



California
Department of
Health Services

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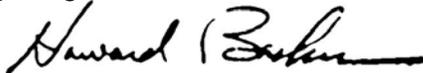
State of California—Health and Human Services Agency
Department of Health Services



Governor

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TO: California Vaccines for Children (VFC) Program Providers
FROM: Howard Backer, M.D., M.P.H., Chief 
Immunization Branch
SUBJECT: QUADRIVALENT HUMAN PAPILLOMAVIRUS (HPV) RECOMBINANT
VACCINE IS NOW AVAILABLE FROM VFC

This memo is divided into sections to enable you to quickly access the information you need:

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SUMMARY

On June 8, 2006, United States Food and Drug Administration (FDA) licensed a quadrivalent human papillomavirus vaccine (trade name *Gardasil™*, Merck & Co., Inc.), for use in females ages 9-26 years. The Advisory Committee on Immunization Practices (ACIP) voted at their June 2006 meeting to recommend the routine use of quadrivalent HPV vaccine as a three-dose series for females ages 11-12 years. Quadrivalent HPV vaccine is also recommended for females ages 13-26 years who did not complete or receive the vaccine when they were younger. The series can be started in females as young as the age of nine years. Quadrivalent HPV vaccine is now available from the VFC Program (http://www.cdc.gov/nip/vfc/acip_vfc_resolutions.htm) for females 9 through 18 years of age. This letter summarizes information about the use of quadrivalent HPV vaccine in the VFC program. The Immunization Branch is following ACIP's provisional recommendations for use of this quadrivalent HPV vaccine. Once available, the Immunization Branch will provide ACIP's final recommendations as well as any updated vaccine information.

BACKGROUND AND COMPOSITION

Human papillomavirus types 16 and 18 cause approximately 70 percent of cervical cancer cases along with some cases of other less common anogenital cancers and cancers of the head and neck. Human papillomavirus types 6 and 11 cause approximately 90 percent of genital warts. Quadrivalent HPV vaccine is a prophylactic vaccine against human papillomavirus types 6, 11, 16, and 18; it is not intended as a treatment for active disease or current infection. The vaccine has not been shown to protect against disease caused by non-vaccine HPV types.

Gardasil™ is a non-infectious recombinant, quadrivalent vaccine prepared from highly purified virus-like particles (VLPs) of the major capsid (L1) protein of human papillomavirus types 6, 11, 16, and 18. The L1 proteins are produced by fermentation in recombinant yeast cells. Quadrivalent HPV vaccine is a sterile liquid suspension that contains the adsorbed VLPs of each HPV type, aluminum-containing adjuvant, and purification buffer. After thorough agitation, quadrivalent HPV vaccine is a white, cloudy liquid. The product does not contain any preservative or antibiotics.

In women who were not infected with the human papillomavirus types 16 and 18 prior to dose one and through one month after dose three, quadrivalent HPV vaccine had an efficacy of 100 percent against high grade cervical, vulvar or vaginal cancer precursors [CIN2/3, AIS, VIN2/3, ValN2/3] associated with human papillomavirus types 16 and 18. Quadrivalent HPV vaccine had an efficacy of 95 percent against any grade of cervical intraepithelial neoplasia (CIN) [CIN1, CIN2/3] or adenocarcinoma in situ (AIS) related to human papillomavirus types 6, 11, 16, and 18. The vaccine had an efficacy of 99 percent against genital warts associated with human papillomavirus types 6, 11, 16, and 18. The vaccine does not protect against HPV types already acquired prior to vaccination.

RECOMMENDATIONS FOR VACCINE USE

Eligible Persons for Receipt of VFC Vaccine

Females ages 9 through 18 years are eligible for quadrivalent HPV vaccine provided by the VFC program.

Dosing Schedule

Routine immunization with three doses of quadrivalent HPV vaccine is recommended for females 11-12 years of age. The vaccination series can be started in females as young as nine years of age. Catch-up vaccination is recommended for females 13-26 years of age who have not been vaccinated previously or who have not completed the full vaccine series, though VFC vaccine is not available past the age of 18 years. Ideally, the vaccine should be administered before potential exposure to HPV through sexual contact; however, females who are already sexually active should still be vaccinated.

At present, cervical cancer screening recommendations have not changed for females who receive the HPV vaccine. Thirty percent of cervical cancers are caused by HPV types that are not prevented by the HPV vaccine, and sexually active females could have been infected prior to vaccination. Providers should continue to educate women about the importance of cervical cancer screening.

Quadrivalent HPV vaccine should be administered intramuscularly as a series of three separate 0.5 mL doses. The second dose should be given two months after the first dose, and the third dose should be given six months after the first dose.

Administration

Thoroughly shake the vial prior to use. The vaccine should appear as a white, cloudy liquid after agitation. The vaccine should be inspected visually for particulate matter and discoloration prior to administration. Do not use the product if particulates are present or if it appears discolored. For single dose vials, 0.5 mL dose of the vaccine should be withdrawn from the single-dose vial using a sterile needle and syringe free of preservatives, antiseptics, and detergents. Once the single-dose vial has been penetrated, the withdrawn vaccine should be used promptly, and the vial must be discarded.

Administration with other vaccines

Quadrivalent HPV vaccine may be given at the same visit when other age appropriate vaccines are provided, such as Tdap and MCV4.

HOW SUPPLIED FOR CALIFORNIA VFC PROGRAM PROVIDERS

Vials

Gardasil™ is supplied as a carton of ten 0.5mL single dose vials (NDC 0006-4045-41).

Storage

- Quadrivalent HPV vaccine should be refrigerated at 36 - 46 degrees F (2 - 8 degrees C).
- Do not freeze.
- Protect from light.

ORDERING AND BILLING

How to Order

VFC Providers may order quadrivalent HPV vaccine using the enclosed VFC Vaccine Order Form (DHS 8501 (11/06)). Vaccine orders for this vaccine should be based on the number of VFC-eligible females, in the recommended age category, expected to be seen at your practice during the particular ordering period. Previous usage of vaccines routinely recommended for adolescents in the 11-12 years age range, such as Tdap, may be useful in guiding your initial vaccine order.

Although VFC providers are encouraged to submit vaccine orders every two months, a separate vaccine request for HPV vaccine may be submitted if a regular order for pediatric vaccines has been recently submitted to the VFC Program Office. Otherwise, providers should order HPV vaccine at the same time other pediatric vaccines are ordered. Information is required in all the four columns of the order form to process vaccine orders. Remember to maintain a copy of your order forms for your office files.

Please be aware that your orders of quadrivalent HPV vaccine may be adjusted, especially during this introductory phase.

Billing Information for VFC Vaccine

Children's Health and Disability Prevention (CHDP): Claims may be submitted for doses of quadrivalent HPV vaccine administered on or after November 1, 2006. The CHDP administration fee is \$9.00 using CHDP code **76**. However, providers should wait until notified by CHDP to submit claims. CHDP Provider Information Notices can be found at <http://www.dhs.ca.gov/pcfh/cms/onlinearchive/chdppl.htm>.

Medi-Cal Fee-For-Service (FFS): The CPT code for administration of quadrivalent HPV vaccine for Medi-Cal is **90649-SL**.

Other codes for the use of quadrivalent HPV vaccine that is not supplied by VFC:

- The CPT code for quadrivalent HPV vaccine is **90649**.
- The CPT code for administration of quadrivalent HPV vaccine is **90471** if given alone, and **+90472** if given after (an) additional vaccine(s) at the same visit (e.g., if Tdap and HPV vaccine are given at the same encounter then one of the vaccine administration codes will be 90471 and the other +90472).
- The ICD-9-CM code for quadrivalent HPV vaccine is **V05.8**.

POTENTIAL VACCINE REACTIONS

Serious Adverse Events: The most frequently reported serious adverse events in trials were headache (0.03% vs. 0.02% placebo), gastroenteritis (0.03% vs. 0.01%), appendicitis (0.02% vs. 0.01%), and pelvic inflammatory disease (0.02% vs. 0.01%). Other serious adverse events were rare. Subjects were also evaluated for new medical conditions over the four year follow-up, including systemic immune disorders (0.076% vs. 0.031% placebo). Post licensure safety studies will be conducted to more closely assess safety of the vaccine.

Minor Adverse Events: Quadrivalent HPV vaccine has been associated with pain (84%), swelling (25%), redness (25%) and pruritis (3%) at the injection site. Fever was reported in 10% of quadrivalent HPV vaccine recipients and 9% of placebo recipients.

Report suspected reactions to the HPV vaccine or other vaccines to the Vaccine Adverse Events Reporting System (VAERS) at 800-822-7967 (toll-free) or <http://vaers.hhs.gov>.

CONTRAINDICATIONS

- History of immediate hypersensitivity to yeast or to any vaccine component.

PRECAUTIONS

- Quadrivalent HPV vaccine can be administered to females with minor acute illnesses (e.g., diarrhea or mild upper respiratory tract infections, with or without fever).
- Vaccination of people with moderate or severe acute illnesses should be deferred until after the illness improves.

PREGNANCY

- Quadrivalent HPV vaccine is not recommended for use in pregnancy. The vaccine has not been associated with adverse outcomes of pregnancy or adverse events to the developing fetus. However, data on vaccination during pregnancy are limited. Any exposure to vaccine during pregnancy should be reported to the vaccine pregnancy registry (1-800-986-8999).

SPECIAL SITUATIONS

- Abnormal Pap test/Positive High-Risk HPV Test/Genital Warts: Quadrivalent HPV vaccine can be given to females who have an equivocal or abnormal Pap test, a positive Hybrid Capture II[®] high-risk test, or genital warts. Vaccine recipients should be advised that data from clinical trials do not indicate the vaccine will have any therapeutic effect on existing Pap test abnormalities, HPV infection or genital warts. Vaccination of these

females would provide protection against infection with vaccine HPV types not already acquired.

- Immunocompromise: Females who are immunocompromised either from disease or medication can receive quadrivalent HPV vaccine. However, the immune response to vaccination and vaccine effectiveness might be less than in females who are immunocompetent.
- Lactating women can receive quadrivalent HPV vaccine.

DOCUMENTATION

- Product Insert: The product package insert on Gardasil™ contains additional vaccine information: <http://www.fda.gov/cber/label/hpvmer060806LB.pdf>
- Vaccine Information Statement (VIS): An interim VIS (9/5/06) that can be used with quadrivalent HPV vaccine can be found at <http://www.cdc.gov/nip/publications/VIS/>.
- Center for Disease Control Prevention Fact Sheet: A question and answer sheet on HPV disease and the HPV vaccine can be found at: <http://www.cdc.gov/nip/vaccine/hpv/hpv-faqs.htm> and <http://www.cdc.gov/std/hpv/default.htm>.
- ACIP recommendations: Provisional ACIP recommendations may be found at: http://www.cdc.gov/nip/recs/provisional_rec/hpv.pdf. Final ACIP recommendations for quadrivalent HPV vaccine will later be published at <http://www.cdc.gov/nip/publications/acip-list.htm>
- American Academy of Pediatrics (AAP) recommendations and other information about HPV will be available to AAP members at <http://www.cispimmunize.org/>
- VFC resolution No. 6/06-2: The VFC resolution on quadrivalent HPV vaccine may be found at: http://www.cdc.gov/nip/vfc/acip_vfc_resolutions.htm.
- Vaccine Injury Compensation Program (VICP): HPV vaccine will be covered by the federal VICP. Information on the federal VICP and quadrivalent HPV vaccine will be found at: <http://www.hrsa.gov/vaccinecompensation/>.

Enclosures: Order Form (11/06),
HPV VIS
Timing Schedule, IMM 395

cc: DHS Immunization Branch Field Representatives
Local Health Officers
Local Health Department Immunization Coordinators
Local Health Department CHDP Program Directors
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Villita Lewis, Deputy Director, Benefits and Quality Monitoring, MRMIB
Marcia Ehinger, M.D., Medi-Cal Benefits Branch, CDHS
Kathy Chance, M.D., Children Medical Services Branch, CDHS

VACCINES FOR CHILDREN (VFC) PROGRAM VACCINE ORDER FORM

PIN (6 digit) _____

COUNTY _____

NAME OF PHYSICIAN'S OFFICE, PRACTICE, CLINIC, ETC. _____ DATE _____ CHDP MEDI-CAL PROVIDER
 Yes No

DELIVERY ADDRESS (Number and Street—No P.O. Boxes) _____
 CHECK HERE IF THIS IS A NEW ADDRESS. CITY _____ ZIP CODE _____

DELIVERY: Please specify all days and times you may receive vaccine.  DAY AND TIME DAY AND TIME DAY AND TIME DAY AND TIME
 Tue. _____ Wed. _____ Thu. _____ Fri. _____

CONTACT PERSON _____ TELEPHONE _____ FAX _____

Vaccines¹ Write in the name of the manufacturer you prefer (if any) for DTaP, hepatitis A, hepatitis B, Hib, and Tdap vaccines in the indicated spaces below.	YOU MUST COMPLETE ALL THE BOXES IN THE FOUR COLUMNS BELOW FOR VFC TO PROCESS YOUR ORDER. (EVEN IF YOU ARE ONLY ORDERING ONE VACCINE)			Vaccine Shipped in Vials of the Following Sizes	New Vaccine Order (Minimum 10 doses) Order in multiple of 10 doses
	Number of Doses (VFC Only) Used Since Last Order Enter "0" if None	VACCINE INVENTORY			
	Number of Doses (VFC Only) On-Hand	Lot Number	Expiration Date		

REGULAR ORDER VFC VACCINES

DTaP (Preferred Mfr.: _____)				10 x 1 dose vial	doses
DTaP/Hepatitis B/IPV Combination				10 x 1 dose vial	doses
Hepatitis A (Age 12 months–18 years) (Preferred Mfr.: _____)				10 x 1 dose vial	doses
Hepatitis B (Pediatric/Adolescent) (Preferred Mfr.: _____)				10 x 1 dose vial	doses
Hepatitis B/Hib Combination				10 x 1 dose vial	doses
Hib (Preferred Mfr.: _____)				10 x 1 dose vial 5 x 1 dose vial	doses
IPV (Inactivated Polio Vaccine)				10 dose vial	doses
Meningococcal Conjugate (ONLY for adolescents 11–18 years of age)				5 x 1 dose vial	doses
Pneumococcal Conjugate				5 x 1 dose vial	doses
Rotavirus (Live, Oral Vaccine) (ONLY for infants ages 6 - 32 weeks)				10 x 1 dose in 2mL tubes	doses
Td–Preservative Free (Age 7–18 years)				10 x 1 dose syringe no needle	doses
Tdap (Adolescent Td with acellular pertussis [booster] ages 10-18 years) ² (Preferred Mfr.: _____)				10 x 1 dose vial	doses
HPV (Human Papillomavirus) (ONLY for females 9–18 years of age)				10 x 1 dose vial	doses

REGULAR VFC VACCINES STORED IN THE FREEZER

MMR (Combined Measles, Mumps, and Rubella)				10 x 1 dose vial	doses
Varicella (Chickenpox)				10 x 1 dose vials	doses
MMRV (Combined Measles, Mumps, Rubella, and Varicella [Chickenpox] vaccines for children 12 mos to 12 years)				10 x 1 dose vial	doses

IMPORTANT  **IF THE SPECIFIC VACCINE MANUFACTURERS I HAVE INDICATED ABOVE ARE NOT AVAILABLE:**
 Send another manufacturer's vaccine. Send the manufacturer's vaccine I requested when it is available.

Notes #1: Toxoids and vaccines not available through the VFC Program: DT-Pediatric, DTaP-Hib, OPV, tetanus, measles, MR (measles-rubella), mumps, and rubella vaccines, HBIG, and PPD.
Notes #2: Read the package insert to see if the product selected can be given at 10 years of age.

Instructions: 1. Please Print or Type.
 2. Order no more than once every two months (i.e., no more than six times per year). Place your order with sufficient stock on hand to allow at least 30 days for delivery. (It should not take 30 days to deliver vaccine, but this will prevent you from running out of vaccine if there is a delay in filling your order.)
 3. Fax your order to the VFC Program.
Questions: Toll-free: 877-2Get-VFC (877-243-8832)
FAX orders to: Toll-free: 877-FAXX-VFC (877-329-9832)



STATE USE ONLY

ASSIGNED		
APPROVED		
ASSIGNED		
ENTERED		
SHIPPED		

HPV (HUMAN PAPILLOMAVIRUS) VACCINE

WHAT YOU NEED TO KNOW

1 What is HPV?

Genital human papillomavirus (HPV) is the most common sexually transmitted virus in the United States.

There are about 40 types of HPV. About 20 million people in the U.S. are infected, and about 6.2 million more get infected each year. HPV is spread through sexual contact.

Most HPV infections don't cause any symptoms, and go away on their own. But HPV is important mainly because it can cause **cervical cancer** in women. Every year in the U.S. about 10,000 women get cervical cancer and 3,700 die from it. It is the 2nd leading cause of cancer deaths among women around the world.

HPV is also associated with several less common types of cancer in both men and women. It can also cause genital warts and warts in the upper respiratory tract.

More than 50% of sexually active men and women are infected with HPV at sometime in their lives.

There is no treatment for HPV infection, but the conditions it causes can be treated.

2 HPV Vaccine - Why get vaccinated?

HPV vaccine is an inactivated (not live) vaccine which protects against 4 major types of HPV.

These include 2 types that cause about 70% of cervical cancer and 2 types that cause about 90% of genital warts. ***HPV vaccine can prevent most genital warts and most cases of cervical cancer.***

Protection from HPV vaccine is expected to be long-lasting. But vaccinated women still need cervical cancer screening because the vaccine does not protect against all HPV types that cause cervical cancer.

3 Who should get HPV vaccine and when?

Routine Vaccination

- HPV vaccine is routinely recommended for girls **11-12 years of age**. Doctors may give it to girls as young as 9 years. It is given as a 3-dose series:

1st Dose:	Now
2nd Dose:	2 months after Dose 1
3rd Dose:	6 months after Dose 1

Why is HPV vaccine given to girls at this age?

It is important for girls to get HPV vaccine **before** their first sexual contact – because they have not been exposed to HPV. For these girls, the vaccine can prevent almost 100% of disease caused by the 4 types of HPV targeted by the vaccine.

However, if a girl or woman is already infected with a type of HPV, the vaccine will not prevent disease from that type.

Catch-Up Vaccination

- The vaccine is also recommended for girls and women **13-26 years of age** who did not receive it when they were younger.

No booster doses are recommended at this time.

HPV vaccine may be given at the same time as other vaccines.

4 Some girls or women should not get HPV vaccine or should wait

- Anyone who has ever had a life-threatening **allergic reaction to yeast, to any other component of HPV vaccine, or to a previous dose of HPV vaccine** should not get the vaccine. Tell your doctor if the person getting the vaccine has any severe allergies.

- **Pregnant women** should not get the vaccine. The vaccine appears to be safe for both the mother and the unborn baby, but it is still being studied. Receiving HPV vaccine when pregnant is **not** a reason to consider terminating the pregnancy. Women who are breast feeding may safely get the vaccine.

Any woman who learns that she was pregnant when she got HPV vaccine is encouraged to call the **HPV vaccine in pregnancy registry** at 800-986-8999.

Information from this registry will help us learn how pregnant women respond to the vaccine.

- People who are mildly ill when the shot is scheduled can still get HPV vaccine. People with **moderate or severe illnesses** should wait until they recover.

5 What are the risks from HPV vaccine?

HPV vaccine does not appear to cause any serious side effects.

However, a vaccine, like any medicine, could possibly cause serious problems, such as severe allergic reactions. The risk of **any** vaccine causing serious harm, or death, is extremely small.

Several **mild problems** may occur with HPV vaccine:

- Pain at the injection site (about 8 people in 10)
- Redness or swelling at the injection site (about 1 person in 4)
- Mild fever (100°F) (about 1 person in 10)
- Itching at the injection site (about 1 person in 30)
- Moderate fever (102°F) (about 1 person in 65)

These symptoms do not last long and go away on their own.

Life-threatening allergic reactions from vaccines are very rare. If they do occur, it would be within a few minutes to a few hours after the vaccination.

Like all vaccines, HPV vaccine will continue to be monitored for unusual or severe problems.

6 What if there is a severe reaction?

What should I look for?

- Any unusual condition, such as a high fever or behavior changes. Signs of a serious allergic reaction can include difficulty breathing, hoarseness or wheezing, hives, paleness, weakness, a fast heart beat or dizziness.

What should I do?

- **Call** a doctor, or get the person to a doctor right away.
- **Tell** your doctor what happened, the date and time it happened, and when the vaccination was given.
- **Ask** your doctor, nurse, or health department to report the reaction by filing a Vaccine Adverse Event Reporting System (VAERS) form.

Or you can file this report through the VAERS website at www.vaers.hhs.gov, or by calling 1-800-822-7967.

VAERS does not provide medical advice.

7 How can I learn more?

- Ask your doctor or nurse. They can show you the vaccine package insert or suggest other sources of information.
- Call your local or state health department.
- Contact the Centers for Disease Control and Prevention (CDC):
 - Call **1-800-232-4636 (1-800-CDC-INFO)**
 - Visit CDC's website at www.cdc.gov/std/hpv and www.cdc.gov/nip.



**DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES**



Immunization Timings

Age 2 months	Interval from previous dose
DTaP	
Hib	
PCV (Pneumo)	
Polio (IPV)	
RV² (Rotavirus)	
Hepp¹	1-2 months after birth dose

Age 4 months	Interval from previous dose
DTaP	1-2 months
Hib	1-2 months
PCV (Pneumo)	1-2 months
Polio (IPV)	1-2 months
RV² (Rotavirus)	4-10 weeks
Hepp¹	1-2 months if 1st dose if given at 2 months of age

Age 6 months	Interval from previous dose
DTaP	1-2 months
Hib³	1-2 months
PCV (Pneumo)	1-2 months
Polio (IPV)	1-14 months
RV² (Rotavirus)	4-10 weeks
Hepp¹	2-12 months and at least 4 months after first dose

Age 12 months	Interval from previous dose
HepaA	
Hib⁴	2-8 months
PCV⁴ (Pneumo)	6-8 weeks
MMR⁵	
Varicella⁵	

Age 15 months	Interval from previous dose
DTaP	6-12 months

Age 18 months	Interval from previous dose
HepaA	6-12 months

For School-Age Kids
Before Kindergarten

Polio, DTaP, MMR #2, and
Varicella #2.

Before 7th Grade

Varicella,
HPV⁷ and
Tdap booster.

Every Fall: **6-59 months and high-risk kids**
Flu Vaccine⁶

This is a suggested schedule. For alternatives and details, consult the latest "Recommended Childhood Immunization Schedule, United States 2006."¹

¹ Hepp series: In absence of documented birth-dose, a schedule starting at 2 months is acceptable. If using combination vaccines, a fourth dose is allowable. If using ComVax[®] (combined Hib and HeppB vaccine), final dose is at 12-15 months.

² The first dose should be given between 6-12 weeks. Maximum age for Rotavirus vaccine is 32 weeks. This six month Hib dose can be skipped if Pedvax Hib[®] and/or ComVax[®] are used exclusively for the 2 and 4 month infant doses.

⁴ Final dose of Hib and PCV series should be given at ≥12 months.

⁵ MMRV vaccine can be used when both MMR and Varicella vaccines are indicated.

⁶ All routine vaccines are available in a thimerosal-free option. See California Health and Safety Code §124172. ⁷ Human Papillomavirus vaccine is recommended for girls only.



CAIFORNIA KIDS

Love them. Immunize them.

State of California Department of Health Services • Immunization Branch
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