

Merck & Company's Development of Gardasil

In 2006, the United States branch of Merck & Co. received FDA approval for Gardasil, a human papillomavirus, or HPV, vaccine that protects against HPV and the cervical cancer that can come with it. In 1891, George F. Merck founded the US branch of the company to distribute chemicals with high purity for use in research, in New York City, New York, and other areas nearby. HPV is a common sexually transmitted infection that can cause genital warts, regular skin warts, cervical cancer, and other cancers. Since 2016, Gardasil has been the only HPV vaccine in use in the US and over people received 28 million doses in the country between 2014 and 2017, reducing people's chances of contracting cancer.

Merck & Co. developed Gardasil to protect against cervical cancer and other cancers caused by HPV. Cervical cancer is uncontrolled cell division in the cervix, the lowest part of the uterus, and it affects twelve thousand women every year in the US. If cervical cancer spreads to the kidney, it can block the channel through which urine travels. That can cause urine build up in the kidneys, which can lead to death if left untreated.

Gardasil contains particles that act in some ways like HPV particles, which helps the body to recognize HPV particles in case of infection and develop an immune response. After the vaccine particles enter the body through an injection, the body releases antibodies that can bind to those particles. Antibodies are blood proteins that combine with the virus particles to inactivate the virus and help to activate other cells in the immune system. If an individual with the HPV vaccine contracts HPV, the body has an antibody to defend itself against the virus. By preparing the body to protect itself against HPV, Gardasil also helps reduce an individual's risk of contracting cancer caused by the virus.

The company that eventually became Merck & Co. began in Darmstadt, Germany, in 1668. George F. Merck's ancestor, Friedrich Jacob Merck, founded the company when he purchased a local pharmacy in Darmstadt. The company continued operating in Darmstadt over the next centuries. In the nineteenth century, his direct descendant, Heinrich Emanuel Merck began expanding the company. By 1887, a branch of the company had opened in New York City, New York, and George F. Merck began to oversee it in 1891.

The existence of a Merck company in the US and a different one in Germany became an issue once the US declared its involvement in World War I in 1917 against Germany and its allies. Since Merck was affiliated with a German family, the US Government seized Merck & Co. and made it a nationally owned company. In 1919, after the end of World War I, George F. Merck reprivatized that US branch and gained ownership.

During the rest of the 1900s, Merck & Co. continued to grow. Merck & Co. merged with other pharmaceutical companies in the 1950s and had new medical breakthroughs in biotechnology. One of those breakthroughs was the development of the MMR vaccine in 1971, which combined three vaccines into one. The MMR vaccine protects against the viral diseases measles, mumps, and rubella. Some symptoms of those include fever, rash, cough, runny nose, red and watery eyes, ear infection, brain damage, headache, and fatigue.

In the 1980s, Merck & Co. developed a vaccine against hepatitis B using recombinant DNA technology, the same technology that would later be used to develop the HPV vaccine. Hepatitis B is a liver infection that spreads via bodily fluids. Hepatitis B includes symptoms of fever, fatigue, loss of appetite, abdominal pain, and can result in liver scarring and liver cancer if left untreated. In May 1986, Merck & Co. developed Recombivax HC to treat hepatitis B, the first vaccine that uses recom-

binant DNA technology. Recombinant DNA technology uses specific parts of the genetic material of the virus instead of all the genetic material. In vaccines, the recombinant DNA codes for just the antigens, so they include none of the DNA that makes the virus harmful. Antigens are the identifiers on a virus that trigger the body's immune system. Since Recombivax HC uses recombinant DNA, it allows the body to create antibodies against those specific antigens. The antibodies can identify specific antigens based on their structure.

In the 1990s, scientists around the world began working to develop an HPV vaccine. The development began with researchers Ian Frazer and Jian Zhou, who developed a technique to replicate certain parts of the virus while working in Brisbane, Australia in 1991. Frazer, Zhou, and various other researchers filed patent applications for the vaccine technology, which would allow them to control the intellectual property of the technology. At the same time, Merck & Co. wanted to start producing the vaccine, so the company had to license the technology from multiple research groups at once. The company finally succeeded at licensing the technology and began producing Gardasil in 1995. In January 2006, Merck & Co. submitted for approval from the Food and Drug Association, or FDA. Six months later, the FDA approved Gardasil for females nine to twenty-six years of age. In 2013, Merck voluntarily recalled one lot of Gardasil due to the possibility that a small number of vials contained glass particles that may have come from a breakage during manufacturing. No adverse events related to that lot have been reported to the CDC.

With the approval of Gardasil came reports of its side effects and its effectiveness in preventing HPV-related diseases, including cervical cancer and genital diseases. The trials that led to the approval of Gardasil found the vaccine to be nearly 100 percent effective in preventing cervical, vulvar and vaginal diseases caused by five types of HPV. According to the US Centers for Disease Control, or CDC, side effects of the vaccine include pain, redness or swelling where the shot was administered, fever, lethargy, nausea, and pain in the muscles and joints. The United Kingdom's National Health Service, or NHS, reports that more than one in ten people who have the Gardasil HPV vaccine experience redness, swelling or pain at the site of the injection and headaches. Usually, those side effects do not last longer than a couple of days. The NHS reports that more than one in one hundred people, but less than one in ten people, who have that vaccine experience bruising or itching at the site of the injection, a high temperature or feeling hot and shivery, nausea, or pain in the extremities. Less than one in ten thousand people with that HPV vaccine have trouble breathing and restriction of airways, and some people may have an allergic reaction immediately after vaccination according to the NHS. The safety data that the CDC reported shows no additional or unexpected safety concerns following vaccination.

After the vaccine was released, researchers criticized that the vaccine was only approved for girls and women. New York University, or NYU, Langone Health, a US health center based in New York City, New York, reports that some researchers and health professionals argued that the vaccine's limited approval disregarded boys and men, who are susceptible to genital warts alongside anal and oral cancer from HPV. After those concerns, in September 2009, approval was expanded to males aged nine to twenty-six.

After the vaccine's introduction, various researchers and health professionals also began studying the age range through which it could still be effective. In 2018, the FDA expanded Gardasil's approval to include men and women twenty-seven to forty-five years old as an opportunity to prevent HPV-related diseases for a broader age range, according to Peter Marks, the director of the FDA's Center for Biologics Evaluation and Research. That addressed the question of age as well as the inclusion of men. Reproductive health involves both sexes, so inclusion of males in the FDA approval of to expand access. According to the CDC, the vaccinating males for HPV, which some colleges and public schools require for admission as of 2022, and the expanded approval for a larger age range can lower HPV transmission rates.

More ethical questions regarding the vaccine arose in debates over whether the HPV vaccine would be mandatory to attend school. After the vaccine's release, some argued that the chance of getting cervical cancer was too low to need compulsory vaccination. Researcher Joseph E. Balog, who studies Public Health and Health Education at State University of New York, The College at Brockport in Brockport, New York, claims that other health professionals argue in favor of voluntary vaccination and improved screening and treatment for cervical cancer. That is after the health professionals

examined mortality trends in cervical cancer and potential unknown long-term effects of HPV.

Some of the public's concerns surrounding HPV vaccination also included the vaccination's supposed potential to promote what critics called sexual promiscuity in young teenage women. In 2014, according to researchers Pedro Navarro-Illana, Justo Aznar, and Javier Díez-Domingo, the public argued that without the vaccine removing the fear of developing cancer or other illnesses, it can encourage teenage sexual intercourse. However, those researchers argue that HPV vaccination in young women confers medical advantages, including lower chance of cervical cancer, genital warts, and other human cancers.

As of 2022, fifteen jurisdictions in the US have passed some sort of approval or requirement of the HPV vaccine since its introduction in 2006. For some universities, the HPV vaccine is mandatory as part of the required immunizations for every student. However, individuals can apply for an exemption under medical or religious reasons with proper documentation given to the school. Controversies regarding the vaccine continue to exist among the public, but researchers in the public health field continue to advocate for the vaccine.

Despite ethical dilemmas voiced regarding the administration and efficacy of the vaccine, expansions have accommodated varying demographics with no significant findings of adverse effects. After Gardasil, Merck & Co. has continued to be active in the medical world including producing and distributing new vaccines, antivenom products, and anti-nausea medication. The development of Gardasil allowed the rates of HPV-related diseases including certain cancers, specifically cervical, vulvar, vaginal, and anal, to decrease by having lower transmission rates. Since 2016, Gardasil is the only HPV vaccine available to use in the US. In 2018, 39.9 percent of individuals from ages eighteen to twenty-six in the US had at least one dose of the vaccine.

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