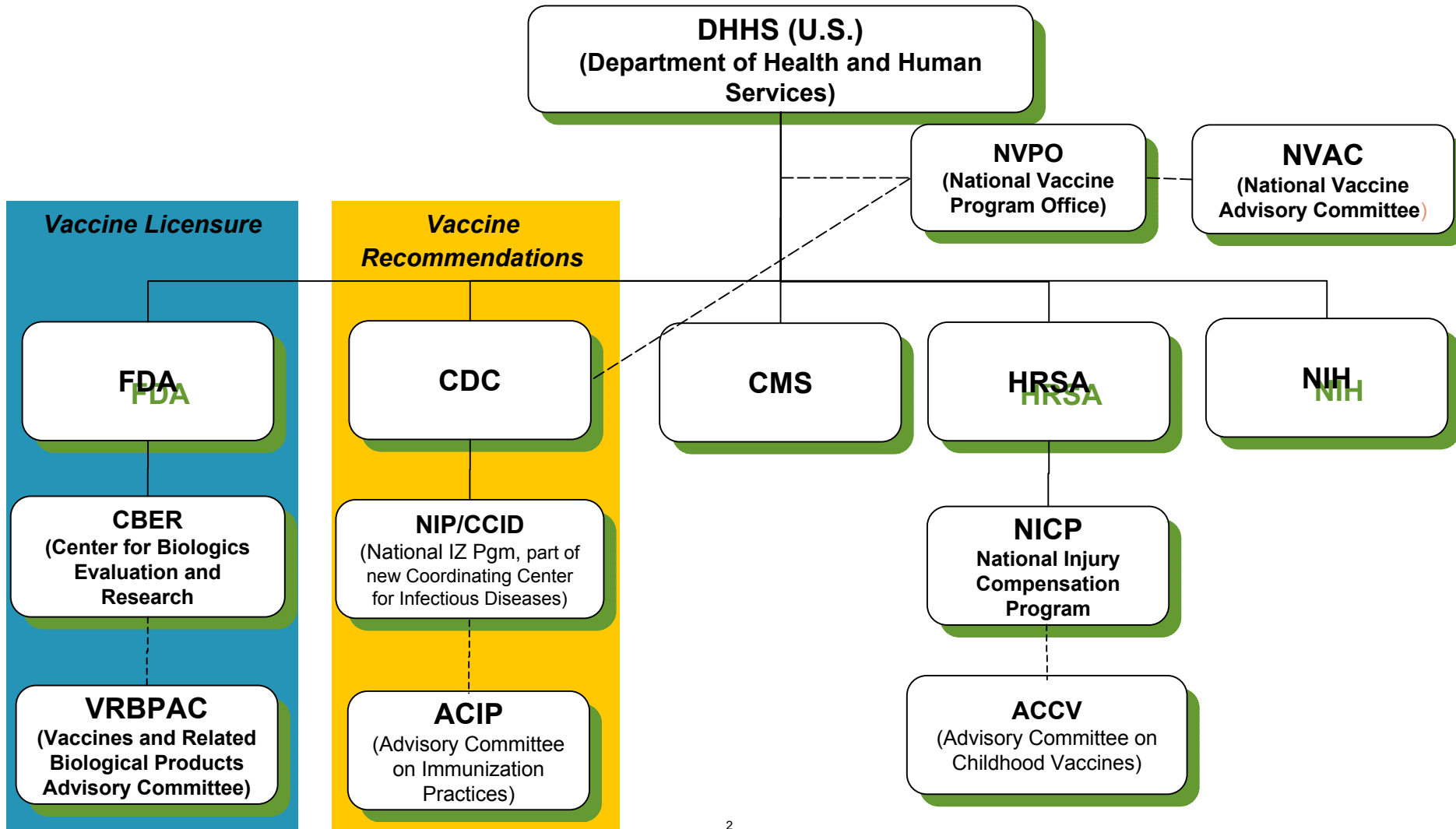


U.S. Advisory Committee on Immunization Practice (ACIP) Recommendations for a Quadrivalent HPV Vaccine

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Selected U.S. Government Agencies and their Advisory Committees

Within the U.S. Department of Health and Human Services, ACIP provides guidance and recommendations to the CDC while the Vaccines and Related Biological Products Advisory Committee (VRBPAC) provides guidance to the FDA.

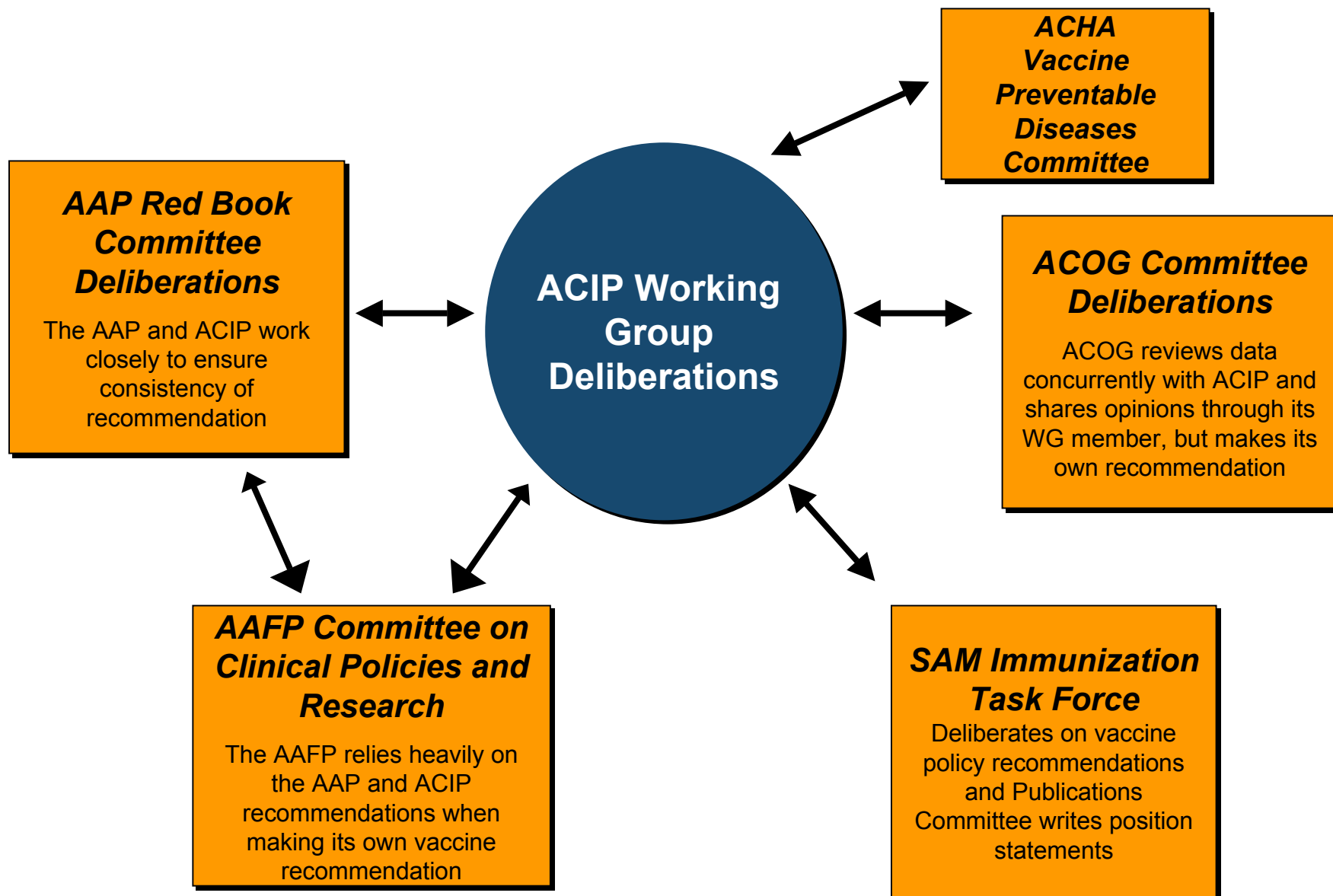


ACIP Overview

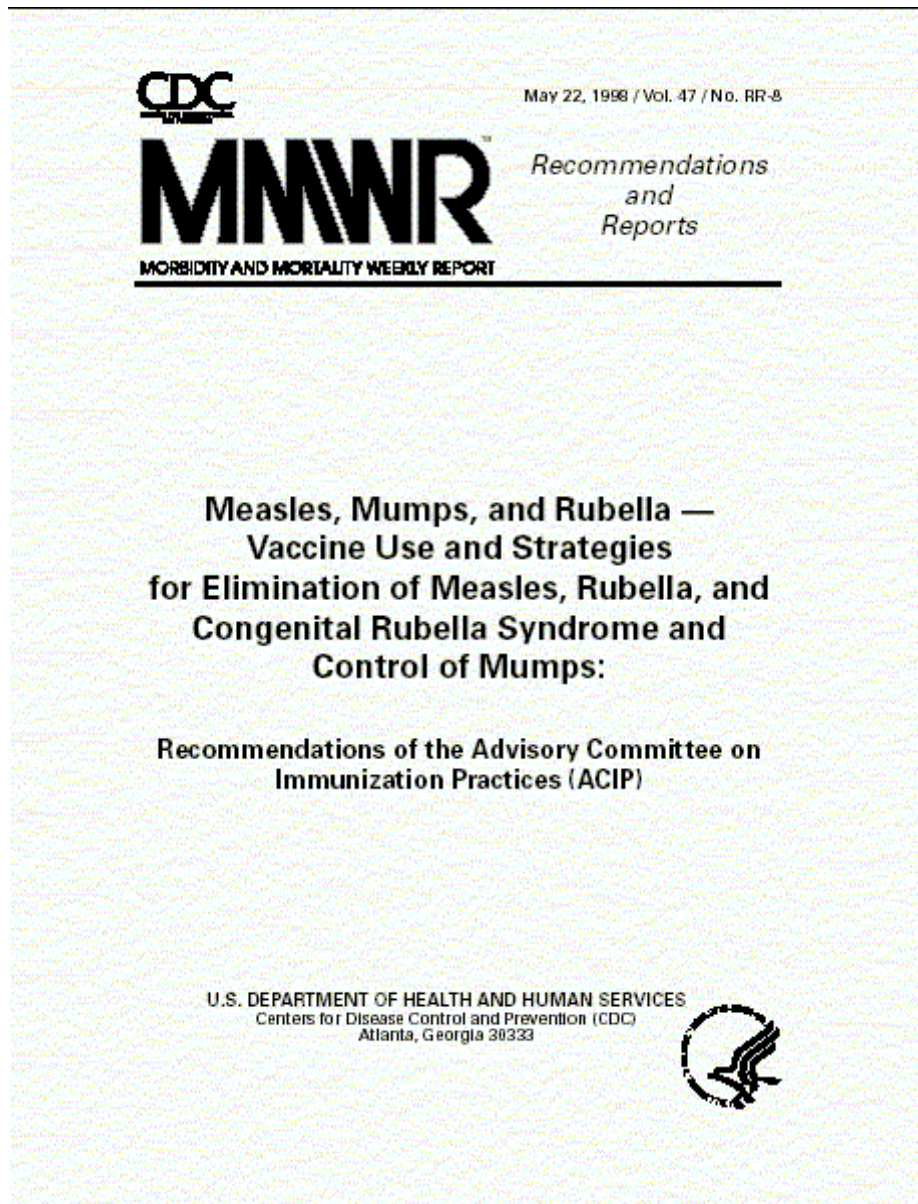
The Advisory Committee on Immunization Practices (ACIP) is a federal advisory committee of experts that:

- **Provides advice and guidance to the Centers for Disease Control & Prevention (CDC) on reducing the incidence of vaccine preventable diseases and increasing the safe usage of vaccines and related biological products**
- **Develops written recommendations for the routine administration of vaccines to pediatric and adult populations**
- **Reviews immunization practices and recommends improvements in national immunization efforts**
- **Establishes a list of vaccines for administration to children eligible to receive vaccines through the Vaccines for Children Program**

How does the ACIP interact with Professional Organizations?



ACIP Publication of Recommendations



Format for Recommendation

- Summary
- Purpose of recommendation
- Clinical description of disease
- Diagnosis and treatment
- Epidemiology of disease (e.g., Morbidity, mortality, disability, cost association with illness, risk groups)
- Route(s) of transmission
- Efficacy, effectiveness and cost effectiveness of interventions
- Precautions and contraindications
- Adverse events
- Recommendation(s) of ACIP with summary of score for evidence and strength of recommendation
- Recommendations of other groups
- Discussion for rationale for ACIP recommendation(s)
- Recommended surveillance, research, education and program evaluation activities

ACIP Childhood and Adolescent Immunization Schedule

DEPARTMENT OF HEALTH AND HUMAN SERVICES • CENTERS FOR DISEASE CONTROL AND PREVENTION

Recommended Childhood and Adolescent Immunization Schedule UNITED STATES • 2006

Vaccine ▼	Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	24 months	4-6 years	11-12 years	13-14 years	15 years	16-18 years
Hepatitis B ¹		HepB	HepB	HepB ²	HepB			HepB Series							
Diphtheria, Tetanus, Pertussis ²			DTaP	DTaP	DTaP		DTaP			DTaP	Tdap	Tdap			
<i>Haemophilus influenzae</i> type b ²			Hib	Hib	Hib ³	Hib									
Inactivated Poliovirus			IPV	IPV	IPV					IPV					
Measles, Mumps, Rubella ⁴						MMR				MMR	MMR				
Varicella ⁵						Varicella					Varicella				
Meningococcal ⁶												MCV4			MCV4
Pneumococcal ⁷				PCV	PCV	PCV	PCV				PCV	PPV			
Influenza ⁸						Influenza (Yearly)					Influenza (Yearly)				
Hepatitis A ⁹										HepA Series					

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2005, for children through age 18 years. Any dose not administered at the recommended age should be administered at any subsequent visit when indicated and feasible. Indicates age groups that warrant special effort to administer those vaccines not previously administered. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever

any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective ACIP statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.

 Range of recommended ages Catch-up immunization 11-12 year old assessment

ACIP Gardasil® Recommendations

June 29, 2006

HPV

Presentations on June 29, 2006

- Data from quadrivalent HPV vaccine trials (Barr, Merck)
- Information on post-licensure studies (Dana, Merck)
- Information on post-licensure safety studies (Iskander, CDC)
- Review of cost-effectiveness analyses (Chesson, CDC)
- Public comment
- Presentation of proposed recommendations for quadrivalent HPV vaccines (Markowitz, CDC); **VOTE**
- Presentation of VFC resolution (Calugar, CDC); **VOTE**

ACIP Provisional Recommendations

ACIP Provisional Recommendations for the Use of Quadrivalent HPV Vaccine

Date of ACIP vote: June 29, 2006

Date of posting of provisional recommendations: August 14, 2006

Tentative date of publication of recommendations in *CDC Morbidity and Mortality Weekly Report*: November 2006

Provisional recommendations for use of quadrivalent HPV vaccine:

- Routine vaccination 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 9 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. Ideally, vaccine should be administered before potential exposure to HPV through sexual contact.
- Each dose of quadrivalent HPV vaccine is 0.5 mL, administered intramuscularly.
- Quadrivalent HPV vaccine is administered in a three dose schedule. The second and third doses should be administered 2 and 6 months after the first dose.
- Quadrivalent HPV vaccine can be administered at the same visit when other age appropriate vaccines are provided, such as Tdap, Td and MCV4.
- At present, cervical cancer screening recommendations have not changed for females who receive quadrivalent HPV vaccine.

HPV Vote – Routine Vaccination

- ACIP recommends routine vaccination for females 11-12 years of age with three doses of quadrivalent HPV vaccine
- The vaccination series can be started as young as 9 years of age at the discretion of the provider

HPV Vote – Vaccination of Females 13-26

- Vaccination is recommended for females 13-26 years of age who have not been previously vaccinated
- Ideally vaccine should be administered before sexual activity, but females who are sexually active should still be vaccinated

HPV *Other Recommendations and Wording*

- Cervical cancer screening – no change
 - Vaccinated females could subsequently be infected with non-vaccines HPV types
 - Sexually active females could have been infected prior to vaccination
- Decision to vaccinate should not be based on Pap testing, HPV DNA or HPV serologic testing

HPV *Special Situations*

Equivocal or Abnormal Pap Test

- Vaccination recommended; however
 - Could already have been infected with a vaccine HPV type
 - Data do not indicate vaccine will have therapeutic effect on existing cervical lesions or HPV infection

HPV *Special Situations*

Positive HPV test

- Vaccination recommended; however
 - Could already have been infected with a vaccine HPV type
 - Data do not indicate vaccine will have therapeutic effect on existing cervical lesions or HPV infection

HPV *Special Situations*

Genital Warts

- Vaccination recommended; however
 - Data do not indicate vaccine will have therapeutic effect on existing genital warts or HPV infection

Immunosuppression

- Can be vaccinated
 - Not a live vaccine
 - Immune response and vaccine efficacy might be less than in immunocompetent persons

Lactating women

- Lactating women can receive vaccines

HPV *Special Situations*

Genital Warts

- Vaccination recommended; however
 - Data do not indicate vaccine will have therapeutic effect on existing genital warts or HPV infection

Immunosuppression

- Can be vaccinated
 - Not a live vaccine
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Lactating women

- Lactating women can receive vaccines

HPV Vaccination During Pregnancy Moved to Special Situations from Precautions and Contraindications

Pregnancy

- Initiation of the vaccine series should be delayed until after completion of the pregnancy
- If a woman is found to be pregnant after initiating the vaccination series, completion should be delayed until after the pregnancy
- If a vaccine dose has been administered during pregnancy, there is no indication for intervention

Pregnancy Outcomes in the Phase III Program Database as of 11-Nov-2005

	Vaccine (N = 10,418)	Placebo (N = 9120)
Subjects with Pregnancies	1115	1151
Number of Pregnancies	1244	1272
Pregnancies With Unknown Outcomes	258	264
Pregnancies With Known Outcomes	996	1017
Live Births (% of preg w/known outcomes)	621 (62%)	610 (60%)
Fetal Loss (% of preg w/known outcomes)	375 (38%)	407 (40%)

>90% of unknown outcomes are ongoing pregnancies

Pregnancy Outcomes – Phase III Efficacy Studies Database as of 11-Nov-2005

	Vaccine		Placebo	
	(N=996)		(N=1017)	
	n	(%)	n	(%)
Normal Baby	570	(57.2)	568	(55.9)
EOP Within 30 Days of a Vaccination	56		58	
EOP Beyond 30 Days of a Vaccination	512		509	
Spontaneous Loss	260	(26.1)	265	(26.1)
EOP Within 30 Days of a Vaccination	21		26	
EOP Beyond 30 Days of a Vaccination	236		237	
Elective Abortion	114	(11.4)	142	(14.0)
EOP Within 30 Days of a Vaccination	21		23	
EOP Beyond 30 Days of a Vaccination	93		117	

Estimated Onset of Pregnancy (EOP) could not be precisely ascertained in 10 women.

N = Number of fetuses/infants with known outcomes.

Pregnancy Outcomes – Phase III Efficacy Studies

Data as of 11-Nov-2005

	Vaccine	Placebo
	n	n
Infant/Fetus Congenital Anomalies	15	16
EOP Within 30 Days of a Vaccination	5	0
Anomaly in Live-Born Infant	5	0
Anomaly in Fetal Loss	0	0
Intrauterine Observation	0	0
EOP Beyond 30 Days of a Vaccination	10	16
Anomaly in Live-Born Infant	9	13
Anomaly in Fetal Loss	0	2
Intrauterine Observation	1	1

Congenital Anomalies Among Pregnancies With an EOP Within 30 Days of a Study Vaccination

- Pyloric Stenosis and Ankyloglossia
- Congenital Megacolon
- Congenital Hydronephrosis
- Hip Dysplasia
- Club Foot

HPV Vote – Precautions and Contraindications

- Moderate or severe acute illnesses
(*precaution*)
- History of ‘immediate’ hypersensitivity or severe allergic reaction to yeast or to any vaccine component
(*contraindication*)

ACIP Vote – Unanimous Approval

- ACIP recommends routine vaccination for females 11-12 years of age with three doses of quadrivalent HPV vaccine
- Vaccination is recommended for females 13-26 years of age who have not been previously vaccinated
- Special Situations
 - Equivocal or abnormal Pap test
 - Positive HPV test
 - Genital warts
 - Immunosuppression
 - Lactating women
 - Vaccination during pregnancy

Thank you