

## **KEY MESSAGES**

### **JAMA Article: Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine**

*This article, which appears in the August 19<sup>th</sup> issue of the Journal of the American Medical Association, is a summary of reports to the Vaccine Adverse Events Reporting System (VAERS) of adverse events following receipt of quadrivalent human papillomavirus vaccine from June 1, 2006, through December 31, 2008. The article was coauthored by scientists from the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA).*

#### **Summary**

- This study looked at all of the adverse events (AEs) following administration of the human papillomavirus (HPV) vaccine that were reported to the Vaccine Adverse Events Reporting System (VAERS) from when the vaccine was first licensed/approved in June 2006 through December 31, 2008.
- After vaccine licensure, CDC and FDA review and follow-up all serious AEs reported to VAERS, and routinely do analyses of VAERS data.
- This is the first **published** CDC/FDA comprehensive analysis of health events reported to VAERS following HPV vaccination in which we looked for patterns of reporting. VAERS reports are regularly reviewed for safety concerns.
- The findings were generally not that different from what is seen in the safety reviews of other vaccines recommended for a similar age group, 9 to 26 years old (meningitis and Tdap). Based on the review of available information by FDA and CDC, the HPV vaccine continues to be safe and effective, and its benefits continue to outweigh its risks.
- There has been a great deal of media coverage on this vaccine--from the advertisement by the manufacturer promoting the use of the vaccine to reports of a variety of health problems following its administration. Consumers, parents, healthcare professionals and others have raised questions regarding the safety of the HPV vaccine.
- Past publications have reported the findings from pre-licensure studies. These studies involved smaller populations (several hundred to several thousand individuals). Also, there have been individual reports of adverse events covered by the news media. However, this is the first nationwide **published** postlicensure study that includes clinical review of medical records associated with reports to VAERS.
- Public health and safety are priorities for CDC and FDA. As with all licensed vaccines, we will continue to closely monitor the safety of the HPV vaccine. FDA and CDC continue to find that the HPV vaccine is a safe and effective vaccine that will potentially benefit the health of millions of women by providing protection against the types of HPV that cause the majority of cervical cancer.

## Key Points

### This study's main findings include the following:

- More than 23 million doses were administered nationally since the HPV vaccine was licensed in 2006. There were a total of 12,424 reports to VAERS of adverse events following HPV vaccination.
- Since the HPV vaccine was approved, the vast majority (94%) of adverse events reported to VAERS after receiving this vaccine have not been serious. An adverse event is considered serious if it is life threatening, or results in death, permanent disability, congenital anomaly, hospitalization or prolonged hospitalization.
- The most common events reported were:
  - Syncope (or fainting)—common after needle injections, especially in pre-teens and teens
  - Local reactions at the site of immunization (pain and redness)
  - Dizziness
  - Nausea
  - Headache
- Of the 12,424 reports of adverse events, 772 (6% of all reports) described serious adverse events, including 32 reports of deaths.
- The 32 death reports were reviewed, and there was no common pattern to the deaths that would suggest they were caused by the vaccine. In cases where there was an autopsy, death certificate, or medical records, the cause of death could be explained by factors other than the vaccine. Some causes of death determined to date include diabetes, viral illness, illicit drug use, and heart failure.
- There were two reports of unusual neurological illness (per autopsy, probable variants of Amyotrophic Lateral Sclerosis/ALS) that resulted in the death of two young females. There is no current evidence suggesting that the HPV vaccine caused these illnesses, but researchers from several highly regarded academic centers are studying the cases.
- There was increased reporting of syncope and blood clots compared with what has been found for other vaccines given to females of the same age. This does not mean there is a definite causal association, but this finding needs further investigation.

## CDC/FDA Actions

- FDA and CDC have taken steps to remind immunization providers about the recommendation that individuals be watched carefully for 15 minutes after any vaccination, including administration with the HPV vaccine, to avoid potential injury from a fall in the event of syncope. FDA requested the manufacturer to change the HPV vaccine's **prescribing information** to include syncope in the warnings and precautions section of the label. Post-vaccination observation is crucial to prevent syncope and traumatic injury associated with fainting. CDC and FDA are working on continued public health communication campaigns, including the Back-to-School immunization programs, to educate the public about fainting after vaccination.
- CDC is working with researchers to provide assistance in the follow up of the two neurological (probable ALS variant) deaths after HPV vaccination. Tissue samples have been sent to the CDC laboratory.
- The Vaccine Safety Datalink (VSD) has been using real-time surveillance studies for multiple AEs, including blood clots and pulmonary emboli; thus far, VSD has **not** detected an elevated risk for any of these adverse events after receipt of HPV vaccine.
- CDC and FDA are both undertaking studies on the disproportional reporting (increased reporting with HPV vaccine compared to what has been found for other vaccines given to females of the same age) noted for syncope and blood clots in VAERS.

## VAERS Facts

- VAERS is a joint program run by CDC's Immunization Safety Office and FDA. VAERS receives information from individuals (vaccine recipients, parents, other family members, doctors, other healthcare workers, and the vaccine manufacturer) across the United States who choose to make a report of an adverse event occurring after vaccination. VAERS is designed to identify potential adverse events that warrant additional study.
- All reports are reviewed by medical officers, nurses and trained staff at both FDA and CDC. VAERS receives reports of many events that occur following immunization. It can detect patterns in reports to show that a vaccine *may be associated with* a possible side effect.
- An adverse event is a health problem that is reported after someone gets a vaccine or medicine. It *may or may not* have been caused by the vaccine or medicine. Some of these events *may occur coincidentally* during the time period following vaccination, while others may actually be caused by vaccination.
- Anyone who thinks that they may have had an adverse event after receiving HPV vaccine (or any vaccine) should file a VAERS report. This can be done on the web, by regular mail or by fax. For more information, visit [www.vaers.hhs.gov](http://www.vaers.hhs.gov).

## HPV Facts

- Every year in the United States, about 11,000 women are diagnosed with cervical cancer and almost 4,000 die from this disease. Most cases of cervical cancer are caused by HPV.
- The HPV vaccine protects against the main types (16, 18) of HPV that cause 70% of cervical cancer. Clinical trials indicate that the vaccine is 99-100% effective in preventing infection caused by the strains/serotypes (6, 11,16,18) included in the vaccine, in women who have not been infected prior to vaccination. Studies are currently evaluating the long-term effectiveness and impact of HPV vaccination.