

Human Papillomavirus Questions and Answers for Public Health Nurses

SEPTEMBER 2008

COMMUNICABLE DISEASE CONTROL

Communicable Disease Control Branch
Public Health Division
Manitoba Health and Healthy Living

September 11, 2008

Manitoba 

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Background Information

- In July 2006, the regulator for vaccines in Canada, the Biologics Genetics and Therapeutics Directorate (BGTD) approved for license Merck's GARDASIL® Human Papillomavirus (HPV) vaccine¹ for use in Canada.
- In February 2007, the National Advisory Committee on Immunization (NACI)^{2,3} issued recommendations for the use of GARDASIL® for females aged 9 to 26.
http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/acs-02/t1_ef.html
- The Chief Public Health Officer of the Public Health Agency of Canada (PHAC) reviewed these recommendations and strongly supports this vaccine³.
- In the 2007 Federal budget, the Canadian Government announced funding to the provinces and the territories in support of a \$300 million national program for the Human Papillomavirus (HPV) vaccine. The vaccine will be used in a publicly funded HPV immunization program for residents, including all First Nations and Inuit residents both on and off reserve.
- In the spring of 2007, the Minister of Healthy Living, Kerri Irvin-Ross, committed to providing a publicly funded HPV vaccine program in Manitoba.
- The Canadian Immunization Committee's (CIC) Recommendations on a Human Papillomavirus Immunization Program, December 2007⁴ provided the following recommendations:
 - to reduce by 60 per cent the Cervical Intraepithelial Neoplasia (CIN) 2/3 caused by HPV 16/18 in Canada within 20 years of introduction of HPV vaccination program.
 - The national goal of HPV immunization programs is to decrease the morbidity and mortality of cervical cancer, its precursors and other HPV related cancers in women in Canada through combined primary prevention (immunization) and secondary prevention (screening) programs.
 - CIC recommends school-based HPV vaccination of one female cohort to be implemented in all Canadian provinces and territories.
 - The Canadian disease modeling and economic analyses indicate that vaccinating a school based cohort is a cost-effective strategy.
 - The HPV immunization program is recommended for girls and women for cervical cancer prevention only at this time.
 - For more detailed information on the recommendations see Recommendations on a Human Papillomavirus Immunization Program, December 2007 –
<http://www.phac-aspc.gc.ca/publicat/2008/papillomavirus-papillome/papillomavirus-papillome-1-eng.php>
- Routine HPV immunization programs for the prevention of cervical cancer have been implemented in a number of industrialized countries including the United States, Australia and western European countries.

- Routine immunization programs primarily target females prior to adolescence and before onset of sexual activity, age ranging from 9 to 17 years. HPV vaccines are currently licensed in more than 60 countries.
- Both NACI and the CIC have deemed that there is sufficient evidence to support the implementation of routine HPV immunization programs as part of cervical cancer prevention programs in Canada, while recognizing that there are important research questions that need to be further addressed after implementation.
- Both committees stress that HPV immunization does not replace the need for fully implemented, organized cervical cancer screening programs and the promotion of safer sex practices.
- As new knowledge and new vaccines become available, the recommendations will be reviewed and updated as needed.
- From September 2007 to June 2008, the Communicable Diseases Control Branch, Public Health Division, Manitoba Health and Healthy Living convened two groups, the Human Papillomavirus Immunization Program (HPVIP) Advisory Group and the HPVIP Working Group to identify the issues related to the HPV Immunization Program in Manitoba and to offer recommendations on the HPV Immunization Program implementation to the Chief Medical Officer of Health, and then subsequently to the Minister of Healthy Living.
- In March 2008, the HPV Immunization Program design recommended to the Minister of Healthy Living was:
 - One cohort, grade six females only, to commence in the 2008-09 School year, a three-dose vaccine schedule administered by Public Health Nurses, in the school setting.
- The recommendation was based on the following factors which are consistent with CIC recommendations:
 - Maximum vaccine effectiveness is achieved when girls are immunized prior to the onset of sexual activity.
 - Public health nurses currently provide publicly funded immunization programs in school settings.
 - Immunizing females in a school setting is a cost effective approach.
 - Information on Reproductive Health is introduced in the Manitoba Education Grade Five curriculum.
 - School attendance is better in Middle years than in Senior years, therefore supporting the completion of the HPV vaccine series.
- On May 1, 2008, the Minister of Health Living, Kerri Irvin-Ross formally announced the introduction of the HPV Immunization Program for Grade Six girls, along with other important cervical cancer reduction initiatives.
<http://news.gov.mb.ca/news/index.html?archive=2008-5-01&item=3597>

Human Papillomavirus

What is Human Papillomavirus?

- There are over 100 types of human papillomavirus (HPV). HPV is a virus that can infect many parts of the body.
- Approximately 40 HPV genotypes are able to infect the genital tract and can cause warts or other consequences such as cancer (for example cervical, penile and anal) in the anogenital region of women and men.
- The types of HPV that infect the anogenital area are not the same as the ones that infect other areas of the body such as the fingers, hands and face.
- The types which cause anogenital warts do not usually cause cancer.
- The various types of HPV are often classified into low and high risk according to their association with cancer. The “low-risk” types are rarely associated with cancer. The “high-risk” types are more likely to lead to the development of cancer³.
- **High-RISK (oncogenic or cancer associated) types are:**
 - Common types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82
 - Possible high-risk types: 26, 53, and 66
- **Low-risk (non-oncogenic) types:**
 - Common types: 6, 11, 40, 42, 43, 44, 54, 61, 72, 73, 81
- Types 16 and 18 are present in 70% of cervical cancers in North America as in many other parts of the world⁴.

How Common is Sexually Transmitted HPV?

Incidence and Prevalence

- HPV is not a nationally notifiable disease in Canada and, to date, no population-based studies have been published².
- Estimates of HPV infection and associated disease burden are based on Canadian prevalence and incidence studies in select populations, such as patients in routine cervical screening clinics, family planning clinics, STI/HIV clinics and university health clinics².
- All published Canadian studies have been conducted in women².
- The risk of acquiring an HPV infection occurs shortly after the onset of sexual activity⁴.
 - The prevalence of HPV infection rises rapidly after the onset of sexual activity and then declines with age.
 - The highest prevalence of HPV is found in the 20-29 age range.
 - Approximately 20% of 15-year-old Canadians have had a sexual encounter⁴.

- The prevalence of genital HPV infections increases with increasing numbers of sexual partners; a clinical study of women who have had more than one sexual partner showed that 46% had cervical HPV infection at three years after their first intercourse⁵.
- HPV infection is so common that most women are likely to be in contact with one or more of the subtypes of this virus at some time in their lives⁴.
 - In North America, the lifetime cumulative incidence of HPV infection is estimated at more than 70% for all types together, which makes HPV the most common sexually transmitted infection.
 - It is estimated that 75% (3 out of 4) of sexually active Canadians will have at least one HPV infection in their lifetime).
 - In a multi-year study of aboriginal women in Nunavik, northern Quebec, infections with any type and high risk HPV types were detected in 29.1% and 20.2 % of women respectively. The most common HPV type was HPV-16 infections with HPV-16 and HPV-18 accounted for 23.8% of all HPV infections. HPV prevalence in this population was found to be similar to that observed among female university students in Montreal and health clinic attendees in Winnipeg and Nunavut.²
 - The prevalence of any HPV infection among women attending an inner-city primary care clinic in Winnipeg did not differ significantly between Aboriginal and non-Aboriginal women. It was found, however, that HPV type 18 was the most prevalent type in Aboriginal women, and it was significantly more common in Aboriginal than non-Aboriginal women².
- Cervical cancer is the first type of cancer to have been associated with HPV: the virus is present in 99.7% of cervical cancer cases⁴.
 - Within one year of an initial HPV infection, low-grade cervical pre-cancerous condition may develop.

Natural History of HPV Infection

*For detailed information, refer to Canadian consensus guidelines on human papillomavirus. – *Journal of Obstetrics and Gynaecology Canada 2007;29(8, supplement 3):S1-S56* – <http://www.sogc.org/home/pdf/hpv-guideline-full.pdf>

- The virus enters the epithelium, usually through a break in the skin, and then infects the cells.
- The time from infection to release of virus is approximately three weeks. However, the period between infection and appearance of lesions can be weeks to months.
- Most infections are unnoticed and resolve spontaneously within 24 months.
- There is essentially no inflammatory response, which permits immune evasion in the early stages of infection.
- People with compromised immune systems (such as HIV) have higher rates of HPV infection and are more likely to manifest large, multifocal, and dysplastic lesions.

- Drugs (steroids), diseases (such as diabetes, renal failure, and HIV infection), and cigarette smoking compromise the immune system and may potentiate the problem.
- Herpes simplex and bacterial vaginosis may facilitate cutaneous and mucosal entry of the virus.
- Classic genital HPV lesions include benign genital warts and cervical, vaginal, anal, and vulvar cancers.
- Concurrent oral, hand, and genital HPV infection is frequent.
- Persistent infection with HPV 16 or 18, although infrequent, may lead to cervical dysplasia and cancer.
- Almost all cervical and vaginal cancers and a large proportion of vulvar, anal, and oral cancers are associated with high-risk, oncogenic strains of HPV.
- Low-risk HPV types cause genital warts, Recurrent Respiratory Papillomatosis (RRP), and oral or conjunctival papillomas.
- HPV infection is difficult to prevent in sexually active adults, and preventing transmission is much more difficult to achieve with HPV infection than with other STIs.
- Vaccination may represent the best primary prevention method, as condoms have limited efficacy without consistent use, and abstinence is unacceptable to many.
- Pap testing is an effective secondary prevention and screening method and with appropriate care and follow-up, most cervical cancers can be detected at an early stage and treated successfully.

Clearance or Persistence of HPV

- 80% of these infections appear to clear; that is, HPV DNA can no longer be detected on the mucosal or epithelial surface.
- The time required for clearance appears to vary with different HPV genotypes, ranging from 5 to 6 months for low-risk types and 8 to 14 months for high-risk types.
- It is unclear whether the virus is completely eliminated in some cases or whether it remains latent in basal cells and can reactivate under immune-permissive conditions⁴.

How is Genital HPV Spread?

- Any person who has sexual contact can get the virus.
- Some types of HPV can be spread during sexual contact with a person who is already infected.
- Sexual contact includes (skin-to-skin contact) with the vagina, vulva (the outside parts of a woman's genitals), penis, scrotum, anus and/ or the mouth.
- Co-infection with more than one type has been seen, and the risk of getting a specific HPV type is not substantially decreased among those with prior infection of a similar type.

Risk Factors Associated with HPV Infection

- Younger age is associated with high rates of HPV infection, the peak age being less than 25 years.
- Number of sexual partners may increase the risk of acquisition of HPV.
- HPV infection has also been associated with current and past cigarette smoking but is not correlated with the amount smoked.
- The possible association of oral contraception with HPV infection has been very difficult to assess, as oral contraception is highly associated with sexual activity.

Genital Warts

Genital Warts:

- usually appear as small bumps or groups of bumps, usually in the genital area;
- can be raised or flat, single or multiple, small or large, and sometimes cauliflower shaped;
- can appear on the vulva, in or around the vagina or anus, on the cervix, and on the penis, scrotum, groin, or thigh;
- may appear within weeks or months after sexual contact with an infected person,
- or, may not appear at all;
- if left untreated, may go away, remain unchanged, or increase in size or number;
- will not turn into cancer.

Cervical Dysplasia and Cancer

Burden of Disease

- Cervical cancer does not have symptoms until it is quite advanced. For this reason, it is important for women to get screened regularly for cervical cancer.
- Other less common HPV-related cancers, such as cancers of the vulva, vagina, anus and penis, also may not have signs or symptoms until they are advanced.
- Persistence of oncogenic HPV viruses is required for the cellular changes associated with cervical dysplasia.
- Pap smear screening is designed to detect such changes before progression, which permits ablative therapy to remove the abnormal cells.
- Canada has low rates of cervical cancer but high rates of pre-invasive disease owing to reasonably effective strategies for Pap smear screening.
- Because of the young age of women with cervical dysplasia and cancer, the burden is significant.
- The link between HPV and cervical cancer has been solidly shown. Most cases of cervical cancer can be found to be attributable to HPV infection. In a pooled analysis of 1918 patients with cervical cancer, HPV DNA was detected in 90.7%⁴.

- The most frequent high risk types detected, in decreasing order of frequency, were 16, 18, 45, 31, 33, 52, 58, and 35.
- Cervical cancer is the third most frequent cancer in women during their child bearing years — between the ages of 20 to 49.
- It was estimated that 1,350 Canadian women were diagnosed with cervical cancer; lower socio-economic, immigrant and Aboriginal women are all under-screened so these numbers could be much higher⁶.
- Approximately 390 died from the disease in 2006⁶.
- **In Manitoba** (2006 stats CCMB⁷)
 - Approximately 45 women are diagnosed with cervical cancers annually and approximately 15 deaths are reported annually⁵.
 - In 2006, there were 300 women with abnormal Pap tests for every women diagnosed with cervical cancer.
 - 59 women were diagnosed with invasive cervical cancer.
 - 3,024 women had a high grade Pap test requiring colposcopy and treatment.
 - 11,543 women had a low grade pap test requiring another Pap test and possible colposcopy.

Distinct Female Populations

- HPV is sexually transmitted between women.
- Recommendations on Pap smear screening and vaccination should not vary for this group.
- HIV-positive women carry HPV at high rates and have higher rates of cervical dysplasia.
- Some studies suggest that the cervical dysplasia progresses faster to invasive cancer, in direct relation to the degree of immunocompromise. The high rates appear to be related to HIV virus load, whereas the association with immune status and HPV persistence is modest.
- Inuit women of Nunavut have higher rates of cervical cancer than Canadian women in general in other provinces and territories.⁵
 - Cervical cancer is the most common cancer of women in this region, representing 35% of all cancers diagnosed.
 - The prevalence of oncogenic HPV in this population is 26% and is inversely related to age.

HPV Infection in Males

- To date, studies in males are less extensive than in females.
- Prevalence in males, as in females, varies according to the population studied, limiting the generalizability of results to the broader population.
- HPV prevalence among males has been shown to vary by the sex of their sexual partners, the presence of cervical pathology in their partners and geographic region.

- Despite the limitations in determining HPV infection status in males, infection and asymptomatic HPV infections appear to be common.

Non-cervical HPV Infection

- Among non-cervical genital cancer and cancers of the head and neck, the proportions related to HPV infection vary.⁵
- Cancer of the vulva is rare, with an annual rate of new diagnoses of 0.5 to 1.5/100 000. HPV is associated with 20% to 50% of cases and is more frequent in younger women than in older women.⁵
- Cancer of the vagina is even more rare, with an annual rate of new diagnoses of 0.3 to 0.7/100 000; 40% of cases are attributable to HPV.⁵
- High proportions of anal cancer in both women (95%) and men (83%) are associated with HPV infection.⁵
- Cancer of the penis is rare, with an annual rate of new diagnoses of 1/100 000; HPV DNA is associated with 40% to 50% of all penile cancers, types 16 and 18 being implicated.⁵
- Cancers of the mouth and oropharynx have highly variable incidence rates around the world owing to variations in tobacco and alcohol use.⁵
- It is estimated that 20% of oropharyngeal cancers and 10% of laryngeal and esophageal cancers are attributable to HPV.⁵
- Recurrent respiratory papillomatosis (RRP) occurs in 4.3/100 000 children and 1.8/100 000 adults in the United States.⁵
- It is estimated that 1 in 400 children born to women with genital infection with HPV types 6 or 11 will have subsequent RRP.⁵

How Can Someone Reduce Their Risk for Getting HPV and Cervical Cancer?

- The only way to completely avoid HPV infection is to not have sexual contact (skin-to-skin contact) with the vagina, vulva (the outside parts of a woman's genitals), penis, scrotum or anus.
- Abstinence is the best way to prevent HPV infection and the best method during adolescence.
- Delay onset of sexual activity. The lining of the reproductive tract in teenage girls is still developing which makes it easier for them to get infected with HPV.
- Once sexually active, consider choosing one long term sexual partner, or limiting the number of sexual partners.
- For those who choose to be sexually active, condoms may lower the risk of getting HPV and other sexually transmitted infections, if used correctly all the time.
- Condoms may also lower the risk of developing HPV-related diseases, such as genital warts and cervical cancer.

- HPV can infect areas that are not covered by a condom — so condoms may not fully protect against HPV.
- Consider partner's sexual history, as they may not know they are infected with HPV (ex: if they have had a previous partner).
- Get immunized with the HPV vaccine prior to the onset of sexual activity.

Will Girls/Women Who Have Been Vaccinated Still Need Cervical Cancer Screening?

- The HPV vaccine does not protect against all types of HPV, it only protects against the four most common types of HPV that cause cervical cancer and anogenital warts.
- Even when someone is vaccinated it is still possible to become infected with one of the less common types of HPV that the vaccine does not protect against.
- It is important that vaccinated girls/women continue to have regular Pap tests.

For More Information, see Manitoba Cervical Cancer Screening Program

Who is at risk of cervical cancer

http://www.cancercare.mb.ca/home/patients_and_family/prevention_and_screening/

Human Papillomavirus Vaccine

Manitoba HPV Immunization Program

- Manitoba Health and Healthy Living will offer the GARDASIL® vaccine to grade six females only, (majority born in 1997), commencing the school year 2008-09 and annually in the future.

The Manitoba HPV immunization program is voluntary.

What is GARDASIL®

- GARDASIL® is a recombinant, quadravalent vaccine that offers protection against two high-risk types of HPV (Type 16 and Type 18) which cause approximately 70 per cent of cervical cancers, and against two low-risk types of HPV (Type 6 and Type 11), which cause approximately 90 per cent of genital warts.
- It is a sterile liquid suspension prepared from the highly purified virus-like particles (VLPs) of the recombinant major capsid (L1) protein of HPV Types 6, 11, 16, and 18.
- The L1 proteins are produced by separate fermentations in recombinant *Saccharomyces cerevisiae* (yeast) CANADE 3C-5 (Strain 1895) and self-assembled into VLPs.

Who is GARDASIL® Recommended For?

- GARDASIL® is a vaccine indicated in girls and women 9-26 years of age for the prevention of infection caused by the HPV types 6, 11, 16, and 18 and the following diseases associated with these HPV types:
 - Cervical cancer
 - Vulvar and vaginal cancers
 - Genital warts (condyloma acuminata)
 - Cervical adenocarcinoma in situ (AIS)
 - Cervical intraepithelial neoplasia (CIN) grade 2 and grade 3
 - Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3
 - Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3
 - Cervical intraepithelial neoplasia (CIN) grade 1
- The vaccine is thought to be most effective before the onset of sexual activity; however, females between the ages of 9 and 26 years can still receive the vaccine even if they have already been sexually active.
- Women who are already sexually active may be infected with an HPV type contained in the vaccine, but they can still benefit from protection against the other HPV types the vaccine protects against.
- **The vaccine does not treat existing HPV infections, genital warts or cervical abnormalities.**

How Effective is the Vaccine?

Efficacy and Immunogenicity

- HPV vaccination has been shown to be highly immunogenic and is very efficacious in preventing persistent HPV infection in women not previously infected with the HPV types used in the vaccine⁵.
- When injected intramuscularly, the vaccine induces immunity without actual infection.
- Clinical trials involving monovalent, bivalent, and quadrivalent vaccines have shown over 90% protection against persistent HPV infection and related cervical dysplasia due to the vaccine subtypes in young, healthy females who have not begun sexual activity.
- Trials have also shown more than 90% efficacy in preventing incident HPV infection.
- Antibody response has been excellent in the vaccinated females and much greater than with natural infection.
- At the end of follow-up, the vaccine-induced antibody titres were 17 and 14 times higher than the titres induced by naturally occurring infection with HPV types 16 and 18, respectively.
- At five years after enrollment, there was 96% protection against persistent HPV infection, and there were no cases of CIN related to HPV 16 or 18 or genital warts related to HPV 6 or 11.
- After 36 months, 94% remained seropositive for HPV type 6, 96% for type 11, and 100% for type 16. However, only 76% remained seropositive for type 18. The significance of antibody levels and seropositivity is unknown at this time².

Who is Eligible for the Vaccine, at No Cost, in Manitoba?

- All females, entering grade six (the majority born in 1997), beginning in the 2008/2009 school year, will be offered the vaccine.
- Once eligible, the individual may receive the vaccine at a later time (as with other vaccine eligibility criteria in Manitoba) at no additional cost.
- To receive the vaccine, arrangements can be made with the local public health office and public health nurse.
- This voluntary immunization program will continue to be offered every year to girls in grade six.
- In special circumstances, the family physician may administer the HPV vaccine to the eligible female student and can order the vaccine from the Provincial Warehouse. (The first and second can be ordered at the same time, and the third dose can be ordered at a later date to accommodate the recommended six month schedule).

If I Am Not Eligible for Free Vaccine, Can I Still Get the Vaccine?

- Yes.
- Contact your doctor who will discuss your individual care.
- The doctor will provide a prescription.
- The cost of the vaccine series may vary.
- If an individual requests the vaccine and is receiving financial assistance from Employment and Income Assistance (EIA), refer the individual to the EIA case coordinator in their area.

Will Manitoba Health and Healthy Living Reimburse Individuals Who Purchase the Vaccine Privately?

- No.
- If an individual has private health insurance coverage, refer the individual to their provider regarding financial reimbursement.
- Manitoba Health and Healthy Living's Pharmacare does not cover the cost of this vaccine.

Who Should Not Receive the Vaccine?

- females under the age of nine or over the age of 26
- **anyone who is allergic to any of the ingredients listed in the vaccine package information – See Summary Product Information**
- pregnant women
- males
- The vaccine is not currently licensed or recommended for use in males, but studies are underway to see if this will be an option in the future.

Contraindications

- Patients who are hypersensitive to the active substances or to any of the excipients of the vaccine.
- Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of GARDASIL® should not receive further doses of GARDASIL®.

Warnings and Precautions

General

- As for any vaccine, vaccination with GARDASIL® may not result in protection in all vaccine recipients.
- This vaccine is not intended to be used for treatment of active genital warts; cervical, vulvar, or vaginal cancers; CIN, VIN, or VaIN.

Is the Vaccine Safe?

- Yes, the vaccine is considered safe, but as with all vaccines, adverse events may occur.
- You cannot get HPV from the vaccine as it does not contain a live virus.
- Health Canada has done a scientific review of the quality, safety and effectiveness of the vaccine and has approved it for use.
- Once a vaccine is in use, Health Canada and the Public Health Agency of Canada continues to monitor its use.

What Are the Common Side Effects of the Vaccine?

- The most commonly reported side effects are:
 - Pain, swelling, itching, and redness at the injection site.
 - Fever, nausea, dizziness, headache, and vomiting.
 - Fainting has been reported (and may occur) following immunization in the adolescent population.

What Are the Rare Side Effects of the Vaccine?

- As with any vaccine or drug, severe, allergic, life-threatening (anaphylactic) reactions may occur with symptoms such as:
 - difficulty breathing
 - wheezing (bronchospasm)
 - hives or rash

As with other vaccines, side effects that have been observed after vaccination include:

- swollen glands (neck, armpit, or groin).
- Guillain-Barré syndrome, a rare form of paralysis that is usually temporary, has been reported but a confirmed link to the vaccine has not been established.
- See the current product monograph for other rarely reported side effects.

Have There Been Reports of Serious Adverse Events Following HPV Immunization?

- For updated information see the Public Health Agency of Canada website at http://www.phac-aspc.gc.ca/std-mts/hpv-vph/fact-faits_e.html#4
- As of June 30, 2008, the Centers for Disease Control and Prevention have reported 9,749 adverse events. These were primarily mild and common adverse events.
- For more information about adverse events following HPV immunization in the U.S., please visit the **Vaccine Adverse Events Reporting System (VAERS) website**.

Post-Market Adverse Drug Reactions

The following adverse experiences have been spontaneously reported during post-approval use of GARDASIL®. Because these experiences were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish (to confirm or to rule out) a causal relationship to vaccine exposure.

- Blood and lymphatic system disorders: lymphadenopathy.
- Nervous system disorders: dizziness, Guillain-Barré syndrome, headache, syncope.
- Gastrointestinal disorders: nausea, vomiting.
- Immune system disorders: Hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.

How are Vaccines Monitored for Safety in Canada?

The Public Health Agency of Canada coordinates and supports the Canadian Adverse Events Following Immunization Surveillance System, which collects reports from health care providers on adverse events following immunization.

In the event of an adverse event, please ensure reporting by completing the Adverse Event Following Immunization Reporting form.

Canada also has an active surveillance system that is based out of 12 pediatric hospitals across Canada, called IMPACT (Immunization Monitoring Program ACTive). In addition, an expert scientific committee in Canada called the Advisory Committee on Causality Assessment (ACCA) assesses select reports and determines whether or not the vaccine was likely to have caused the reaction.

Can the Vaccine Be Given at the Same Time as Other Vaccines?

- Yes, the vaccine can be given at the same time as most other vaccines.
- When one or more vaccines are given at the same time, they are given in separate arms.
- Concomitant administration of GARDASIL® vaccine and hepatitis B vaccine at all three doses does not diminish the response or Geometric Mean Titers (GMT's) to either vaccine. Studies with conjugate meningococcal vaccine and with adult/adolescent formulations of tetanus, diphtheria and acellular pertussis vaccines (Tdap) are under way.
- GARDASIL® is not a live vaccine and has no components that have been found to adversely affect the safety or efficacy of other vaccines.
- GARDASIL® vaccine can be administered at the same visit as other age-appropriate vaccines, such as the adolescent/ adult formulation of Tdap and meningococcal conjugate vaccines.
- Administering all indicated vaccines together at a single visit increases the likelihood that adolescents and young adults will receive each of the vaccines on schedule.

Summary Product Information

Description

GARDASIL® [Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine] is a recombinant, quadrivalent vaccine that protects against Human Papillomavirus (HPV). It is a sterile liquid suspension prepared from the highly purified virus-like particles (VLPs) of the recombinant major capsid (L1) protein of HPV Types 6, 11, 16 and 18. **The L1 proteins are produced by separate fermentations in recombinant *Saccharomyces cerevisiae* (yeast) CANADE 3C-5 (Strain 1895) and self-assembled into VLPs.**

Composition

Active Ingredients

GARDASIL® is a sterile preparation for intramuscular administration.

Each 0.5-mL dose contains approximately:

- 20 µg of HPV 6 L1 protein
- 40 µg of HPV 11 L1 protein
- 40 µg of HPV 16 L1 protein
- 20 µg of HPV 18 L1 protein

Inactive Ingredients

Each 0.5-mL dose of the vaccine contains approximately:

- 225 µg of aluminum (as amorphous aluminum hydroxyphosphate sulfate adjuvant)
- 9.56 mg of sodium chloride
- 0.78 mg of L-histidine
- 50 µg of polysorbate 80
- 35 µg of sodium borate
- water for injection

The product does not contain a preservative (Thimerosal) or antibiotics.

Dosage

Recommended Dose and Dosage Adjustment

- GARDASIL® should be administered intramuscularly as 3 separate 0.5 mL-doses according to the following schedule:
 - **First dose:** at elected date
 - **Second dose:** 2 months after the first dose
 - **Third dose:** 6 months after the first dose
 - Individuals are encouraged to adhere to the 0, 2, and 6 months vaccination schedule.
- If a deviation from the recommended schedule occurs, it is recommended that the second dose be administered at least 1 month after the first dose, and the third dose be administered at least 3 months after the second dose.
- All 3 doses should be given within a 1-year period.

Interrupted Vaccine Schedules

- If the GARDASIL® vaccine schedule is interrupted, the vaccine series does not need to be restarted.
- If the series is interrupted after the first dose, the second dose should be given as soon as possible, and the second and third doses should be separated by an interval of at least 12 weeks.
- If only the third dose is delayed, it should be administered as soon as possible.
- Individuals who have accessed the immunization program in other provinces but have not completed the series are advised to contact their nearest Public Health Office to consult with a Public Health Nurse. The PHN will review the vaccine schedule for completion of the series and eligibility in accordance with Manitoba's publicly funded program. **See chart below.**

Effective 2008/2009

Province	Grade(s)	Year Program Started
British Columbia	6 & 9	2008
Alberta	5 & 9 (2009-2012)	2008
Saskatchewan	6 & 7 (2008 only)	2008
Manitoba	6	2008
Ontario	8	2007
Quebec	4 & 9	2008
New Brunswick	7 & 8 (2008 only)	2008
Nova Scotia	7	2007
PEI	6	2007
Newfoundland	6	2007
NWT	TBA	
Yukon	TBA	
Nunavut	TBA	

How Long Does Vaccine Protection Last?

- Recent studies have indicated good protection against HPV for five years of follow-up.

Are Additional Doses (Boosters) Required?

- Additional booster doses are not recommended at this time; future recommendations will be based on scientific evidence.

Two Doses Versus Three Doses of the Vaccine

- NACI's recommendations for providing 3 doses of the HPV vaccine are based on current evidence.
- Further study on the effectiveness of a two-dose HPV vaccine schedule is required and as data from on-going research becomes available, recommendations will be updated accordingly.

Administration

- GARDASIL® should be administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.
- GARDASIL® must not be injected intravascularly.
- Subcutaneous and intradermal administrations have not been studied, and therefore are not recommended.

- The prefilled syringe is for single use only and should not be used for more than one individual. For single use vials, a separate sterile syringe and needle must be used for each individual.
- The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.

Shake Well Before Use.

- Thorough agitation immediately before administration is necessary to maintain suspension of the vaccine.
- After thorough agitation, GARDASIL® is a white, cloudy liquid.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.
- Discard the product if particulates are present or if it appears discolored.

Storage and Stability

- Store refrigerated at 2°C to 8°C.
- Do not freeze.
- Protect from light.
- GARDASIL® should be administered as soon as possible after being removed from refrigeration.
- GARDASIL® can be administered provided total time out of refrigeration (at temperatures at or below 25°C) does not exceed 72 hours.

Packaging

Vials

GARDASIL® is supplied as a carton of:

- one 0.5 mL single-dose vial.
- * Manitoba Health and Healthy Living will be providing the supply in single dose vials

Syringes

GARDASIL® is supplied as a carton of:

- one 0.5 mL single-dose prefilled Luer Lock syringe, preassembled with an UltraSafe Passive® delivery system. One needle is provided separately in the package.

Vials and prefilled syringes components are **latex free**.

References

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2. National Advisory Committee on Immunization (NACI) Statement on Humanpapillomavirus Vaccine, February 15, 2007, Vol.33.ACS – <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07pdf/acs33-02.pdf>
3. The FACTS on the Safety and Effectiveness of the HPV Vaccine – http://www.phac-aspc.gc.ca/std-mts/hpv-vph/fact-faits_e.html
4. Recommendations on Human Papillomavirus Immunization Program, Canadian Immunization Committee, December 2007 – <http://www.phac-aspc.gc.ca/publicat/2008/papillomavirus-papillome/papillomavirus-papillome-1-eng.php>
5. Canadian consensus guidelines on human papillomavirus, *Journal of Obstetrics and Gynaecology Canada* 2007;29(8, supplement 3):S1-S56 – <http://www.sogc.org/home/pdf/hpv-guideline-full.pdf>
6. Canadian Cancer Society, human papillomavirus – http://www.cancer.ca/ccs/internet/standard/0,3182,3649_1242735771__langId-en,00.html
7. Cancer Care Manitoba stats, 2006.

Resources

Canadian

1. Public Health Agency of Canada
 - a) Human papillomavirus (HPV) – <http://www.phac-aspc.gc.ca/std-mts/hpv-vph/facts-faits-eng.php>
 - b) Its Your Health - HPV – <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/hpv-vph-eng.php>
 - c) What Everyone should know about Human Papillomavirus (HPV) – Questions and Answers – http://www.phac-aspc.gc.ca/std-mts/hpv-vph/hpv-vph-qaqr_e.html
 - d) The FACTS on the Safety and Effectiveness of HPV Vaccine – http://www.phac-aspc.gc.ca/std-mts/hpv-vph/fact-faits_e.html
2. Canadian Coalition for Immunization Awareness and Promotion – HPV – <http://www.immunize.cpha.ca/en/diseases-vaccines/hpv.aspx>
3. Health Canada - Summary Basis of Decision (SBD) GARDASIL® – http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/phase1-decision/drug-med/sbd_smd_2007_gardasil_102682-eng.php
4. Society of Obstetricians and Gynaecologists of Canada website – <http://www.hpvinfos.ca/hpvinfos/home.aspx>
HPV Toolkit – order online at the website listed above.
5. Society of Canadian Colposcopists – <http://www.hpvinfos.ca/hpvinfos/professionals/position-statements.aspx>
6. The Society of Gynecological Oncologists of Canada – <http://www.hpvinfos.ca/hpvinfos/professionals/position-statements.aspx>
7. Canadian Medical Association Journal (CMAJ-JAMC) August 28, 2007, Vol.177, No. 5 – <http://www.cmaj.ca/content/vol177/issue5/>
8. Canadian Women's Health Network – http://www.cwhn.ca/PDF/CWHN_HPJuly30.pdf
9. Women's Health Clinic – http://www.womenshealthclinic.org/resources/wih/WHC_HP_policy_statement.pdf
10. Canadian Pediatric Society – Human papillomavirus vaccine for children and adolescents POSITION STATEMENT (ID 2007-01) – <http://www.cps.ca/english/statements/ID/ID07-01.pdf>

Other

Centers for Disease Control and Prevention (CDC) Human papillomavirus – <http://www.cdc.gov/std/HPV/default.htm>

HPV Today – http://www.hpvtoday.com/_english/index_english.htm

