Could Vaccines be a Possible Model For Pediatric Drug Development?

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Comparison of 20th Century Annual Morbidity and Current Morbidity, Vaccine-Preventable Diseases

Disease	20th Century Annual Morbidity	2005**	Percent Decrease
Smallpox	48,164	0	100*
Diphtheria	175,885	0	100*
Measles	503,282	62	99.99
Mumps	152,209	265	99.83
Pertussis	147,271	21,003	85.74
Polio (paralytic)	16,316	1	99.99
Rubella	47,745	16	99.97
Congenital Rubella Syndrome	823	1	99.88
Tetanus	1,314	20	98.48*
H. influenzae, type b and unknown (<5 yrs	20,000	199	99.01

•Record lows ** Provisional

Email: Barry Sirotkin 2/14/06

Diseases Prevented by Vaccination of Children

1986	2006	
Diphtheria	Diphtheria	Hepatitis B
Tetanus	Tetanus	Varicella
Pertussis	Pertussis	Pneumococcal Disease
Polio	Polio	Influenza
Measles	Measles	Meningococcal Disease
Mumps	Mumps	Rotavirus
Rubella	Rubella	Hepatitis A
Hib	Hib	Human Papillomavirus

Major New Vaccines Licensed for Universal Vaccination of Children Between 2000 and May 24, 2006†

Vaccine	Year	Manufacturers
HPV	2006	Merck
Rotavirus	2006	Merck
MMRV	2005	Merck
Tdap	2005	GSK, sanofi
MCV4	2005	sanofi
LAIV	2003	MedImmune
DTaP-HepB-IPV	2002	GSK
PCV7	2000	Wyeth

† Excludes labeling changes, newer versions of same products, and new licenses for similar products already licensed.

Source: www.fda.gov/cber/products.htm

Factors that May Influence Development of Vaccines for Children - I

- Large population covered – universal vaccination recommendation includes at least one birth cohort annually
- Recommending bodies, Advisory Committee on Immunization Practices (ACIP) and American Academy of Pediatrics Committee on Infectious Diseases set standard of care
- Vaccines are folded into routine well clinic visits

Recommended Childhood and Adolescent Immunization Schedule

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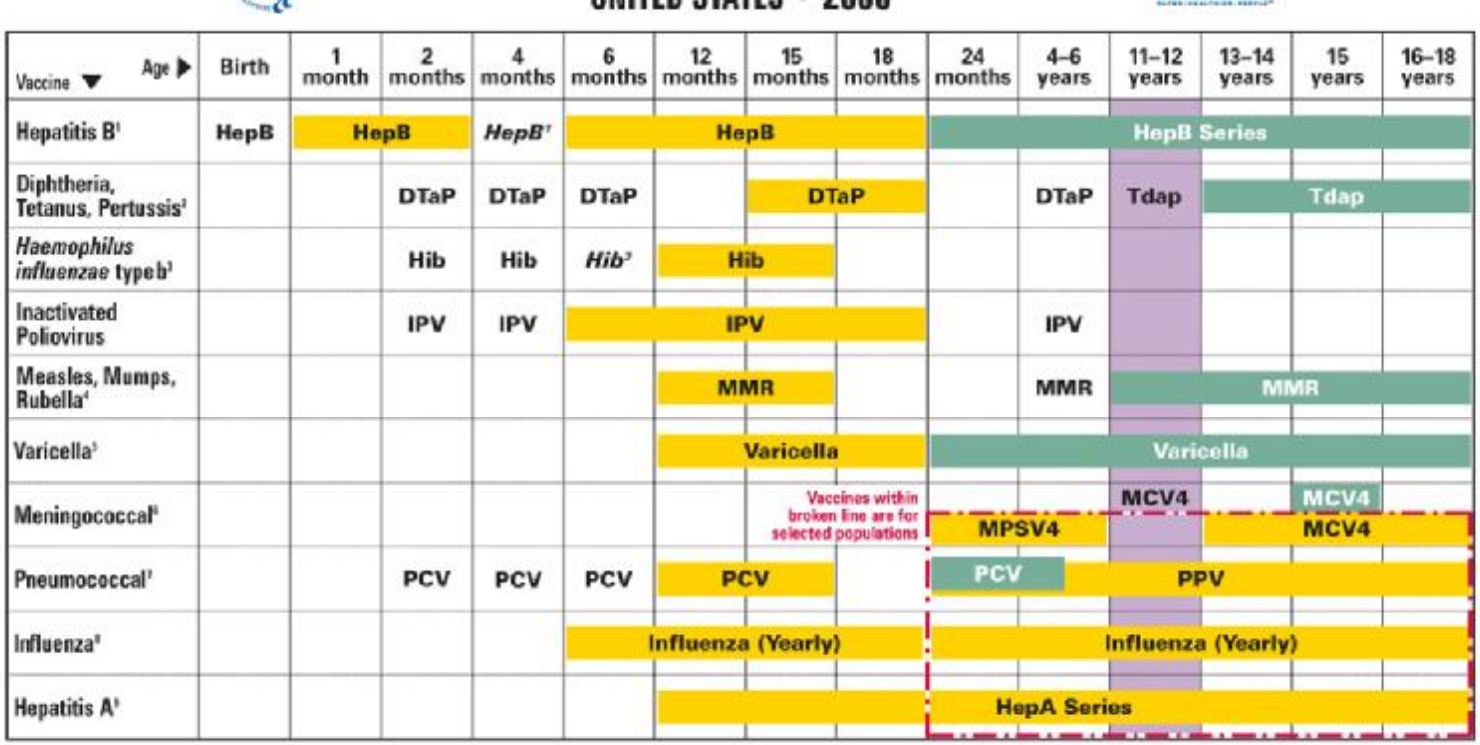

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2005, for children through age 18 years. Any dose not administered at the recommended age should be administered at any subsequent visit when indicated and feasible. Indicates 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

FOOTNOTES:

From: http://www.cdc.gov/nip/recs/child-schedule-image1-ppt.jpg

Factors that May Influence Development of Vaccines for Children - II

- Vaccinations often offer protection to individual and through herd immunity to community as well
- Many vaccines are eventually mandated through school and/or day care laws
- National Vaccine Injury Compensation Program
  - Funded by excise tax
  - Table-related injuries
  - Proof of causation for others
- There are no manufacturers of generic vaccines

Immunization Coverage Among Children 19-35 months of age†, United States, 2004‡

Vaccines	Coverage (%)
DTP-3	95.9%
DTP-4	85.5%
Polio-3	91.6%
MMR-1	93.0%
Hib-3	93.5%
HepB-3	92.4%
Var-1	87.5%
PCV-3	73.2%
Combined Series excluding PCV-3	76.0%

† Median age 27 months. Children Born February 2001-May2003

‡ Source: http://www.cdc.gov/nip/coverage/NIS/04/tab03_antigen_state.xls. Accessed 5/24/06

Safety Monitoring for Vaccines - I

- Vaccine Adverse Event Reporting System (VAERS)
  - Passive reporting
  - Certain adverse events required by law to be reported
  - Stimulated through Vaccine Information Statements mandated by law for vaccines in Injury Compensation Program
  - Maintained by FDA and CDC
  - De-identified data available to public

Safety Monitoring for Vaccines - II

- Vaccine Safety Datalink (VSD)
  - 7 HMO's; 8 plans
  - Allows calculation of rates of adverse events
  - Allows calculation of expected rates in absence of vaccination
  - Allows calculation of expected rates at reference intervals before or after vaccination

Similarities Between Drug and Vaccine Development

- Both covered by the Pediatric Research Equity Act
- Requirements for licensure similar
- Vaccines and drugs often tested first in adults usually in Phase I settings before doing evaluations in children.
- Children are a “vulnerable population” and cannot give their own informed consent
- Testing in adults may provide some evidence of benefit and safety

Example of the Use of the Pediatric Research Equity Act (PREA) with Vaccines

Letter from Norman W. Baylor, PhD, Director, Office of Vaccine Research and Review, 8/31/05 to GlaxoSmithKline Biologicals on Approval of Fluarix

"All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We have reviewed your submission dated May 25, 2005 and agree that a deferral of your pediatric studies for Fluarix in children <18 years of age is justified as you are pursuing with due diligence a pediatric indication for Fluarix."

Source: http://www.fda.gov/cber/approvltr/inflgla083105L.htm. Accessed 5/24/06

Differences Between Drug and Vaccine Development

- Exclusivity has not been important in vaccine development
- Limited numbers of children impacted by many drugs in contrast to relatively large number of children impacted by a vaccine recommendation
- Vaccines often developed with childhood indication in mind. Many of the infectious diseases occur primarily in children
- Vaccines usually given to well children in contrast to drugs

Acknowledgments

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