P6: New Vaccine Updates - Universal Flu, Group A Strep and Schistosomiasis

Preferred Product Characteristics

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PATH

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World Health Organization

BILL & MELINDA GATES foundation

NIH National Institute of Allergy and Infectious Diseases

Background

Global Vaccine and Immunization Research Forum

March 4 - 6, 2014

Hyatt Regency Bethesda, Maryland, USA

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Target Product Profiles

Attribute
Indication
Target Populations(s)
Route of Administration
Product presentation
Dosage schedule
Warnings&Precautions/ Pregnancy & Lactation
Expected Efficacy
Safety Profile
Concomitant use
Shelf-life
Storage
Product registration WHO PreQualification
Demand Forecast
Manufacturing Capacity
COGS
Logistics

- WHO Preferred Product Characteristics (PCCs) were presented at GVIRF 2014 as an element of high level roadmap for vaccine R&D based on public health needs
- It was agreed that WHO's PPC concept is a promising approach to stimulate vaccine development for priority diseases in early development

http://www.who.int/immunization/research/forums_and_initiatives/06_Workshop2_PPC.pdf

PPCs are WHO document

- Pathogen-specific (not product-specific)
- Provide pre-Proof-of-Concept guidance in early stage vaccine R&D (e.g., 5-10 years before licensure):
  - For products that meet priority public health needs with a focus on low and middle income countries
  - For vaccine manufacturers and funding agencies in refining their product development plans
- Clarifies the World Health Organization's preferences with regard to many criteria that form part of Target Product Profiles, particularly:
  - Indication
  - Target populations
  - Safety and efficacy data to be generated in clinical trials
  - Possible immunization strategies

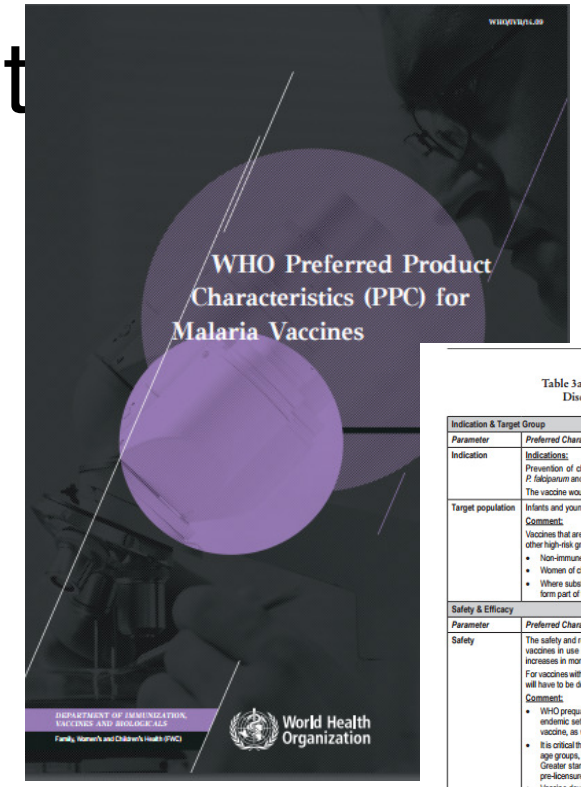


Table 3a: Preferred Product Characteristics: Disease-Reducing Malaria Vaccines

Indication & Target Group	
Parameter	*Preferred Characteristic*
Indication	Indications: Prevention of clinical malaria, including manifestations of severe malaria. caused by either *P. falciparum* and/or *P. vivax*. The vaccine would be indicated primarily for malaria disease control, rather than elimination.
Target population	Infants and young children aged 5 years and under, in most settings Comment: Vaccines that are highly effective at preventing clinical malaria (>75%) can be considered for use in other high-risk groups (depending on available efficacy and safety data in this population) such as:- • Non-immune individu als migrating to, or living temporarily in, areas of malaria transmission. • Women of child-bearing age and pregnant women living in areas of malaria transmission • Where substantial disease burden occurs in children aged over 5 years or adults, these also form part of the target population
Safety & Efficacy	
Parameter	*Preferred Characteristic*
Safety	The safety and reactogenicity of the vaccine is comparable to or better than WHO recommended vaccines in use in low and middle-income countries. Data should allow assessment of deferred increases in morbidity as vaccine-induced immunity wanes. For vaccines within the EPI schedule, absence of clinically important interference with EPI vaccines will have to be documented. Comment: • WHO prequalification and policy recommendations include risk-benefit assessment in malaria endemic settings and safety will be assessed in the context of the data on benefit for each vaccine, as well as risk. • It is critical that clinical studies include high quality data on safety in the relevant populations and age groups, with reporting according to international standards and accepted case definitions. Greater standardisation of data collection and reporting of safety and reactogenicity data in pre-licensure clinical trials is strongly encouraged. • Vaccine developers and vaccine financing agencies are referred to the Global Vaccine Safety Initiative (GVSI). Pharmacovigilance systems strengthening is a high priority as outlined in the GVSI and thus consideration of safety data generation as part of Phase 4 studies and pharmacovigilance systems is strongly encouraged.
Efficacy	The vaccine should reduce incidence of all clinical malaria episodes by at least 75% for no less than one year and preferably at least two years. Booster doses should be required no more frequently than annually. The duration of protection is as important as the short-term efficacy for the primary target group of children under the age of 5 years in medium to high transmission malaria endemic countries. Thus, the initial efficacy and duration of protection will be considered together. Clinical data should allow assessment of the requirement for and timing of booster doses. The public health impact, in terms of cases averted, will be an important element in the public health assessment. Baseline incidence of disease and the vaccine efficacy taken together yield the cases averted. The following efficacy measures are recommended:- • Primary efficacy measure: incidence of all episodes of clinical malaria. • See section 2b for further guidance
Registration & Prequalification	
Parameter	*Preferred Characteristic*
Registration and Prequalification	The vaccine should be WHO pre-qualified according to the process outlined in *Procedures for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies* (WHO/BS/10.2155).

http://apps.who.int/iris/bitstream/10665/149822/1/WHO_IVB_14.09_eng.pdf?ua=1

PPCs are not

- Are not product-specific
  - Although can be seen as a precursor for product-specific Target Product Profiles (TPPs) and Product Inserts
- Do not specify minimally acceptable criteria
- Are not static exit criteria
  - Updated if necessary at least every 5 years
- In no way replace:
  - WHO policy recommendation(s) (e.g., by SAGE)
  - WHO Vaccine Presentation and Packaging Advisory Group (VPPAG)
  - WHO pre-qualification process
- Do not cover topics considered by other WHO entities
  - Programmatic suitability (PSPQ)
  - Vaccine presentation
  - Thermostability
  - Formulation
  - Packaging
  - Disposal
  - etc.

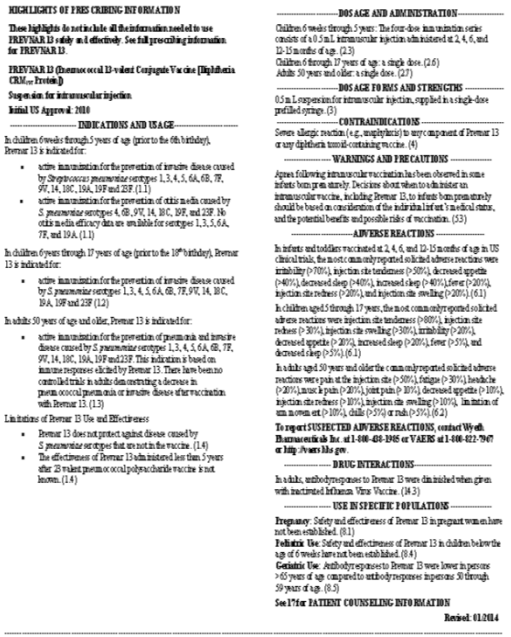
Guidance for Industry and Review Staff

Target Product Profile — A Strategic Development Process Tool

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Attribute	Desired	Minimum
Indication	•	
Target Populations(s)	•	•
Route of Administration	•	•
Product presentation	•	•
Dosage schedule	•	•
Warnings &Precautions/ Pregnancy & Lactation	•	•
Expected Efficacy	•	•
Safety Profile	•	•
Concomitant use	•	•
Shelf-life	•	•
Storage	•	•
Product registration WHO PreQualification	•	•
Demand Forecast	•	•
Manufacturing Capacity	•	•
COGS	•	•
Logistics	•	•



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PREVNAR 13 safely and effectively. See full prescribing information for PREVNAR 13.

PREVNAR 13 (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein])

Suspension for intramuscular injection

Initial US Approval: 2010

INDICATIONS AND USAGE

In children 6 weeks through 5 years of age (prior to the 6th birthday), Prevnar 13 is indicated for:

- active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. (1.1)
- active immunization for the prevention of otitis media caused by *S. pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. No otitis media efficacy data are available for serotypes 1, 3, 5, 6A, 7F, and 19A. (1.1)

In children 6 years through 17 years of age (prior to the 18th birthday), Prevnar 13 is indicated for:

- active immunization for the prevention of invasive disease caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. (1.2)

In adults 50 years of age and older, Prevnar 13 is indicated for:

- active immunization for the prevention of pneumonia and invasive disease caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. This indication is based on immune responses elicited by Prevnar 13. There have been no controlled trials in adults demonstrating a decrease in pneumococcal pneumonia or invasive disease after vaccination with Prevnar 13. (1.3)

Limitations of Prevnar 13 Use and Effectiveness

- Prevnar 13 does not protect against disease caused by *S. pneumoniae* serotypes that are not in the vaccine. (1.4)
- The effectiveness of Prevnar 13 administered less than 5 years after 23-valent pneumococcal polysaccharide vaccine is not known. (1.4)

DOSAGE AND ADMINISTRATION

Children 6 weeks through 5 years: The four-dose immunization series consists of a 0.5 mL intramuscular injection administered at 2, 4, 6, and 12-15 months of age. (2.3)
Children 6 through 17 years of age: a single dose. (2.6)
Adults 50 years and older: a single dose. (2.7)

DOSAGE FORMS AND STRENGTHS

0.5 mL Suspension for intramuscular injection, supplied in a single-dose prefilled syringe. (3)

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) to any component of Prevnar 13 or any diphtheria toxoid-containing vaccine. (4)

WARNINGS AND PRECAUTIONS

Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including Prevnar 13, to infants born prematurely should be based on consideration of the individual infant's medical status, and the potential benefits and possible risks of vaccination. (5.3)

ADVERSE REACTIONS

In infants and toddlers vaccinated at 2, 4, 6, and 12-15 months of age in US clinical trials, the most commonly reported solicited adverse reactions were irritability (>70%), injection site tenderness (>50%), decreased appetite (>40%), decreased sleep (>40%), increased sleep (>40%), fever (>20%), injection site redness (>20%), and injection site swelling (>20%). (6.1)

In children aged 5 through 17 years, the most commonly reported solicited adverse reactions were injection site tenderness (>80%), injection site redness (> 30%), injection site swelling (>30%), irritability (>20%), decreased appetite (> 20%), increased sleep (>20%), fever (>5%), and decreased sleep (>5%). (6.1)

In adults aged 50 years and older the commonly reported solicited adverse reactions were pain at the injection site (>50%), fatigue (>30%), headache (>20%), muscle pain (>20%), joint pain (> 10%), decreased appetite (>10%), injection site redness (>10%), injection site swelling (>10%), limitation of arm movement (>10%), chills (>5%) or rash (>5%). (6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Wyeth Pharmaceuticals Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

DRUG INTERACTIONS

In adults, antibody responses to Prevnar 13 were diminished when given with inactivated Influenza Virus Vaccine. (10.3)

USE IN SPECIFIC POPULATIONS

Pregnancy: Safety and effectiveness of Prevnar 13 in pregnant women have not been established. (8.1)
Pediatric Use: Safety and effectiveness of Prevnar 13 in children below the age of 6 weeks have not been established. (8.4)
Geriatric Use: Antibody responses to Prevnar 13 were lower in persons >65 years of age compared to antibody responses in persons 50 through 59 years of age. (8.5)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 01/2014

PPC /TPP as Driver of Vaccine Product Development

Preferred Product Characteristics

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Storage	•	•
Product registration WHO PreQualification	•	•
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Product Insert

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In adults 50 years of age and older, Prevnar 13 is indicated for:

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