



Report from the U.S. Agency for International Development (USAID) to Congress on the Human Papillomavirus

Pursuant to Section 7019(e) of Division K of Public Law 115-141, the Department of State, Foreign Operations, and Related Programs Appropriations Act, 2018, which incorporates by reference the requirements of Senate Report 115-152, USAID submits this report to Congress on the human papillomavirus (HPV). The relevant part of Section 7019(e) reads as follows:

The USAID Administrator shall report to the Committee not later than 120 days after enactment of the act on ways to utilize low cost Human Papillomavirus vaccines to significantly reduce mortality from cervical cancer in high-prevalence, low-income countries.

HPV is the most-common viral infection of the reproductive tract. There are more than 100 different types of HPV, 13 of which cause cancer; of these, two are responsible for 70 percent of the cases of cervical cancer worldwide. Every year, approximately 230,000 women die of cervical cancer in the developing world, or 90 percent of the deaths from the disease worldwide. Nearly all cervical cancers are preventable through vaccination against HPV, or through the screening and treatment of pre-cancerous lesions among women already infected with HPV. Once the most-common cause of cancer-related death among American women, cervical cancer is now just the 12th-most-common cause, as rates have fallen by 70 percent since the 1950s. However, mortality from cervical cancer has increased in developing countries. Existing and emerging technologies for the prevention of cervical cancer are now becoming available in many countries in which USAID works, but are not yet widely in use because of bureaucratic inertia and regulatory hurdles.

The U.S. Government is the fourth-largest donor to Gavi, the Vaccine Alliance, and contributed \$275 million in Fiscal Year (FY) 2017 and \$290 million in FY 2018. Gavi makes a variety of efficacious, high-quality, cost-effective vaccines available to the poorest countries of the world. Two vaccines available to eligible countries protect against the transmission of the strains of HPV that cause up to 90 percent of the cases of cervical cancer. Gavi has a goal to immunize 40 million girls from HPV by 2020, which will avert an estimated 900,000 deaths from cervical cancer worldwide. Since the initiation of Gavi's funding for HPV vaccination in 2013, and thanks in large part to the Alliance's market-shaping efforts, the poorest countries now have access to the lowest-ever price for HPV vaccine, \$4.50 per dose, compared to a previous low of \$13.

Gavi-eligible¹ countries can apply for funding for HPV vaccination. To date, 30 countries have conducted HPV-vaccination demonstration pilots, and eight countries have been able to introduce and scale up HPV vaccine nationwide, with an expectation that Ethiopia and Sénégal will introduce in 2018.

¹ A country's Gross National Income (GNI) *per capita* determines its eligibility for Gavi resources.

Since at least 2012, researchers have proposed a coverage level in women of 70 percent as the threshold for the ideal cost-effectiveness of the HPV vaccine.² Meta-analysis showed that a vaccination coverage of at least 50% delivered a 68% reduction in HPV types 16 and 18 and a 61% reduction in anogenital warts between the prevaccination and post-vaccination periods.

Two primary challenges exist to scaling up the use of vaccine against HPV. One is that the HPV vaccination requires robust immunization programs capable of pivoting from focusing on infants in health centers to reaching nine-to-fourteen-year-old girls with two doses of vaccine in schools and/or health centers. (The World Health Organization has recommended that HIV-positive girls receive a third dose of HPV vaccine, typically in a clinic.). In a number of countries, the necessary coordination and planning between Ministries of Health, Ministries of Education, and other governmental and non-governmental entities has proven difficult (especially in nations that have recently decentralized or devolved responsibility for the delivery of basic social services to Counties or Districts). A recently published study of the introduction of HPV vaccination in South Africa, a country not eligible for funding from Gavi, identified problems such as obtaining informed consent, limitations in the capacity of the cold chain, and the management of minor adverse events in schools during the administration of the vaccine. Perhaps the most-important conclusion of the study, however, concerned the importance of communications: “While campaign planners anticipated and prepared for some negative media coverage, they did not expect the use of social media for spreading misinformation about HPV vaccination.”³ Strong links with parent-teacher associations, including at private schools, has proven crucial to help bridge gaps in understanding and even logistics at the local level.

Second, the global supply of HPV vaccine is constrained, in part because of the high-demand created by Gavi’s financing. The United Nations Children’s Fund projects a global shortfall of 29 million doses in 2019.⁴ Many countries are in the process of applying for support for rolling out HPV vaccination, and they will have to phase in their introductions as the vaccine supply improves. Although manufacturers expect to resolve supply constraints in the near term, scaling up the coverage of HPV vaccine in low-income countries will require continued technical assistance, particularly in generating country-level demand for the vaccine and supporting the capacity of health and educational authorities and frontline health-workers to reach an often underserved cohort (adolescent girls).

A breakthrough that could help relieve both of the challenges mentioned above is that development of a single-dose, nonavalent strain of the HPV vaccine. A consortium called the Single-Dose HPV Vaccine-Evaluation Consortium, funded by the Bill and Melinda Gates Foundation (BMGF) and led by PATH is conducting clinical and other studies with this goal in mind. Recent modeling suggests a single-dose vaccine effective against the nine most-prevalent types of HPV would have a major impact on mortality from cervical cancer in sub-Saharan Africa and other high-prevalence areas, even among HIV-positive women.⁵

² Canfell K, Chesson H, Kulasingam SL, Berkhof J, Diaz M, Kim JJ Modeling preventative strategies against human papillomavirus-related disease in developed countries. *Vaccine*. 2012; 30: F157-F167

³ <http://www.ghspjournal.org/content/ghsp/early/2018/08/24/GHSP-D-18-00090.full.pdf>

⁴ https://www.unicef.org/supply/files/HPV_2_Status_Update.pdf

⁵ <https://www.sciencedirect.com/science/article/pii/S0264410X1830197X>

Nevertheless, the awareness-raising that Gavi, national governments and civil-society partners have been conducting about cervical cancer and the availability of the vaccine against HPV and other preventative measures appears to be having additional, positive effects on health programming. As the HPV vaccine and testing and other interventions to prevent and control cervical cancer are being implemented in many African countries, some have reported large increases in the voluntary use of contraceptives, particularly long-acting reversible contraceptives, in settings where family planning and reproductive health care are offered in tandem with screening for cervical pre-cancer and the treatment of pre-cancerous cervical lesions.⁶ Expanded implementation and evaluation is needed in different contexts to understand how to integrate voluntary family planning and cervical-cancer screening, which should optimally include implementation models and service-delivery points that are feasible, scalable, and beneficial for both purposes.

As a major donor to Gavi, USAID is well-positioned to work with our country Missions to help increase the uptake of HPV vaccines, and address bottlenecks to their delivery. USAID bilateral programs support governments with capacity-building for frontline health workers; assist with policy and regulatory change; improve data and cold-chain systems; and generate demand for, and improving access to, immunization. USAID obtained Congressional approval in September 2018 to invest \$12,000,000 in funds from Fiscal Year 2017 to support the integration of cervical cancer preventative services into existing voluntary family-planning and reproductive-health programs in Malawi and Mozambique, two low-income countries with some of the highest rates of cervical cancer in the world. Activities will focus on the screening for, and ablation of, pre-cancerous lesions; the training and supervision of providers; strengthening referral networks; building the capacity to provide cryotherapy and thermal coagulation; and introducing improved screening methods through advanced molecular HPV testing.

⁶ <https://srh.bmj.com/content/familyplanning/42/1/17.full.pdf>