Highlghts in Pediatric Infectious Diseases

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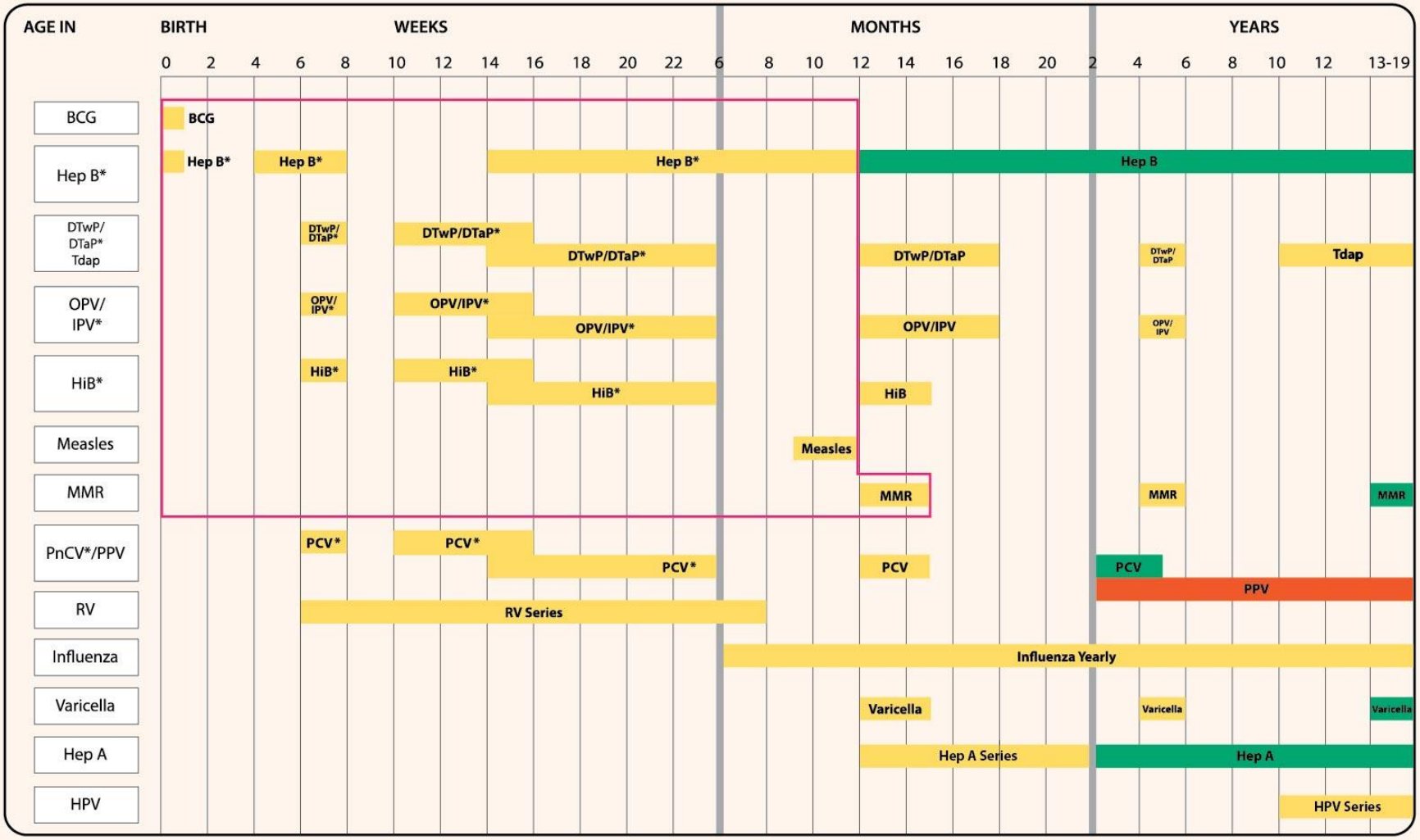
Childhood Immunization Schedule 2012



Disclaimer:

- ***The Childhood Immunization Schedule present recommendations for immunization for children and adolescents based on the knowledge, experience and premises current at the time of publication.***
- ***No claim is made for infallibility, and the PPS, PIDSP and PFV acknowledge that individual circumstances may warrant decisions differing from recommendations given here.***

Disclaimer:

- ***The recommendations are not absolute. Physicians must regularly update their knowledge about specific vaccines and their use because information about safety and efficacy of vaccines and recommendations relative to their administration continue to develop after a vaccine is licensed.***

Childhood Immunization Schedule 2012

Revised as of November 14, 2011

- ***PHILIPPINE EPI VACCINES:***

Vaccines in the pink area, are vaccines given in the Philippine Expanded Program of Immunization (EPI) of the Department of Health. Vaccines in the EPI include:

- ***BCG***
- ***DTwP***
- ***Hepatitis B***
- ***Hib***
- ***Measles***
- ***MMR***
- ***OPV***

Other Recommended Vaccines

- Not part of the Philippine EPI but because of merit are advocated by the PPS, PIDSP and the Philippine Foundation for Vaccination
- These vaccines include:

• DTaP • Hepatitis A • Human Papilloma virus (HPV) • IPV • Influenza	• MMRV • Pneumococcal • Rotavirus • Tdap • Varicella

BCG

- Given intradermally (ID)
- BCG - given at the earliest possible age after birth preferably within the first 2 months of life. For healthy infants and children > 2 months who are not given BCG at birth, PPD prior to BCG vaccination is not necessary. However, PPD is recommended prior to BCG vaccination if any of the following are present:
  - **suspected congenital TB**,
  - **history of close contact to known or suspected infectious cases of TB**,
  - **clinical findings suggestive of TB and/or chest x-ray suggestive of TB**.

  In the presence of any of these conditions, an induration of $\geq$ 5 mm is considered positive.
- The dose of BCG is 0.05 ml for infants < 12 months of age and 0.1 ml for children $\geq$ 12 months of age.

DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTaP)/DTwP:

- Given intramuscularly (IM)
- Given at a minimum age of 6 weeks with a minimum interval of 4 weeks
- The fourth dose may be given as early as 12 months provided there is a minimum interval of 6 months from the third dose. The fifth dose may not be given if the fourth dose was administered at age 4 years or older.

Hepatitis B

- Given intramuscularly (IM).
- 1st dose within the 1st 12 hours of life, and may be counted as part of the 3-dose primary series. Subsequent doses are given at least 4 weeks apart, with the 3rd dose preferably given not earlier than 24 weeks of age.
- **A 4th dose is needed for the following**: (to be administered **not earlier** than 24 weeks of age):
  - If the 3rd dose is given at age < 24 weeks.
  - For patients using the EPI schedule of birth, 6 and 14 weeks.
  - For preterms < 2 kgs whose 1st dose was given at birth
    - Preterm infants born to HBsAg(-) mothers who are medically stable may be given the 1st dose of HBV at 30 days of chronological age regardless of weight, and this can be counted as part of the 3-dose primary series.

- If mother is HBsAg (+), administer HBV and HBIg (0.5mL) within 12 hours of life.
- If HBsAg status is unknown, administer HBV within 12 hours of birth and determine mother's HBsAg
- ASAP if HBsAg (+), administer HBIg no later than 7 days of life.

HAEMOPHILUS INFLUENZAE TYPE B CONJUGATES VACCINE

- Given intramuscularly (IM)
- Given at a minimum age of 6 weeks with a minimum interval of 4 weeks
- If the first dose was given between 7 through 11 months of age, the second dose should be given at least 4 weeks later and the third dose at least 8 weeks from the second dose.
- A booster dose should be given between 12-15 months with an interval of 6 months from the 3rd dose.
- One dose of Hib vaccine should be considered for unimmunized children age 5 years or older who have **sickle cell disease, leukemia, HIV infection, or who had splenectomy.**

MEASLES

- Given subcutaneously (SC)
- Children who received a dose of a measles-containing vaccine at less than 12 months of age should be given **2 additional doses** beginning at 12 through 15 months of age and separated by at least 4 weeks, the latter two preferably as MMR.
- Measles vaccine may be given as early as 6 months of age in cases of outbreaks as declared by public health officials.

MEASLES, MUMPS, RUBELLA (MMR)

- Given subcutaneously (SC)
- Minimum age of MMR is administered at age 12 months. The second dose is administered at age 4 through 6 years but may be administered at an earlier age provided the interval between the first and second dose is at least 4 weeks.
- Children < 12 months of age given any measles-containing vaccine (measles, MR, MMR) should be given 2 additional doses of MMR. The first dose is given at 12 to 15 months of age and should be separated by at least 4 weeks from measles containing vaccine. The second dose is administered at age 4 through 6 years, but may be given at an earlier age provided the interval between the first and second dose is at least 4 weeks.
- Children 12 months or older given any measles-containing vaccine (measles, MR, MMR) should be given one dose of MMR vaccine, separated by at least 4 weeks from the first measles-containing vaccine.

POLIOVIRUS VACCINE (IPV/OPV)

- IPV given intramuscularly (IM) / OPV given per orem
- Given at a minimum age of 6 weeks with a minimum interval of 4 weeks
- The final dose in the series should be given on or after the 4th birthday and at least 6 months after the previous dose. If 4 or more doses have been given prior to age 4 years an additional dose should be administered at age 4 through 6 years.

- If a combination of OPV and IPV are given as part of a series, a total of 4 doses should be administered, regardless of the child's current age.
- If available, IPV is preferred.

TETANUS AND DIPTHERIA TOXOID (Td)/ TETANUS AND DIPTHERIA TOXOIDS AND ACELLULAR PERTUSSIS (Tdap)

- **Given intramuscularly (IM).**
- **In children who are fully immunized*, Td booster doses should be given every 10 years. A single dose of Tdap can be given in place of the due Td dose, and can be administered regardless of the interval since the last tetanus and diphtheria toxoid–containing vaccine**
- **Children and adolescents 7 to18 years of age who are not fully immunized with DPT vaccine should be given a single dose of Tdap. The remaining doses are given as Td.**
- **Children and adolescents 7 to18 years of age who have never been immunized with DPT vaccine should receive the 3-dose series of tetanus-containing vaccine using the 0-1-6 months schedule. A single dose of Tdap is given, preferably as the 1st dose. The remaining doses are given as Td.**

* ***Fully immunized is defined as 5 doses of DTaP or 4 doses of DTaP if the fourth dose was administered on or after the fourth birthday*.**

HEPATITIS A

- Given intramuscularly (IM)
- Hepatitis A vaccine is recommended for all children age ≥12 months. A second dose of the vaccine is given 6 to 12 months after the first dose.

HUMAN PAPILLOMAVIRUS VACCINE (HPV)

- Given intramuscularly (IM)
- Primary vaccination consists of a 3-dose series administered to females 10-18 years of age. The recommended schedule is as follows:
    - Bivalent HPV at 0, 1 and 6 months; Quadrivalent HPV* at 0, 2, and 6 months.
- The minimum interval between the first and second dose is at least one month and the minimum interval between the second and third dose is at least 3 months.

**Use of Quadrivalent HPV in males 10-18 years of age for the prevention of anogenital warts is optional.*

INFLUENZA VACCINE

- Given intramuscularly or subcutaneously (IM/SC)
- All children from 6 months to 18 years should receive influenza vaccine.
- Children 6 months to 8 years receiving influenza vaccine for the first time should receive 2 doses of the vaccine separated by at least 4 weeks. If only one dose was administered during the previous influenza season, administer 2 doses of the vaccine then one dose yearly thereafter.
- In October 3, 2011 WHO recommended using the same 3 influenza strains in next year's Southern Hemisphere vaccine. These are the current strains as in the Northern Hemisphere vaccine.

INFLUENZA VACCINE

- Because the strains in the 2012 influenza vaccine have not changed from the previous season, it is recommended that children age 6 months to 8 years who received at least one dose of the 2011 vaccine will require only one dose of the 2012 vaccine.
- Children who received a single dose of influenza vaccine for 2 consecutive years should continue receiving single annual doses.
- Annual vaccination should preferably be given between February to June, but maybe given throughout the year.

MEASLES, MUMPS, RUBELLA, VARICELLA (MMRV)

- Given subcutaneously (SC)
- Combination MMRV may be given as an alternative to separately administered MMR and Varicella vaccine for healthy children 12 months to 12 years of age. A second dose of MMRV is administered at 4-6 years or at an earlier age provided the interval between the first and the second dose is at least 3 months.

PNEUMOCOCCAL VACCINES (PCV/PPV)

- **Given intramuscularly (IM)**
- **The minimum age for Pneumococcal Conjugate Vaccine (PCV) is 6 weeks and for Pneumococcal Polysaccharide Vaccine (PPV) is 2 years.**
- **A single dose of PCV is recommended for all healthy children ages 2 to 5 years with any incomplete PCV schedule.**
- **For healthy children, no additional doses of PPV are needed if the PCV series is completed. PPV is recommended for high risk children >2 years of age in addition to PCV. PPV should be administered at least 8 weeks after PCV.**

ROTAVIRUS VACCINE (RV)

- Given per orem (po)
- The monovalent human rotavirus vaccine (RV1) is given as a two-dose series with the first dose administered beginning at 6 weeks of age and the second dose administered not later than 24 weeks of age.
- The pentavalent human bovine rotavirus vaccine (RV5) is given as a three-dose series with the first dose given between 6 weeks to 14 weeks of age and the third dose administered not later than 32 weeks of age.
- The minimum interval between doses is 4 weeks.
- There is insufficient data on efficacy and safety of rotavirus vaccines given in older age groups.

January 10, 2012

- The Philippines will begin vaccinating children against rotavirus in 2012
- First Southeast Asian nation to implement WHO 2009 recommendation.
- Another rotavirus vaccine milestone was reached today, as the Philippines became the first country in SEA to implement the WHO recommendation to introduce life-saving rotavirus vaccines through its NIP for Filipino children and the nation's healthcare resources
- During the 13th Asian Conference on Diarrheal Disease and Nutrition (ASCODD) in Manila, Health Secretary Enrique T. Ona announced that the Philippines will introduce rotavirus vaccines with an initial focus on children living in the poorest communities, which have the highest child morbidity and mortality rates from diarrheal diseases

VARICELLA VACCINE

- Given subcutaneously (SC)
- The first dose of the vaccine is administered from age 12-15 months. The second dose of the varicella vaccine is administered at 4-6 years or at an earlier age provided the interval between the first and the second dose is at least 3 months. **A second dose of the vaccine is recommended for children, adolescents, and adults who previously received only one dose of the vaccine.**
- All individuals age ≥13 years and without previous evidence of immunity should receive 2 doses of varicella vaccine given at least 4 weeks apart.

VACCINES FOR SPECIAL GROUPS:

- **These are vaccines which are not part of the Philippine EPI or Other Recommended Vaccines but available data support its use in certain conditions or in selected populations. Vaccines for Special Groups include**:
- Meningococcal
- Rabies
- Typhoid

Philippines: Policymakers' views on Dengue fever/DHF and the need for a dengue vaccine

- National Health Priority
  - Top health priorities in the Philippines
    - Tuberculosis
    - Pneumonia
    - Diarrhea
    - Rabies
  - Dengue
    - Considerable media attention given to Dengue outbreaks
    - Disease strikes urban areas
    - Public and Media view Dengue as a government problem and responsibility -> political issue

Source: Vaccine 22 (2003) 121-129.

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Challenges for Dengue Vaccine R & D: why it has been so difficult?

- **4 different serotypes**
  - Technical difficulties
  - Inter-serotype competition
  - Need for balanced protection against all four serotypes
- **There is no animal model for the disease**
- **Theoretical risk of immunopotentiation after sequential infections (antibody-dependent enhancement - ADE) : need for a combined tetravalent vaccine**

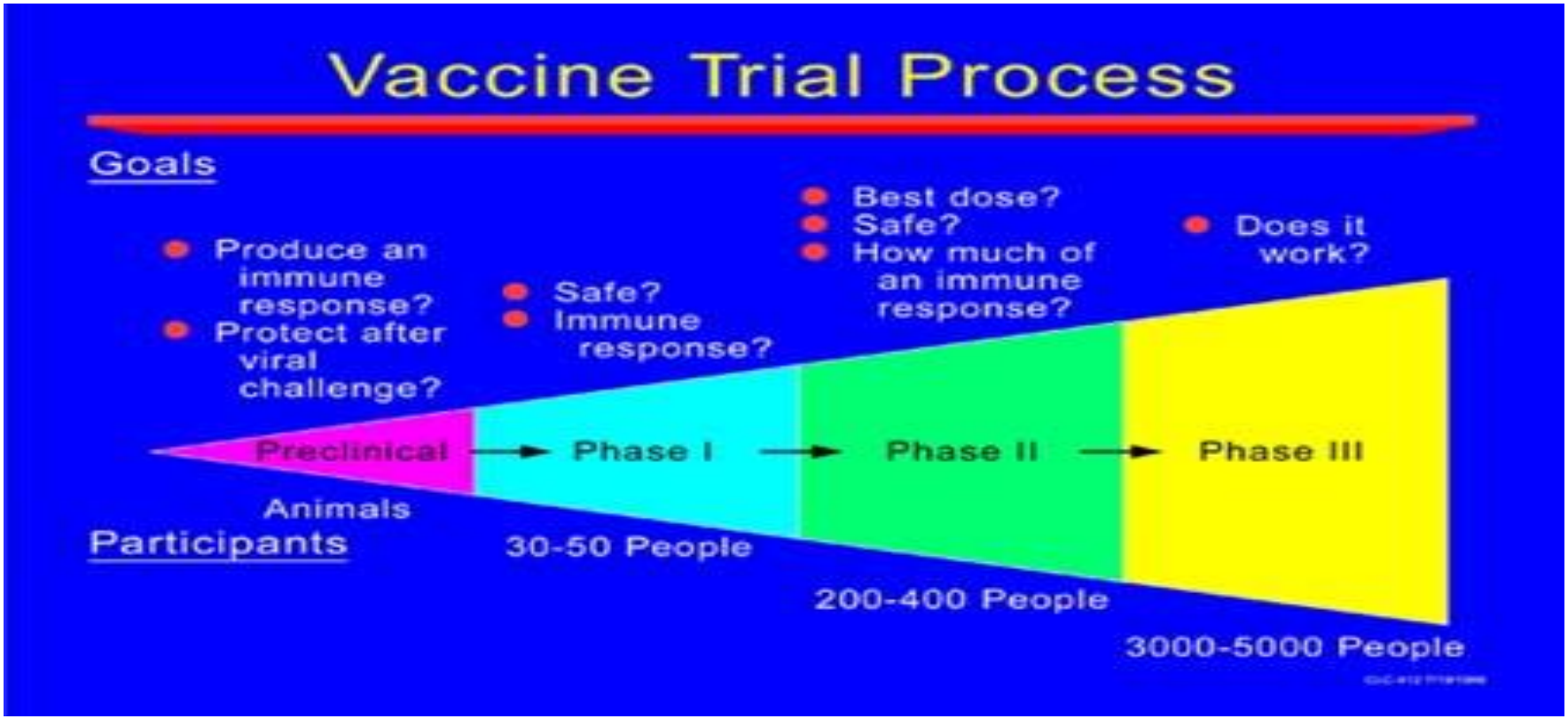
Dengue Vaccine

- Clinical Development: Sp Dengue candidate vaccine first one to enter Phase III clinical trial
  - High seroconversion rate against all 4 sero-types
  - Good safety profile
  - Phase IIb study ongoing in Thailand
  - Other ongoing trials in endemic regions in all age groups

- Availability of the vaccine foreseen in next 3 to 5 years
- New production facility
  - 100m + dose capacity
  - Bulk facility planned to be on line by 2014

Dengue Facility Under Construction
in Neuville, France

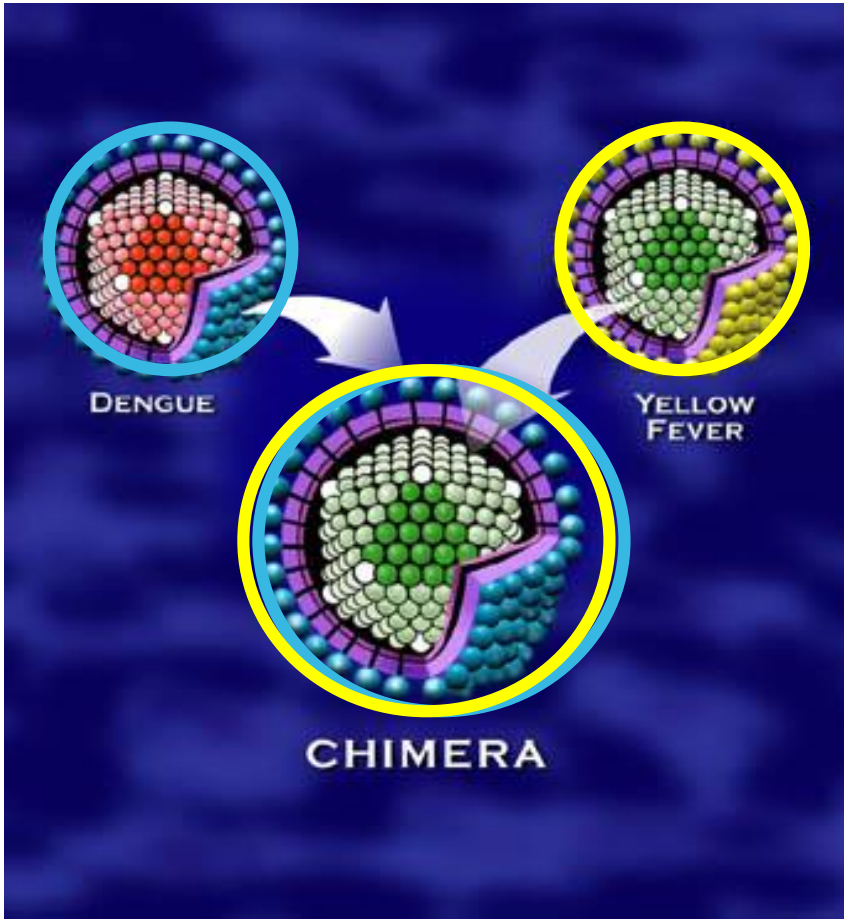
Clinical development plan



- **Phase I clinical results**
- **Phase II clinical results to date**
- **Phase III studies**

Sanofi Pasteur Tetravalent Dengue Vaccine Candidate

- **Molecular biology- based technology (Chimerivax™) licensed-in from former Acambis, Cambridge, USA in 1998***
- **Four live attenuated Dengue viruses with genes encoding for envelope protein of dengue (Pr-M and E) and the non structural and capsid protein of the 17D Yellow Fever vaccine strain.**



Dengue Vaccine Candidate's Current Company Target

Product Profile

Description:
Live attenuated virus, tetravalent
(4 vaccinal strains cultured in serum free Vero cells)

Pharmaceutical form:
Powder and solvent for suspension for injection (0.5 ml)

Route of administration:
Sub-cutaneous

Schedule:
3 injections 0 - 6 - 12 months

Dengue Vaccine Candidate's Current Company Target Product Profile

Indication:
Prevention of symptomatic dengue disease
- covering the spectrum from Dengue Fever to severe Dengue cases due to serotypes 1, 2, 3 or 4.

Populations:
Children - 9 months of age and adults living in endemic areas, people working in (traveling to) endemic areas

Priority:
Endemic countries (Asia/Pacific, Latin America, Caribbean)

Completed clinical trials

Code	dengue vaccine	Population	country	Status
CYD01	Monovalent Den-2 (3&5 log10 PFU)	Adults (18-40 yo) n=56	USA	Completed
CYD02	Tetravalent (4 log10 TCID50/ serotype)	Adults (18-40 yo) n=99	USA	Completed
CYD04	Tetravalent (5 log10 TCID50/ serotype)	Adults (18-45 yo) n=66	USA	Completed
CYD05	Tetravalent (5 log10 TCID50/ serotype)	Adults (18-45 yo) Adolescents (12-17 yo), Children (2-11 yo) n=126	Philippines	Long term follow-up on-going
CYD06	Tetravalent (5 log10 TCID50/ serotype)	Adults (18-45 yo) Adolescents (12-17 yo), Children (2-11 yo) n=126	Mexico	Completed
CYD10	Tetravalent (5 log10 TCID50/ serotype)	Adults (18-40 yo) (DIV12 Trial subjects, VDV1, VDV2 or YF primed) Max n=48	Australia	Completed

Summary of Results :
Phase II Clinical trials

- **Immunogenicity**
  - **Balanced immune response against all 4 serotypes after 3 doses of tetravalent Dengue vaccine**
  - **Higher immune responses observed in children**
  - **Previous flavivirus vaccination has a priming potential**
  - **Booster effect in people previously exposed to wild type dengue**
  - **Stepwise increase of seropositivity rates against each serotype with 3 dose**

Summary of Results :
Phase II Clinical trials

- **Safety**
  - **Reactogenicity profile comparable to control vaccines**
  - **No safety signal with the ongoing Phase II studies, including CYD 23 and CYD 28:**
    - **>5,000 subjects have received ≥ 1 dose (half 2-11 years in endemic countries)**
    - **and > 3,000 subjects have received 2nd dose.**

- *…largely confirming Phase I findings*


Thank You