



**protect now
for the future**

HUMAN PAPILLOMAVIRUS VACCINE

Frequently Asked Questions

for

Health Professionals

Produced by the National Immunisation Office in collaboration with the
Health Protection Surveillance Centre

Version 3 - September 2010



HPV Disease and Cervical Cancer

What is HPV?

Human papillomavirus (HPV) is a virus that infects squamous epithelium including the skin, and mucous membranes of the upper respiratory and anogenital tract. It can exist within its host in an active or latent form. There are over 100 types of HPV. Some types are responsible for common warts (verrucae). Around 40 types can infect the genital tract. Some of these are low-risk types (e.g. HPV 6 and 11) which cause genital warts, while others are high-risk types (e.g. HPV 16, 18, etc.) and are associated with various cancers such as cancer of the cervix, vulva, vagina, anus, penis and oropharynx.

How is HPV spread?

Transmission of genital HPV can occur during vaginal, oral or anal sexual intercourse or genital contact with an infected person. Non-sexual routes of transmission include transmission from mother to baby in the period immediately before or after birth.

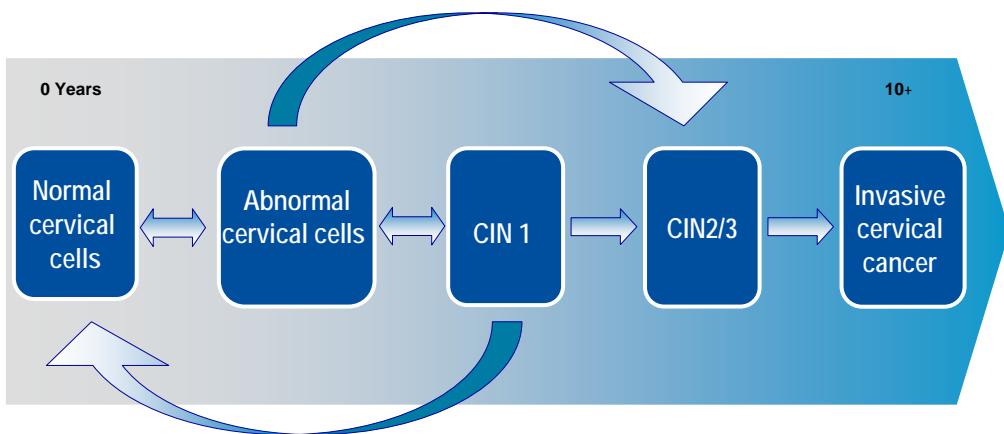
What diseases can HPV cause?

The clinical spectrum of disease ranges from asymptomatic infection, to benign warts, to invasive cancer, depending on the virus type, the route of infection, and the body's immune response.

- Genital HPV is the most common sexually transmitted disease worldwide.
- Risk factors associated with genital HPV infection include younger age at sexual initiation, number of sexual partners, and the sexual history of the partner (number of previous sexual partners).
- The highest rates of HPV infection occur in the 18-28 year age group.
- An estimated 80% of sexually active women become infected with at least one strain of HPV by age 50 years.

How does HPV infection cause cervical cancer?

Cervical cancer can take many years to develop & most lesions never progress



- Most lesions regress spontaneously
- Some abnormalities accelerate to pre-cancerous lesions

IARC. Colposcopy & Treatment of Cervical Intraepithelial Neoplasia: A Beginner's Manual. IARC 2005

- Most genital HPV infections are asymptomatic and transient.
- HPVs associated with cancer are called oncogenic or 'high risk' types. HPVs that do not cause cancer are termed 'low risk' types. Two of these 'low risk' types cause genital warts. HPV types are referred to by number (assigned in the order in which they were discovered).
- 70% of new genital HPV infections clear within one year, and most within two years. High risk strains are more persistent than low risk strains.
- HPV can infect the cells on the surface of the cervix and damage them, causing their appearance to change. This can lead to the development of precancerous lesions over a number of years. These precancerous lesions are called Grade 2 or 3 cervical intraepithelial neoplasia (CIN) and they can lead to cervical cancer.
- Persistent infection by high-risk strains is detectable in more than 99% of cervical cancers.
- Types 16 and 18 are responsible for over 70% of cervical cancers.

What is the incidence of cervical cancer?

Ireland

- In Ireland in 2007 there were 286 new cases of cervical cancer in Ireland and 81 women died from the disease.
- Data from Eurostat indicate that mortality from cervical cancer in Ireland is above the EU-27 and EU-15 average. The average age at diagnosis is 46 years and of death is 56 years.

Worldwide

- HPV is responsible for 5.2% of the cancer burden worldwide
- Cervical cancer is the second most common cancer in women with an estimated 493,000 new cases in 2002 and 274,000 deaths
- Most cases occur in countries without effective screening programmes.

What about HPV infection and genital warts?

- Ano-genital warts are highly contagious; two-thirds of people who have sexual contact with an infected partner will develop warts.
- In the United States, it is estimated that approximately 1% of sexually active adults have visible genital warts and that at least 15% have subclinical infection
- Type 6 and 11 are associated with over 90% of genital warts.
- In Ireland, ano-genital warts account for approximately 30% of all sexually transmitted infection notifications annually.
- In Ireland, the largest proportion of cases occurs in young adults in the 20-29 year age group.

Can HPV infection be prevented?

Individuals can reduce their risk of getting genital HPV infection by changes in sexual behaviour including abstinence from any sexual activity or lifelong monogamy.

Reducing the number of sexual partners and the frequency of new partners will also reduce the risk. Condom use reduces but does not eliminate the risk of sexual transmission of HPV.

Can cervical cancer be prevented?

Cervical screening can detect pre-cancerous lesions and cervical cancer at an early stage when treatment can be successful. In countries where there is an organised cervical cancer screening programme there has been a marked reduction in the incidence of invasive cervical cancer.

Vaccines are available which will reduce but not eliminate the risk of cervical cancer. At present the available vaccines target only two oncogenic (cancer causing) HPV types (16 and 18) which account for 70% of cervical cancer risk. Therefore, cervical cancer screening programmes will continue to be important even in vaccinated populations.

HPV Vaccine

Why is HPV vaccine being introduced into the National Immunisation Programme?

Following recommendations from the National Immunisation Advisory Committee (NIAC), the Minister for Health and Children announced that the HPV vaccine will be introduced into the national immunisation programme in 2010 as part of the national strategy to protect females from cervical cancer. The vaccine will be offered to all girls in First and Second Year of second level schools in 2010.

Girls who are outside of the traditional school system (home-schooled and out-of-school) will also be vaccinated. From September 2010 girls who reach 12 years of age between 1st September 2009 and 31st August 2011 will be vaccinated. Thereafter girls who turn 12 between September and August of the academic year will be vaccinated.

What is HPV vaccine?

HPV vaccines contain virus-like particles (VLPs) produced from the major capsid protein L1 of each HPV type using recombinant DNA technology.

These vaccines,

- contain no viral DNA and are not infectious or oncogenic



- are not live vaccines
- cannot cause HPV infection
- cannot cause cancer

What HPV vaccines are available?

Two HPV vaccines are licensed for use in Ireland, Cervarix, (manufactured by GSK) a bivalent vaccine containing VLPs for two HPV types (16 and 18) and Gardasil (manufactured by Sanofi Pasteur), a quadrivalent vaccine containing VLPs for four HPV types (6, 11, 16 and 18).

What HPV vaccine is being used in the school programme?

The HPV school vaccination programme will use the quadrivalent vaccine Gardasil, manufactured by Sanofi Pasteur MSD. This HPV vaccine is licensed for use in females aged between 9 and 26 for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer and genital warts causally related to HPV types 6, 11, 16 and 18.

Why is it given at this age?

The following is the rationale for administration of HPV vaccine at this age:

- The vaccine is most effective if given before sexual activity occurs
- A superior immune response has been demonstrated at this age

What is the vaccine dose and schedule?

Three doses (0.5ml) are recommended to be given at 0, 2 and 6 months by intramuscular injection in the deltoid region.

Is there an alternative schedule?

There is an alternative vaccination schedule which should be used in exceptional circumstances only.

There should be at least one month between Dose 1 and 2, at least 3 months between Dose 2 and 3, and all 3 doses should be given within 12 months.

If the HPV vaccine schedule is interrupted, does the vaccine series need to be restarted?

No. If the vaccine schedule is interrupted the vaccine series does not need to be restarted.

If the HPV vaccination course takes longer than 6 months to complete is protection adequate?

Yes. Primary analysis of efficacy in trials where all three vaccinations were given within one year of enrolment has demonstrated full protection. However, the largest clinical trials have been carried out on females who completed the course within the recommended 6 month timeframe. Therefore the recommendation is that wherever possible the 0, 2, 6 month schedule should be adhered to.

Can other vaccines be given at or around the same time?

Yes. Gardasil vaccine is not a live vaccine and can be administered either simultaneously or at any time before or after an inactivated or live vaccine, preferably in another limb.

Studies have been carried out on concomitant administration of Gardasil with a combined booster dose of diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis. Results show no significant interference with antibody response to any of the components of either vaccine. Studies on the co-administration of Gardasil and hepatitis B (recombinant) vaccine showed no reduction in efficacy. No significant difference in reactogenicity and safety was seen between subjects receiving Gardasil co-administered with hepatitis B vaccine (recombinant). Recent data from the USA also demonstrates safe and effective co-administration of Gardasil with a quadrivalent meningococcal vaccine and with a combined dose of tetanus, diphtheria and acellular pertussis.

How effective is Gardasil?

- Gardasil is highly effective at preventing infection of susceptible women with the HPV types covered by the vaccine.
- Gardasil has been found to be over 99% effective in preventing pre-cancerous lesions associated with HPV types 16 and 18 in young women.
- Gardasil has been found to be over 99% in preventing HPV 6 or 11-related genital warts .



- Partial cross-protection has been demonstrated for the vaccine against infection with several non-vaccine oncogenic HPV types, including HPV 45 and 31 the commonest non vaccine oncogenic types.

Vaccination provides less benefit to females if they have already been infected with one or more of the HPV vaccine types. This is why the national programme is targeting girls in First Year of second level school before they are likely to be exposed to HPV infection.

How long does protection last?

Data from clinical trials indicate that sustained protective efficacy has been observed for at least 4.5 years after completion of a 3 dose course of Gardasil. Further trials and post-marketing surveillance are ongoing and it is expected that the vaccine will provide longer term protection.

Is a booster dose of HPV vaccine needed?

Studies and trials are ongoing to determine whether or not a booster dose is required. The results of these will indicate if a booster dose is necessary and if a booster is required the girls will be informed.

What are the constituents of Gardasil?

Virus

- HPV Type 6 (20 μ g)
- HPV Type 11 (40 μ g)
- HPV Type 16 (40 μ g)
- HPV Type 18 (20 μ g)

Other constituents

- Sodium chloride
- L-histidine
- Polysorbate 80
- Sodium borate
- Water for injection
- Traces of yeast protein which is used in the manufacturing process



Adjuvant (substance that enhances an immune response)

- Amorphous aluminium hydroxyphosphate sulphate

These constituents are present in many other vaccines and other authorised products

Are aluminium containing vaccines safe?

The World Health Organisation's Global Advisory Committee on Vaccine Safety stated that at present there is no evidence of a health risk from aluminum-containing vaccines.

Does Gardasil contain thiomersal?

No. There is no thiomersal in Gardasil.

Is latex used in either the manufacturing process for Gardasil?

No. Latex is not used in the manufacturing or packaging process for Gardasil.

How is the vaccine presented?

- Gardasil is presented as a suspension for injection in a pre-filled syringe with no needle attached.
- Prior to agitation it may appear as a clear liquid with a white precipitate. After thorough agitation it is a white, cloudy liquid.
- Two needles are included in the packaging – a 23G needle (0.6x25mm) and a 25G needle (0.5x16mm).
- Gardasil will be provided in a single dose presentation

Are there any reasons not to give the vaccine?

Contraindications

- Known hypersensitivity to the active substances, the adjuvant, or any of the vaccine constituents or severe (anaphylactic) allergy to yeast
- Previous allergic reaction to Gardasil
- Pregnancy.

Precautions

- Acute severe febrile illness; defer until recovery
- Vaccine should be administered with caution to individuals with coagulation defects. If vaccines are given intramuscularly to those with a bleeding disorder or receiving anticoagulant treatment it is prudent to use a 23-gauge (blue) needle, and to apply pressure to the vaccine site for 1-2 minutes after the injections. In those with a severe bleeding tendency vaccination can be scheduled shortly after administration of clotting factor replacement or similar therapy. There are no data with HPV vaccines using the subcutaneous route. Administration by the subcutaneous route may be considered in those with severe bleeding disorders. However, immunogenicity of vaccines recommended for IM administration may not be as long-lasting if they are given subcutaneously. The patient or parent should be advised of this.
- There is no data on the use of Gardasil in individuals with impaired immune responsiveness, whether due to treatment or illness. These individuals may not respond as effectively to the vaccine.

When there are doubts as to whether or not to give a vaccine contact a Paediatrician or Consultant in Public Health Medicine

Can Gardasil be administered during pregnancy?

No. Gardasil is not currently recommended during pregnancy, although there is no known risk associated with using recombinant viral vaccines during pregnancy.

Can Gardasil be given to breastfeeding mothers?

Yes. Gardasil vaccine can be given to breastfeeding mothers.

How safe is the vaccine?

Gardasil is considered safe and well tolerated.

Side effects profile

- Very common (1/10): Pyrexia, and erythema, pain, or swelling at the injection site
- Common (1/100, <1/10): Pain in extremity, and bruising and pruritus at the injection site
- Rare (1/10,000, <1/1,000): Urticaria



- Very rare (<1/10,000): Bronchospasm.

Syncope (fainting) has occurred after vaccination with Gardasil, especially in adolescents.

Post-vaccination fainting has been reported with most vaccines. Based on data from the USA, syncope is most common after three adolescent vaccines HPV, MCV4 (4th dose Meningococcal vaccine), and TdaP. It is not known whether this is due to the vaccines or if the increased incidence in this age group merely reflects that adolescents are generally more likely to experience fainting. The onset of syncope is usually immediate. A review of syncope after vaccination found that 89% occurred within 15 minutes of vaccination. (See Guidelines for staff involved in the HPV programme for further management)

How do I report an adverse event following vaccination?

All adverse events should be reported to the Irish Medicines Board (IMB).

Adverse events can be reported online at:

<http://www.imb.ie/EN/Safety--Quality/Online-Forms/Human-Medicine-Adverse-Drug-Reaction.aspx>

Or an adverse event form can be downloaded from:

<http://www.imb.ie/EN/Publications/Safety-Quality/Reporting-Suspected-Product-Problems/Safety-Related-Problems/Adverse-Reaction-Form.aspx?page=1&year=0&categoryid=58&letter=&q> and returned by FREEPOST.

HSE HPV Vaccination programme

When will the school based programme begin?

The programme will target all girls in 1st year of second level schools.

For the first year of the programme the vaccine will be given to all girls who will be entering 1st Year AND 2nd Year in September 2010.

All girls require three doses of vaccine with a two month interval between the 1st and 2nd dose and a four month interval between the 2nd and 3rd doses.

The HSE vaccination teams will visit second level schools three times on agreed dates in September, November and March to provide the vaccinations. Some



schools may have only a small number of girls eligible for HPV vaccination and these girls may be invited to attend a HSE clinic.

From 2011 onwards the vaccine will be provided to girls in first year of second level schools nationally.

A 'Blitz and Mop up' approach will be adopted to enable adherence to the recommended schedule, the vaccination of the entire cohort, the completion of the full vaccine course within one academic year with provision for school holidays and examination periods. (See Guidelines for staff involved in the HPV programme for further information)

Girls who are home schooled or out-of-school will be invited to attend a HSE clinic. From September 2010 girls who reach 12 years of age between 1st September 2009 and 31st August 2011 will be vaccinated. Thereafter girls who turn 12 between September and August of the academic year will be vaccinated.

Is there a catch-up programme?

No. At this point in time there are no plans to proceed with a catch-up programme.

Why is there no catch-up programme?

The priority is the establishment of a successful national programme for all girls in First Year in second level schools and girls of an equivalent age outside of the school system in order to meet the NIAC recommendation to vaccinate all 12 year old girls.

Why is it given to girls only?

The aim of the HPV vaccination program is to protect females from cervical cancer which does not affect males. There is no evidence to date that vaccinating males is effective at reducing the incidence of cervical cancer in women. Consideration may be given to vaccinating males in the future if indicated by the scientific evidence.

Who can give consent for vaccination?

- For girls aged under 16, consent must be obtained from one parent or guardian
- For girls aged 16 years of age and over they can consent on their own behalf

- Consent is given by the child/parent/guardian to a course of vaccination therefore it covers all three doses necessary to complete a course and consent remains valid until the course has been completed unless consent has been withdrawn
- Further guidance on consent, if required, is contained in “*A Practical Guide to Immunisation*” which is available at
http://www.immunisation.ie/en/Downloads/PDFFile_15165_en.pdf

What happens if a parent consents and a girl refuses to be vaccinated?

- If a parent consents but a girl refuses vaccination on the day of the school clinic the girl should not be vaccinated

What happens if a parent refuses consent and a girl requests the HPV vaccine?

- If a parent refuses but a girl expresses a desire to be vaccinated on the day of the school clinic, a girl may be vaccinated if she is aged 16 years or over as she can provide her own consent. If a girl is less than 16 years of age she cannot be vaccinated.

What happens if a girl is absent from school and misses a dose?

The girl should be given an appointment for a mop-up clinic to be held at the end of the three week period of school vaccination clinics.

What happens if a girl or her parents refuse vaccination prior to the first school visit but consent at a later school clinic?

The girl should receive her first dose at this clinic and the course should be continued as per the allowed alternative schedule. This may extend the course into the next academic year.

What happens if a girl changes school during a school year?

If the girl started the HPV programme in her previous school she will have received a record card detailing her vaccination history to date. Her vaccination course can be continued in her new school if the routine or alternative schedule can be followed.

What happens if a girl has had one or more previous doses of Gardasil vaccine outside of the school programme?

If a child has previously completed a three dose course of Gardasil they should not participate in the school programme. If a girl has not completed the course of vaccination and if her parents can provide a record of her previous vaccinations she can be considered for inclusion in the school based programme.

Are Gardasil and Cervarix interchangeable?

There is no evidence that the HPV bivalent and quadrivalent vaccines are interchangeable. If an individual has started a course of one vaccine then the vaccination series should be completed with that vaccine.

Is Gardasil vaccine used in the UK programme?

No- the vaccine used in the UK is Cervarix, (manufactured by GSK) a bivalent vaccine containing VLPs for two HPV types (16 and 18)

Can the vaccine be given if the girl is already sexually active?

Yes. The vaccine should still be administered as it protects against four HPV types. However, it is important to stress that vaccination will not alter the progression of a pre-existing HPV infection or the development of any consequences of this infection.

Can the vaccine be given to a girl who has previously been diagnosed with HPV infection?

Yes. The vaccine can be given to a girl who has previously acquired a HPV infection.

What protection is provided by one or two doses?

Data are not available on the efficacy of one or two doses. Efficacy studies to date are bases on a 3 dose vaccination course.



What happens if a dose of vaccine is given too early i.e. dose 2 given less than one month after the 1st dose 3 given less than 3 months after the 2nd dose?

There is no data available on the administration of the second dose or third dose before the recommended schedule. If a dose is given early then that dose should be repeated.

What should happen if the 2nd dose is given late i.e at 10 months- should there still be a 3 month gap between the 2nd and 3rd dose?

Yes the schedule should be resumed and the 3rd dose given 3 months after the 2nd dose.

What should happen if a girl finds out she is pregnant and has received the vaccine?

If a girl who was vaccinated subsequently finds out that she was pregnant at or conceived around the time of vaccination, any further HPV vaccination should be postponed. There is no evidence to date that the vaccine will have caused any harm to her, the pregnancy, or the foetus. She should be advised to discuss the matter with her GP and the IMB should be informed that she was vaccinated whilst pregnant. The course of Gardasil HPV vaccination may be finished when the pregnancy is completed.

What should parents do if they want to get younger or older siblings vaccinated?

Gardasil HPV vaccine is licensed for females aged 9 to 26 and Cervarix is licensed for females aged 10 to 25. If siblings fall within this age category, parents and girls may visit their GP to obtain the vaccine but they will have to bear the cost. Parents of younger siblings should be advised to wait until they reach First Year in second level schools when they will be vaccinated free-of-charge through the school based programme.

How will girls who do not attend schools get vaccinated?



Girls who are outside of the traditional second level school setting, including home-schooled girls and girls who have dropped out of school, will be vaccinated at the HSE clinics. In the first year of the programme girls who turn 12 between 1st September 2009 and 31st August 2011 will be vaccinated. Thereafter girls who turn 12 between September and August of the academic year will be vaccinated.

Do vaccinated females need to attend for cervical screening?

Yes.

Currently HPV vaccines only protect against types 16 and 18 which cause approximately 70% of cervical cancers. A small number of girls (<1%) may not develop an adequate immune response post vaccination and a small number of girls may be already infected. Thus it is essential that girls participate in the National Cervical Screening Programme when they are of an appropriate age.

More information on the cervical screening programme is available at
<http://www.cervicalcheck.ie/>.

Where can one get information for parents whose first language is not English

Factsheets are available in the following languages

- English
- Irish
- Arabic
- Simplified Chinese
- German
- French
- Polish
- Portuguese
- Romanian
- Russian

These are available for download at www.hpv.ie and www.immunisation.ie

Where to look for further information

Further information regarding HPV, cervical cancer and HPV vaccine can be found on the following websites.



- National Immunisation Office available at <http://www.immunisation.ie>
- Immunisation Guidelines for Ireland 2008 Edition HPV chapter available at <http://www.immunisation.ie/en/HealthcareProfessionals/ImmunisationGuidelines2008/>
- Department of Health and Children available at www.dohc.ie
- Health Protection Surveillance Centre available at <http://www.hpsc.ie>
- Irish Medicines Board available at <http://www.imb.ie>
- Medicines Information online available at www.medicines.ie
- National Cancer Screening Service available at <http://www.cancerscreening.ie>
- National Cancer Registry Ireland available at <http://ncri.ie/ncri/index.shtml>
- Irish Cancer Society available at <http://www.cancer.ie>
- World Health Organisation HPV information available at <http://www.who.int/immunization/topics/hpv/en/>
- Centre for Disease Control and Prevention – HPV information available at <http://www.cdc.gov/hpv/>
- Australian Government, Department of Health and Education HPV programme available at <http://www.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-hpv>
- New Zealand, Ministry of Health HPV programme available at <http://www.moh.govt.nz/moh.nsf/indexmh/immunisation-diseasesandvaccines-hpv-programme>
- United Kingdom HPV programme available at <http://www.immunisation.nhs.uk/Vaccines/HPV>
- Canadian HPV programme available at <http://www.phac-aspc.gc.ca/std-mts/hpv-vph/fact-faits-eng.php>
- European Medicines Agency available at <http://www.ema.europa.eu/>