

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

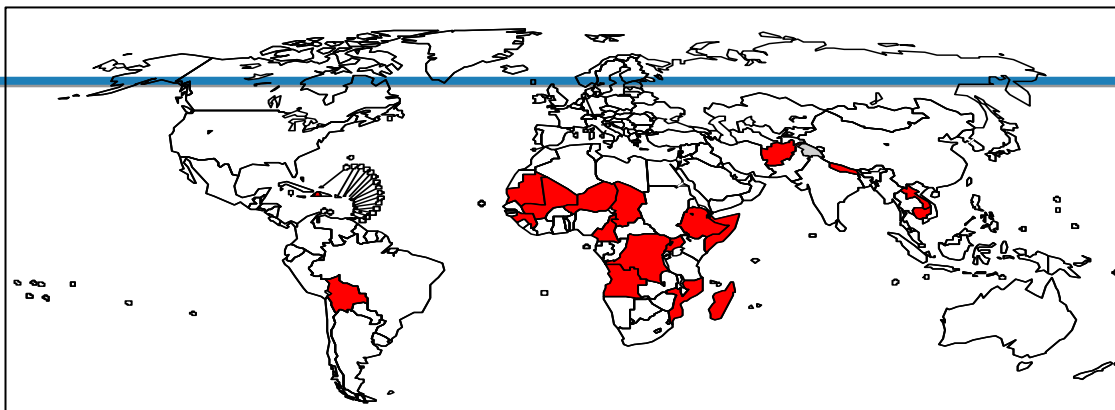
And highlights of WHO activities



World Health
Organization

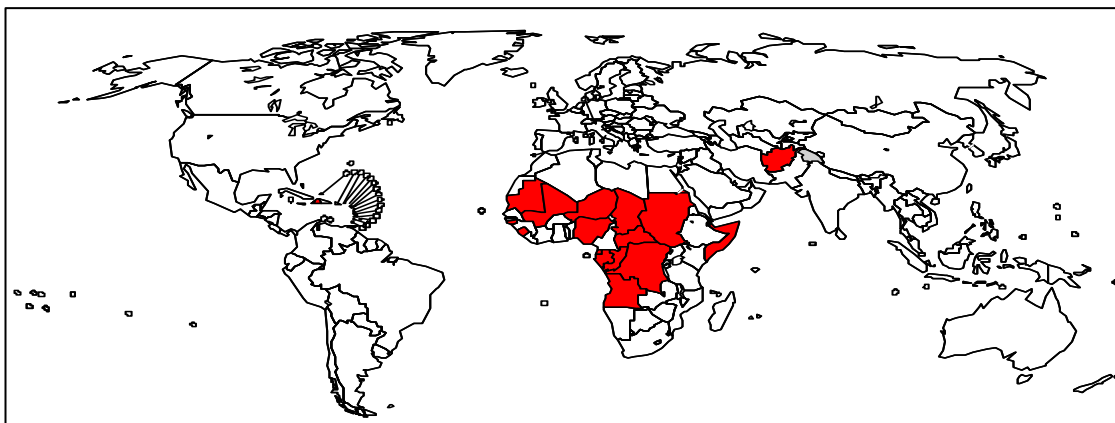
Global Immunization Progress

Countries with DTP3 Coverage below 50%

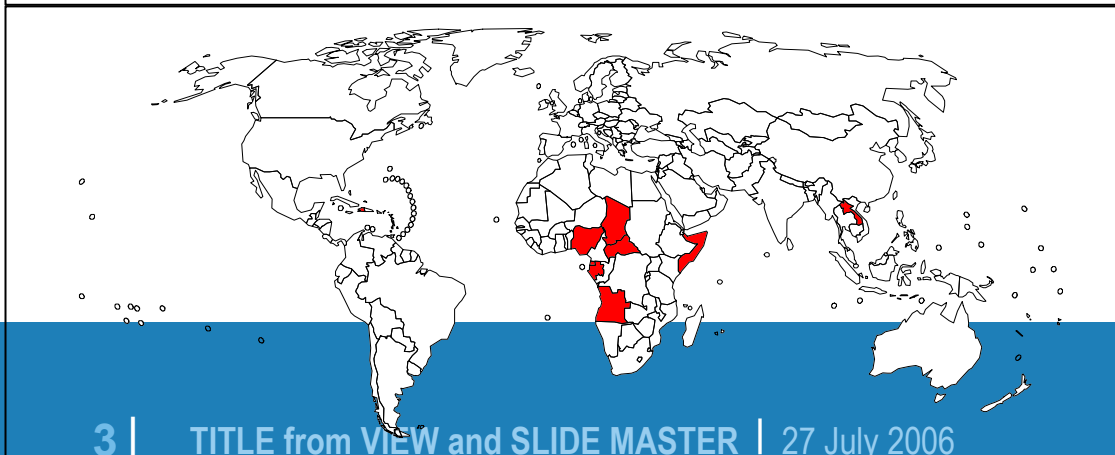


■ DTP3 coverage < 50%

19 countries in 1990

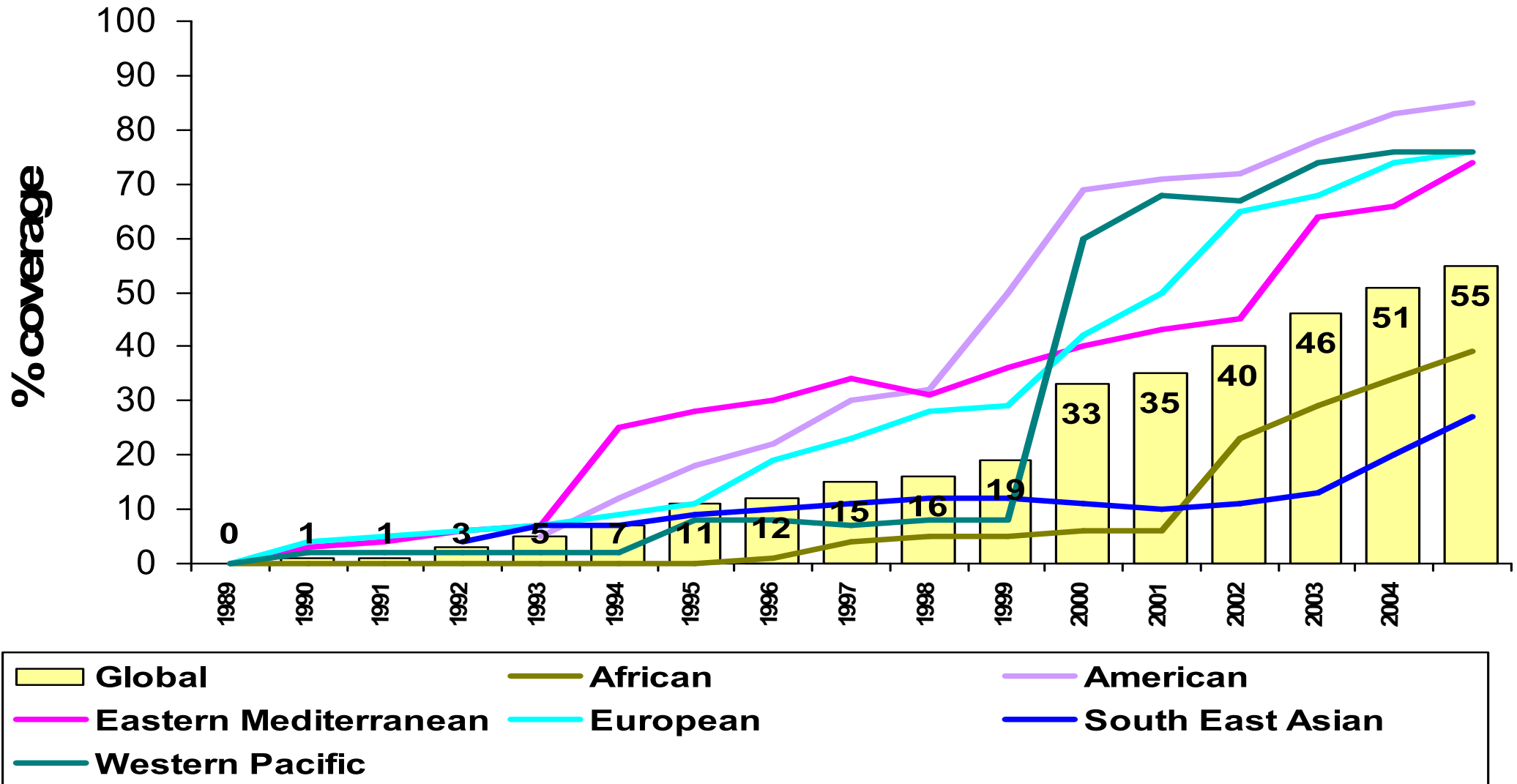


20 countries in 2000



9 countries in 2005

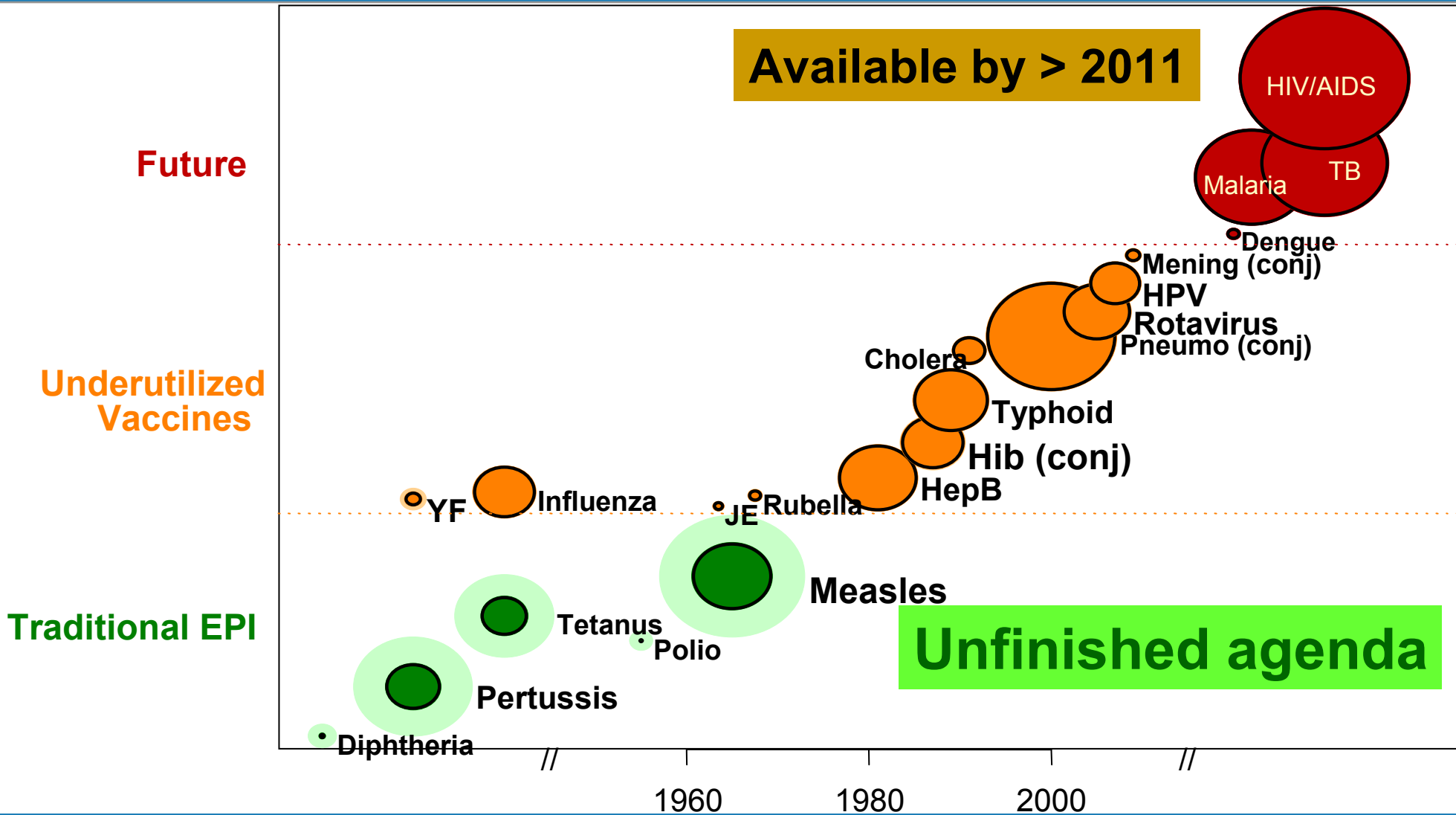
Global Immunization 1989-2005, HepB3 coverage in infants



World Health Organization

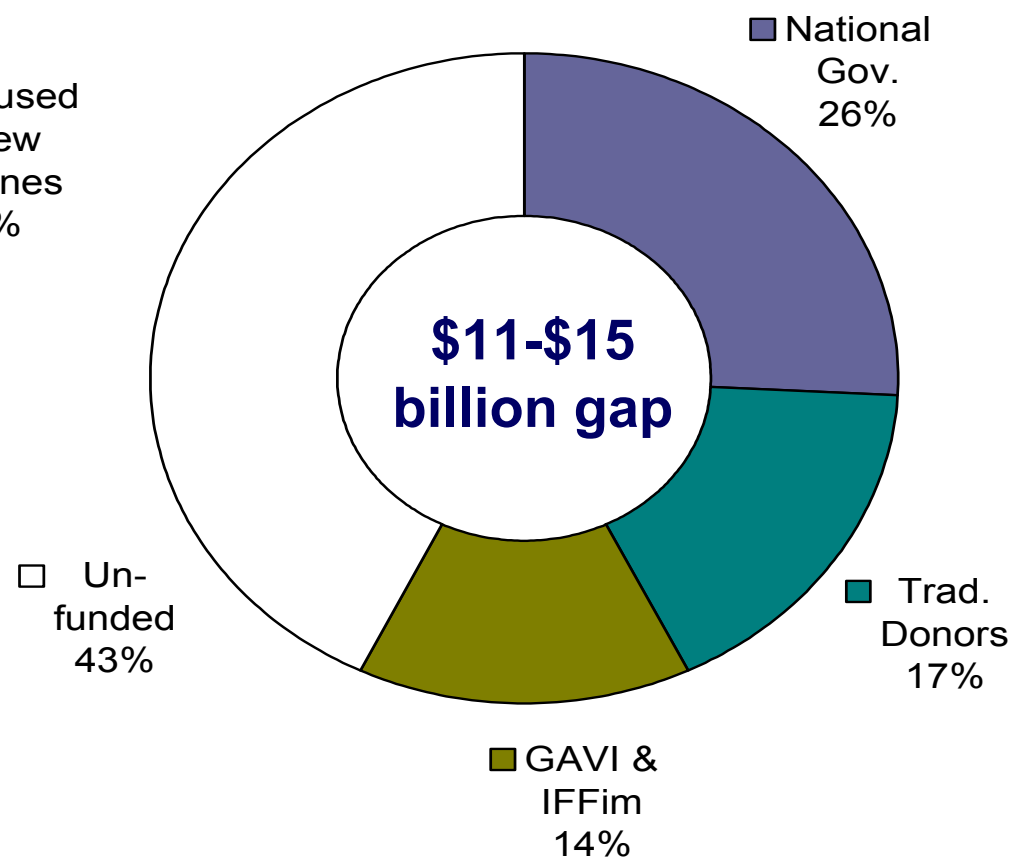
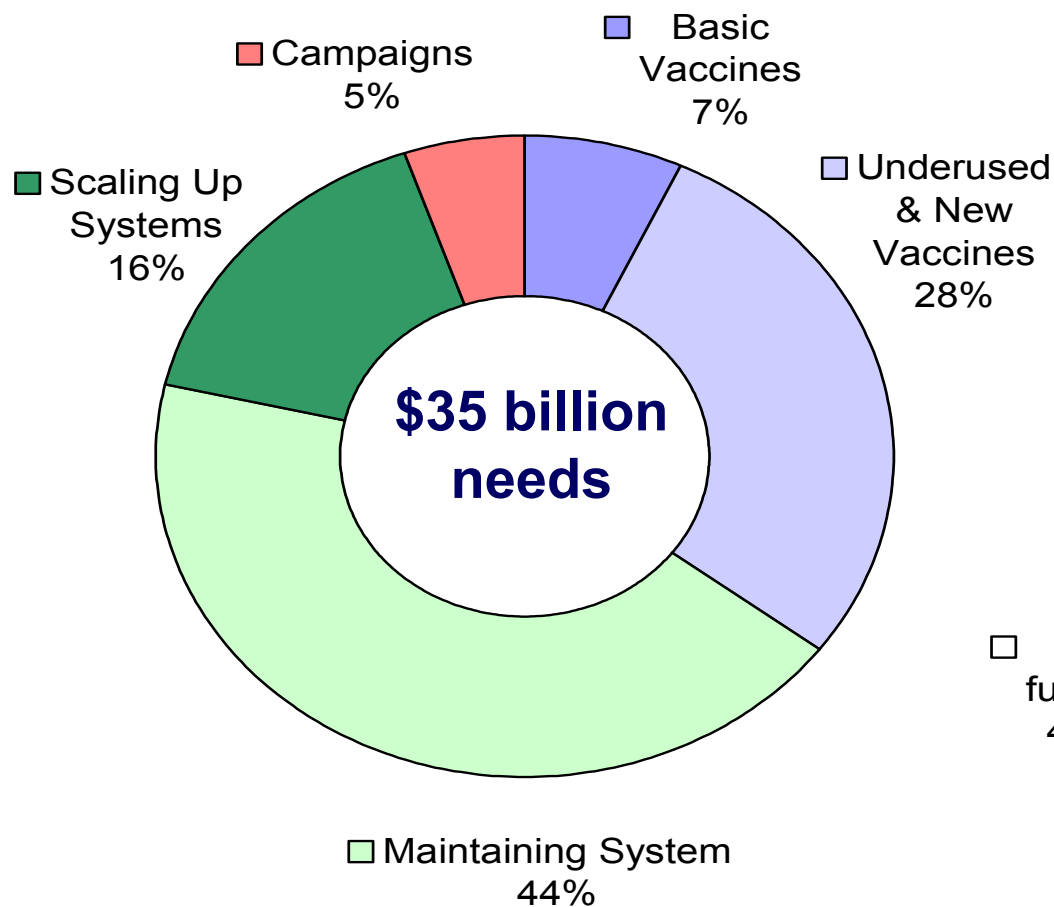


The vaccines pipeline



The Cost of Reaching GIVS goals

- \$11-15 billion funding gap for immunization (2006-2015)



Source: GIVS Costing Analysis (WHO-UNICEF, 2005)



New funding for Immunization through GAVI

- International Finance Facility for Immunization (IFFIm)
 - >\$1Bn raised in November
- Advanced Market Commitments (AMCs)
 - AMC pilot for Pneumo vaccine (1Bn pledged for 1.5Bn total)



Malaria
Tuberculosis
HIV

Malaria Vaccine Development

- Global Strategy
 - Malaria Vaccine Technology Roadmap published and endorsed by major funders of malaria vaccine development
 - **Roadmap to be launched at the GVRF in Bangkok**
- Vaccine candidates
 - RTS,S/AS02 duration of vaccine efficacy (50% against severe disease) is up to 18 months
 - Multi-site pivotal trials of RTS,S planned in 2007-2008
 - Results from "Proof of concept" trials of other leading candidates expected soon
 - Numerous other candidates in Phase 1

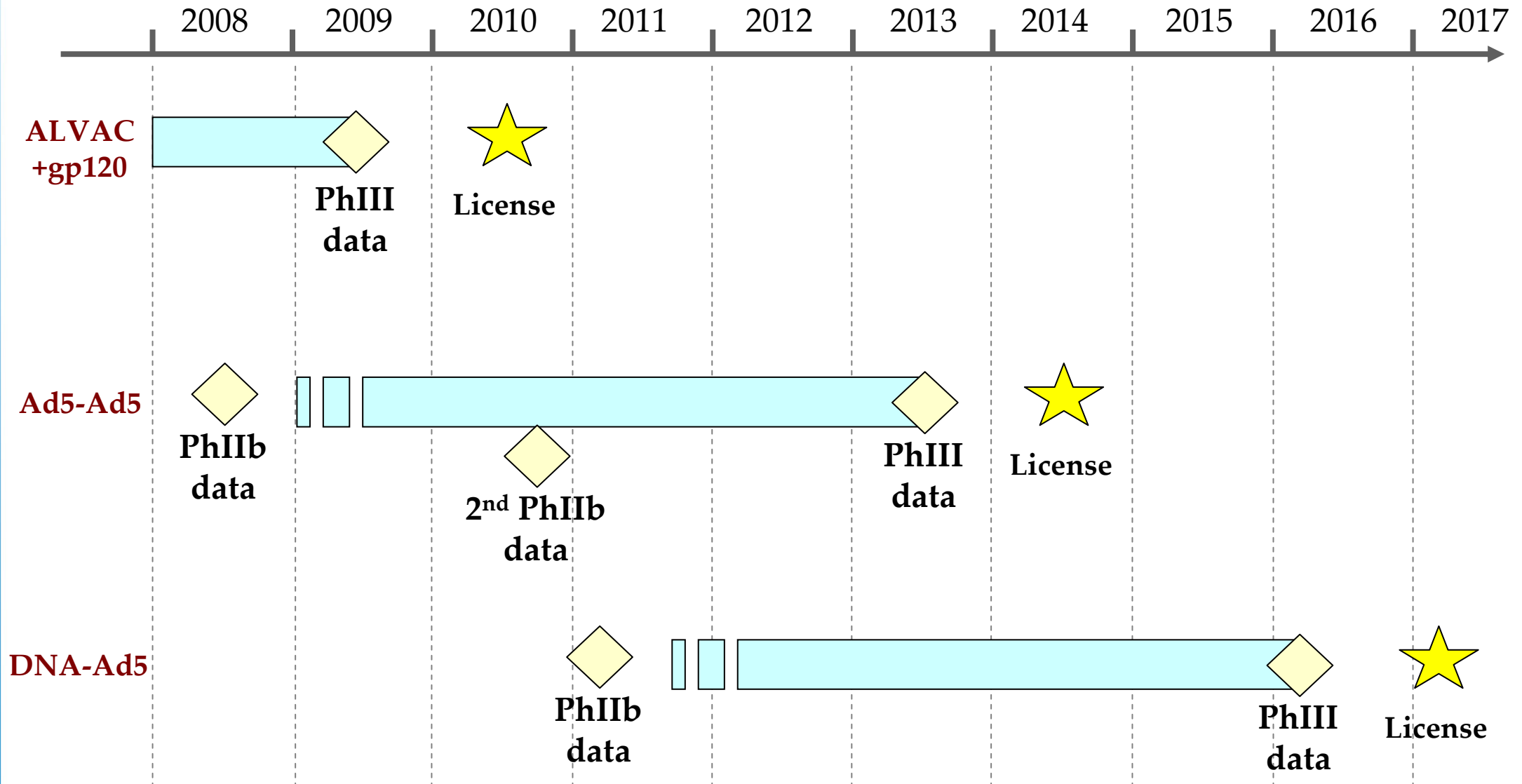


HIV vaccines: Global landscape

- The **2006 G8 Summit** (St Petersburg, Russia) reaffirms high level political support to global efforts to promote the development of HIV vaccines
- US NIH/NIAID establishes the **Centre for HIV Vaccine Immunology (CHAVI)**
- The Bill & Melinda Gates Foundation provides the first grants for the establishment of the **Collaboration for AIDS Vaccine Discovery (CAVD)**
- Growing number of low- and middle-income countries participating in preparation and conduct of **HIV vaccine clinical trials**
- WHO-UNAIDS provides a forum for discussions relevant for the development of **policies, norms and standards** in support of HIV vaccine trials with a special focus on developing countries

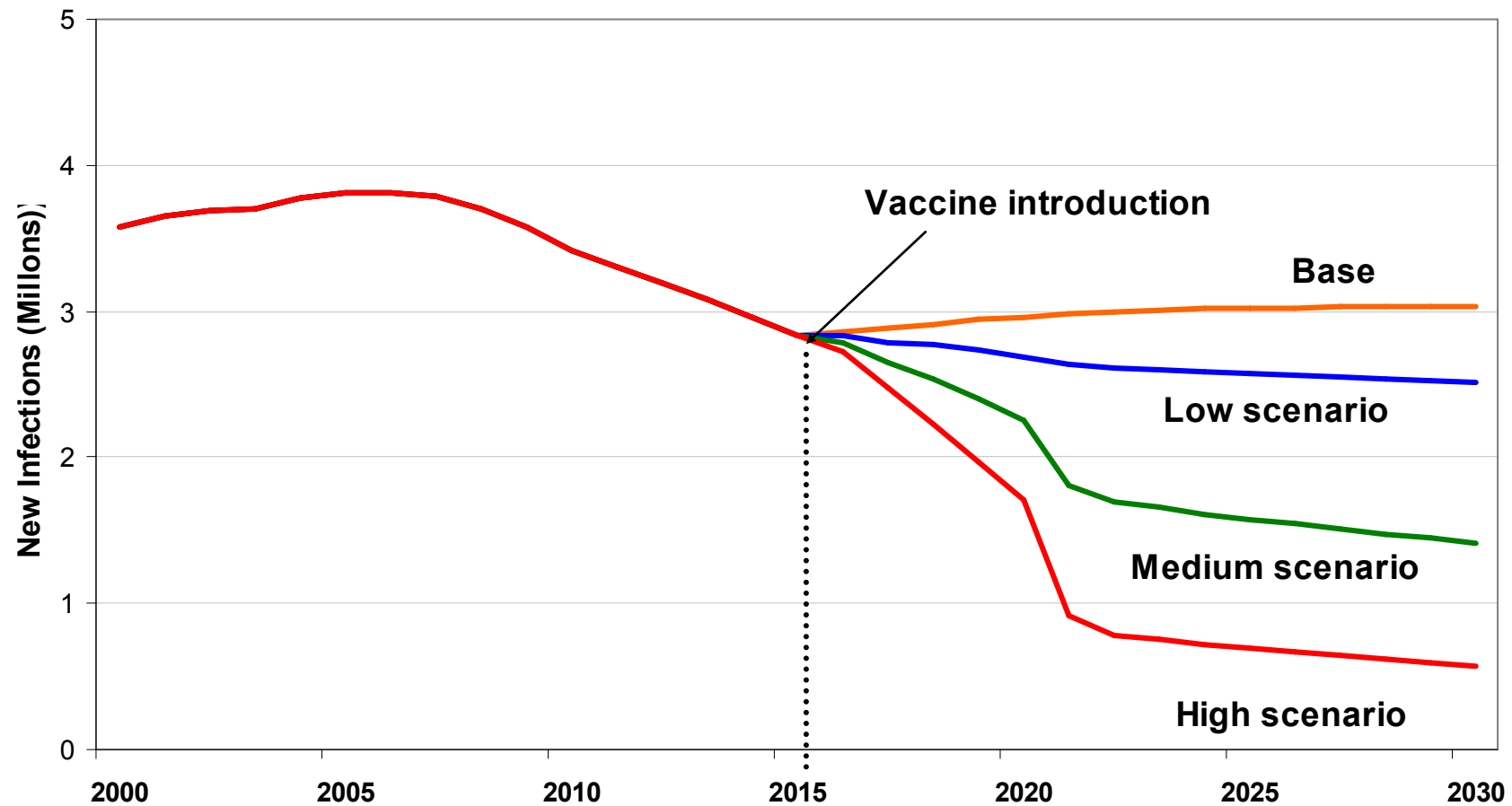


Pending efficacy data & possible licensures



Partial efficacy HIV/AIDS vaccines

New adult HIV infections in low- and middle-income countries



Tuberculosis vaccine development

- **Five vaccine candidates are/have undergone phase 1 clinical trials :**
 - 2 adjuvanted protein subunits
 - 1 MVA-vectored product
 - 1 recombinant adenovirus-35 vector
 - 1 recombinant BCG (abandoned due to regulatory shortcomings)
- **In 2006, the most advanced candidate, MVA85A has entered phase I/II evaluation in South Africa, one of the 22 TB highest-burden countries**
- **Seven more products in the immediate pipeline (1-3 years before entrance into clinical trials)**



Influenza

WHO's Contribution to the Global Action Plan

- Strengthening of NRA for licensing of influenza vaccines
- Capacity building for H5N1 vaccine manufacturing in developing countries
- Systematic evaluation of available technologies
- Contribution to the development of practical antigen dose reduction strategies through clinical trials of intradermal jet-injector delivery methods
- Facilitation of access to potent adjuvants to enhance immunogenicity of vaccines (collaboration with IDRI)
- Regular update on clinical trials of prototype H5N1 vaccines and on R&D for influenza vaccines with broad spectrum and long lasting immunogenicity
- Evaluation of delivery strategies (with UNICEF)



Rotavirus
Pneumococcus
HPV

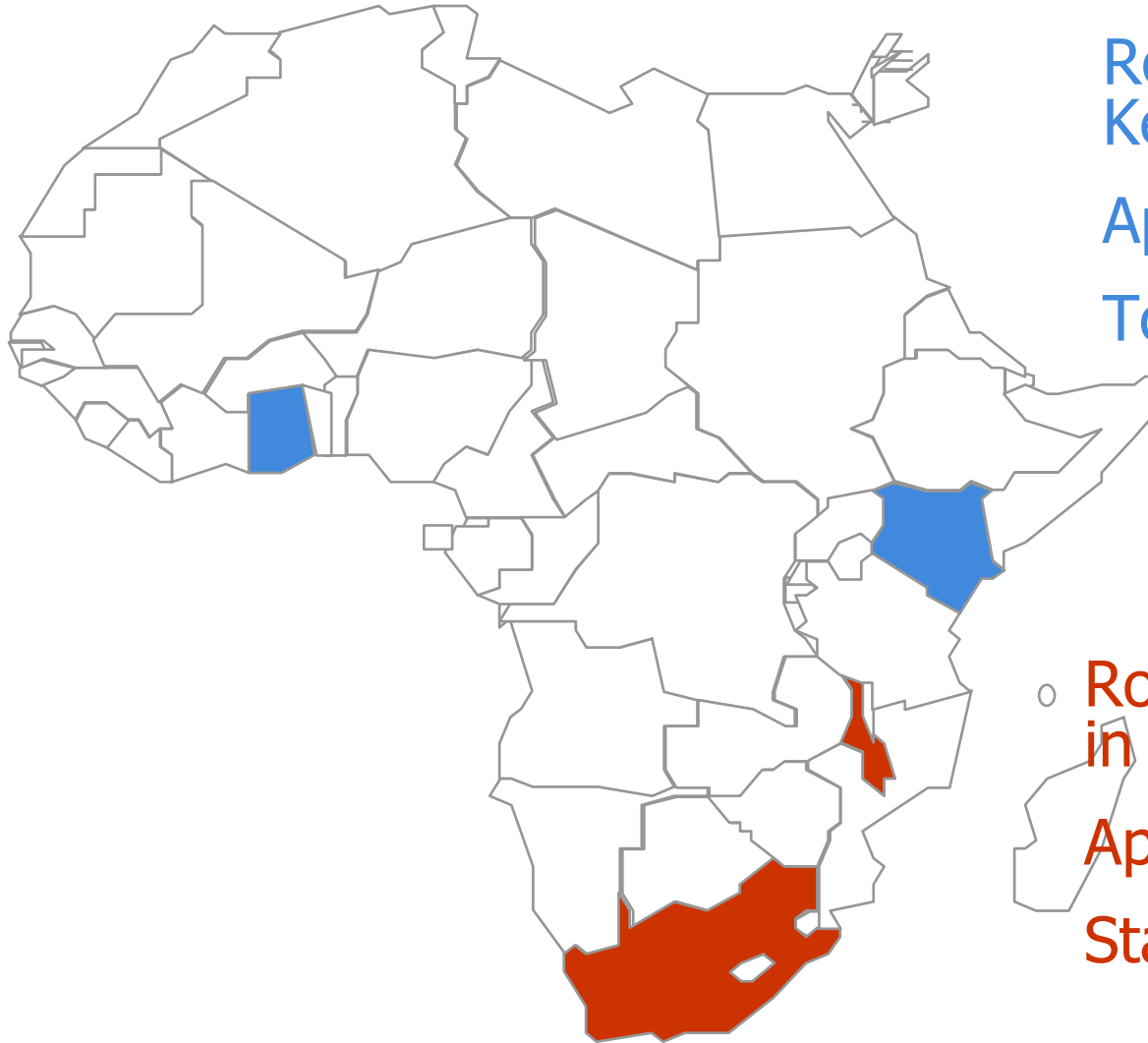
Rotavirus Vaccine Landscape

- Two recently licensed live rotavirus vaccines
- Upstream Rotavirus Vaccine Candidates
 - Reassortant rhesus-human rotavirus strain (BioVirx)
 - Reassortant UK bovine-human strain (NIH license to vaccine producers in Brazil, China and India)
 - Australian neonatal human RV3 strain (QIMR and BioFarma)
 - Indian bovine-human reassortant strains – 116E (USA/Indian consortium - SII)
- Support from the BMGF (UK and 116E)



Rotavirus Vaccine Trials in Africa

WHO collaboration with PATH (2002 – 2009)



RotaTeq® Phase III trials in Kenya and Ghana and 3rd site

Approximately 5,000 infants

To start in 1Q2007

○ Rotarix® Phase III vaccine trials in South Africa and Malawi

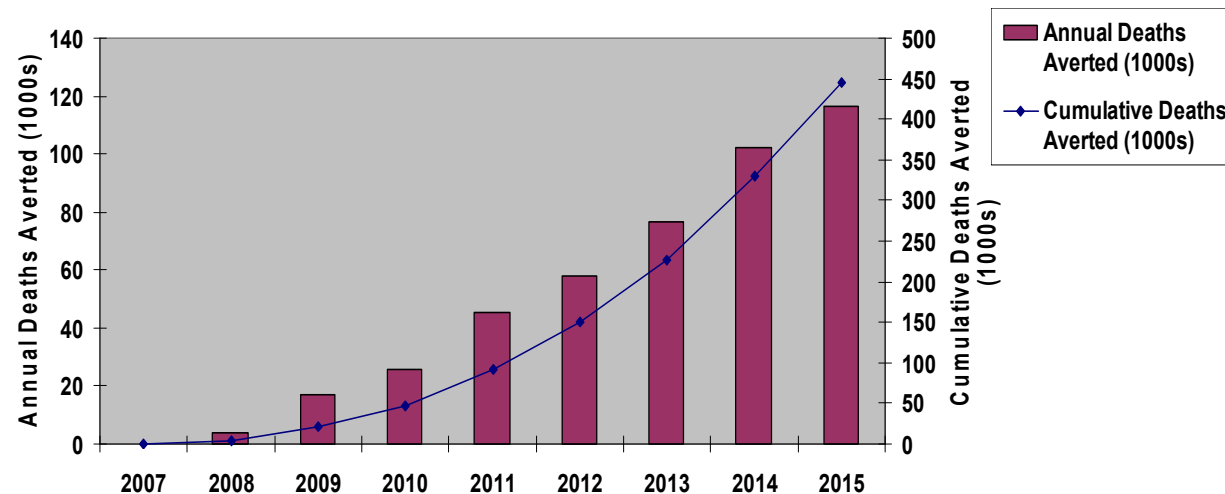
○ Approximately 5,600 infants

○ Started in 2005 (SA) & 2006 (M)

Pneumococcal Vaccines: Global Highlights

- GAVI Alliance Board approved the Investment Case for accelerated introduction of pneumococcal vaccines and ...
- Pneumococcal conjugate vaccines have been chosen for to pilot the Advance Market Commitment (AMC) process.
- PATH finances development protein vaccines, with grant from BMGF
- 11v PCV (TT/DT conjugate)* shows efficacy against radiological pneumonia in Philippines

*further development not planned



HPV/cervical cancer vaccines

- Licensed vaccine: **GARDASIL Merck**
HPV 16, 18 (cervical cancer)
HPV 6, 11 (genital warts)
- Advanced candidate vaccine: **CERVARIX GSK**
HPV 16, 18 (cervical cancer)
Licensing expected during 07



WHO Global HPV Lab Network

Sentinel centres for monitoring HPV DNA and antibody detection



established



Under negotiation



Bacterial enteric diarrhoea

Dengue

New International Enteric Bacterial Initiatives

All funded by the Bill and Melinda Gates Foundation – new synergy of activities

- Aetiology and burden of disease study in multi-centres using similar techniques and methodology (Mike Levine, CVD)
- Cholera Vaccine Initiative (John Clemens, IVI)
- Pre-emptive use of a Cholera Vaccine Stockpile (Marie Paule Kieny, WHO)
- Enteric Vaccines Initiative (still to be awarded)

BMGF Cholera Vaccine Grant to WHO

- WHO currently does not recommend a cholera vaccine stockpile with the only available international vaccine
- Project to learn lessons for future stockpile
 - Develop tools for risk assessment of situation and mass immunization campaigns
 - Examine financing and sustainability of stockpile, revolving stock and replenishment of stock
 - Examine specific research questions
 - Herd protection and specifically in <2 year olds
 - Safety in HIV infected individuals
 - Use in endemic situations for predictable seasonal cholera



Dengue vaccines

- Global developments:
 - Phase 2 pediatric trials with YF-Den chimeras started
 - New tetravalent dengue trials expected soon (CDC & NIH candidates), all live Den/Den recombinants
- WHO emphasis:
 - Measure of immunity to dengue: Neutralization assay guidance document and standard reagents to be available soon
 - New clinical trial guidance document close to completion
 - Support innovative virus attenuation strategies
- Challenges ahead:
 - Manage interference in tetravalent formulations, which also occur in clonal live vaccines
 - Demonstrate efficacy and long-term safety of candidate vaccines



New delivery systems

Global landscape in Vaccine Delivery Systems

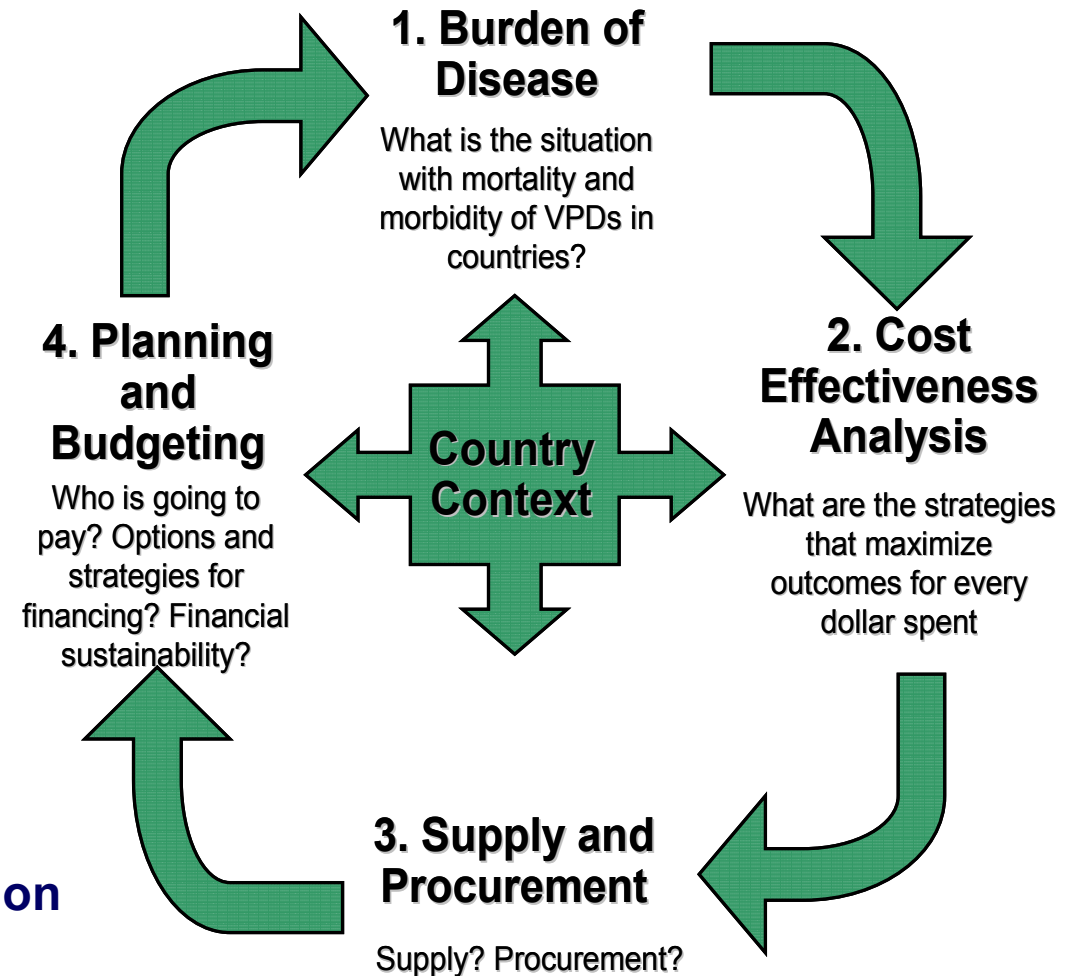
- Adjuvants to enhance immunogenicity
 - For pandemic flu two proprietary adjuvants (MF59 and AS03) shown to significantly increase immunogenicity and permit dose-reduction.
 - The only publicly available potent adjuvant (ISA720) raises safety concerns.
- Vaccine delivery
 - Large volume of formulated rotavirus vaccine places a burden on cold chain storage space.
- Injection
 - Mostly provided with needles and syringes. Needle stick injuries and disease transmission still a potential hazard.
 - Jet-injector ID administration under evaluation for IPV and influenza vaccine

Tools and strategies for decision-making on vaccine introduction

Setting Standards for Evidence-Based Decision Making

- **QUESTION:** Supporting evidence-based decision making for priority setting and implementation of immunization interventions
- **CHALLENGES:** multiplicity of tools that need to be
 - Streamlined
 - Harmonized
 - Ensure adequacy of methods

Evidence Based Decision Making Loop



Covered in other sessions of the GVRF...

- The Measles Aerosol Project (Michel Greco)
- The Global Action Plan to increase supply of pandemic influenza vaccines (Alejandro Costa)
- The Meningitis Vaccine Project (Marc LaForce)
- Japanese encephalitis (December 3 satellite)

