



HPV Vaccine Update November 2008

*Merck's human papilloma virus (HPV) vaccine, **Gardasil®**, was approved on June 8, 2006 by the Food and Drug Administration (FDA) for use by girls and women ages 9-26. In June 2008, the FDA denied Merck approval for a supplemental application for use of the vaccine in adult women age 27 through 45 due to lack of data. GlaxoSmithKline also developed an HPV vaccine, Cervarix, which was approved by the European Medicines Agency (EMA) in September 2007. An application for approval was submitted to the FDA in March 2007 but approval is not expected before late 2009.*

According to 2007 data from the Center for Disease Control, approximately one in four girls aged 13-17 has started the three-shot HPV vaccination series. This October, the Advisory Committee on Immunization Practices (ACIP), the independent panel of health experts that advises the CDC on US vaccine policies, reported that safety monitors detect no major safety problems with the HPV vaccine.

On July 1, 2008, the US Citizenship and Immigration Services (USCIS) added HPV to the list of mandatory vaccinations for immigrants. As a result, the HPV vaccine is mandatory for immigrant women and girls between the ages of 11 and 26.

What is the Link between HPV and Cervical Cancer?

Over 99.7% of cervical cancer cases worldwide are associated with HPV, the most common sexually transmitted viral infection in the United States. Of its 120 different strains, about 40 HPV strains affect the genitals and are sexually transmitted, and at least 15 of these strains have the potential to cause cervical cancer. The four types believed to cause most genital HPV disease include strains 16 and 18 which cause about 70 percent of cervical cancer, and strains 6 and 11, which cause 90 percent of genital warts. The virus has also been found in other less common cancers including those of the oral cavity, oropharynx, anus, penis, vagina, and vulva.

Although not all HPV infection leads to cervical cancer, according to the American Cancer Society, in 2008, approximately 11,070 cases of cervical cancer will be diagnosed in the US and approximately 3,870 women will die from cervical cancer¹. According to the National Cervical Cancer Coalition, women in developing countries account for about 85 percent of both the yearly cases of cervical cancer (estimated at 473,000 cases worldwide) and the yearly deaths from cervical cancer (estimated at 253,500 deaths worldwide). For more information on cervical cancer and HPV please refer to "[The Role of the Cervix in Reproductive Health](#)," available on RHTP's website.

¹ "What Are the Key Statistics about Cervical Cancer," American Cancer Society Website. Retrieved October 29, 2008 from http://www.cancer.org/docroot/CRI/content/CRI_2_4_1X_What_are_the_key_statistics_for_cervical_cancer_8.asp?nav=cri

What are the Facts on the HPV Vaccines?

- **Safety:** Both Gardasil and Cervarix have low risk profiles. The vaccines consist of papilloma virus like particles, empty shells of viral structural proteins from brewer's yeast, and cannot transmit the virus. In safety studies of boys and girls 9 -15 years of age, and women 16-26, the only known adverse reactions attributed to the vaccine included injection site pain and incidence of low grade fever². As of June 30, 2008, 94% percent of total reports received by the FDA and CDC monitored Vaccine Adverse Event Reporting System (VAERS) indicated fainting and nausea after the injection in adolescent aged girls.³ The FDA and CDC have taken steps to remind immunization providers to watch individuals for 15 minutes after vaccination to avoid potential injury from fall.
- **Efficacy:** Clinical trial results for both Gardasil and Cervarix in women 16 to 26 and bridged to girls 9-15⁴, show high levels of protection against “persistent HPV infection” – more than 99% of the more than 20,000 women who enrolled had a seroconversion rate in the trials⁵. Both vaccines are “prophylactic,” or protect against contraction of HPV, but do not eliminate an already existing infection.
- **Duration of Protection:** Gardasil has shown 100% percent effectiveness after the third vaccination in females, and proven immunization for up to 5 years⁶. Cervarix has shown 100% effectiveness and proven immunization up to 4.5 years⁷. The FDA has not recommended a booster shoot. There is strong evidence that the protective efficacy of the vaccines will be long lasting, however studies are being conducted to determine if a booster shot will be necessary.
- **Cost:** Both vaccines must be administered in three separate visits within a period of six months (0, 1 or 2, and 6 months). Gardasil costs approximately \$360 for complete immunization. This cost does not include any additional healthcare provider fees.
- **Impact:** Both vaccines target the most common cancer causing HPV strains, 16 and 18⁸, and Gardasil also protects against strains 6 and 11; linked to genital warts. Although an impact on preventing HPV lesions will be sooner, an impact on preventing cervical cancer will not be seen for many years⁹. In addition, even were we to achieve a high impact on elimination of cervical cancer, public health experts remind us that there are other oncogenic strains of HPV and there is little evidence of cross strain protection. Therefore, **routine Pap screenings are still necessary to protect against cervical cancer**

² “FAQ about HPV vaccines,” American Cancer Society Website. Retrieved April 19, 2006 from http://www.cancer.org/docroot/CRI/content/CRI_2_6x_FAQ_HPV_Vaccines.asp?sitearea=

³ “Information from CDC and FDA on the Safety of Gadasil Vaccine,” US Food and Drug Administration Website. Retrieved November 21, 2008 from <http://www.fda.gov/cber/safety/gardasil071408.htm>

⁴ It is not feasible to collect genital samples and discuss sexual activity in children; therefore the data was bridged to girls.

⁵ Markowitz, Lauri. “Considerations and Options for HPV Vaccine Recommendations in the US,” presented at ACIP Meeting. Atlanta, GA. February 2006.

⁶ Ibid.

⁷ GlaxoSmithKline Release. April 6, 2006.

⁸ According to research conducted by Gynecologic Cancer Prevention Research Group at Dartmouth Medical School, Cervarix has shown protection against strains 35 and 41 as well which together make up 10% of the cause of cervical cancer (GSK Release, April 6, 2006).

⁹ Markowitz, Lauri. February 2006.

- **Acceptability:** Studies have found high acceptability among parents and providers for routine adolescent vaccination (higher acceptability for older adolescents); rates of acceptance increase with education about the safety, efficacy, and appropriateness of the vaccine¹⁰.

Is the HPV vaccine approved for use by boys and men?

In November 2008, Merck released results from a Phase III clinical trial study of Gardasil use by boys and men aged 16 to 26. This study concluded that the vaccine reduced the incidence of external genital lesions caused by human HPV types 6, 11, 16 and 18 by 90 percent. As a result of this study, Merck plans to submit a supplemental Biologics License Application for Gardasil use in boys to the FDA by the end of 2008.¹¹

What is ACIP and Why Does Their Recommendation Matter?

The Advisory Committee on Immunization Practices (ACIP) is a fifteen member panel, organized under the Centers for Disease Control (CDC), which provides recommendations to public health systems nationwide on who should receive a vaccination, when and how often they should receive it, and the appropriate dosage. Their recommendations take a number of factors into account including: safety, efficacy and duration of protection, impact and cost effectiveness, and acceptability.¹²

ACIP itself does not mandate vaccination, but their recommendations strongly influence standards of practice, and are relied upon by insurers for setting reimbursement policy and by states for public funding purposes. ACIP offers recommendations for:

- **Routine childhood and adolescent vaccination schedules.** Although states have the ultimate decision making power, and some states allow exclusion for routine vaccination on the basis of religious or philosophical beliefs, if ACIP puts a vaccine on this schedule, evidence of vaccination is required before allowing a child to be enrolled in school, thereby making a vaccine *de facto* nearly universal. Further, if a vaccine is added to the “routine” schedule, it can be added to the “Vaccines for Children” (VFC) program, which provides free vaccines to doctors serving eligible low-income children. HPV vaccine advocates argue that a “yes” vote on this second question is necessary to ensuring wide scale availability, particularly among lower socioeconomic people.
- **Adult immunization schedule:** ACIP provides recommendations for “catch up” and booster schedules for adults, provides recommendations for specific subpopulations (for example, pregnant women), and, if it has decided a vaccine should not be administered to the entire population, the committee makes recommendations for groups at highest risk of contracting the disease. In general, these recommendations are largely voluntary with exceptions for public health personnel, persons enrolling in the military, or persons immigrating to the US.

What Has ACIP Said About the HPV Vaccine?

In February 2006, ACIP reviewed the data and proposed recommendations presented by the *HPV Vaccine Workgroup* concerning Gardasil, On June 29, the ACIP unanimously voted for “**routine**

¹⁰ Liddon, Nicole, CDC. “The Future of Cervical Health for Underserved Populations.” Congressional Black Caucus, Washington, DC. March 16, 2006.

¹¹ Merck Release. November 13, 2008.

¹² “ACIP Charter,” ACIP. Retrieved April 18, 2006 from <http://www.cdc.gov/nip/ACIP/charter.htm>.

vaccination of females 11 to 12 years of age,” with voluntary vaccination allowed for women as young as 9 years old. ACIP also recommended “catch up” vaccination of girls and women 13-26 years old. Finally, and importantly, the committee also recommended Gardasil as one of 16 mandatory vaccines covered by the Vaccines for Children Program, a key step in ensuring universal access of the vaccine. Reasons for this suggestion include:

- The prevalence of HPV in the US – nearly three in four Americans between the ages of 15 and 49 has been infected with HPV at some point in their life.
- Because HPV is sexually transmitted, experts say the vaccine needs to be administered to as many young adolescent females as possible *prior to sexual activity* and 13% of American females have sexual intercourse prior to age 15¹³.
- Merck’s trials found the vaccine produced a stronger immunological response in adolescents aged 10-15 than in women aged 16-23.
- Gaps in adolescent health care, including immunizations, and the fact that public health experts have estimated that we would need to achieve 80% saturation to achieve “herd immunity” (a highly colorful term to shorthand the level at which we could expect to see the disease wiped out).

HPV Vaccination Mandates

The Reproductive Health Technologies Project is concerned with the growing trend mandating the vaccine for school entry. In 2007, at least **24 states and the District of Columbia introduced this type of legislation**. More recently, the US Citizenship and Immigration Services (USCIS) added HPV to the list of mandatory vaccinations for immigrant women and girls between the ages 11 and 26. While data have shown that the vaccine is safe, a mandate is premature for several reasons:

- **Low Threat to Public Health**— Human Papilloma Virus is the leading cause of cervical cancer; however, it is not spread by casual contact and thus poses a lower risk to all Americans than other vaccine-prevented diseases, such as influenza. In addition, under the USCIS policy, only the first dose is mandated for immigrant women and girls making this directive a less than meaningful way to improve public health.
- **Cost**—Gardasil costs approximately \$360 for all three doses (excluding any additional healthcare provider fees), which can create a tremendous financial barrier for women without insurance coverage.
- **New to the Market**—Gardasil was introduced to the market in 2006 and is still undergoing post market research to assess the vaccine’s long term safety and efficacy.
- **Broken Health Care Infrastructure**—A good vaccine requires a good public health infrastructure. Unfortunately, HPV vaccine mandates are one part of a broken health care system that often looks to quick fixes and easy shortcuts. We need a comprehensive preventive approach to decrease the incidence of HPV and cervical cancer that includes continuous education, regular pap smears, as well as timely vaccinations.

¹³ “Teenagers in the US: Sexual Activity, Contraceptive Use, and Childbearing,” Series No. 23 Volume 24. National Survey for Family Growth. 2002.