FDA Response to questions about Gardasil

Does the FDA believe the vaccine to be safe?

Yes. Studies involving approximately 21,000 girls and women in the United States and around the world were conducted to evaluate the safety and effectiveness of Gardasil before receiving approval by the FDA. Approximately half of the study participants received the vaccine, and the other half received a control or placebo. These studies demonstrated that the potential benefits of the vaccine exceeded the potential risks.

Since Gardasil was licensed by FDA in June 2006, the Centers for Disease Control and Prevention’s (CDC) data indicates more than 46 million doses of Gardasil have been distributed in the United States as of July 2012 (http://www.cdc.gov/vaccines/vpd-vac/hpv/vac-faqs.htm).

Further information about the safety of the Gardasil vaccine can be found at: http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/ucm179549.htm

Is the FDA concerned about the 30 thousand complaints into VAERS?

Postmarketing surveillance is necessary to ensure that safety is continually monitored after licensure. As of February 2, 2014, VAERS has received a total of 31,870 reports of possible adverse events following immunization with Gardasil. A report to VAERS generally does not prove that the identified vaccine caused the adverse event described. An event described in a VAERS report is not necessarily a confirmed medical condition diagnosed by a physician.

What is the FDA doing to investigate these complaints? Are there any plans to look more in depth to see if there are any patterns among the kids who have had reactions?

When evaluating whether an adverse event might be caused by a vaccine, the FDA applies several approaches. After a vaccine is approved for use in the United States, the FDA and CDC use the Vaccine Adverse Event Reporting System (VAERS) to monitor vaccine safety. Each day, the FDA medical officers review all serious adverse events, which for regulatory purposes (21 CFR 600.80) are defined as those reported as fatal, disabling, life-threatening, requiring hospital admission, prolonging a hospital stay, resulting in a congenital anomaly, or requiring medical intervention to prevent such an outcome. When available, medical records, clinic notes, and autopsy reports are also reviewed. VAERS data may be used to detect new or rare adverse events, monitor known reactions, perform vaccine lot surveillance, identify risk factors, and evaluate the safety of newly licensed vaccines.

At the FDA, routine safety surveillance for Gardasil includes a monthly summary of new VAERS reports (serious and non-serious), follow-up on previous reports, data mining, literature search, case series analysis, regulatory updates, and an overall safety assessment by physician epidemiologists. Additionally, in accordance with Title IX, Section 915 of the Food and Drug Administration Amendments Act of 2007, physicians at the FDA perform a formal comprehensive safety review. See here for more details: http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/surveillance/ucm204091.htm.
FDA also presents these ongoing safety analyses to an independent Pediatric Advisory Committee, which assesses the reviews and makes recommendations for action. More information on the Pediatric Advisory Committee presentations can be found here:

- http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/PediatricAdvisoryCommittee/ucm2005361.htm
- http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/PediatricAdvisoryCommittee/ucm283814.htm
- http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/PediatricAdvisoryCommittee/ucm234285.htm
- http://www.fda.gov/ScienceResearch/SpecialTopics/PediatricTherapeuticsResearch/ucm123229.htm

These evaluations are performed to determine whether there are any new serious adverse events that were not previously identified during product development, known side effects that have been reported with unusually high frequency, or potential new safety concerns that have emerged. For Gardasil, two such reviews have been performed and presented: in 2010 (after the indication was expanded to include the prevention of vulvar and vaginal cancer) and in 2012 (after the indication was expanded to include the prevention of genital warts in males, and the prevention of anal cancer in females and males).

VAERS reports are not the only source of information used to evaluate the safety of a vaccine. When patterns or clusters of reports are detected, more in-depth analyses are performed using the FDA’s Post-licensure Rapid Immunization Safety Monitoring (PRISMA) program and the CDC’s Vaccine Safety Datalink (VSD).

The FDA’s Post-licensure Rapid Immunization Safety Monitoring (PRISMA) program is part of the Agency’s Sentinel Initiative, which has expanded the use of large health care databases to evaluate medical product safety. Information about PRISMA can be found on the FDA’s website at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/ucm196251.htm

The VSD is a large-linked database of managed care organizations (MCOs) administered by the CDC. The VSD enables scientists to test hypotheses regarding the associations of vaccines and health outcomes. Unlike the VAERS system, studies through the VSD are able to calculate rates of adverse events among persons who did or did not receive a particular vaccine, thus elucidating whether an adverse event is more common among persons who received the vaccine. In 2011, the VSD published the results of their real time safety surveillance of Gardasil conducted between August 2006 – October 2009. In this study, the VSD studied the occurrence of specific adverse events following more than 600,000 doses of Gardasil. Adverse events in the HPV vaccinated population were compared to another appropriate population (such as adolescents vaccinated with vaccines other than HPV) and included Guillain–Barré syndrome (GBS), stroke, venous thromboembolism (VTE), appendicitis, seizures, syncope (fainting), allergic reactions, and a potentially life-threatening allergic reaction called anaphylaxis. None of these adverse events were found to be any more common after HPV vaccination than among the comparison groups.

Further information about VSD can be found at: http://www.cdc.gov/vaccinesafety/Activities/vsd.html
As it does with all vaccines, the FDA continues to monitor the safety of Gardasil. For example, the FDA recently evaluated the results of a postmarketing study, which included 189,629 females ages 9 to 26 years, 51% of whom were 9 to 15 years of age, to assess the risk for onset of new autoimmune diseases after vaccination with Gardasil. Examples of these types of diseases include juvenile rheumatoid arthritis, lupus, multiple sclerosis, etc. The results of this study showed that there is no elevated risk for onset of new autoimmune disease associated with the use of Gardasil. The FDA evaluated the results of another postmarketing study that evaluated all emergency visits and hospitalizations after Gardasil vaccination in a large cohort of females aged 9 to 26 years, and the results of a pregnancy registry assessing the safety of Gardasil administered inadvertently to pregnant women. See the following studies:


FDA continues to monitor the safety of Gardasil and believes that the benefits of vaccination outweigh the potential risks.

Some parents say they have never been contacted by the FDA about their complaints. Is this typical?

Follow up from FDA or CDC is not conducted for every report. The FDA, CDC and the VAERS contractor work together to conduct a review and follow-up of all serious AE reports (as defined above). VAERS staff follow up on all serious and other selected adverse event reports to obtain additional medical records, laboratory results, and/or autopsy reports to help understand the concern raised.

Some doctors have noticed the research supporting the vaccine has a major flaw. They say of the thousands of people in the original trial—Merck was only able to follow up with about 100.

The doctors that you reference have received inaccurate information. In the studies that the FDA evaluated to support original licensure in 2006, over 11,000 females were followed for safety after receiving Gardasil and approximately 9,000 were followed for efficacy.

Is the FDA concerned about this issue?

See previous response.

Does the FDA have a threshold of how many people are needed to follow up with?

No. This type of scientific information is determined on a case-by-case basis for each vaccine’s clinical development program taking into account various factors, such as the mechanism of action and the clinical performance of the vaccine, the epidemiology and pathophysiology of the disease, and the feasibility of potential approaches to long term follow up.
Some doctors have also pointed out because of this...the efficacy of the vaccine can only be 5 years. Does the FDA agree or disagree?

The FDA disagrees. In studies conducted to date, protection against HPV-related disease has been observed through 8 years after vaccination with Gardasil, and assessment of effectiveness is ongoing as the population of Gardasil recipients increases and as more follow-up time since vaccination is gained. One example, as noted in the approval letter to Merck in 2006, some who participated in the original study will be followed out to 2018 (approximately 15 years of follow-up after vaccination).

It is important to note that the prescribing information states that Gardasil does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening.