

Eighteen months of immunization and vaccine R&D at WHO...



**World Health
Organization**

Presentation outline

- Global progress in access to immunization
- Research and development update
 - Meningitis A
 - Measles aerosol
 - Adjuvants
- Pneumococcal Vaccine AMC: Target Product Profile
- Ethics of vaccine clinical trials
- WHO prioritization of vaccine-preventable diseases



Global Momentum on Child Survival

The New York Times

Number of deaths in children under 5 falls below 10 million



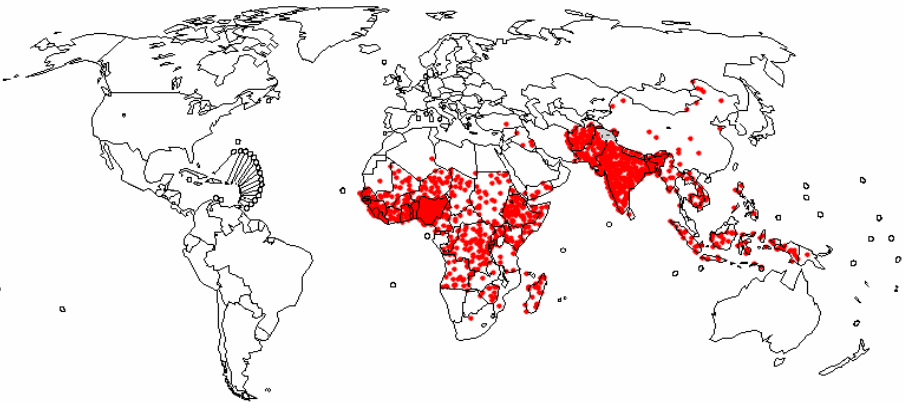
Vaccination campaigns, as in Indonesia, cut childhood deaths.

Source: http://www.nytimes.com/2007/09/13/world/13child.html?_r=2&hp&oref=slogin&oref=slogin

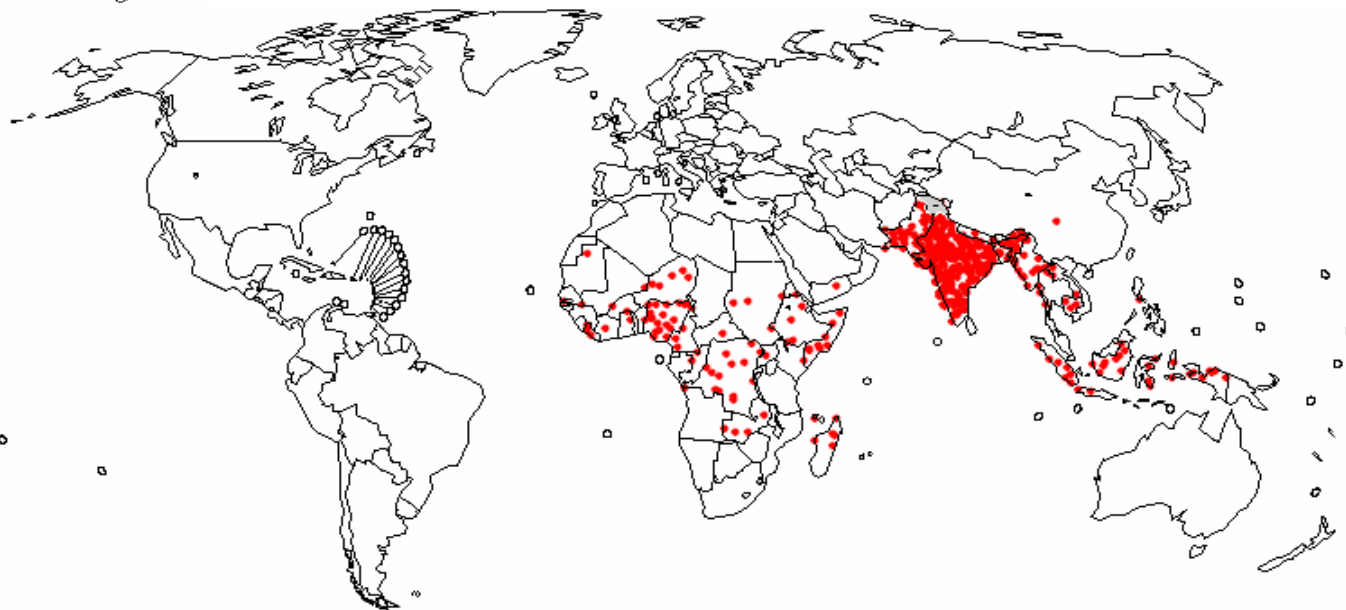
Published: September 13, 2007

Estimated measles deaths, 2000, 2006

2000 757 000 deaths



2006 242 000 deaths



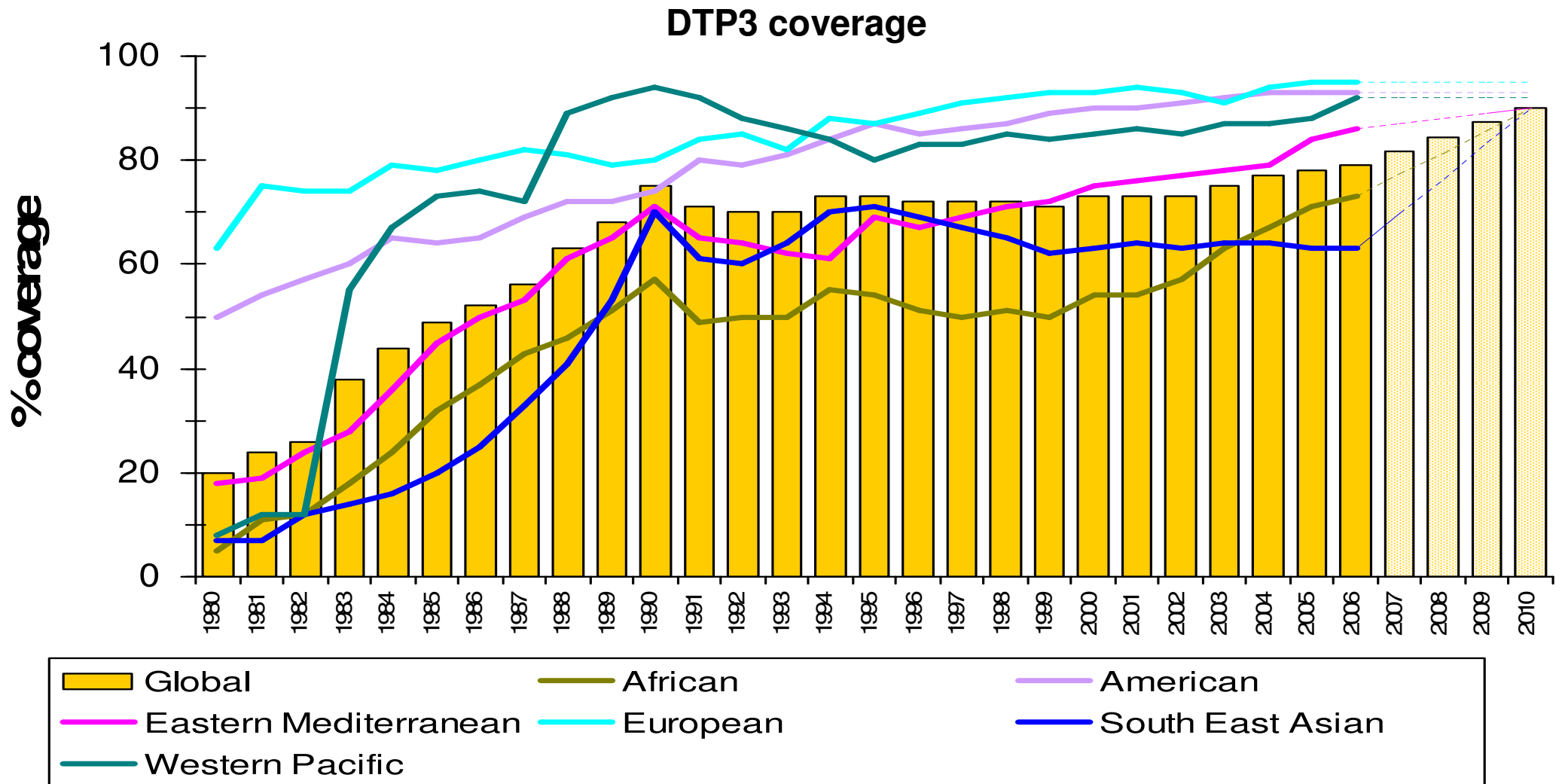
= 500 deaths

dots are randomly distributed
countries.

Data source: WHO/IVB, November 2007

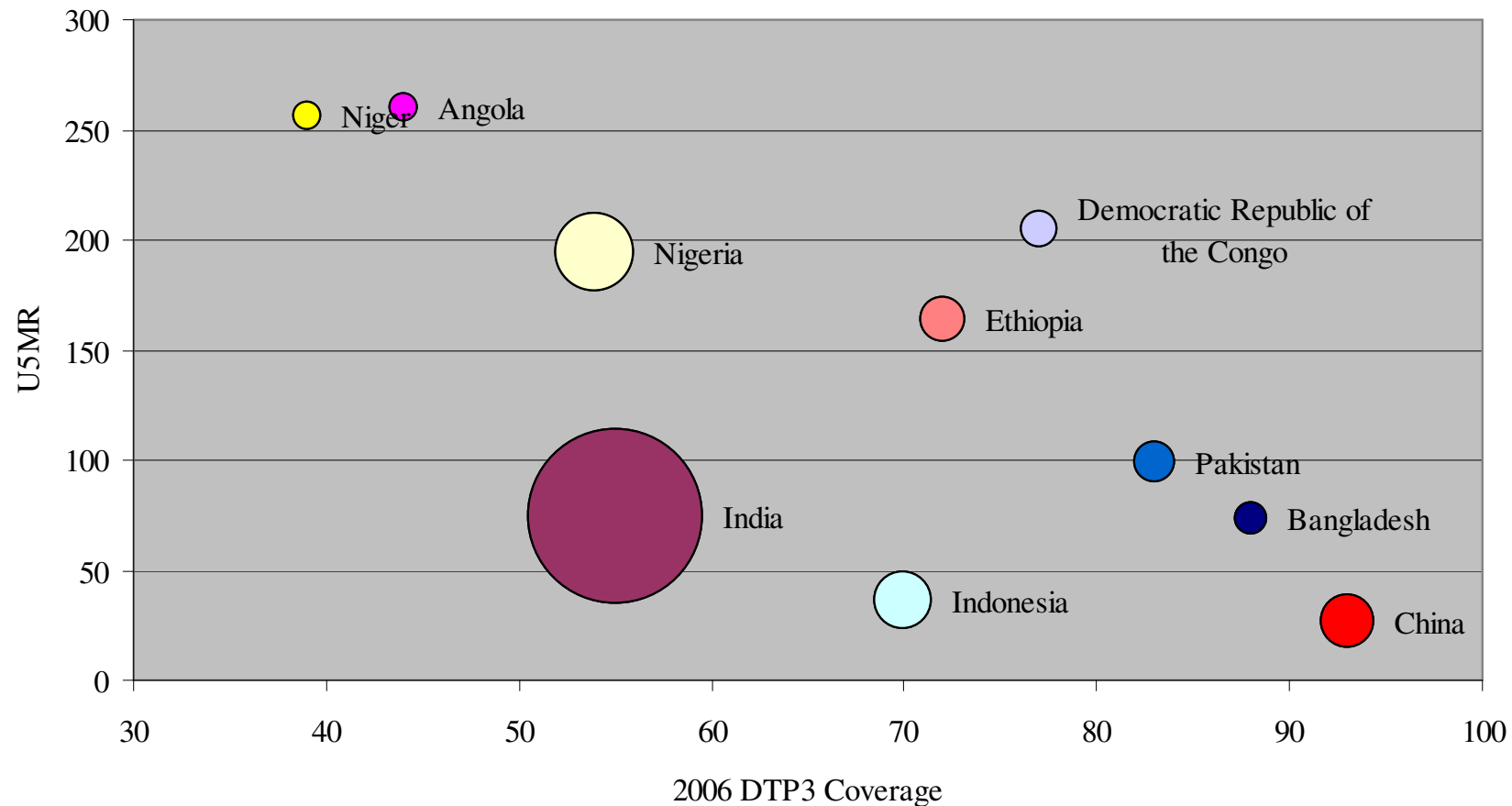
ARE WE ON TRACK TO REACH OUR COVERAGE GOALS?

Global Immunization 1980-2006, and projections 2007-2010 to reach 90% global coverage goals in 2010



Countries with the largest numbers of unimmunized children

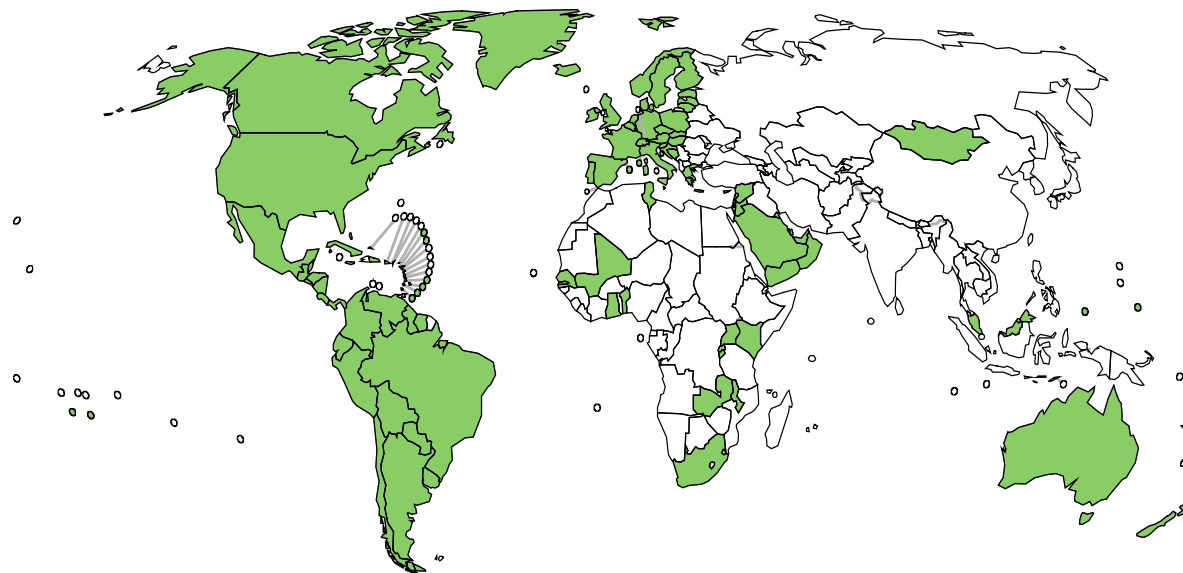
Unimmunized Children 2006



Countries having introduced Hib vaccine in 2000 and 2006



2000: 64 countries introduced



2006: 106 countries introduced

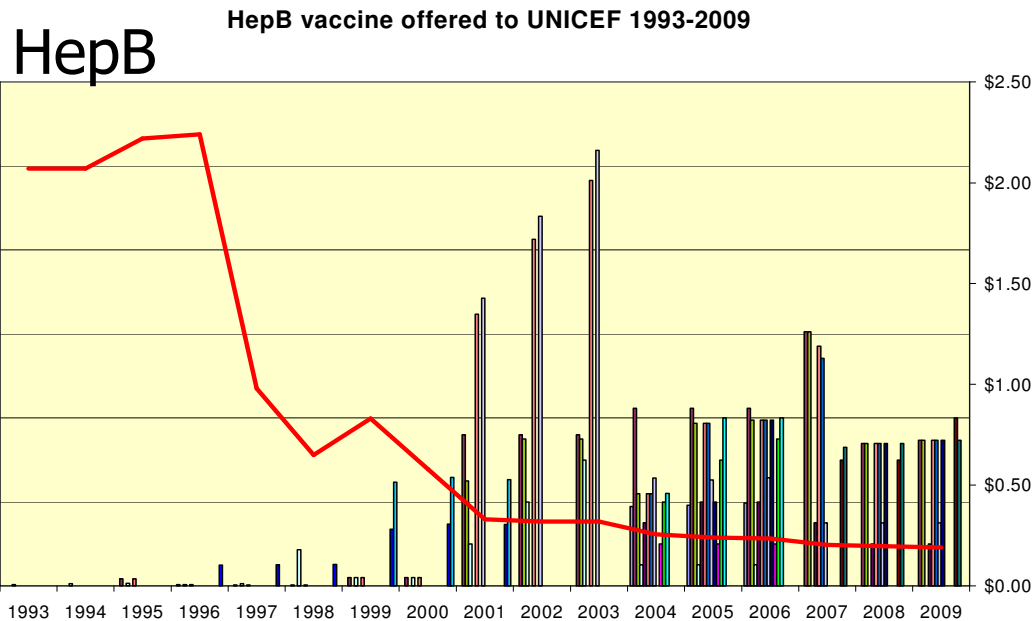
Source: WHO/UNICEF estimates, 2006

WHO Member States. Date of slide: 15 February 2007

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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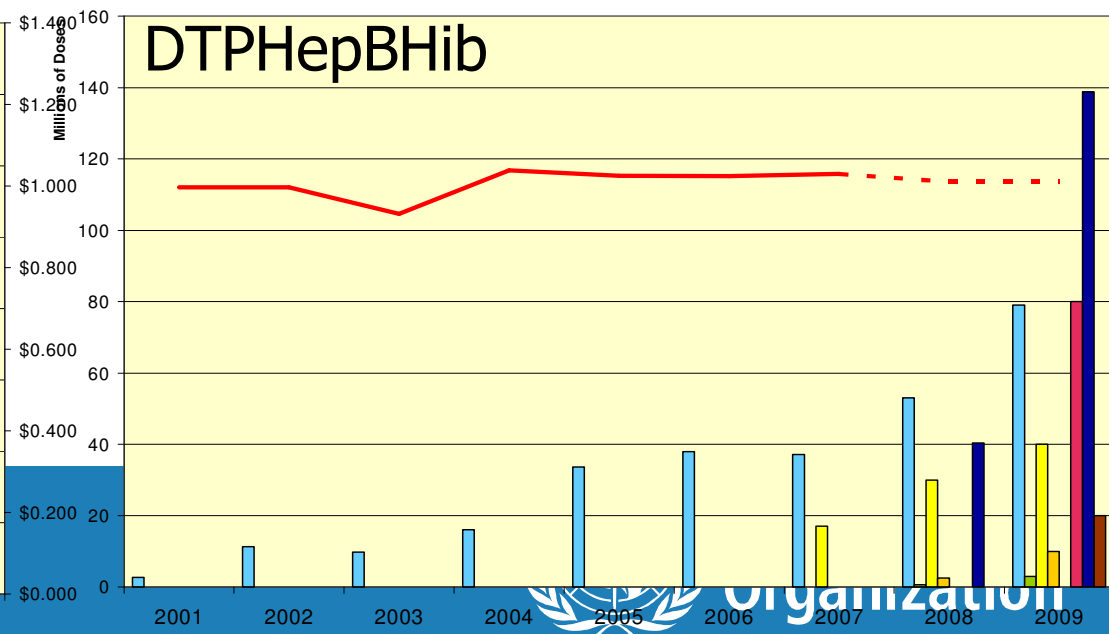
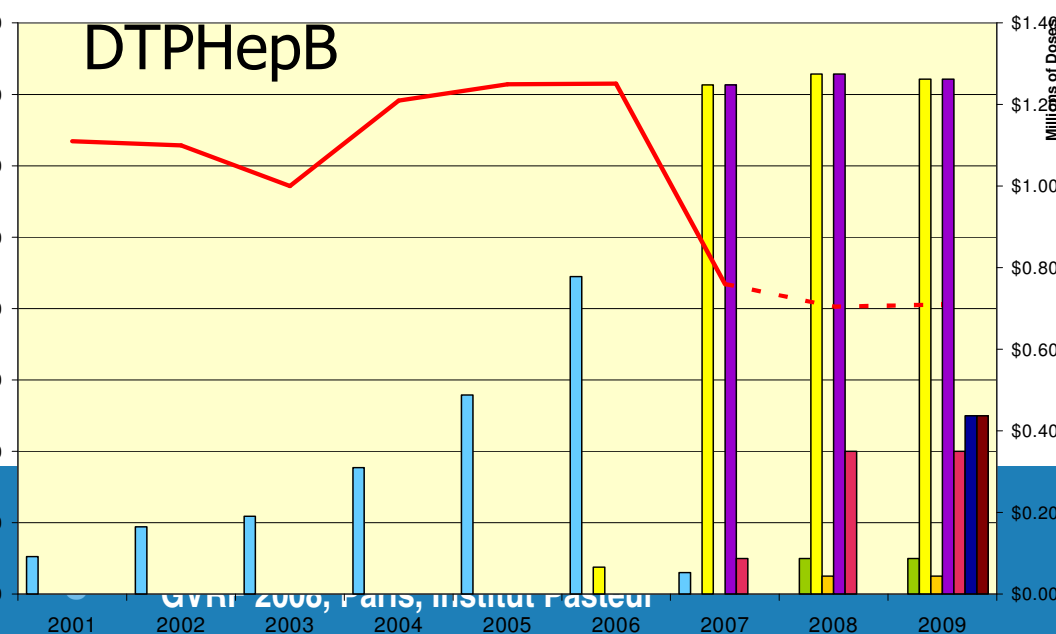
Impact of number of suppliers (and volume) on price



HepB price dropped with entry of many manufacturers (number of bars)

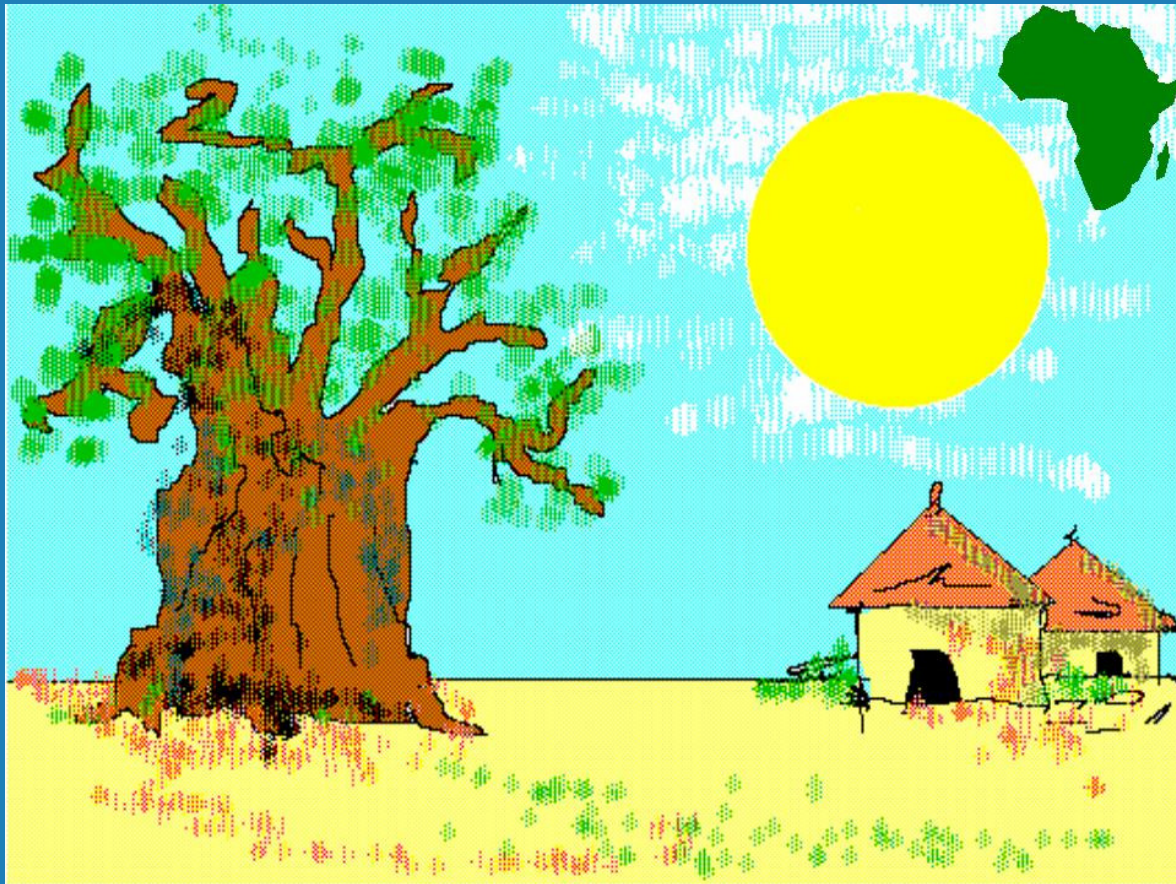
Same experience starting to be seen with DTPHepB in 2007

For DTPHepBHib by 2009?



New vaccines research, development and introduction

Facilitating & Promoting the Development of Meningococcal Conjugate Vaccines for Africa – a partnership with PATH



World Health
Organization

Progress towards the development of Men A-containing conjugate vaccines in 2005-2006

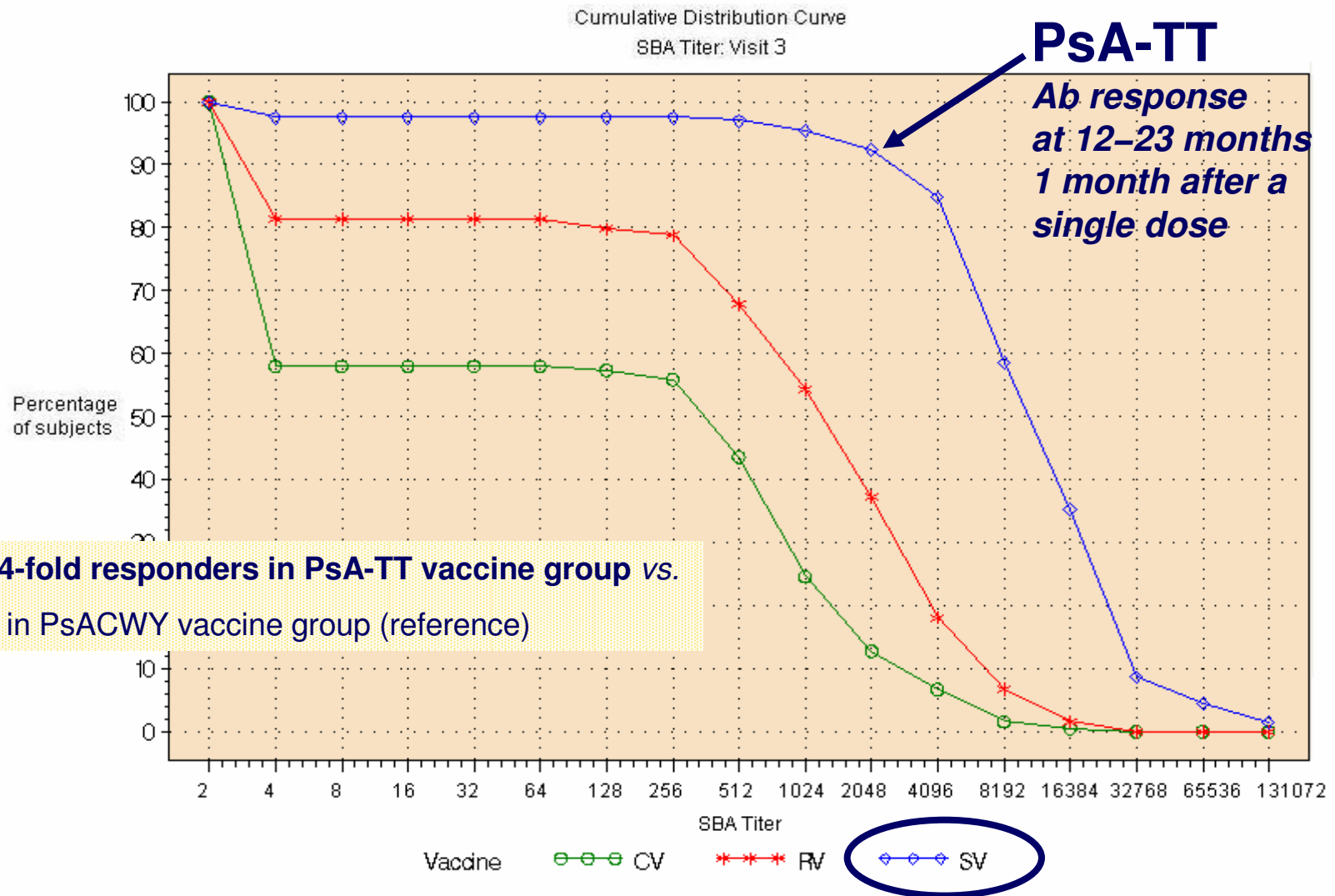
- **Conjugate Tetravalent Men A/C/Y/W135 Vaccines**
 - Sanofi Pasteur, Novartis Vaccines
 - GSK, *under development*
- **Conjugate Bivalent Men A/C & Monovalent Men A Vaccines**
 - Chengdu Institute of Biological Products, *under development likely for use in China only*

- **Conjugate Monovalent Men A Vaccine**

- manufactured by Serum Institute of India, developed within the Meningitis Vaccine Project (WHO & PATH)
under development for use among 1 to 29 year-olds, with an extension in infants
Introduction planned in Burkina Faso 2009
- Introduction price: 0.40 cts/dose
- Deployment in Africa through GAVI funding?



Week 4 Men A rSBA Titres Reverse Cumulative Distribution Curves



WHO Measles Aerosol Project

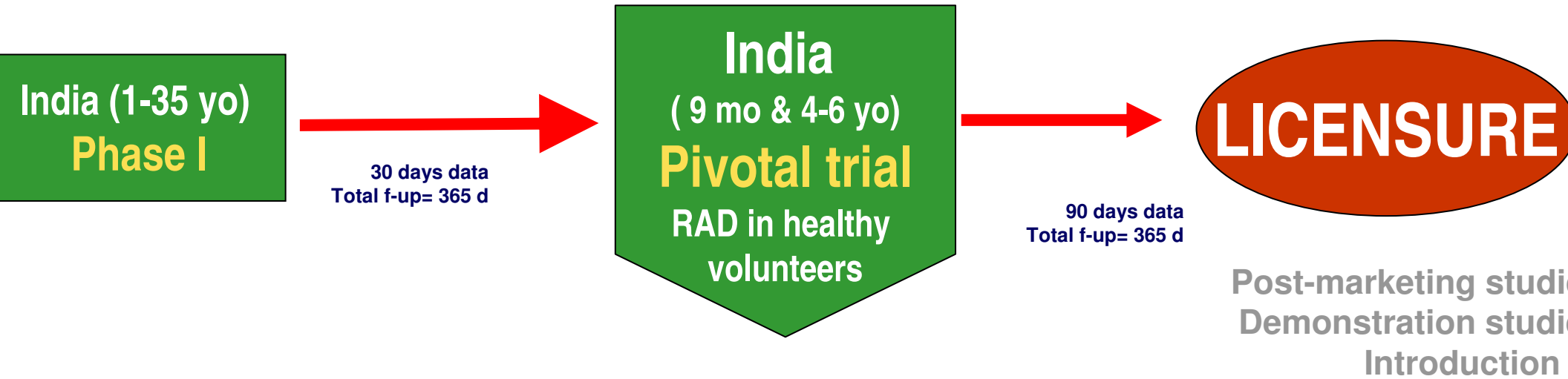
- Intends to **license** at least one method (vaccine and delivery device) for respiratory delivery of currently licensed measles vaccines



A measles vaccine that is safe, immunogenic, inexpensive and, easier to administer than injection.

Same vaccine, same dose, same vaccination schedule, same use recommendations.

Measles Aerosol Project Clinical Trials & device usability



Usability /logistics characteristics
Optimal device design



2007 **2008** **2010**

Product Research and Development: Global Adjuvant Development Initiative

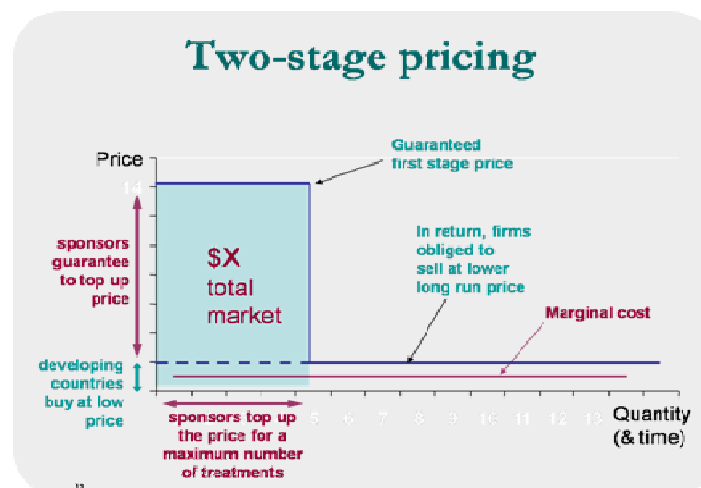
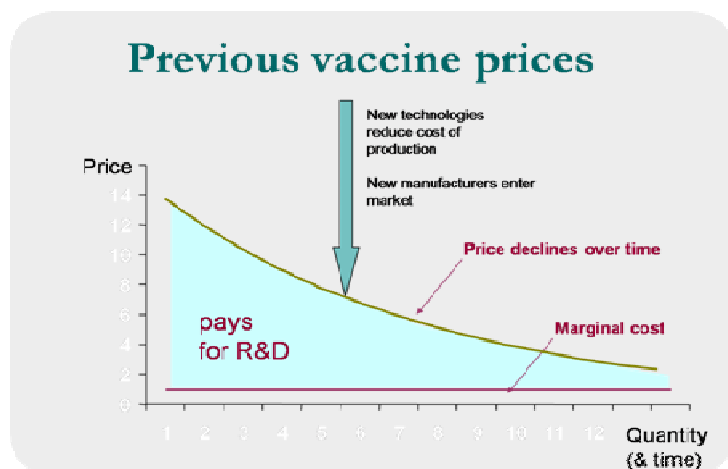
- Why?
 - Availability of potent adjuvants could accelerate development of vaccines. But
 - Lack of knowledge and know-how in public sector, and issues of comparability, safety and access
- What?
 - GADI will comprise a research centre in Switzerland and in India, to:
 - Evaluate, optimize and develop adjuvants using standardized readouts
 - Generate new scientific knowledge and innovation
 - Create and share public sector expertise
 - Provide vaccine formulation services for public sector
- Progress
 - Intellectual Property Rights and Freedom to Operate analysis
 - Initiation of AdjuNet
 - Linking with the Infectious Disease Research Institute (IDRI), Seattle
 - Discussion of funding options with Wellcome Trust and the EU



Pneumococcal Vaccine AMC: Target Product Profile

AMC Concept

A financial commitment by donors, to subsidize vaccine purchase at a set price, if it meets a specified target product profile and is in demand by GAVI-eligible countries with the goal of motivating increased supplier participation and investment to accelerate the introduction of life-saving vaccines in the world's poorest countries.



What is the Target Product Profile (TPP)*?

TPP sets the required minimal public health performance standards for AMC eligibility, such as:

- Effectiveness in target populations
- Safety, reactogenicity, contra-indications
- Dose-scheduling and compatibility with available delivery systems
- Product presentation, stability and packaging

**as defined in the AMC framework document*

Consultation process - 2007 (*)

- ✓ *ad hoc* expert panel technical consultation, with observers from SAGE, UNICEF and others;
- ✓ Draft formulation of consensus TPP;
- ✓ TPP endorsed by SAGE, and submitted to WHO Director-General for approval;
- ✓ TPP communicated to AMC secretariat (GAVI).

(*process approved by the Donor Committee)

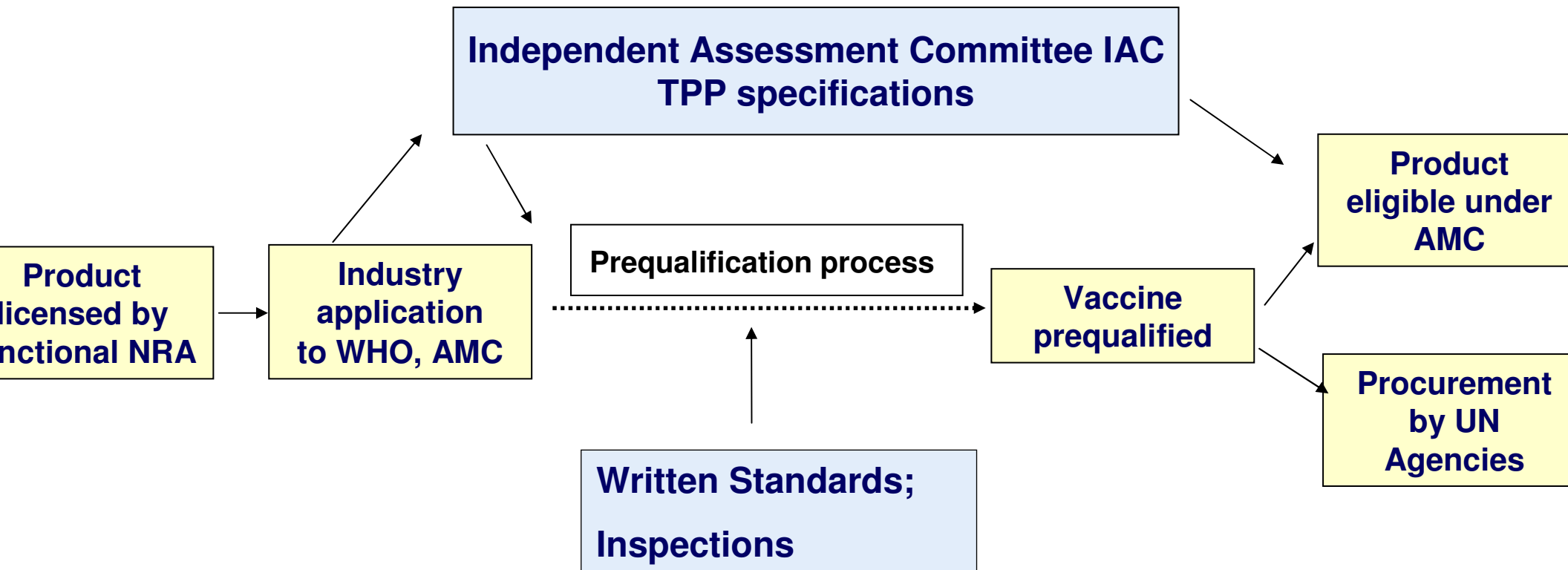


Pneumo vaccine Target Product Profile

Attribute (partial list)	Minimally Acceptable Profile
A. Vaccine serotypes	The serotypes included must cover at least 60% of the invasive disease isolates in the target region, and must include serotypes 1, 5 and 14.
E. Dosage schedule	Compatible with EPI schedule and consist of not more than 3 doses in the first year of life.
H. Product presentation	Mono-dose (vial or auto-disposable syringe) or low multi-dose presentations.
J. Storage and cold chain requirements	Stable at 2-8° C with a shelf-life of at least 24 months; Vaccine Vial Monitor.
L. Product registration and prequalification	The product must be WHO pre-qualified



Determining the eligibility of AMC funding



Ethical conduct of vaccine clinical trials

Recent publications

07

Ethical considerations
in biomedical HIV prevention trials

UNAIDS/WHO guidance document



Ethical considerations related to the provision of care and treatment in vaccine trials

Tarantola D^a, Macklin R^b, Reed ZH^c, Osmanov S^d, Stobie M^e, Hankins C^f, Kieny MP^g

Abstract: Ethical principles of beneficence and justice combined with international human rights norms and standards create certain obligations on researchers, sponsors and public health authorities. These include treatment provision for participants enrolled in clinical trials of vaccines, drugs and other new preventive and curative technologies and methods. However, these obligations are poorly defined in practical terms, inconsistently understood or inadequately applied. Vaccine clinical trial designs normally define standards of prevention applicable to the population where the trial is to take place. The present document addresses specifically the setting of standards applicable to care and treatment in vaccine trials. The lack of clear guidance on how to achieve the optimal synergy between the development of new health technologies, on the one hand, and the promotion and protection of ethical and human rights principles, on the other, is a barrier to the progress of health research and therefore to the advancement of public health. The World Health Organization and UNAIDS have engaged in a series of consultations in Africa, the Americas, Asia and Europe to reflect on how this aim could best be achieved. This document highlights the outcome of these consultations. It proposes a structured approach to consensual decision making in the context of the clinical trial of vaccines against such public health challenges as HIV and newly emerging or threatening epidemics. A structured approach involving investigators and sponsors in a consultative process with trial communities and other stakeholders in research will ensure that the needs and legitimate expectations of trial participants are appropriately met, obligations towards them are delivered and, as a result, ethical research is facilitated in the interest of public health.

Vaccine, Volume 25, Issue 26, 21 June 2007, Pages 4863-4874

Discussed at GVRF 2006, Bangkok, Thailand



WHO Prioritization of Vaccine-Preventable Diseases

Objectives and Methodology

● Objectives

- Prioritize/Categorize vaccine-preventable diseases by public health priority
 - Diseases with vaccines currently available (but not routinely recommended/widely used) or available in the near-term
- Provide guidance to WHO Member States, partners, and industry: for which diseases to prioritize activities

● Features

- “Rational consensus“ decision-making method
 - Input (structured) from global health community and experts on diseases and criteria used to make public health priorities



Results of Landscape Analysis: Diseases Considered in the Project

Diseases for which vaccines are currently licensed and available (but not routinely recommended or widely used)

- Cervical cancer (human papillomavirus infection)
- Cholera
- Hepatitis A
- Influenza (seasonal)
- Japanese encephalitis
- Meningococcal disease (groups ACYW135)
- Meningococcal disease (group B)
- Mumps

- Pneumococcal disease
- Rabies
- Rotaviral enteritis
- Rubella
- Typhoid fever
- Varicella
- Yellow Fever

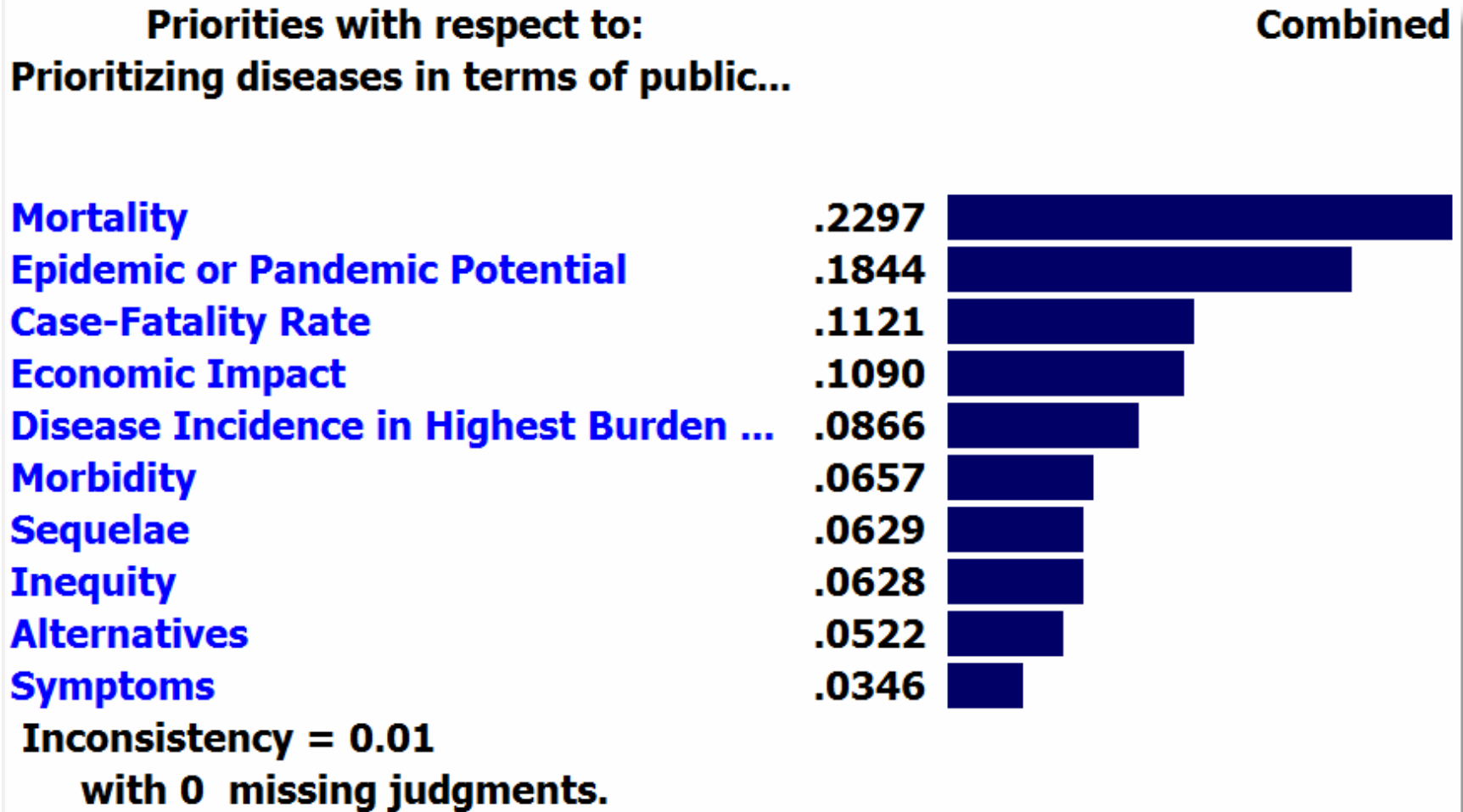
Diseases for which vaccines may be available (licensed) by 2012

- Dengue
- Hepatitis E
- Malaria



Phase II: Criteria Priorities

Priorities of Criteria for Respondents Group (N=32)
(Normalized to Sum to 1.0)



Combining Phase II and Phase III for global level Disease Prioritization:

What are our the global results (**preliminary**)?

Very High Priority:
Malaria, S. Pneumo

High Priority:
Cervical Cancer (HPV), Cholera, Dengue,
Japanese Encephalitis, Meningococcal ACWY, Rabies,
Rotavirus, Seasonal influenza, Typhoid Fever,
and Yellow Fever;

Medium Priority:
Hepatitis A, Hepatitis E, Meningococcal B,
Mumps, Rubella, and Varicella

Summary

- A rich pipeline of new or near market vaccines.
- Potential for significant impact on MDG-4.
- Increasing role of developing country suppliers in R&D.
- Need to finish the agenda with Hep B and Hib vaccine introduction; prepare for introduction of pneumococcal and rotavirus vaccines.
- Increasing cost of immunization is a challenge but there are new opportunities for financing, like the AMC.
- Clear decision making pathways to make informed and rational choices on vaccine introduction should be in place for use by countries



and finally

We thank the scientific organisation committee for their guidance, and our sponsors for their generous financial support

- The Bill and Melinda Gates Foundation and the Wellcome Trust
- Merck, Sanofi-Pasteur, GSK, Serum Institute of India, BioFarma, Shanta, Transgene

We also acknowledge the Institut Pasteur for hosting the GVRF 2008

