CDC Questions and Answers Concerning the Safety and Efficacy of Gardasil®

June 4, 2007

1. What is the ability of Gardasil® to prevent cervical cancer in girls/young women?

Gardasil® protects against infection from 4 HPV types, including 2 types (HPV 16 and 18) that cause about 70% of cervical cancers. In clinical trials among women who had not yet been infected with a specific vaccine HPV type, the efficacy of the vaccine was close to 100% for prevention of pre-cancer lesions of the cervix due to that type. For example, a woman who participated in the study and who did not have HPV type 16 before vaccination was afforded almost 100% protection against cervical pre-cancer lesions caused by HPV type 16. Therefore, if girls/women are vaccinated before their first sexual experience, Gardasil® should be very effective in preventing about 70% of cervical cancers.

2. Are there any concerns about the safety of this vaccine?

The clinical trials found no increased number of serious adverse events in girls/women who received vaccine compared with those who received placebo. Before the Advisory Committee on Immunization Practice (ACIP) recommends any vaccine, it weighs the known and potential benefits against known risks. Like all vaccines, Gardasil® has some side effects, but ACIP determined that the benefits outweigh the risks.

Since the vaccine has been licensed, the most common reports to the Vaccine Adverse Events Reporting System (VAERS) have been local injection site reactions - as was seen in the clinical trials. There were some cases of fainting after vaccination. This has been found with other vaccines administered to adolescents. Many people have a fainting episode at some point in their life and there are many potential causes. The ACIP's general recommendations for all vaccines include a suggestion for a 15 minute post-vaccination waiting period.

Since the vaccine was licensed, there have been 13 reports of Guillain-Barre Syndrome (GBS) among persons who received Gardasil®. CDC investigators are in the process of confirming GBS. Of the 13 reports, six individuals received Gardasil® given alone, five received Gardasil® and Menactra®, one received Gardasil®, Menactra®, and Hepatitis A vaccine, and one received Gardasil® and Pneumococcal Polysaccharide Vaccine given within 30 days of one another. At least one media article has incorrectly reported the number of GBS cases as forty. Because GBS occurs at a rate of 1-2/100,000 person years during the second decade of life, some cases will occur by coincidence following vaccination (but not due to vaccination).

Since the vaccine was licensed, there have been three deaths reported among persons who received Gardasil®: One involving a pulmonary embolism; one involving myocarditis due to influenza A infection; and one from a blood clot. These deaths are being fully investigated. Since more than 5 million doses have been distributed, some deaths will occur coincidentally following vaccination (but not due to vaccination).

3. How is the safety of this vaccine being monitored?

Before any vaccine is licensed and made available to the American public, the Food and Drug Administration (FDA) must approve it as safe and effective. Prior to being licensed by FDA in June 2006, the HPV vaccine was tested in more than 11,000 females, ages 9 through 26 years, from the U.S. and several countries around the world. There appeared to be no serious side effects, and the vaccine was found to be safe and effective. The most common side effect was brief soreness at the injection site.

Now that the vaccine is in general use, the CDC, working with FDA, continues to closely monitor the safety of the HPV vaccine. One tool that is used in monitoring vaccine safety is the Vaccine Adverse Event Reporting System (VAERS). VAERS is a national reporting system that accepts and monitors approximately 18,000 reports of adverse events submitted annually by a variety of sources.

VAERS serves as an early-warning system to detect problems that may be related to vaccines. CDC and FDA physicians and scientists review all reports of serious side effects reported to VAERS in order to identify potential new vaccine safety concerns that may need further study. It is important to know that many adverse events reported to VAERS may not be caused by vaccines. Reports to VAERS may be submitted by anyone, including healthcare providers, patients and family members. Because of this, VAERS is subject to several limitations including underreporting and incomplete information.

VAERS receives reports of many events that occur after immunization. Some of these events may occur coincidentally following vaccination, while others may be caused by vaccination. The fact that an adverse event occurred following immunization is not conclusive evidence that the event was caused by a vaccine. Factors such as medical history and other medications taken near the time of the vaccination must be examined to determine if they could have caused the adverse event.

4. Some people have said that boosters of HPV vaccine may be needed. If so, how might this change opinions about the vaccine?

At this time, we don't know if boosters will be needed. Data available to date show persistent high protection from the vaccine through 5 years and suggest protection will last much longer. If boosters are needed, this would not change the recommendation for vaccination. It might change the cost effectiveness of the vaccine if boosters are needed. However, based on analyses by economic experts, vaccination is expected to remain cost-effective if booster doses are needed.

5. How likely is it that the vaccine might prevent pre-cancerous lesions yet not prevent the actual cancer?

The vaccine trials used pre-cancer lesions of the cervix as the main endpoint to measure efficacy. The trials found the vaccine to have close to 100% efficacy in preventing pre-cancer lesions in women who had not yet been infected with any of the four HPV types contained in the vaccine. Most cancers progress through well-defined stages that include such pre-cancer lesions; therefore, prevention of the pre-cancer lesion will prevent the cancer. It is unethical to use cervical cancer as an endpoint since cervical cancer can be prevented by detection and treatment of pre-cancer lesions. Women's lesions would have to be left untreated and allowed to progress to cancer if cervical cancer was used an endpoint in the trials.

6. Will the HPV vaccine divert dollars and efforts away from Pap testing ?

No. Pap testing will remain one of the main public health measures to prevent cervical cancer. ACIP recommendations state that vaccinated women should have regular Pap testing as currently recommended by national organizations. There are several reasons why women will still need regular cervical cancer screening:

> The vaccine does NOT protect against all HPV types that cause cancer. Approximately 30% of cervical cancers are caused by types not covered by the vaccine, so vaccinated women would still be at risk for some cancers,
>
> Women may not get the full benefit of vaccination if they receive it after they have already acquired one or more of the four HPV types covered by the vaccine. The vaccine does not treat existing HPV infections, nor does it prevent the development of diseases caused by existing infections.

7. Some news articles have claimed that some women who received at least one shot of Gardasil® went on to develop pre-cancer lesions on their cervix within three years of vaccination, just 14% fewer than in a placebo control group.

These results are from an analysis which included women who developed pre-cancer lesions caused by any HPV type, not just types prevented by the vaccine (specifically, HPV types 6,11,16 and 18). There are over 40 types of sexually transmitted HPV. Some of the pre-cancer lesions observed in the study may have been from any of these types. Additionally, since 27% of the women were already infected with an HPV type contained in the vaccine at the time of vaccination and the vaccine does not prevent disease due to an HPV type already present, some women in the study developed pre-cancer lesions due to the HPV vaccine types.

Women would have had to be followed for a longer time to see the full benefit of the vaccine. More benefit would be observed in vaccinated women because the vaccine would keep preventing new infections with HPV 6, 11, 16, and 18 , while unvaccinated women in the placebo group would remain vulnerable to acquiring new infections and disease due to those four HPV types.