference number for this study is 09/H0720/25.

**Further information and contact details:**

If you have any questions, you can ask your VRN or contact the organisers, Professor Elizabeth Miller on 0208 200 6868 or Dr Anu Ohrling 020 8327 7434.

Further information about our trials programme including links to the organisations reviewing research and the guidance we follow can be found at [www.hpa.org.uk](http://www.hpa.org.uk) and typing *clinical trials* into the search bar.

We do hope that you will take part in this study. Your contribution would be an important step towards the continual improvement of vaccine policy in the UK. You may be invited to take part in future studies with us by virtue of the surgery you attend. We reassure you that invitations for future studies will not be because of anything to be concerned about from results of this study.

Sticker with Vaccine Research Nurse Name and Contact Details