

# Do We Have Evidence to Support a Hepatitis B Booster Policy for Persons Vaccinated as Infants

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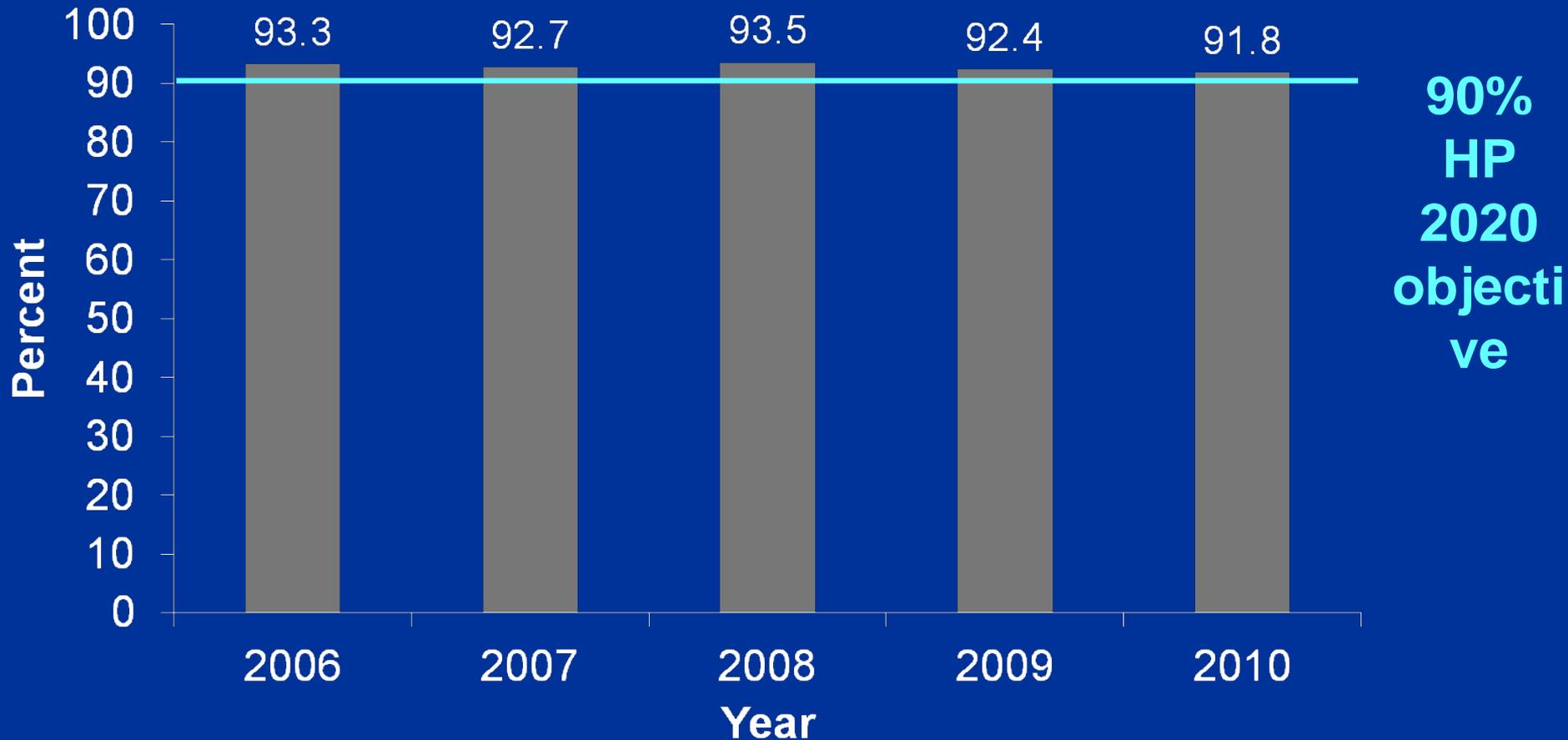


National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention

Division of Viral Hepatitis

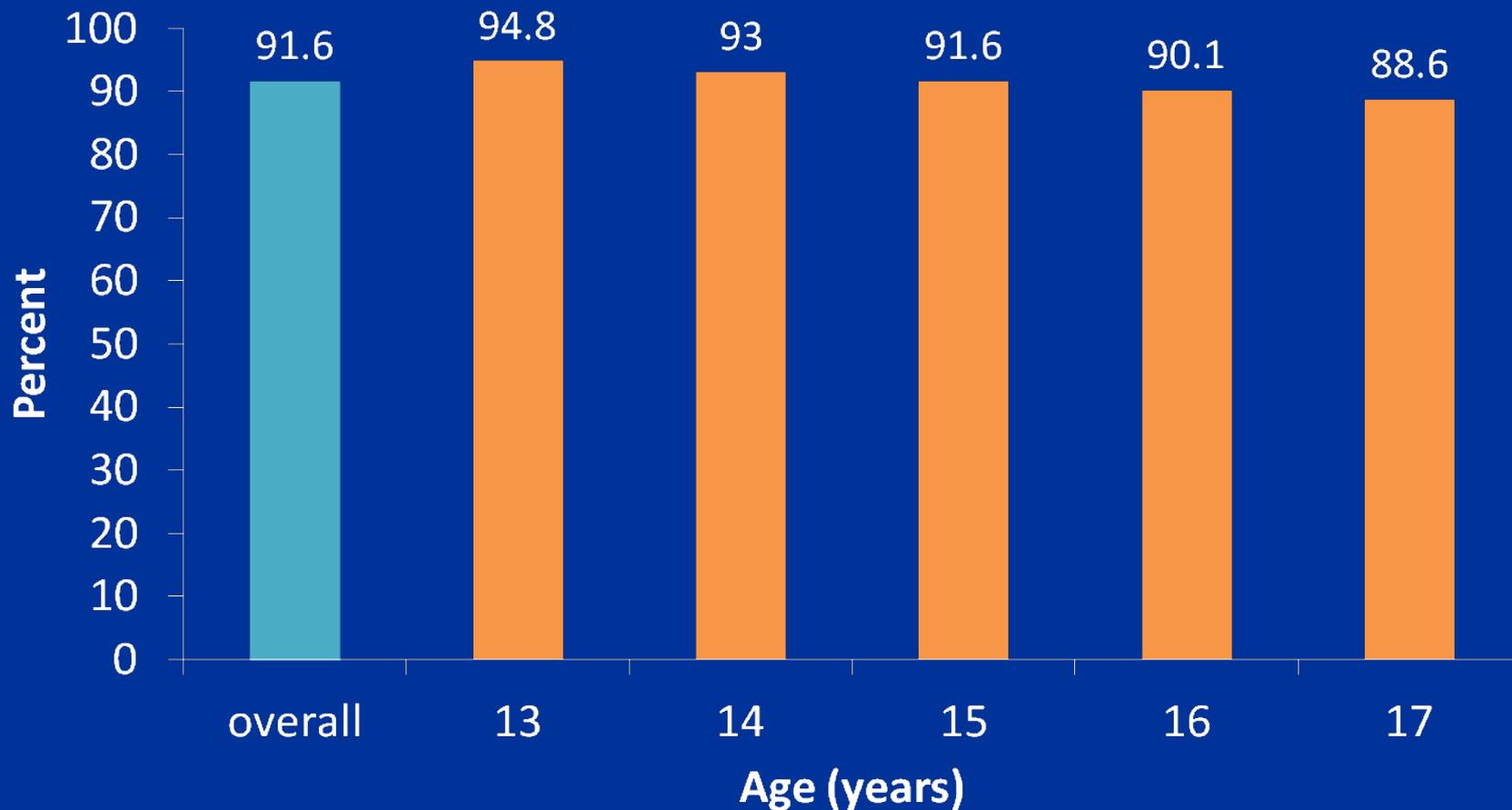


# Hepatitis B Vaccination Coverage Among Infants Aged 19-30 mos. – United States, 2006-2010



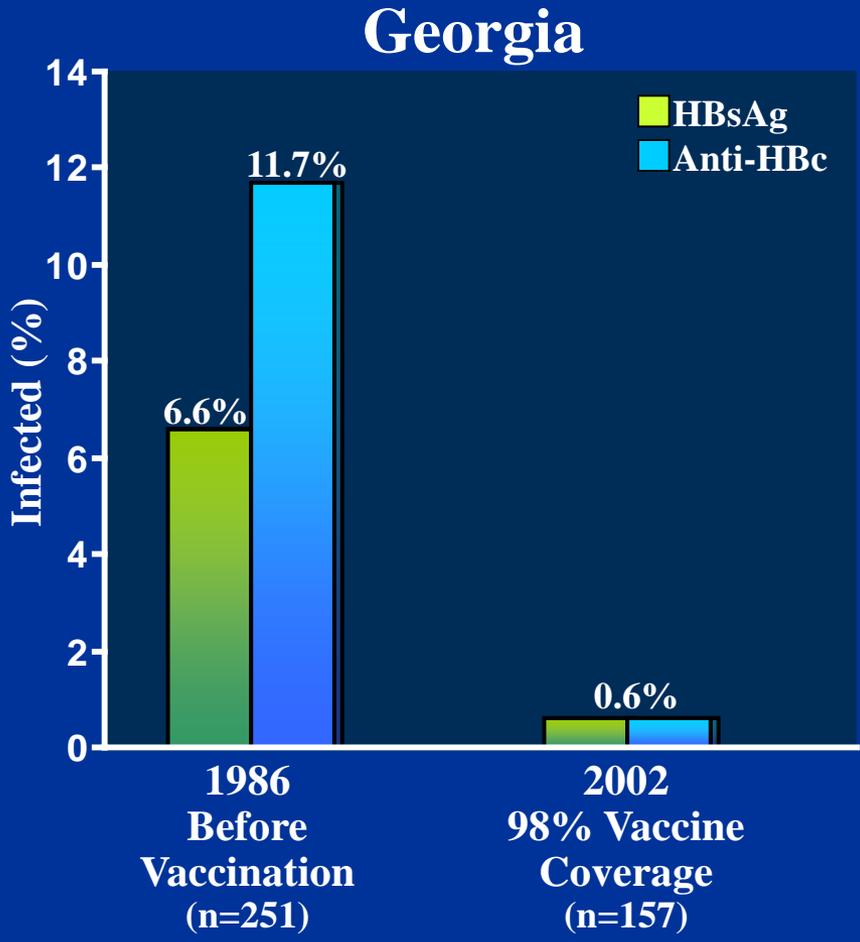
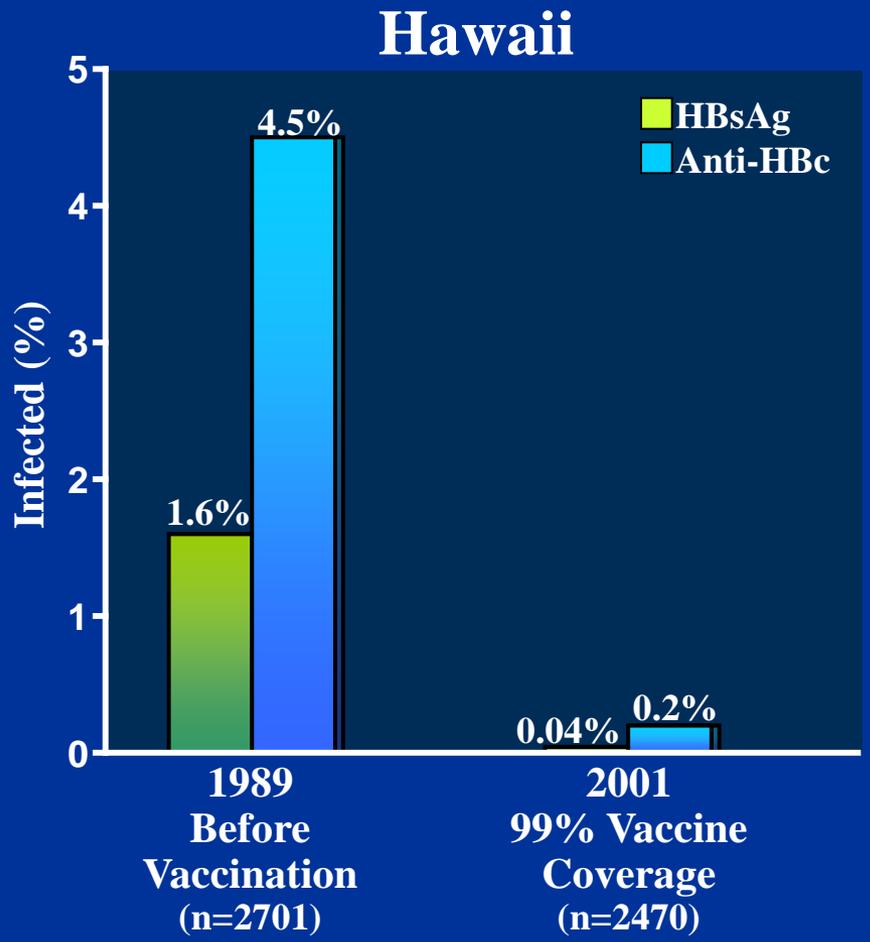
Source: CDC. National and state vaccination coverage among children aged 19-35 months – United States, 2010. *MMWR*. 2011;60(34):1158.

# Hepatitis B Vaccination Coverage Among Adolescents Aged 13-17 yrs. – United States, 2010



Source: CDC. National and state vaccination coverage among adolescents aged 13 through 17 years – United States, 2010. *MMWR*. 2011;60(33):1119.

# Effectiveness of Hepatitis B Immunization Among API Children, Hawaii and Georgia



Franks AL, et al. *N Engl J Med.* 1989;321:1301-1305.  
 Pon EW, et al. *Pediatrics.* 1993; 92:574-578.  
 CDC. Hawaii and Georgia Health Departments.

# CDC/ACIP Statements Regarding a Booster Dose following Routine Infant Hepatitis B immunization

- 1982: The duration of protection and the consequent need for booster doses are not yet known. <sup>1</sup>
- 1985: The duration of protection and need for booster doses are not yet defined <sup>2</sup>
  - only 10%-15% of persons who develop adequate antibody will lose antibody within 4 years
  - among those who lose antibody, protection against viremic infection and liver inflammation appears to persist

# CDC/ACIP Statements Regarding a Booster Dose following Routine Infant Hepatitis B immunization (continued)

- **1991:** For children and adults whose immune status is normal, booster doses of vaccine are not recommended, nor is serologic testing to assess antibody levels necessary. The duration of protective efficacy for adolescents who were vaccinated during infancy or childhood must be evaluated; the results will determine future recommendations concerning booster doses. <sup>1</sup>
- **2005:** Studies are needed to assess long-term protection after vaccination and the possible need for booster doses of vaccine. <sup>2</sup>
- **2006:** Booster doses are not recommended for persons with normal immune status who were vaccinated as infants, children, adolescents, or adults. <sup>3</sup>

# Supportive Evidence for CDC Policy Regarding a Booster Dose following Routine Hepatitis B immunization

- Implementation of hepatitis B vaccination programs in populations with a high endemicity of HBV infection has resulted in virtual elimination of new HBV infections.
- Immunocompetent persons who achieve anti-HBs concentrations of  $\geq 10$  mIU/mL after preexposure vaccination have nearly complete protection against both acute disease and chronic infection.
- Even when anti-HBs concentrations decline to  $< 10$  mIU/mL, nearly all vaccinated persons remain protected against HBV infection
- Persistence of vaccine-induced immune memory among persons who responded to a primary adult vaccine series with anti-HBs  $< 10$  mIU/mL has been demonstrated by an anamnestic increase in anti-HBs concentrations
- Among vaccine recipients, breakthrough infections (detected by the presence of anti-HBc or HBV DNA) are limited, typically transient and asymptomatic and rarely resulting in chronic HBV infection.

# Response to Hepatitis B Vaccine Booster Dose Among Children and Adolescents Vaccinated as Infants \*

- Alaskan study of persons vaccinated < 7 days of birth; measure of anti HBs amnestic response 4 weeks after a booster dose
  - 74 adolescents received plasma derived vaccine. **Response 69%**
  - 138 adolescents received 2.5 $\mu$  recombinant vaccine; **Response 83%**
  - 166 children (5.0-7.0yrs) received 5.0  $\mu$  dose; **Response 99%**
  - 309 (83%) of 378 participants had antiHBs <10mIU/ml; amnestic response related to participant age
- Conclusions
  - Despite loss of protective antibody, nearly all participants had levels of protection
  - No evidence that loss of demonstrable amnestic response indicated susceptibility

# **CDC SUPPORTED STUDIES OF LONG TERM EFFICACY**

# Follow-Up Study of Hepatitis B Vaccine Recipients 22 Years After Vaccination \*

- Of 493 recipients > 6 mos of age at vaccination with primary response to vaccination
  - Evidence of HBV infection
    - ★ 5 participants anti-HBc +; none HBsAg+ or HBV DNA+
    - ★ 0.74 (95% 0.31-0.45) /1000 persons per year.
  - 298 (60%) had anti-HBs  $\geq$  10mIU/ml at study baseline
  - 133 (81%/ 164 developed anti-HBs  $\geq$  10mIU/ml 30-60 days after booster
- Conclusions
  - After 22 years, 93% had evidence of protection
  - No need for a booster dose

# Follow-Up Study of Adolescents 15 years after Hepatitis B Vaccination\*

- Micronesia- 237 adolescents participants in national health survey
  - 193/237 (81%) vaccinated  $\leq$  2 days of age
  - At 35 months of age, 116 (49%) anti-HBs  $\geq$ 10 mIU/ml, no HBV
- 105/196 eligible adolescents participated, median age 15.8 years
  - 8 (7.6%) antiHBc+, none HBsAg+
  - Of other 97, 7( 7%) had anti-HBs  $\geq$ 10 mIU/ml
  - Of 96 boosted, 46 (48%) anti-HBs  $\geq$ 10 mIU/ml 14 days after vaccination
- Conclusions
  - Fifteen years after vaccination, breakthrough infections remain rare.
  - HepB vaccination prevents infection years after vaccination

# Follow-Up Study of Adolescents 15 years after Hepatitis B Vaccination\*

Alaska-37 adolescents vaccinated in first week of life; 2.5 $\mu$  dose anti-HBs  $\geq$ 10 mIU/ml by 18 months of age

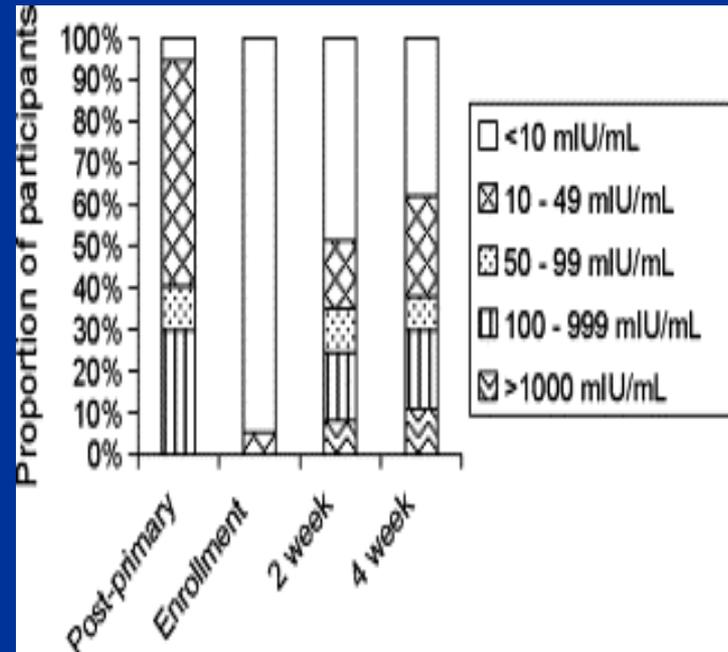
All negative for anti-HBc

35 (95%) anti-HBs < 10 mIU/ml at enrollment

After 5 $\mu$  dose, 18 (51%) amnestic response < 15 days

Discussion:

Additional studies needed to see if protection persists into adolescents and adulthood



\* Hammitt, et al. Vaccine 2007;25: 6958-6964

# **STUDIES AND SURVEILLANCE IN PROGRESS**

# Study of Long Immunity from Hepatitis B Vaccination

- Enrolled 16-19 yr-olds from the Houston TX metro area (target N=400)
  - HBsAg-negative mothers
  - Documented receipt of 3 dose primary vaccine doses < 12 mos.
- Two comparison groups
  - 1<sup>st</sup> dose HepB vaccine ≤7 days of birth
  - 1<sup>st</sup> dose HepB vaccine >4 weeks of birth
- Each group randomized to receive 10 µg vs. 20 µg booster Engerix-B
- Anti-HBs measured at baseline (pre-booster) and 2 weeks post-booster
  - % anti-HBs ≥10 mIU/L
  - Geometric mean titers (GMTs)
  - % positive for anti-HBc
- ~ One half of subjects recruited; few have anti-HBs ≥10 IU/L at baseline; most are ≥10 IU/L post-booster, none positive for anti-HBc
- Completion date- Spring 2012

# Investigation of Breakthrough HBV infections Among Persons < 29 years of Age Reported With Acute Hepatitis B

- 1451 cases of acute hepatitis B reported 2008-2010
  - 1079 (74%) missing vaccination history
  - 39 (3%) report vaccination; 7 misclassified and excluded
  - Of 32 cases meeting case definition
    - ★ Median age at event 20.5 yrs
    - ★ Median age at vaccination 12.5 yrs
    - ★ 22 had completion of vaccine series documented /reported
      - 9 (41%) None identified
      - 11 (59%) Risk reported- health care worker (5), MSM (2), tattoo (3), IDU (1)
- Future surveillance activities will direct states to collect vaccination information on all HBV cases among persons < 20

# Hepatitis B Vaccination among Healthcare Students \*

- 4,075 health care students entering training 2000-2010<sup>1</sup>
  - Most vaccinated >1999, average age of vaccination 22 years (0-59.6)
  - **Of 253 students 11-12 yrs in 1995-1997, 11 (4%) vaccinated .**
- 2,481 health care students with history of 3 dose hepB vaccination
  - Median age at start of hepB series – 14.7 years ( 0-49)
- Both schools require documentation of seroprotection and HepB booster for those anti-HBs < 10 mIU/ml

\* Tohme, et al. Infect Control hosp Epid 2011;32. <sup>2</sup> CDC unpublished data

# Conclusions Regarding Long-term Efficacy of Hepatitis B Vaccine

- CDC booster dose policy is long standing
  - Stated in 1991 and reaffirmed in 2006
- Policy based on evidence
  - Declines in HBV incidence, no/few cases of vaccine failures
  - Absence of acute hepatitis B, HBsAg or HBV DNA among cohorts of persons vaccinated as infants, children and adults up to 22 years after vaccination
- Data published from CDC studies support current policy
- US population of persons vaccinated as children now aging into adulthood; Studies of seroprotection must continue
- CDC asked by ACIP to reconsider current policy

# Review of Current ACIP Policy

# Advisory Committee on Immunization Practices Structure

- 15 voting members including chairperson (non-government)
  - 4 year terms
  - ACIP steering committee nominates, HHS selects
  - One consumer representative
  - Members screened for conflicts of interest
- 8 *ex officio* members – representing other government agencies that are involved in immunization (non-voting)
- 27 liaison members – representatives of professional societies and organizations responsible for vaccine development and immunization programs (non-voting)

# ACIP Work Groups (WG) - December 2010

PERMANENT WG	1	Adult Immunization
	2	General Recommendations
	3	Harmonized Schedule
	4	Influenza Vaccines
TASK ORIENTED WG	5	Hepatitis Vaccines
	6	Human Papillomavirus Vaccines
	7	Meningococcal Vaccines
	8	Pertussis Vaccines
	9	Pneumococcal Vaccines
	10	Herpes-zoster (singles) Vaccine
	11	Measles
	12	Japanese Vaccines

# Example: ACIP Hepatitis Vaccines Work Group

- Established in 2008
  - Chaired by ACIP member
  - CDC Lead Staff- Dr Trudy Murphy
- Tasks
  - Hepatitis B vaccination for persons with diabetes (ACIP endorsed, October 2011)
  - Management of health care workers and trainees with documented history of vaccination
  - Booster dose of Hepatitis B vaccine
  - Update of vaccine recommendations
    - ★ Hepatitis B- children
    - ★ Hepatitis A

# Considerations Regarding a Booster Dose following Routine immunization

- Goals
- Long term efficacy studies
- Surveillance data
- Immunization coverage
- Special populations
- Cost effectiveness
- Research- new adjuvants
- Program/implementation issues

# Key Elements for Developing Evidence Based Recommendations

- Vaccine safety
- Vaccine efficacy/effectiveness
- Burden of disease
- Economic analysis and implementation issues

**Evidence tables will be used to summarize benefits and harms and strengths and limitations studies**