



Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive



protect now
for the future

HUMAN PAPILLOMAVIRUS VACCINE

Frequently Asked Questions for Health Professionals



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 200 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, 31, 33, 45, 52, and 58) 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.

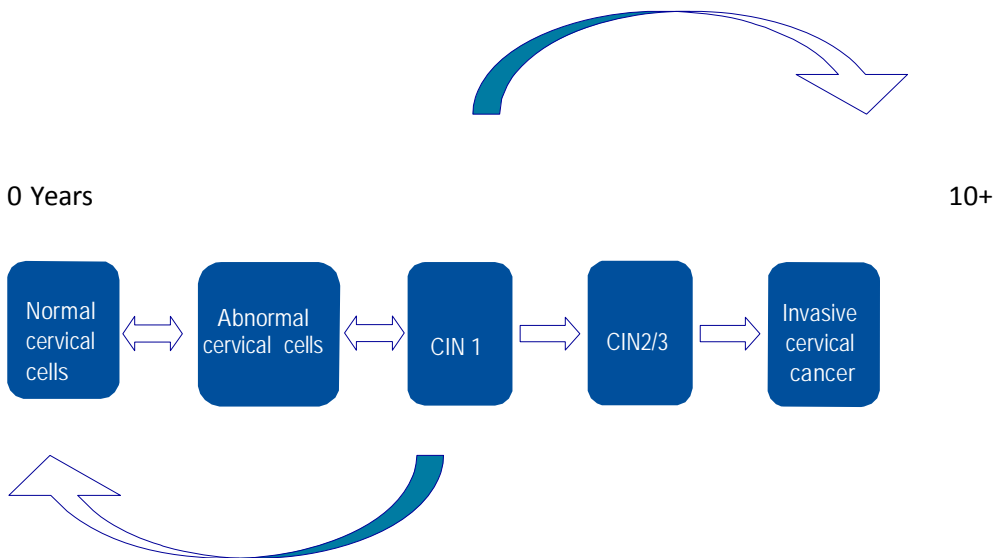
What diseases can HPV cause?

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 immuneresponse.

- 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 globally.
- 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



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

- Most lesions regress spontaneously
- Some abnormalities accelerate to pre-cancerous lesions
- 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 most 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. Highrisk 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 cervicalcancers.
- Types 16 and 18 are responsible for over 70% of cervical cancers.

What is the incidence of cervical cancer?

Ireland

- In Ireland there was an annual average of 290 new cases of cervical cancer and 90 deaths from the disease –annually.
- 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 45years and the average age of death is 56 years.

Worldwide

- HPV is responsible for 5.2% of the cancer burden worldwide.
- Cervical cancer is the fourth most common cancer in women with an estimated 528,000 new cases and 266,000 deaths in 2012.
- Most cases occur in countries without effective cervical cancer 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 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.
- 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.
- Over 90% of genital warts are associated with Type 6 and 11 HPV

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 vaccines available in Ireland target only two oncogenic (cancer causing) HPV types (16 and 18) which

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account for 70% of cervical cancer risk. Therefore, cervical cancer screening programmes will continue to be important even in vaccinated populations.

HPV Vaccine

History of the HSE HPV Vaccination Programme

Following recommendations from the National Immunisation Advisory Committee (NIAC), the Minister for Health and Children announced that the HPV vaccine would be introduced into the national immunisation programme in 2010 as part of the national strategy to protect females from cervical cancer.

HPV vaccine was offered to all girls in first and second year of second level schools in 2010/2011 and age equivalent in special schools. Girls outside of the traditional school system (home-schooled) were also vaccinated.

In 2011/2012 a HPV catch-up vaccination programme for girls in sixth year in second level schools and age equivalent attending special schools, home schooled, Youthreach and Community Training Centres was added to the routine HPV programme for First year girls. This catch-up vaccination programme finished at the end of the 2013/2014 academic year.

Since September 2014 the programme targets all girls in first year of second level schools and age equivalent attending special schools and home schooled.

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 licensed?

Three HPV vaccines are licensed for use in Ireland

- Cervarix, (manufactured by GSK) a bivalent vaccine containing VLPs for two HPV types (16 and 18)
- Gardasil (manufactured by MSD), a quadrivalent vaccine containing VLPs for four HPV types (6, 11, 16 and 18).

A new HPV vaccine, Gardasil 9, was licensed by the European Medicines Agency in July 2015. The vaccine

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contains VLPs for nine types of the human papillomavirus (HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58). The additional 5 HPV types targeted by this vaccine, 31, 33, 45, 52, and 58, cause about 20% of cervical cancers. This vaccine therefore will protect against most cervical cancers. See SmPC at http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d124&jsenabled=true

What HPV vaccines are available in Ireland?

Currently Cervarix and Gardasil are the only HPV vaccines available in Ireland.

Are Cervarix and Gardasil interchangeable?

NIAC advises

“There is no evidence that the HPV2 (Cervarix) and HPV4 (Gardasil) vaccines are interchangeable. The same HPV vaccine should be used for the vaccination series. However, if the previously administered HPV vaccine is unknown or unavailable, either vaccine can be used to complete the series, to provide protection against HPV 16 and 18.

Less than the required number of doses of HPV vaccine will provide less protection against HPV vaccine types than a complete course of HPV vaccine.

Due to lack of information, no recommendation regarding the administration of HPV4 (Gardasil) vaccine to a person previously fully vaccinated with HPV2 (Cervarix) vaccine can be given”.

What HPV vaccine is being used in the school programme in Ireland?

The HPV school vaccination programme uses the quadrivalent vaccine Gardasil, manufactured by MSD.

This HPV vaccine is licensed for use from the age of 9 years for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer, anal cancer and genital warts causally related to HPV types 6, 11, 16 and 18.

Is Gardasil a live vaccine?

Gardasil is not a live vaccine. It is made from proteins like those that coat the HPV virus known as virus like particles (VLPs). These VLPs cannot cause HPV infection or cancer.

How does Gardasil work?

Gardasil vaccination causes the mounting of the humoral immune response to develop antibodies to the antigens in the VLPs.

How long has Gardasil been in use?

Gardasil has been licensed for use since 2006. By July 2016, over 200 million doses of Gardasil have been distributed globally either as part of national immunisation programmes or privately. Gardasil is currently used in over 25 European countries, the United States, Canada, Australia and New Zealand.

Why is Gardasil recommended for all First year girls?

NIAC recommended that HPV vaccine be given to 12 year old girls (equivalent to First year of second level school) because

- 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?

For those girls aged less than 15 years* at the first dose, two doses (0.5ml) are recommended at 0 and 6 months.

For girls aged 15 years and older at the first dose, three doses (0.5ml) are recommended as there is no evidence to support a two dose schedule in those aged 15 and older. The first 2 doses should be given at 0 and 6 months and the third dose can be given at least three months and preferably four months after the 2nd dose. The vaccine is given by intramuscular injection in the deltoid region.

“In some circumstances, advice in the Immunisation Guidelines from the National Immunisation Advisory Committee (NIAC) may differ from that in the Summary of Product Characteristics (SmPC). When this occurs, the recommendation in the guidelines, which are based on current expert advice from NIAC should be followed”.

The SmPC for Gardasil states that the vaccine according to a 2 dose schedule can be given to girls up to 14 years.

NIAC have advised that a 2 dose schedule can be given to girls up to 15 years.

What is the minimum interval between the first and second dose of vaccine?

While every effort should be made to comply with the recommended interval of six months, NIAC now recommends that the minimum interval between HPV1 and HPV 2 is 24 weeks (168 days). In addition the four day rule applies.

This means the second dose of HPV vaccine can be considered valid if given at an interval of $168 - 4 = 164$ days after the first dose.

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

Gardasil vaccine is not a live vaccine and can be administered the same time as or at any interval before or after any other vaccines such as Tdap (tetanus, low dose diphtheria and low dose acellular pertussis

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vaccine) and MenC (meningococcal vaccine).

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 vaccine (Tdap). NIAC recommends that MMR vaccine can be given at the same time as HPV vaccine.

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 period of school vaccination clinics.

When is the latest time for a girl to start her 1st dose of HPV vaccine in 2016/2017?

Only girls who are clinically unwell and unable to have the vaccine in September/October and girls who are new to the school when the team visit the schools in 2017 can get their 1st dose of HPV in March/April. This means a very small number should start the programme in March/April.

If parents choose to defer HPV vaccination in September/October they will need to purchase the vaccine privately outside of the schools programme.

What consent form should I use if a girl requires a 3rd dose of HPV vaccine?

You need to contact the National Immunisation Office to obtain a copy of the 3rd dose HPV consent form. The parent or patient (if they are over 16 years of age) needs to complete this consent form before the vaccine is given.

The completed consent form should be attached to the patient's original consent form.

What should a vaccinator check before giving the second or third dose of Gardasil?

Vaccine scheduling In relation to the 2nd dose:

The minimum interval of 24 weeks less 4 days (164 days) should have passed since the 1st dose.

If a girl presents for her 2nd dose less than the minimum interval after her 1st dose, vaccination should be deferred and she should be given an appointment to attend at a later date.

In relation to the 3rd dose for those girls aged 15 years and older at time of first dose: it is acceptable to give the 3rd dose if at least three calendar months (12 weeks / 84 days) have passed since the 2nd dose. If a girl presents for her 3rd dose less than three calendar months after her 2nd dose, vaccination should be deferred and she should be given an appointment to attend at a later date.

The 3rd dose may be given at the start of the next academic year when the school vaccination team are next in the school unless there is a mop up clinic being set up at least three calendar months after date of 2nd dose.

Clinical Issues

- Did the girl have any reaction/adverse effects to the first/second dose of Gardasil?
- Has the girl developed any new medical condition or is she on any new medication?
- Is there any possibility that the girl may be pregnant?
- Is the girl feeling well today?

These clinical issues are dealt with in the "Guidelines for Staff: Schools Immunisation Programme 2065/2017" - available at www.immunisation.ie and it is essential that all clinical staff involved in the programme are familiar with this document.

What should happen if a girl receives a dose of HPV (Gardasil) vaccine before the recommended minimum time interval?

Those aged under 15 years at the first dose require two doses of Gardasil vaccine. The minimum interval between dose 1 and dose 2 is 24 weeks less 4 days (164 days).

If the second vaccine dose is administered earlier than 24 weeks) less 4 days (164 days) after the first dose, a third dose should be administered at least three months after the second dose".

Those aged 15 years and older at the first dose require three doses of Gardasil vaccine. The minimum interval between dose 1 and dose 2 is 1 month (4 weeks / 28 days)

The minimum interval between dose 2 and dose 3 is three months (12 weeks / 84 days)

If a dose is given earlier than the minimum interval it should be considered invalid. If there is an adverse event after this dose, the event should be notified to the Health Products Regulatory Authority (HPRA) as a medication error. A repeat dose of Gardasil vaccine should be given after the recommended minimum interval has elapsed since the invalid ~~do~~

For example a girl aged under 15 years received HPV1 on 1st October 2016 and HPV2 on 1st March 2017 (<24 weeks - 4 days interval)

This HPV 2nd dose will be an invalid vaccine as 24 weeks less 4 days have not elapsed since HPV 1st dose

- A 3rd dose (valid HPV 3rd) should be given on or after 24th May 2017 (12 weeks/84 days after the invalid dose)

OR

For example, a girl aged 15 years or older received HPV2 on 1st April 2017 and HPV3 on 1st June 2017 (<12 weeks interval)

- A 3rd dose (valid HPV 3rd) should be given on or after 25th August 2017 (12 weeks/84 days after the invalid dose)

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 even if this means that it will take more than 12 months to complete the vaccine course. Clinical studies with Gardasil show persistence of immune response in those trial subjects who had received the complete vaccine schedule (SmPC section 5.1 Pharmacodynamic properties). There is also evidence of an anamnestic (immune memory) response (SmPC section 5.1 Pharmacodynamic properties).

What about a girl who received her 1st dose of HPV vaccine in 2015/2016 but missed subsequent doses?

If a girl was less than 15 years of age at her 1st dose of vaccine she only needs one further dose at least 6 months after the first dose to complete the course.

If she was 15 or older at the 1st dose she needs two further doses with at least 3 months between the 2nd and 3rd doses.

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 aged 16-26 years.
- Gardasil has been found to be over 99% effective 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 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?

Efficacy studies have shown the vaccine to be effective for nine years, with no evidence of waning immunity.

It is expected that the vaccine will provide long term protection.

What protection is provided by one dose?

Data are not available on the efficacy of one dose. Efficacy studies to date are based on a 2 or 3 dose vaccination course.

What are the constituents of Gardasil?

Virus like particles (VLPs)

- HPV Type 6 (20µg)
- HPV Type 11 (40µg)
- HPV Type 16 (40µg)
- HPV Type 18 (20µg)

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

How commonly are these constituents found in other products?

These constituents outlined above are commonly found in some other vaccines and in other medicinal compounds. Examples are outlined below:

- L-histidine is an essential amino acid available in food., A small amount is required in the vaccine. L-histidine is also a component of some hepatitis vaccines,
- Polysorbate 80 is a component of several of the childhood vaccines and other medication e.g. mycostatin used for oral thrush, feldene gel used as an anti-inflammatory medication and in making ice cream.

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- Sodium borate is a component of some vaccines and medicinal compounds such as Optrex eye drops,
- Aluminium hydroxyphosphate sulphate is a component of several of the childhood vaccines. Aluminium salts have been used in many vaccines for 70 years. The quantity of aluminium in the vaccine is very small (most adults will get approximately 35x more aluminium in their diet each day, than exists in the vaccine).

Are aluminium containing vaccines safe?

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

Does Gardasil contain thiomersal?

No. There is no thiomersal in Gardasil.

Is latex used in either the manufacturing or packaging process for Gardasil?

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

Are there any reasons not to give the vaccine?

Contraindications

- Known hypersensitivity to the active substances, the adjuvant, or any of the vaccine constituents.

Note: Allergy to yeast is no longer considered a contraindication to vaccination (see Chapter 10 HPV in Immunisation Guidelines for Ireland available at <http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter10.pdf>)

- Pregnancy.

Precautions

- Acute severe febrile illness; defer until recovery.
- Vaccine should be administered with caution to individuals with coagulation defects. When vaccines are given intramuscularly to persons with bleeding disorders or on anticoagulants, it is prudent to use a 23 gauge or wider needle to reduce the pressure gradient and cause less trauma to the tissues, and to apply gentle pressure to the vaccine site for 1-2 minutes after the injections. If using a 25 gauge needle, the vaccine should be injected into the muscle over 5 seconds to reduce the risk of tissue damage. In those with a severe bleeding tendency vaccination can be scheduled shortly after administration of clotting factor replacement or similar therapy. There is no recommendation on the subcutaneous administration of the HPV vaccine. The patient or parent should be advised of this.

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

How safe is the vaccine?

Gardasil is considered safe and well tolerated.

Side effects profile

- Very common (1/10): Erythema, pain, or swelling at the injection site; headache.
- Common (1/100, <1/10): Pain in extremity; bruising and pruritus at the injection site; fever; nausea
- Rare (1/10,000, <1/1,000): Urticaria
- Very rare (<1/10,000): Bronchospasm.

Post marketing adverse events have also been reported, e.g. dizziness; syncope (fainting); fatigue; chills; malaise; vomiting; injection site cellulitis.

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 given in the USA), 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 faint. 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: Schools Immunisation Programme 2016/2017 - available at www.immunisation.ie for further management).

In some countries there have been deaths reported following HPV vaccination – however further investigation has shown that none of these deaths were causally associated with the HPV vaccine and were due to other unrelated causes such as road traffic accidents, drowning, malaria and an undiagnosed tumour.

The most recent post licensure safety report for Gardasil was published in MMWR July 2014.: CDC. Human Papillomavirus Vaccination Coverage Among Adolescent Girls, 2007–2013, and Postlicensure Vaccine Safety Monitoring, 2006–2014 — United States. MMWR 2014; 63 620-624 available at <http://www.cdc.gov/mmwr/pdf/wk/mm6329.pdf>

In March 2015 the US CDC reported that ‘HPV vaccines are safe and effective vaccines’ <http://www.cdc.gov/vaccinesafety/Vaccines/HPV/Index.html>

In November 2015 the European Medicines Agency (EMA) reported on a review of HPV vaccines. This report found no evidence the vaccine was linked to chronic fatigue like conditions.

On January 12 2016 the EMA issued a final report on this review of HPV vaccines: “EMA confirms evidence does not support that they cause CRPS or POTS” Please see link for full details at http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/HPV_vaccines_20/European_Commission_final_decision/WC500196773.pdf

In January 2016, the European Commission endorsed the conclusion of the EMA, that there is no need to change the summary of product characteristics for HPV vaccines including Gardasil vaccine.

In May 2016 The UK Medicines and Healthcare Regulatory Agency reported : *“More than three million girls have been vaccinated so far in the UK with HPV vaccine, and tens of millions more have been vaccinated globally. As with all vaccines, safety remains under continual review, and HPV vaccine has a very good safety record”*.

The HSE is guided by the recommendation of the EMA and the HPRA.

How do I report an adverse event following vaccination?

All adverse events should be reported to the HPRA.

More information at

<http://www.hpra.ie/homepage/about-us/report-an-issue>

(Also See “Guidelines for Staff: Schools Immunisation Programme 2016/2017” Section 7.0 -available at www.immunisation.ie for further details).

What should happen with a girl who has a hypersensitivity reaction post vaccination?

The Immunisation Guidelines for Ireland state that those who have had a non- anaphylacticallergy may be given a subsequent dose of that vaccine if indicated.

<http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter10.pdf>

This recommendation differs from the contents of section 4.3 of the Summary of Product Characteristics (SmPC) of Gardasil (HPV vaccine), which states as a contraindication “Hypersensitivity to the active substances or to any of the excipients. Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of Gardasil should not receive further doses of Gardasil.”

NIAC wishes to draw attention to the following, in order to clarify this apparent conflict of advice.

1. There are degrees of severity of hypersensitivity reactions.
2. The only absolute contraindication to most vaccines is previous anaphylaxis to the vaccine or any of its constituents.
3. Cases of hypersensitivity need to be considered on a case by case basis.
4. Mild hypersensitivity reactions are not contraindications to a subsequent dose of a vaccine.
5. More severe hypersensitivity reactions should be discussed with a Consultant in Public Health Medicine and/or Pediatrician. In these cases vaccination in a hospital setting may be appropriate.
6. Recommendations from NIAC, including those in the Immunisation Guidelines for Ireland, may differ from those of the SmPC and the Health Products Regulatory Authority (HPRA).

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As advice from NIAC is evidence-based, does not differ substantially from that of other national vaccine advisory bodies, and is a national recommendation, there should not be concerns if that advice differs from the contents of the SmPCs.

To assist in the assessment of reactions it is important that the HPRA adverse reaction report form is completed in full for all cases. A medication error does not need to be routinely reported to the HPRA unless the student experiences harm (i.e. an adverse reaction) associated with it. In any such cases involving adverse reactions, an adverse reaction report should be submitted to the HPRA, including information on the nature of the error involved.

Up to the end of May 2016, the HPRA had received 1025 reports of suspected adverse reactions/events associated with use of the Gardasil in Ireland (please note that each report may include one or more suspected adverse reactions).

Of these reports, thirteen include the term 'Chronic Fatigue Syndrome', generally along with a range of other symptoms such as joint swelling, nausea, flu like illness, menstrual disorders.

Six reports include clinical information indicating that a diagnosis of POTS and two reports indicate a diagnosis of CRPS in association with Gardasil.

These reports have been received from a number of sources, including some directly from patients/family members, with variable levels of information on the clinical assessment, investigation and diagnoses.

The majority of reports received have been consistent with the expected pattern of adverse effects associated with use of Gardasil, as described in the product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PIL)).

What needle should be used to vaccinate girls with bleeding disorders?

NIAC states that

“There is little published information regarding the administration of intramuscular vaccines to persons with bleeding disorders or receiving anticoagulant treatment.

Those with inherited coagulopathies should receive factor replacement before intramuscular injection. When vaccines are given intramuscularly to persons with bleeding disorders or on anticoagulants, it is prudent to use a 23 gauge or wider needle and to apply gentle pressure to the vaccine site for 1-2 minutes after the injections. If using a 25 gauge needle, the vaccine should be injected into the muscle over 5 seconds to reduce the risk of tissue damage.

Is Gardasil contraindicated in girls allergic to penicillin?

No. An allergy to penicillin is not a contraindication to Gardasil, the vaccine used in the HSE's HPV vaccination programme.

Is Gardasil contraindicated in immunosuppressed girls?

No. Gardasil is NOT contraindicated in girls who are immunosuppressed as long as they are well and do not have a high fever. Again there is no risk to receiving HPV vaccine if their immune system is lowered – however the vaccine manufacturer has stated that those with reduced immune responses may not respond to HPV vaccine as well as those with healthy immune systems (this is the same as with most other vaccines) but there is no long term data about this yet. If the immunosuppression is temporary vaccination may be deferred until her immune system is functioning normally.

There is a report in Gardasil SmPC of a study of Gardasil in 126 HIV positive individuals aged 7 - 12 years – of whom 96 were vaccinated with Gardasil. Seroconversion to all four antigens occurred in 96% of subjects. However, the antibody titre was lower than in non-HIV infected subjects. The clinical relevance of the lower response is unknown. There is no data on the use of Gardasil in other individuals with impaired immune responsiveness, whether due to treatment or illness. Immunosuppressed individuals may not respond as effectively to the vaccine.

NIAC recommends that HPV vaccine should be considered for HIV infected females up to the age of 45 years.

What should happen to a girl who receives her first or second dose of HPV and then becomes immunosuppressed?

As above, there is no contraindication to a girl receiving a further dose of HPV vaccine (if indicated) as long as she is well and does not have a high fever. However, she may not respond to HPV vaccine as well as those with healthy immune systems. If the immunosuppression is temporary, vaccination may be deferred until her immune system is functioning normally.

Is Gardasil contraindicated in girls with coeliac disease?

No. Gardasil is not contraindicated in girls who have coeliac disease. However the vaccine manufacturer has stated that those with reduced immune responses may not respond to HPV vaccine as well as those with healthy immune systems (this is the same as with most other vaccines) but there is no long term data about this yet.

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 Versio

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 Gardasil be given to a girl using hormonal contraceptives?

Yes. In clinical studies of Gardasil the use of hormonal contraceptive did not appear to affect the immune response to Gardasil – see SmPC Section 4.5.

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.

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. The HPRA should only be informed if there is harm to the patient or foetus which is considered to be related to the vaccine. The HPRA would appreciate information re gestation of pregnancy at time of vaccination in relation to Gardasil vaccination. The outcome of pregnancy should be followed up with the girl when completing her course of HPV vaccine or when the pregnancy is completed. The course of Gardasil HPV vaccination may be finished when the pregnancy is completed.

Can Gardasil be given to breastfeeding mothers?

Yes. Gardasil vaccine can be given to breastfeeding mothers.

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. 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 Gardasil affect a girl's fertility?

No. Gardasil does not affect a girl's future fertility.

See link to Frequently Asked Questions about HPV Vaccine Safety at

<http://www.cdc.gov/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html#A6>

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

Gardasil and Cervarix HPV vaccines are licensed for use from the age of 9 years onwards.

Parents should be advised to wait until younger girls reach First year in second level schools when they will be vaccinated free-of-charge through the HSE school programme. Older girls may visit their GP or a private provider to obtain the vaccine but they will have to bear the cost.

Which HPV vaccine is used in the UK programme?

The vaccine used in the UK from 2008 to 2012 was Cervarix, (manufactured by GSK) a bivalent vaccine containing VLPs for two HPV types (16 and 18). From September 2012 the UK have used Gardasil in the national HPV vaccination programme.

Do fully vaccinated girls need cervical screening?

Yes. Currently HPV vaccines only protect against types 16 and 18 which cause approximately 70% of cervical cancers. Girls who have been fully vaccinated still need to be screened for cervical cancer caused by the remaining HPV types which the vaccine does not protect against. In addition 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.

Dr. Philip Davies, Director General of the European Cervical Cancer Association stated in January 2016: *“30,000 women die from cervical cancer each year in Europe; many of these deaths are preventable. Through CervicalCheck and the HPV vaccination programme, Ireland has one of the best cervical cancer prevention programmes in Europe and it’s completely free.”*

More information on the cervical screening programme is available at www.cervicalcheck.ie

Is information available in other languages?

The HPV Leaflet is available in the following languages:

English, Irish, Arabic, Simplified Chinese, German, French, Polish, Portuguese, Romanian and Russian

These are available for download at 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.

- Department of Health and Children available at <http://health.gov.ie/>
- Health Protection Surveillance Centre available at www.hpsc.ie
- Health Products Regulatory Authority available at www.hpra.ie
- Immunisation Guidelines for Ireland HPV chapter available at <http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter10.pdf>
- Irish Cancer Society available at www.cancer.ie
- Medicines Information online available at www.medicines.ie
- National Cancer Screening Service available at www.cancerscreening.ie
- National Cancer Registry Ireland available at www.ncri.ie/ncri/index.shtml
- National Immunisation Office available at www.immunisation.ie
- Australian Government, Department of Health and Education HPV programme available at <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-hpv>
- Canadian HPV programme available at <http://www.immunize.ca/en/diseases-vaccines/hpv.aspx> Centers for Disease Control and Prevention – HPV information available at www.cdc.gov/hpv/
- European Medicines Agency available at www.ema.europa.eu/
- New Zealand, Ministry of Health HPV programme available at <http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/hpv-immunisation-programme/hpv-vaccine>
- United Kingdom HPV programme available at www.nhs.uk/conditions/vaccinations/pages/hpv-human-papillomavirus-vaccine.aspx
- World Health Organization HPV information available at www.who.int/immunization/topics/hpv/en/