COMMONWEALTH of VIRGINIA

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September 11, 2008

Kim Snead, Executive Director
Joint Commission on Health Care
900 E. Main Street, 1st Floor West
Richmond, VA 23219

Dear Kim:

In response to the Joint Commission on Health Care's (JCHC) request for information concerning the human papillomavirus (HPV) vaccine, I have attached five powerpoint slides which provide a quick overview. In the event that the JCHC desires more detailed information, the following summary discusses the HPV vaccine, Virginia's statutory provisions concerning the HPV vaccine, and the potential for adverse effects resulting from the vaccine. Information pertaining to the potential for adverse effects was, I believe, of particular interest to the JCHC.

Overview of HPV and Cervical Cancer

HPV is the virus that causes most cases of cervical cancer. Every year, about 12,000 women are diagnosed with cervical cancer and almost 4,000 die from this disease in the United States. Worldwide, cervical cancer is the second most common cancer in women, causing an estimated 470,000 new cases and 233,000 deaths per year. The U.S. Food and Drug Administration (FDA) approved Gardasil as a vaccine against HPV in June, 2006 for use in girls and women ages 9 through 26. This approval followed the testing of the vaccine on over 11,000 women in the U.S. and around the world.

Virginia's HPV Immunization Requirement for School Entry

In 2007, the General Assembly enacted legislation requiring HPV immunization for females as a condition of entry into the sixth grade. This new immunization requirement is effective on October 1, 2008, and will first affect girls who enter the sixth grade in September 2009. Parents and guardians are allowed to have their children opt out of this requirement, after having reviewed materials describing the link between the human

papillomavirus and cervical cancer approved for such use by the Board of Health. VDH is working with the Department of Education to develop these educational materials. No form needs to be completed, signed, etc. in order for a parent/guardian to opt their child out of this requirement.

Potential for Adverse Events Associated with HPV Vaccine

More than 16 million doses of Gardasil have been distributed in the U.S. Given the large number of doses distributed, it is expected that, by chance alone, serious adverse events and some deaths will be reported in this large population during the time period following vaccinations. The FDA and the U.S. Centers for Disease Control and Prevention (CDC) closely monitor the safety of all vaccines through the Vaccine Adverse Event Reporting System (VAERS). This monitoring and analysis of reports, including in-depth medical review, is designed to detect serious events that occur at rates greater than expected, compared to what would be expected by chance alone. In addition, FDA routinely reviews manufacturing information, and has not identified any issues affecting the safety, purity or potency of Gardasil.

Between the date the vaccine was licensed (June 8, 2006) and June 30, 2008, there were 9,749 VAERS reports of adverse events following Gardasil vaccination (6,667 were U.S. reports, 3,082 were foreign reports). Among the U.S. reports, more than 94% were classified as reports of non-serious events such as brief soreness at the injection site and headache. Less than 6% were reports of serious adverse events, about half of the average for vaccines overall. Please note that VAERS defines serious adverse events, in the Code of Federal Regulations, as adverse events involving hospitalization, death, permanent disability, and life-threatening illness

Reports of Non-Serious Events (94% of total reports). Since Gardasil was approved by the FDA through June 30, 2008, the vast majority (94%) of adverse events reported to VAERS after receiving this vaccine have not involved serious events. These reports include fainting, pain at the injection site, headache, nausea and fever. Fainting is common after injections and vaccinations, especially in adolescents. Falls after fainting may sometimes cause serious injuries, such as head injuries, which can be prevented with simple steps, such as keeping the vaccinated person seated for up to 15 minutes after vaccination. Both the FDA and CDC have taken steps to remind immunization providers about the recommendation that individuals be watched carefully for 15 minutes after vaccination to avoid potential injury from a fall. The vaccine's prescribing information was changed to include this information.

Reports of Serious Events (6% of total reports). Concerns have been raised about reports of deaths occurring in individuals after receiving Gardasil. As of June 30, 2008, 21 deaths had been reported to VAERS (17 were U.S. reports, 4 were foreign reports). Patient identifying data was not available for four of the 17 U.S. reports and one report is currently under investigation. For the remaining 12 reports, after careful review, VAERS could not establish a causal relationship between vaccination and death. There was not a common pattern to the deaths that would suggest they were caused by the vaccine. In cases where autopsy, death certificate and medical records were available, the cause of death was explained by factors other than the vaccine. Please note that while Gardasil was being tested in the U.S. before it was licensed, 10 people in the group that received the HPV vaccine and 7 people in the placebo group died during the trials. No deaths were considered vaccine-related.

Guillain-Barré Syndrome (GBS) has also been reported in individuals following vaccination with Gardasil. GBS, a rare neurological disorder that causes muscle weakness, may occur spontaneously in unvaccinated individuals after a variety of specific infections. The FDA and CDC have reviewed the reports of GBS that have been submitted to VAERS. To date, there is no evidence that Gardasil has increased the rate of GBS above that expected in the population. The data do not currently suggest an association between Gardasil and GBS.

Thromboembolic disorders (blood clots) have also been reported to VAERS in people who have received Gardasil. Most of these individuals had risk factors for blood clots such as use of oral contraceptives which are known to increase the risk of clotting. Thromboembolic disorders as well as other medical events are being studied through the Vaccine Safety Datalink (VSD) in previously planned controlled studies. The Vaccine Safety Datalink project is a collaborative effort between CDC's Immunization Safety Office and eight large managed care organizations. The VSD project monitors immunization safety and address the gaps in scientific knowledge about rare and serious adverse events following immunization.

I hope that this information is useful and helpful to the JCHC. Please contact me if I may be of any further service to you.

Sincerely,

Karen Remley, MD, MBA, FAAP

Enc.
cc: The Honorable Marilyn B. Tavenner

HPV Immunization School Entry Requirement (§32.1-46)

- Three doses of properly spaced human papillomavirus (HPV) vaccine for females. First dose shall be administered before the child enters the sixth grade.
- "Because the human papillomavirus is not communicable in a school setting, a parent or guardian, at the parent's or guardian's sole discretion, may elect for the parent's or guardian's child not to receive the human papillomavirus vaccine, after having reviewed materials describing the link between the human papillomavirus and cervical cancer approved for such use by the Board (of Health)."

HPV Immunization

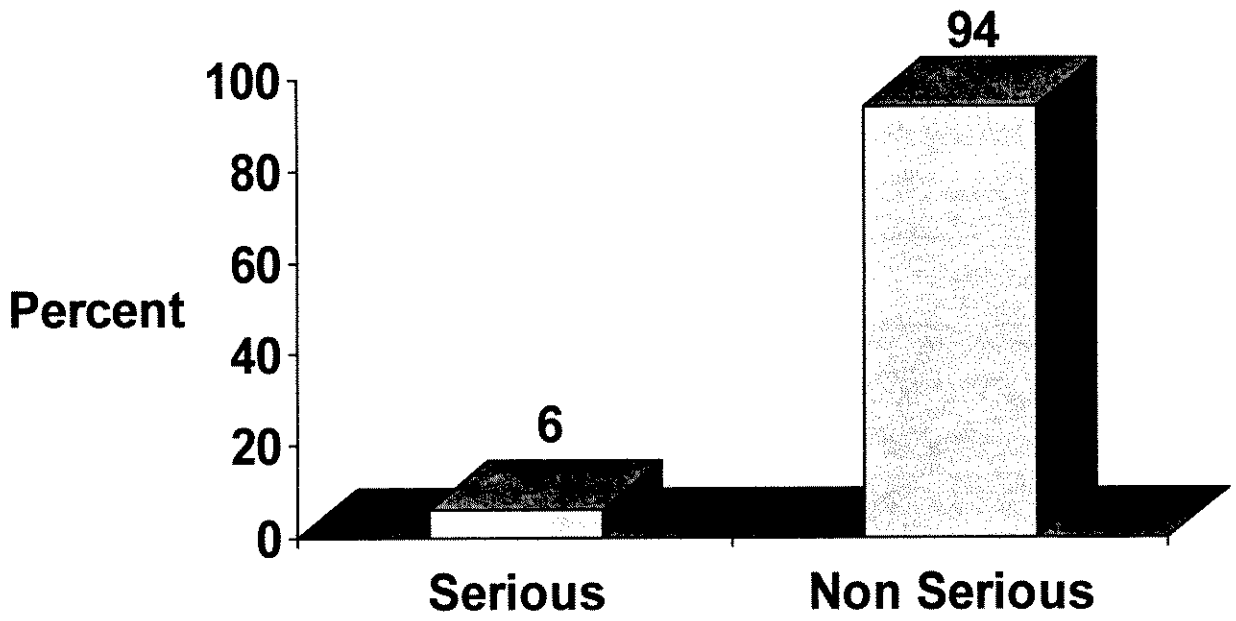
- FDA approved the human papillomas virus (HPV) vaccine, Gardasil, on June 8, 2006 for use in girls and women 9 through 26 years of age.
- Gardasil was tested in over 11,000 women in the United States and around the world, and found to be safe and effective in preventing serious HPV-related diseases.
- This vaccine is an important cervical cancer prevention tool that will potentially benefit the health of millions of women.

HPV Immunization

- FDA and CDC closely monitor the safety of all vaccines through the Vaccine Adverse Event Reporting System (VAERS).
- As of July 22, 2008 Merck and Co. has distributed over 16 million doses of Gardasil in the United States.

HPV Immunization

9,749 Adverse Events Reported Concerning Gardasil through 6/30/08



Non serious includes fainting, pain at injection site, headache, nausea, and fever. Serious adverse events involve hospitalization, death, permanent disability and life threatening illness.

HPV Immunization

- Based on the review of available information by FDA and CDC, Gardasil continues to be safe and effective, and its benefits continue to outweigh its risks.
- CDC has not changed its recommendations for use of Gardasil. FDA has not made any changes to the prescribing information for how the vaccine is used or to the vaccine's precautions.