In 2006, the first vaccine against human papilloma virus (HPV) infection, Gardasil® (MSD) was approved for use in Thailand. A second vaccine, Cervarix® (GlaxoSmithKline), is currently undergoing regulatory review by the Thai FDA. Both vaccines are designed with the goal of preventing cervical cancer. This article provides a review of the HPV vaccines, Gardasil and Cervarix.

HPV epidemiology and clinical presentation
Genital human papilloma virus (HPV) is one of the most common sexually transmitted infections. The global age standardized prevalence of HPV among women varies by location, ranging from 1.4% in Spain to 25.6% in Nigeria. In Thailand, the prevalence of HPV infection in women ≥ 15 years of age from Lampang and Songkla was studied. Overall, 6.3% of women were HPV DNA positive, the most common types were HPV 16, 52 and 58.

Over 100 different types have been identified internationally. There are about 40 types of HPV that can infect the genital tract. The viruses are divided into 2 groups (high or low risk) based on their oncogenic potential. High risk HPV includes 16, 18, 31, 33, 35, 45, 52 and 58 types. High risk types are well established as the primary etiologic agent in greater than 90% of cervical cancer. In a ten year cohort study of 20,810 women, the cumulative incidence of cervical intraepithelial neoplasia grade 3 among women positive for HPV type 16 was 17.2%, and the incidence among women positive for HPV type 18 was 13.6%. The risk among women who tested positive for high risk HPV types other than types 16 and 18 was 3%. However, the 10 year incidence of cervical intraepithelial grade 3 among women negative for oncogenic high risk HPV infection was 0.8%.

Globally, HPV type 16 and 18 account for more than 70% of cervical cancers. Six HPV genotypes (type 31, 33, 35, 45, 52 and 58) account for an additional 20% of cervical cancers world wide.

HPV vaccine
Gardasil®
Gardasil® is a quadrivalent vaccine that offer protection against HPV type 6, and 11 which are genital warts and HPV type 16, and 18 which are associated with 70% of cervical cancers. In young women (16-26 years), Gardasil® induced antibody titers peak 7 months following initiation of the vaccine series. The titers then decline reaching a plateau 18-24 months later. This plateau is maintained for at least 5 years, with a 5 year level that is similar to the titer naturally induced by HPV type 6 and 18 and that is higher than the titers naturally induced by HPV type 11 and 16. In young adolescents (9-15 years), the titers are 1.7-2.4 times higher than those among women aged 16-26 years. Vaccine efficacy for grade II or higher cervical intraepithelial neoplasia caused by HPV type 16 and 18 is 98%.

Cervarix®
Cervarix® is a bivalent vaccine that protects against HPV type 16 and 18. The vaccine is formulated with a new ASO4 adjuvant with was claimed to increase the antibody titer. In young women (16-26 years), Cervarix® induced antibody titers at a peak of 7 months after initiation of the vaccine. However the 18 month plateau level is many fold higher than the levels induced by natural infection, and after 51-53 months 100% of women were seropositive for both HPV types 16 and 18. In young adolescents, the titers are also higher than those among women age 16-26 years. Vaccine efficacy for high grade precancerous lesion caused by HPV type 16 and 18 is 90%.

Vaccine safety
Both vaccines have a good safety profile. Both produced local reactions that were 6-8% more frequent than reactions produced by an alum placebo. Both vaccines are not approved for pregnant women.

Recommendations
The U.S. Food and Drug Administration (FDA) licensed the first vaccine shown to be effective at preventing infection with some genotypes of HPV. The prophylactic quadrivalent human papillomavirus L1 virus like particle vaccine offers protection against cervical cancer, cervical dysplasia and genital warts associated with HPV genotypes 6, 11, 16, and 18. The U.S. FDA approval is for administration of this 3 dose vaccine to females aged 9-26 years at intervals of 0, 2 and 6 months. The need for booster doses remains unclear. To date protection has been shown to last at least 5 years.

A second bivalent HPV vaccine is in development. Results of initial studies of this vaccine showed the good protection against HPV type 16 and 18.
Cervical cytology screening
HPV vaccine can prevent around 70% of cervical cancers. Current cervical cytology screening recommendations still remain unchanged and should be followed regardless of vaccination status.

HPV testing
Testing for HPV is currently not recommended before vaccination. Testing for HPV DNA would not identify past HPV infections, only a current HPV infection.

Vaccination of sexually active women
Sexually active women can receive the quadrivalent HPV vaccine. The patients should be counseled that the vaccine may be less effective in women who have been exposed to HPV before vaccination than in women who were HPV naïve at the time of vaccination.

Vaccination is not treatment
The quadrivalent HPV vaccine is a prophylactic vaccine, not intended to treat patients with cervical cytology abnormalities or genital warts.

Vaccination of women older than 26 years and males
Research regarding vaccination of women older than 26 years and males is currently under investigation. Data available are insufficient to make recommendations for these populations.

REFERENCES