# Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children

# Advisory Committee on Immunization Practices

Larry K. Pickering, MD, FAAP

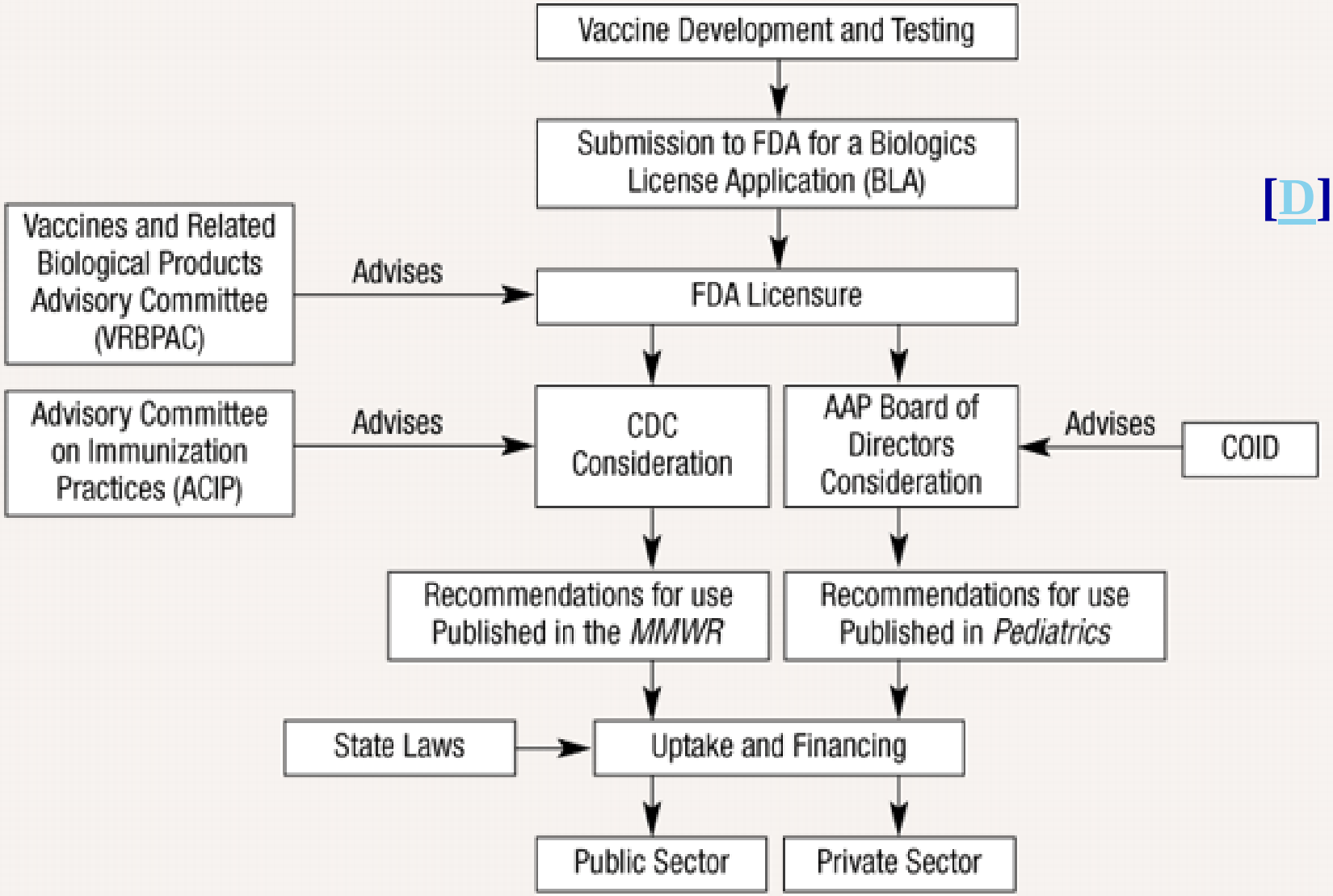
October 20, 2005

Washington, DC

# Objectives

- To review vaccine approval process
- To discuss the responsibilities, structure, and function of the ACIP
- To review the interaction of ACIP with public and private organizations and societies
- To summarize issues facing ACIP

## Development of pediatric vaccine recommendations and policies

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Modified from Pickering LK, Orenstein WA. Development of pediatric vaccine recommendation and polices. *Semin Pediatr Infect Dis.* 2002;13:148-154. Reprinted with permission.

# ACIP Responsibilities

- Since 1964: Provides advice and guidance to Office of Secretary, DHHS and Director, CDC on most effective means to prevent vaccine-preventable diseases
  - Application of antigens and related agents (e.g. vaccines, antisera, immune globulins, antiviral agents, chemotherapy and chemoprophylaxis)
  - Licensed vaccines and unlicensed vaccines if warranted

# ACIP Responsibilities

- Since 1993: Vaccines for Children (VFC) Program
  - Unique statutory authority established by Omnibus Budget Reconciliation Act of 1993 (42 U.S.C. § 1396s) gives ACIP authority to determine the vaccines, number of doses, schedule and contraindications for the VFC
  - **VFC is a $1.5 billion annual entitlement program**

# Advisory Committee on Immunization Practices

## Structure

- 15 voting members including the chair
  - 4 year terms
  - CDC nominates, OS DHHS selects
  - Chairman selected from current members
- 8 ex-officio members – representing FDA, DoD, HRSA, NVPO, CMMS, NIH, IHS and DVA
- 22 liaison members – representatives of professional societies and organizations responsible for vaccine development and immunization programs

# ACIP Liaison Organizations

- American Academy of Family Physicians
- American Academy of Pediatrics
- America's Health Insurance Plans
- American College Health Association
- American College of Obstetricians and Gynecologists
- American College of Physicians
- American Medical Association
- American Pharmacists Association
- Association of Teachers of Preventive Medicine
- Biotechnology Industry Organization
- Canadian National Advisory Committee on Immunization
- Healthcare Infection Control Practices Advisory Committee
- Infectious Diseases Society of America
- London Department of Health
- National Association of County and City Health Official
- National Coalition for Adult Immunization
- National Foundation for Infectious Diseases
- National Immunization Council & Child Health Program
- National Medical Association
- National Vaccine Advisory Committee
- Pharmaceutical Research & Manufacturers of America
- Society for Adolescent Medicine

# Function

- 3 meetings annually – February, June, and October
- Agenda items
  - Solicited from ACIP members, liaisons, CDC staff and others using standard form
  - Finalized by ACIP Chair, Executive Secretary, CDC Steering Committee
- Follow FACA rules and procedures
- Recommendations published in MMWR

# Expertise of ACIP Members

- Infectious diseases
- Immunology
- Pediatrics
- Internal medicine
- Public health
- Vaccine research and policy
- Consumer concerns

# Advisory Committee on Immunization Practices

- Working Group Function
  - Develop draft policies/options for review/vote by full ACIP
  - Work by teleconference and before/during ACIP meetings
  - Working group guidelines regularly updated
  - Contain at least 2 ACIP members, CDC staff, ex-officio representatives, liaisons and consultants
  - 14 active Working Groups as of October 2005

# Product Approval Information - Licensing Action

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20852-1448

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May 3, 2005

Our STN: BL 125106/0

GLAXOSMITHKLINE BIOLOGICALS
Attention: Ms. Donna Boyce
Director, CMC, Pediatric Vaccines
U.S. Regulatory Affairs
2301 Renaissance Boulevard
Building 510,
P.O. Box 61540
King of Prussia, PA 19406-2772

Dear Ms. Boyce:

We have approved your Biologics License Application (BLA) for Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed under your existing Department of Health and Human Services U.S. License No. 1617. Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed is indicated for booster immunization against tetanus, diphtheria and pertussis as a single dose in adolescents 10-18 years of age.

Under this authorization, you are approved to manufacture Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed at GlaxoSmithKline Biologicals in Rixensart, Belgium. The final formulation is performed by GlaxoSmithKline Biologicals SA in Rixensart, Belgium. Product will be filled by GlaxoSmithKline Biologicals SA in Rixensart, or Wavre, Belgium. Labeling and packaging will be performed by GlaxoSmithKline Biologicals SA at the latter facility. You may label your product with the proprietary name Boostrix and you will

# ACIP Working Groups

- Permanent
  - Adult Immunization
  - General Recommendations
  - Harmonized Schedule
  - Influenza Vaccine

# ACIP Working Groups

- Task Oriented
  - Bioterrorism
  - Evidenced Based
  - Hepatitis
  - HIV Vaccine
  - Human Papillomavirus
  - Meningococcal
  - MMR-VZV
  - Pertussis
  - Rabies
  - Rotavirus

# Key Documents

- ACIP Charter –amended October 2004
- ACIP Policies and Procedures –October 2002
- Guidelines for Working Groups
  - October 2004 version (being updated)
  - Updated list of Working Groups
  - Calendar of ACIP activities
- New member orientation booklet

# CDC Management

- Executive Secretary
  - Leads CDC management of ACIP
  - Assures meetings follow guidelines, approves meeting agendas, guides development/revision of procedures, charter, and other documents.
  - Prepares briefing documents of meetings for the CDC Director
  - Historically CDC Associate Director for Science
- National Immunization Program
  - Provides critical management support services
  - 2 FTEs and a Preventive Medicine Resident
    - Assistant to the Director for Immunization Policy
    - ACIP Committee Program Analyst

# CDC Management

- CDC ACIP Steering Committee
- CDC Federal Advisory Committee Management
  - Provides FACA support and liaison with DHHS
- CDC Office of General Counsel
  - Advice on legal issues
- Funding for ACIP Operations

# Steering Committee

- Coordinates ACIP Activities across the Coordinating Center for Infectious Diseases (CCID)
- Develops consensus CDC position on: ACIP issues, policies and procedures, ACIP meeting agendas, nominees for ACIP
- Convened by Executive Secretary with ACIP Chair
- Composition
  - Director, NIP
  - Representatives from CCID Centers
  - AD for Immunization Policy
  - ACIP Program Analyst
  - FDA Ex-Officio
- Works through consensus

# Activities of ACIP Steering Committee

- Develop agenda for ACIP meetings
  - Begins 2 months in advance of each meeting
  - CIO representatives work with lead staff in CIOs to define agendas, length, speakers for each topic, issues for vote vs. discussion
- Develop nomination slate to replace departing members and chair
  - Anticipate 3 to 4 vacancies annually
  - Review nominees and select lead and alternate candidate for each position

# Activities of ACIP Steering Committee

- Other Activities
  - Refine policies and procedures, including conflict of interest
  - Forum for considering how to prioritize development of new recommendations
  - Determine need for new liaison organizations
  - Deal with structure/function activities of working groups

# Participants in the U.S. Immunization System

- Government: federal, state, and local
- Private industry
- Academic institutions
- Private providers
- Insurers

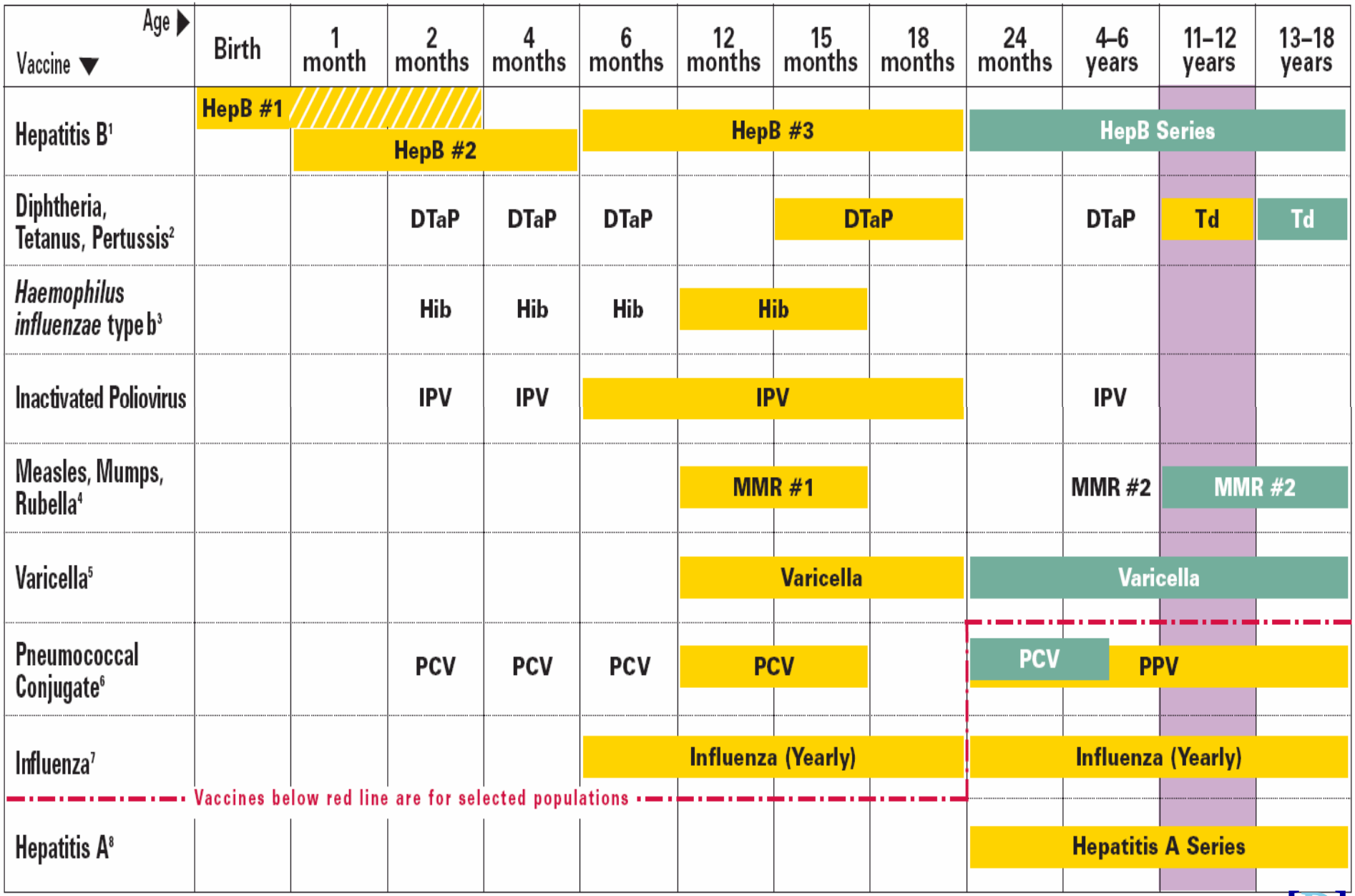
# Childhood Vaccine Policy Recommending Bodies

- CDC's Advisory Committee on Immunization Practices
- American Academy of Pediatrics Committee on Infectious Diseases
- American Academy of Family Physicians

# Vaccine Policy Product: Two Immunization Schedules

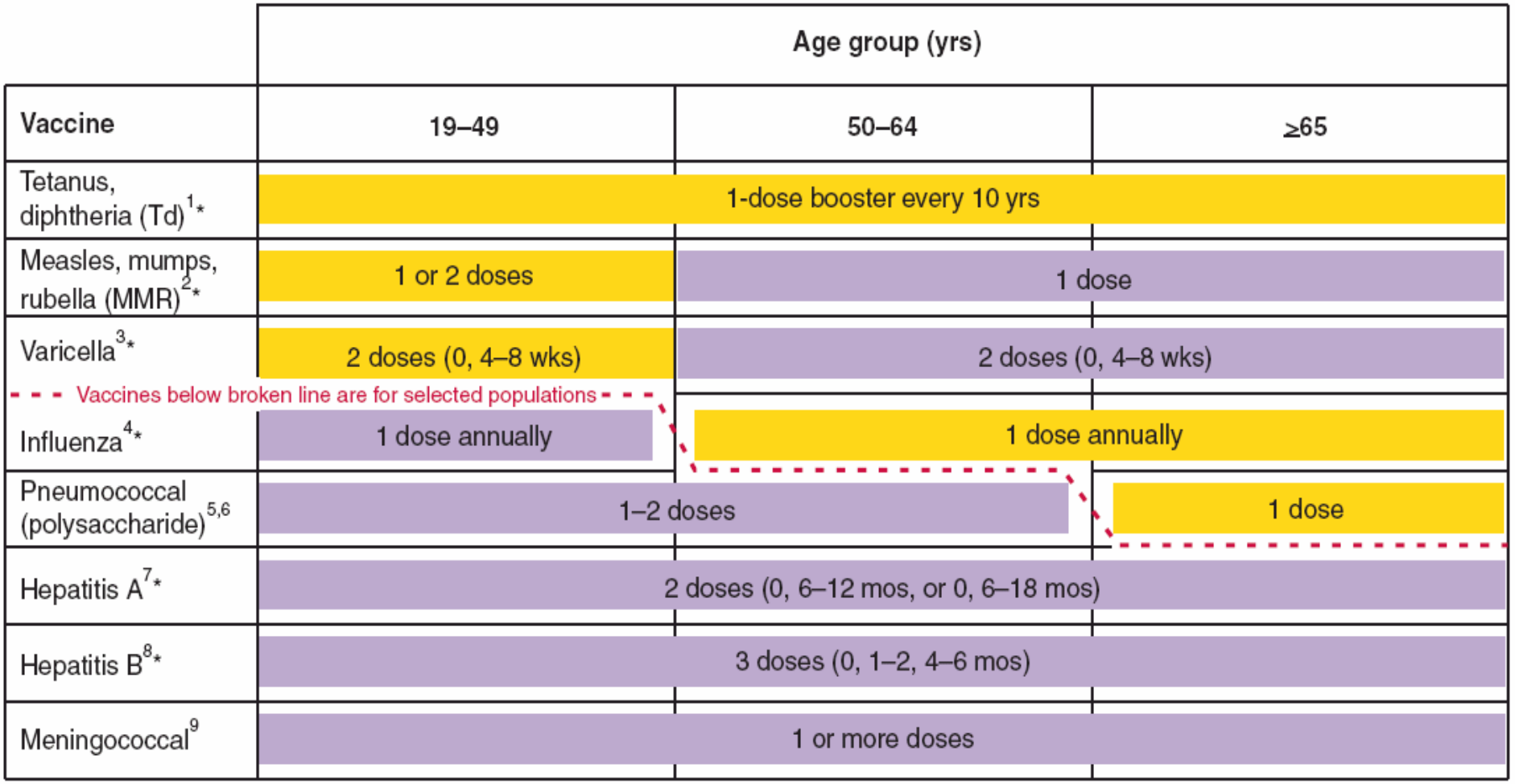
- ACIP, AAP, and AAFP produce a harmonized childhood and adolescent immunization schedule
  - First harmonized in 1994
  - Before 1994, differing schedules existed
- ACIP, AAFP produce a harmonized adult immunization schedule
- Schedule updated once per year
- Look at the complete schedule, with each vaccine in the context of the other vaccines

# Recommended Childhood and Adolescent Immunization Schedule UNITED STATES • 2005




http://www.cdc.gov/nip/recs/adult-schedule.htm

# Recommended adult immunization schedule by vaccine and age group – United States. October 2005-September 2006

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**http://www.cdc.gov/nip/recs/child-schedule.htm**

# Evidence Considered in Vaccine Policy Development

- Preventable burden of disease
- Efficacy and effectiveness in various age groups and population
- Safety of the vaccine
- Interactions with other vaccines
- Economic analysis

MMWR Weekly
January 7, 2005 / 53(51);Q1-Q3

# Recommended Childhood and Adolescent Immunization Schedule -- - United States, 2005

**Harmonized Childhood and Adolescent Immunization Schedule, 2005**

The Advisory Committee on Immunization Practices (ACIP) periodically reviews the recommended childhood and adolescent immunization schedule to ensure that the schedule is current with changes in vaccine formulations and reflects revised recommendations for the use of licensed vaccines, including those newly licensed. Recommendations and format of the childhood and adolescent immunization schedule for July--December 2004 were approved by ACIP, the American Academy of Family Physicians (AAFP), and the American Academy of Pediatrics (AAP) and were published in April 2004 (*1*). That schedule updated previous ones by adding the recommendation that, beginning in fall 2004, healthy children aged 6--23 months, as well as household contacts and out-of-home caregivers for healthy children aged 0--23 months, receive annual influenza vaccine (*2*).

The childhood and adolescent immunization schedule for 2005 is unchanged from that published in April 2004 (Figure). In addition, the catch-up immunization schedule for children and adolescents who start late or who are >1 month behind remains unchanged from that published in January 2004 and again in April 2004 (Table). The childhood and adolescent immunization schedule and the catch-up immunization schedule for 2005 have been approved by ACIP, AAFP, and AAP.

**Vaccine Information Statements**

The National Childhood Vaccine Injury Act requires that all health-care providers provide parents or patients with copies of Vaccine Information Statements before administering each dose of the vaccines listed in the schedule. Additional information is available from state health departments and at http://www.cdc.gov/nip/publications/vis.

Detailed recommendations for using vaccines are available from package inserts, ACIP statements on specific vaccines, and the *2003 Red Book* (*3*). ACIP statements for each recommended childhood vaccine can be viewed, downloaded, and printed from the CDC National Immunization Program website at http://www.cdc.gov/nip/publications/acip-list.htm. In addition, guidance on obtaining and completing a Vaccine Adverse Event Reporting System form is available at http://www.vaers.org or by telephone, 800-822-7967.

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# AMERICAN ACADEMY OF PEDIATRICS

## POLICY STATEMENT

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of All Children

Committee on Infectious Diseases

# Recommended Childhood and Adolescent Immunization Schedule: United States, 2005

The annual recommended childhood and adolescent immunization schedule of the American Academy of Pediatrics, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention, and the American Academy of Family Physicians is issued for 2005.

Licensure applications have been submitted to the Food and Drug Administration for a conjugate meningococcal vaccine and 2 new preparations of diphtheria-tetanus-acellular pertussis vaccine. The American Academy of Pediatrics is considering recommendations for use of these vaccines in adolescents. If new recommendations emerge, a midyear schedule will be released.

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 can be obtained on the Internet at www.vaers.org or by calling 1-800-822-7967. Information on new vaccine

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National Vaccine Program Office

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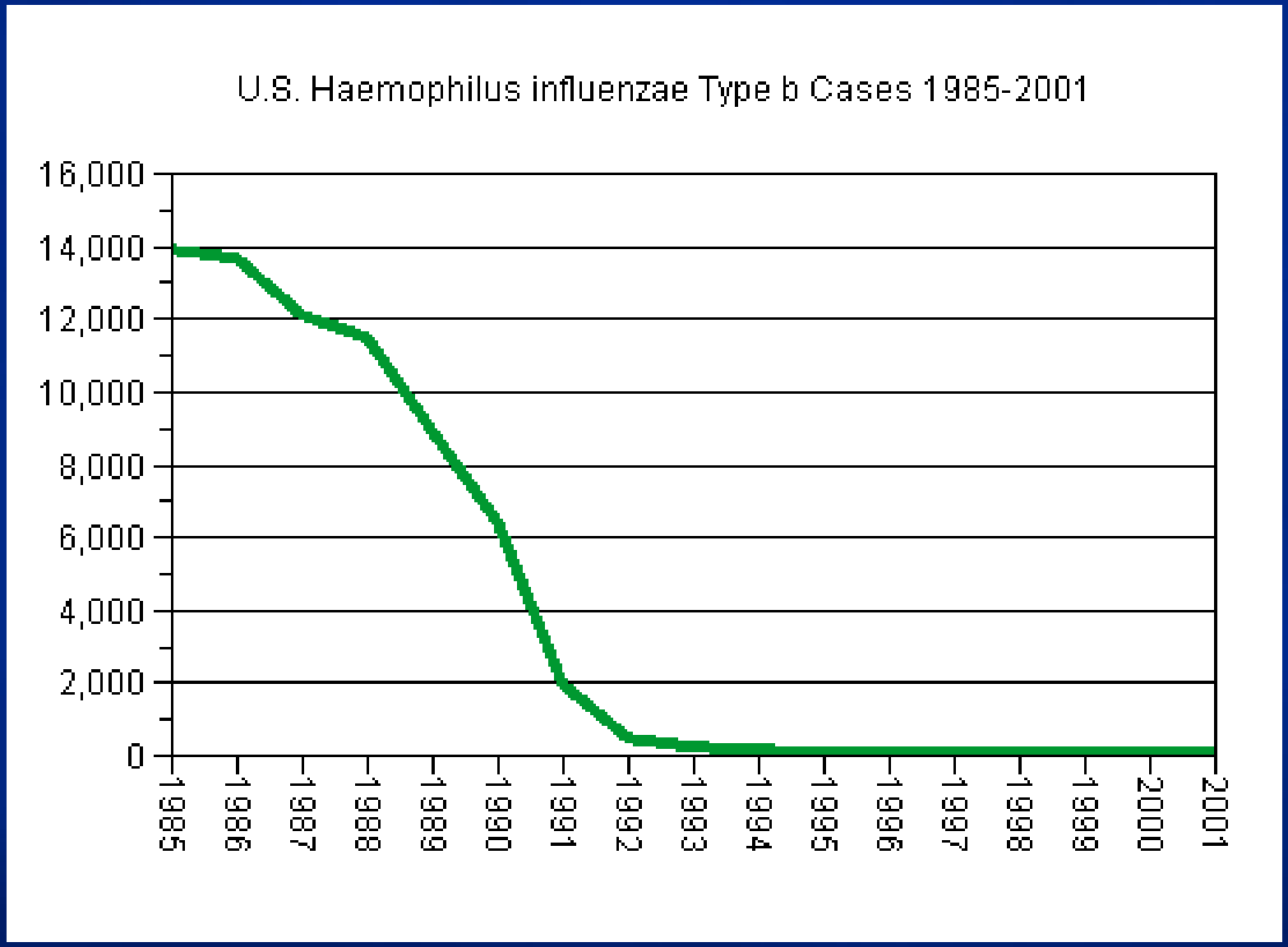
# Types of ACIP Recommendations

- Universal use
  - Age-based recommendation
  - Least confusing and easiest to implement
  - Vaccine must benefit all
- Risk-based
  - Medical, occupational, behavioral risk
  - Difficult for providers to identify those who should be vaccinated
  - Much less well implemented than universal


U.S. Haemophilus influenzae Type b Cases 1985-2001
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
1985
1986
1987
1988
1989
1990
1991
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2001

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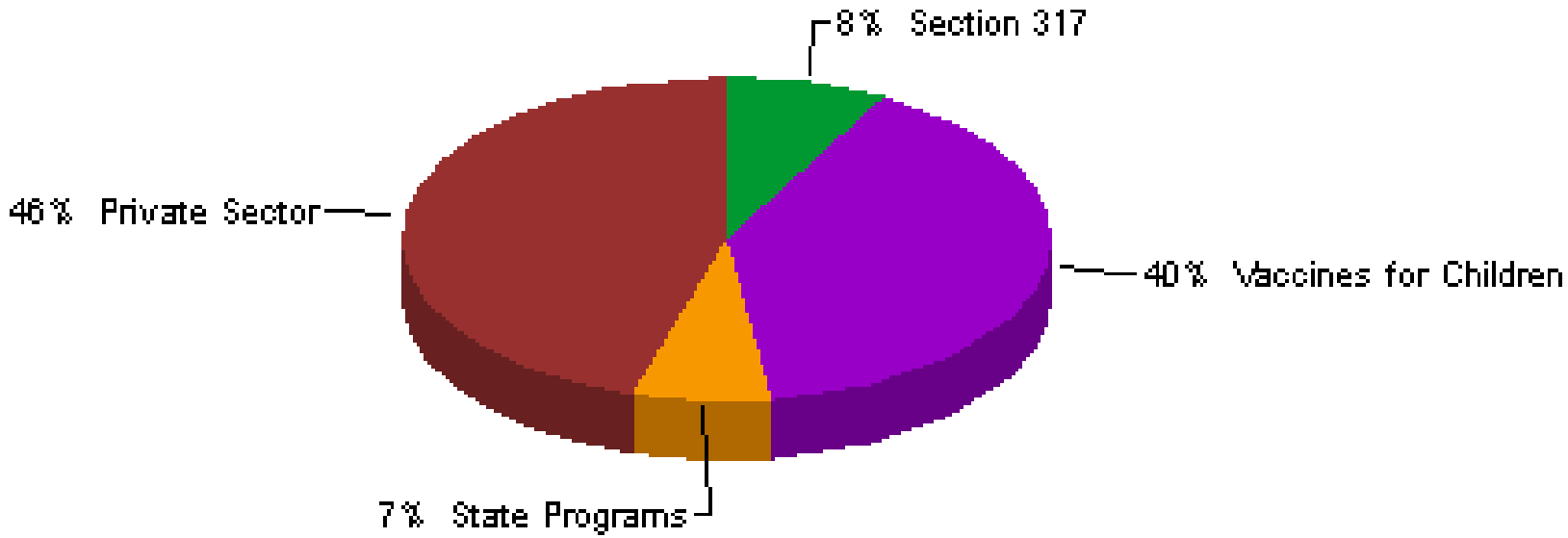
# Assuring Purchase of Recommended Vaccines

- Shared public sector and private sector responsibility
- Cost of vaccines to parents is a significant barrier to vaccination
- Adequate financing of vaccines is critical to successful implementation

## Who Paid for Childhood Vaccines in FY 2004?




Source: Biologics Surveillance Data 2004 from vaccine manufacturers

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# Federal Government Role in Purchasing Childhood Vaccines

- Vaccines for Children program (VFC)
  - Entitlement to certain vulnerable children
  - 45% of young children eligible for VFC
  - Mandatory funding
  - Inclusion of vaccines into VFC controlled by CDC's ACIP
- Section 317 vaccine funding
  - Discretionary
  - No restrictions on vaccine or population

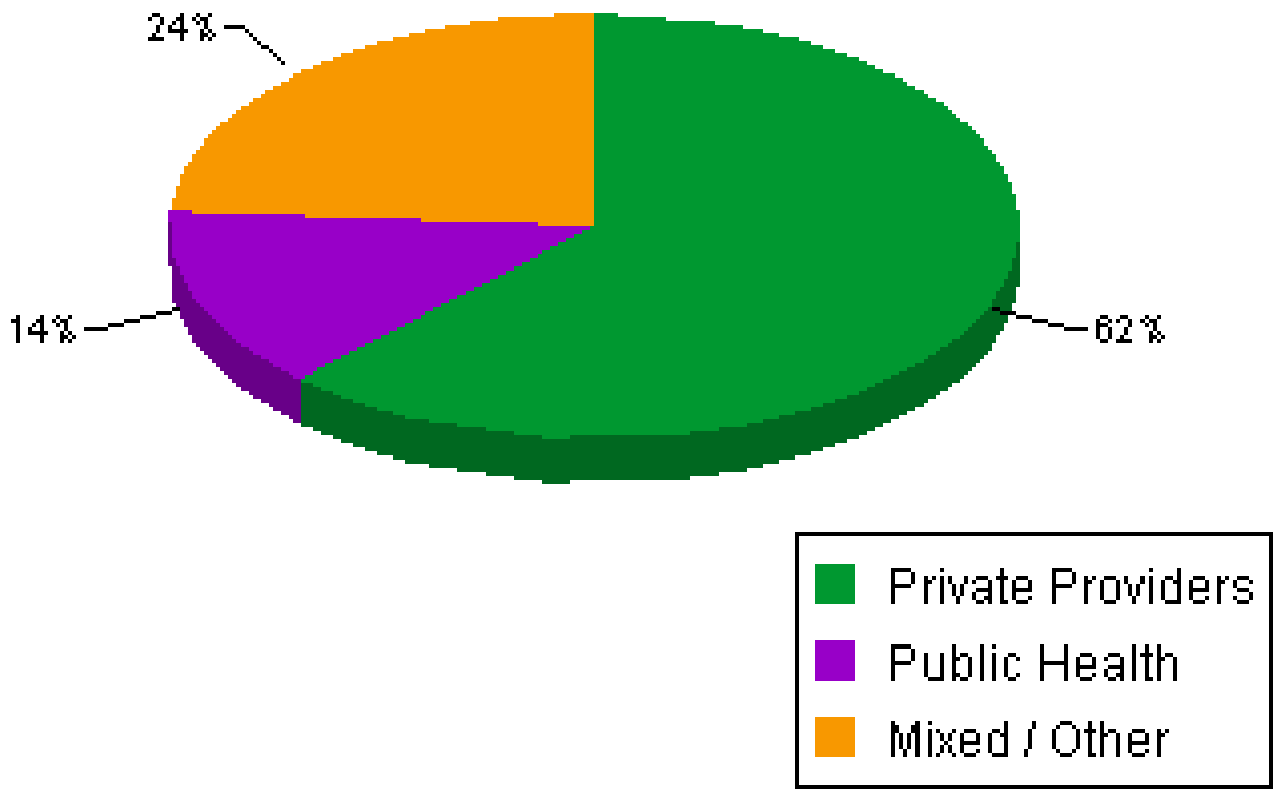
# Private Sector Role in Vaccine Financing

- Private health insurance usually includes immunization benefit
- Some children have insurance that does not cover vaccines
  - In general, their parents must pay for the vaccines
  - Only about 2% of the U.S. childhood population

# State Government Role in Purchasing Vaccine

- Varies substantially by state
  - Most states contribute some funding
- Some states have purchase policies in which they guarantee purchase of all vaccines
- States regulate most insurance companies and can mandate inclusion of vaccines into insurance packages

## Who Vaccinated Children in the U.S. in 2003 and 2004?

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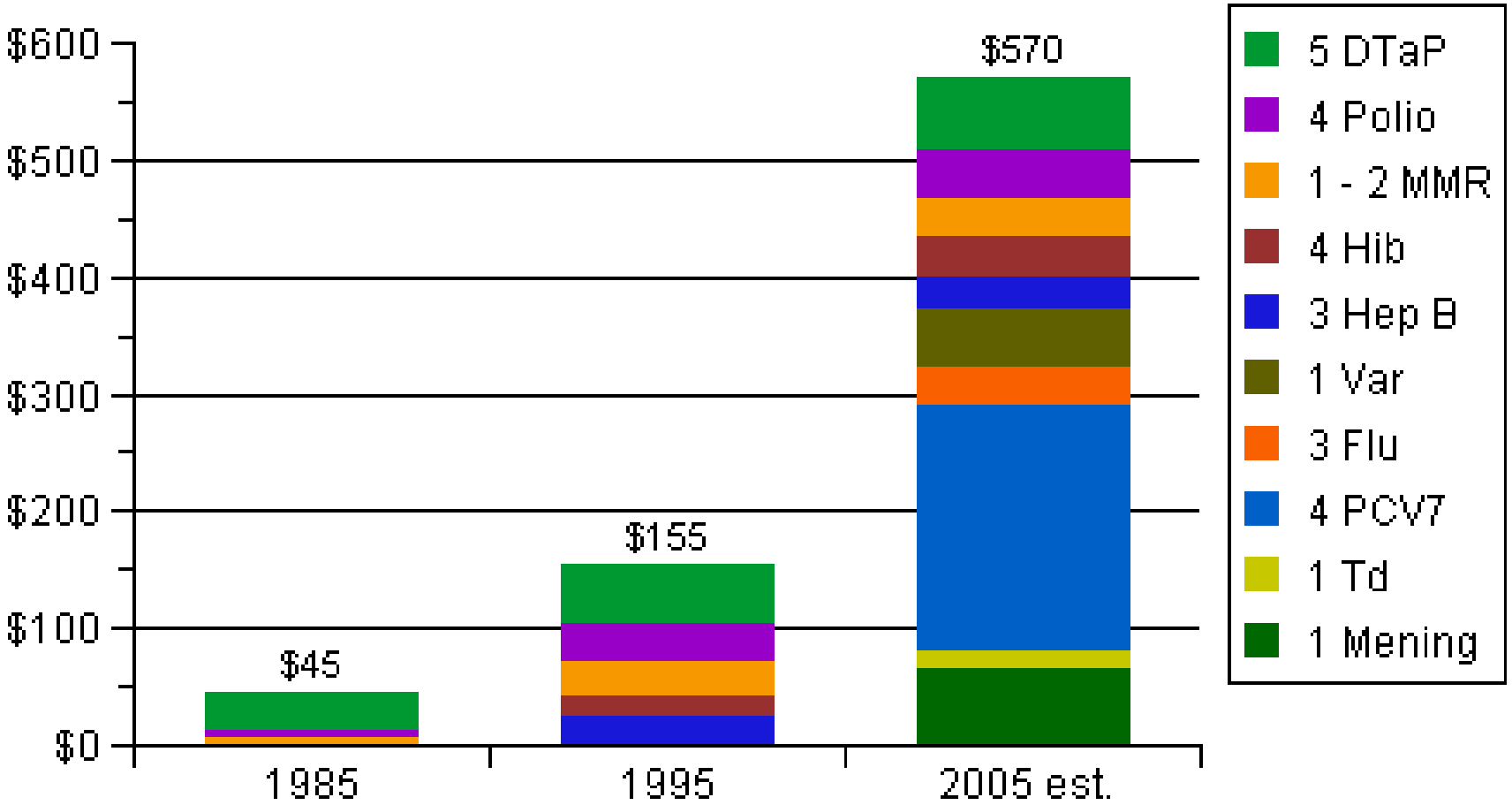
# How Does Public Health Reach Children

- VFC program has 45,000 provider sites
  - 75% of sites are private providers
  - 25% are public sector sites
- Collectively, VFC providers vaccinate 90% of children
  - VFC vaccine for VFC-eligible children
  - Private purchase vaccine for other children
- Improving VFC providers' practices improves vaccinations for almost all children

# Number of Vaccines in the Routine Childhood Immunization Schedule

| 1985 (7) | 1995 (10) | 2005 (13) |
|---|---|---|
| Measles | Measles | Measles |
| Rubella | Rubella | Rubella |
| Mumps | Mumps | Mumps |
| Diphtheria | Diphtheria | Diphtheria |
| Tetanus | Tetanus | Tetanus |
| Pertussis | Pertussis | Pertussis |
| Polio | Polio | Polio |
| | Hib (infant) | Hib (infant) |
| | HepB | HepB |
| | Varicella | Varicella |
| | | Pneumococcal Disease |
| | | Influenza |
| | | Meningococcal |

# Federal Contract Prices for Vaccines Recommended Universally for Children and Adolescents 1985-2000




Federal contract prices shown for 1985 and 1995 are averages that account for price changes within that year.
An estimate is provided for 2005 since contract prices are renegotiated in April and August.
The 2005 estimate factors in the cost to vaccinate one adolescent with one dose of Meningococcal & one dose of Td.

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## Status of Licensure and Recommendations for New Vaccines*

| Vaccine | Manufacturer | BLA submitted to the FDA | BLA age indications** | FDA licensure status | Status of AAP/ACIP recommendations*** |
|---|---|---|---|---|---|
| MCV4 (Menactra™) | sanofi pasteur | Dec-03 | 11-55 years of age | Licensed 14-Jan-05 | AAP: www.aap.org/advocacy/releases/mengpolicyfinal.pdf MMWR: www.cdc.gov/mmwr/preview/mmwrhtml/rr5407a1.htm |
| | | Supplement to original BLA March 2005 | 2-10 years of age | To be reviewed | Pending FDA licensure |
| Varicella virus second dose (Varivax®) | Merck | Supplement to original BLA: optional second dose | children 12 months to 12 years of age (3 month minimum interval) | Licensed 5-Apr-05 | Not Recommended Jun-05 |
| Tdap (Boostrix™) | GlaxoSmithKline (GSK) | Jul-04 | 10-18 years of age | Licensed 3-May-05 | NIP: http://www.cdc.gov/nip/vaccine/tdap/default.htm |
| Tdap (ADACEL™) | sanofi pasteur | Aug-04 | 11-64 years of age | Licensed 10-June-05 | NIP: http://www.cdc.gov/nip/vaccine/tdap/default.htm |
| MMRV (ProQuad®) | Merck | Aug-04 | Same as for MMR dose 1 or dose 2; 12 months to 12 years | Licensed 6-Sep-05 | Pending review |
| Hepatitis A (VAQTA®) | Merck | Supplement to original BLA | greater than or equal to 12 months | Licensed 15-Aug-05 | Pending review |
| Hepatitis A (HAVRIX®) | GlaxoSmithKline (GSK) | Supplement to original BLA | greater than or equal to 12 months | To be reviewed | Pending FDA licensure |
| Rotavirus (ROTATEQ®) | Merck | Apr-05 | 2,4, and 6 months of age | To be reviewed | Pending FDA licensure |
| Zoster vaccine (ZOSTAVAX™) | Merck | Apr-05 | older adults | To be reviewed | Pending FDA licensure |
| Influenza (FLUARIX™) | GlaxoSmithKline (GSK) | 25-May-2005 | over 18 years of age | Licensed 31-Aug-05 | MMWR: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5434a4.htm |
| HPV (Gardasil™) | Merck | Possible submission 4th Quarter 2005 | 11-26 years of age (3 doses) | Pending BLA submission | Pending FDA licensure |
| HPV (Cervarix™) | GlaxoSmithKline (GSK) | TBD | Pending submission | Pending BLA submission | Pending FDA licensure |
| Hib/DTaP/IPV (PENTACEL™) | sanofi pasteur | 25-July-2005 | 2, 4, 6, and 15 to18 months | To be reviewed | Pending FDA licensure |

**Table Updated: 10/6/05**

**Table available on Red Book Online: http://aapredbook.org/news/vaccstatus.shtml**

BLA = biologics license application, VRBPAC = Vaccines and Related Biological Products Advisory Committee, FDA = Food and Drug Administration
AAP = American Academy of Pediatrics, ACIP = Advisory Committee on Immunization Practices, MCV4 = Meningococcal conjugate vaccine
MMRV = measles, mumps, rubella, varicella, Tdap = Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, absorbed
HPV = human papillomavirus vaccine, Hib = Haemophilus b, DtaP = Diphtheria, Tetanus and Pertussis, IPV = Inactivated Poliovirus Vaccine
* information from vaccine manufacturers, from ACIP meetings and from AAP
** age licensure can change following FDA review; not final until package insert approved
*** ACIP recommendations become official after approval by the CDC Director and Department of HHS and publication in MMWR; AAP recommendations become official after approval by the Board of Directors

# Status of Licensed Vaccines

| Vaccine | FDA licensed | AAP/ACIP recommended |
|---|---|---|
| MMRV | Yes | Pending |
| Varicella: 2nd dose | Yes | No |
| Hepatitis ≥ 12 months | Yes | Pending |
| MCV7 | Yes | Yes |
| Tdap (adolescents) | Yes | Yes |
| Tdap (adults) | Yes | Pending |
| Influenza (adults)(GSK) | Yes | Yes |

# Conclusions

- Routine immunizations provide a tremendous benefit to infants, children, adolescents, adults and to society
- Immunization is a shared public / private responsibility
- The ACIP is a well functioning, well respected FACA committee
- Many challenges face ACIP including vaccine financing, vaccine supply and vaccine acceptance issues

# Vaccines Recently Licensed or Near Licensure

| age | vaccine | |
|---|---|---|
| children | MMRV* | |
| | Varicella: second dose* | |
| | Hepatitis A: 12 months* | |
| | Oral rotavirus | |
| | LAIV | |
| adolescents | MCV4* | HPV |
| | TdaP* | hepatitis A |
| adults | Zoster | Influenza* |
| | Tdap* | |

*Recently licensed by the FDA