

The concept and status of Full Public Health Value Propositions (FPHVP) for Vaccines

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Universal health coverage (UHC) is a public health imperative



- At least half of the world's population do not have full coverage of essential health services.
- About 100 million people are still being pushed into extreme poverty (living on \$ 1.90 or less a day) because they have to pay for health care.
- Over 800 million people (almost 12% of the world's population) spend at least 10 percent of their household budgets on health care.
- > The development of new vaccines for infectious diseases and improved access to existing vaccines are fundamental pillars to achieving UHC

WHO's IVR develops guidance to accelerate development, licensure, and uptake of vaccines in LMICs



Research & Development

Translational gap

Licensure

Introduction gap

Uptake

Needs and preferences for LMIC countries must be clearly articulated and included early in vaccine product development and implementation research, to support an eventual policy recommendation



Mind the gap: jumping from vaccine licensure to routine use The Lancet 387: 1887 – 1889, 2016

WHO Preferred Product Characteristics (PPCs) seek to broaden the scope of Target Product Profiles (TPPs) to incorporate LMIC needs



Parameter	WHO PPC	TPP
Focus	Pathogen-specific	Product candidate-specific
Content	Describes preferences for LMICs	Sets minimal criteria for development
Purpose	Encourage innovation, broaden vaccine target populations	Guide investment decision-making
Audience	Entities seeking eventual WHO PQ/LMIC market	Stakeholders interested in return on investment
Criteria defined	Describes only preferences	Describes minimal and ideal ranges
Process of development	Public health stakeholder consultation	Within institutions

Inter-relationship of WHO vaccine development guidance from early development to licensure



Preferred Product Characteristics describe vaccine preferences

Pathogen-specific guidance for LMIC use

PPC:

Indication, target population, schedule, efficacy target, route of admin....

gPPP:

Formulation, primary container, packaging

generic Preferred Product **Profile** describes presentation and packaging preferences

Developed by Vaccine Presentation

and Packaging Advisory Group (VPPAG)

Roadmaps and pathway consultations facilitate how to achieve PPCs



IVR guidance to inform product development of pipeline vaccines for LMIC contexts



Pathogen-specific documents developed by WHO's PDVAC	Purpose/description
Full public health value proposition (FPHVP) (proposal)	Describes the full health, economic and societal value of a vaccine to a broad range of global stakeholders, including from a LMIC perspective, and aims to articulate the full direct (individual) and indirect (population) effects of a vaccine
Preferred product characteristics (PPC)	Describe preferred characteristics for vaccines with emphasis on the LMIC use context
Vaccine R&D roadmap	Provides a high-level vision, near and long term goals, and strategic framework of priority activities
Considerations for product development pathways	Considers the manufacturing, clinical development, regulatory, policy and commercialization pathways and barriers

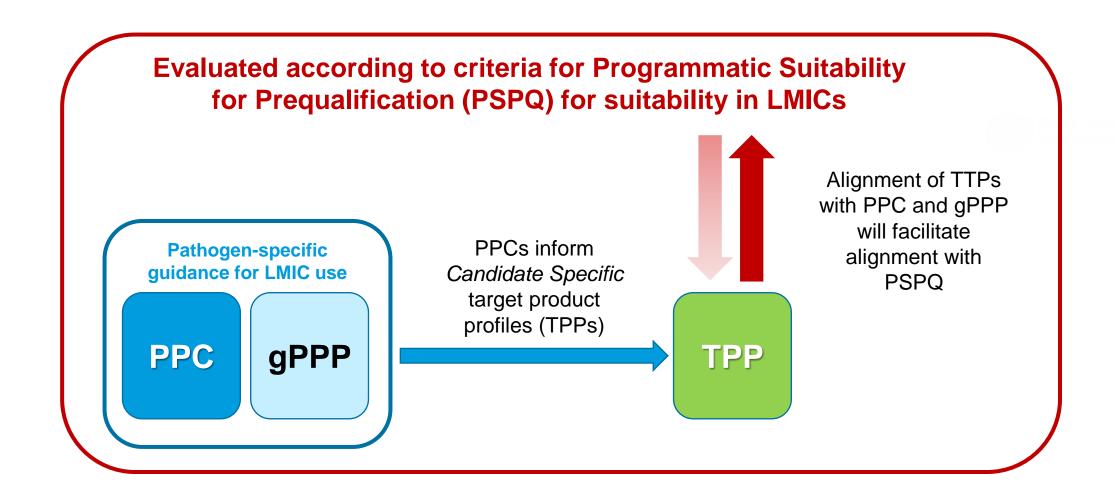
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WHO generic guidance that informs vaccine development				
Generic Preferred Product Profile for Vaccines (gPPP) (2015)	Recommendations on presentation and packaging of new vaccines for use in LMICs			
Assessing the programmatic suitability of vaccine candidates for WHO prequalification (2014)	Process and criteria for prospective vaccine PQ in terms of their programmatic suitability for LMICs			

WHO PSPQ criteria and pathogen specific WHO preferences inform TPPs to improve LMIC suitability





Status of guidance document development for vaccines against PDVAC prioritized pathogens



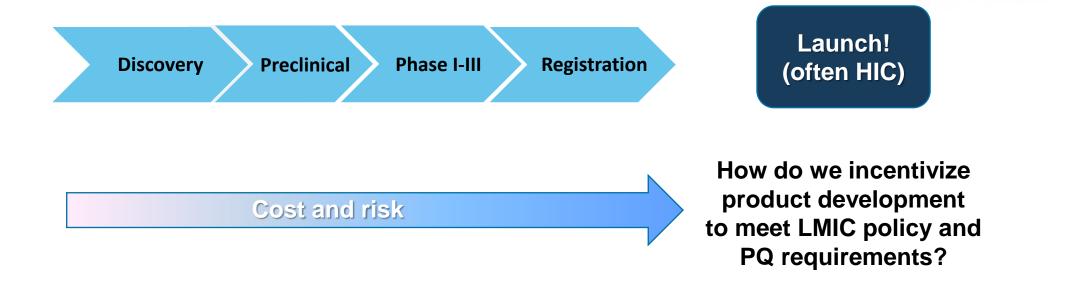
Pathogen	Landscape analysis	PPC	Roadmap	Pathways	Scoping consultations*
Tuberculosis	✓	✓			✓
HIV	✓				✓
Malaria	✓	✓	\checkmark		✓
Influenza	✓	√ (improved vaccines)			✓
RSV	✓	✓	✓	✓	✓
GBS	✓	✓	\checkmark	\checkmark	✓
HSV	✓	✓			✓
ETEC	✓	√ (in progress)			✓
Shigella	✓	√ (in progress)		√ (in progress)	✓
GAS	\checkmark	√ (drafted)			\checkmark

http://www.who.int/immunization/research/ppc-tpp/preferred_product_characteristics/en/

HIV: human immunodeficiency virus; RSV: respiratory syncytial virus; GBS: group B Streptococcus; HSV herpes simplex virus; GAS: group A streptococcus. PPC: Preferred product characteristics; RM: Roadmap; * meeting reports publically available

The FPHVP for vaccines *is a concept in development* that describes the <u>global</u> value of a vaccine



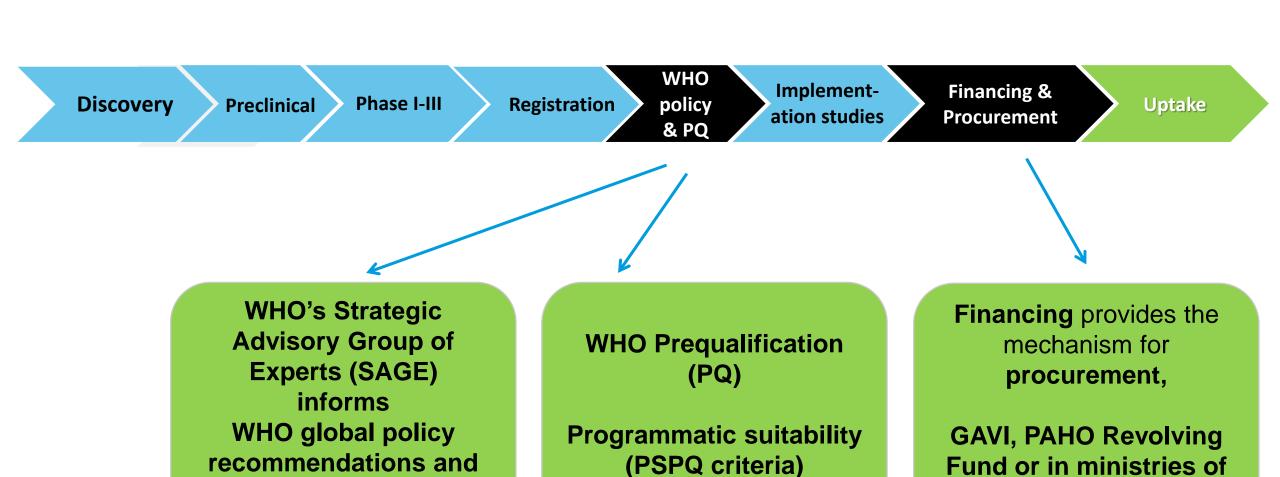


Additional steps for vaccine uptake in LMICs

strategies



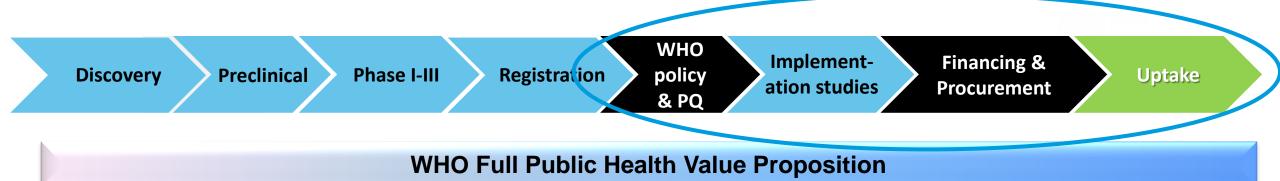
finance



The FPHVP for vaccines *is a concept in development* that describes the <u>global</u> value of a vaccine



...and considers the data needed to support policy recommendations & uptake in LMICs



- Articulates the value of the vaccine from the perspective of multiple stakeholders
- Serves as an end-to-end compendium of available evidence to support advocacy and inform decision making at various stages of product development
- Identifies gaps to guide funding decisions and assessment of risk

Traditional v FPHVP approach



Traditional approach based on:

- Efficacy (individual direct benefit) & effectiveness (direct and indirect health benefits)
- Risk/safety profile (individual)
- Cost-benefit analysis

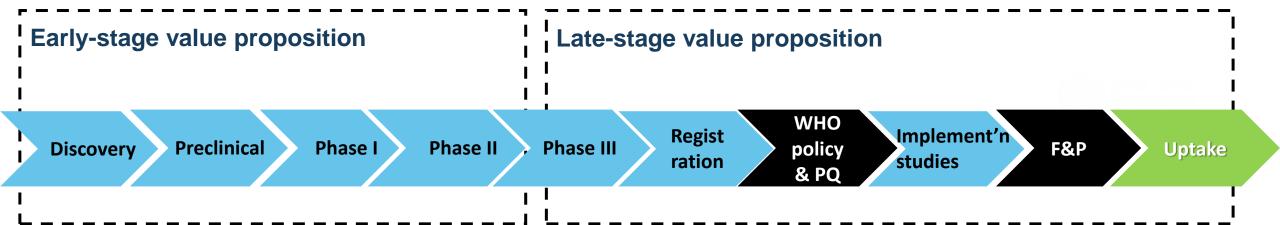


FPHVP approach also based on:

- Disease reduction directly and indirectly by reducing:
 - Vaccine preventable disease incidence
 - All cause mortality
 - Under 5 mortality
 - Long-term sequelae
 - Pathogen transmission
 - Anti-microbial resistance
- Reducing frequency and size of outbreaks
- Stabilizing health systems
- Social and economic benefits
- Equity, access, affordability, acceptance and sustainability
- Protecting against financial risk

The availability of data to describe the FPHVP varies by development stage





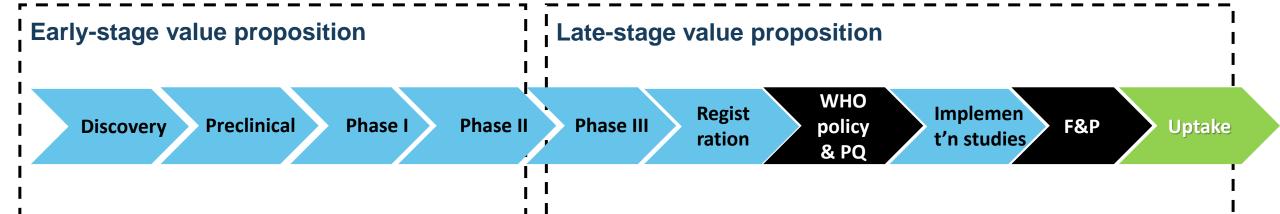
Qualitative
Significant data gaps
Analysis based on assumptions and proxies

Quantitative

More comprehensive and robust data to provide evidence for decision making

The purpose of the FPHVP





Goal of early stage FPHVP:

- improve epidemiology/burden estimates
- consider the landscape of other interventions
- evaluate the technical and commercial feasibility
- prime the vaccine pipeline
- articulate the demand for a vaccine and create in-country champions/advocates

Goal of late stage FPHVP:

- evaluate the full market potential of vaccine, considering individual- and populationbased benefit
- inform return on investment/business case
- articulate evidence to support recommendation
 & uptake
- Create political will for vaccine implementation

Case Studies



Meningococcal A

Group B Streptococcus

Enterotoxigenic *E.coli*



Poster child?



Gestating?



Languishing?

▶1996: Ministers of Health and Interior from16 African countries recognized epidemic meningitis as a high priority

2001: Creation of MVP (partnership between PATH and WHO) with a grant from the Bill & Melinda Gates Foundation

2001–2002: African public health officials emphasize the key importance of a low vaccine price for a sustainable supply

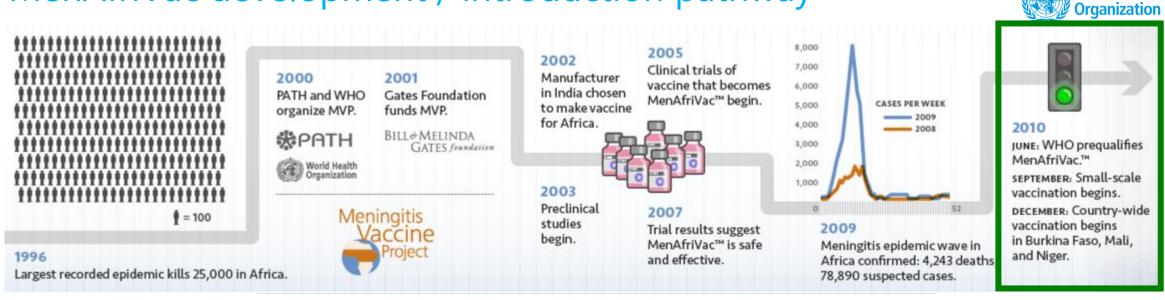
Affordability is key to ensure sustainability, < \$US 0.50/dose



Case study: MenAfriVac development by the Meningitis Vaccine Project (MVP)



MenAfriVac development / introduction pathway



In collaboration with health authorities of 26 countries in sub-Saharan Africa and of India



Norwegian Institute of Public Healt

BILL&MELINDA

World

Health

Organization



accine



PATH A catalyst for global health





Michael & Susan Dell





>300MM doses delivered

World Health





Meningitis



















ROBERT KOCH INSTITUT



➤ 2015/16: WHO PDVAC identified development of GBS vaccines suitable for maternal immunization (MI) in pregnancy and use in LMICs as public health priority

2016: WHO developed a PPC and roadmap

2017: BMGF funded the WHO/LSHTM GBS value proposition project

Case study: Group B Streptococcus vaccine





- ➤ Project goal to define the value of GBS vaccine by:
- Assessing the preventable burden of disease,
- o- Estimating expected costs/gains from vaccinating pregnant women

In order to:

- o- Inform investments in product development and implementation research in readiness for Maternal Immunization vaccination platform
- o- Identify major data gaps as they relate to the creation of a favourable environment for future vaccine introduction in low resource countries

Preparation for policy recommendation and uptake for a vaccine EARLY in product development!

Case study: Group B Streptococcus vaccine





- ➤ Most advanced candidate approaching pivotal efficacy testing in travelers (currently in POC testing), within the next few years.
- ➤ Global mortality estimates of ETEC are declining, but still significant morbidity that is detrimental to long term health, social and economic prospects in LMICs
- Funding to support an LMIC indication for ETEC is at risk because of declining mortality
- Travelers vaccine may be available soon, but not appropriate for LMIC uptake

FPHVP approach may incentivise development of LMIC indication for ETEC



Case study: Enterotoxigenic E.coli vaccine



<u>Early-stage</u> value proposition focuses on vaccines up to clinical proof-of-concept



Burden of disease (mortality, DALYs, strain variation); the public health need for Intervention

Competitive landscape analysis (other inventions) and potential Vx market

Activities undertaken

Preferred Product Characteristics

Integrated Product Development Plan

Potential demand forecast for Vx (Use-case scenarios)

Discovery Preclinical Phase I Phase II

Academic institutions, biotech & pharma

Governmental organizations, product development partnerships & philanthropies

Key stakeholders

Vaccinees, Healthcare workers, Communities, Civil societies...

Global stakeholders (e.g., WHO, GAVI, UNICEF)

<u>Late-stage</u> value proposition focuses on vaccines <u>post</u> clinical proof-of-concept



Components of early stage Vx VP (accuracy refined, robustness improved)

Market assessment, strategic demand forecast and market shaping; return on investment

Vaccine impact on burden of disease and transmission (individual & population/societal effects)

Economic analysis of the value of the vaccine

Phase III

Registration

WHO policy & PQ

Implementation studies

Financing & Procurement

Uptake

Vaccinees, Healthcare workers, Communities, Civil societies...

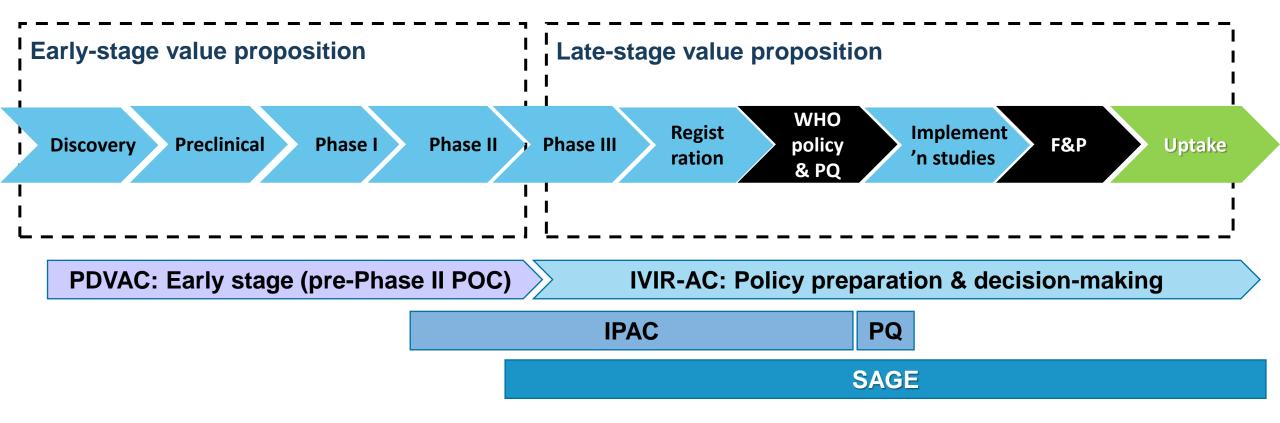
Governmental organizations, product development partnerships & philanthropies

Global stakeholders (e.g., WHO, GAVI, UNICEF)

Country MoH & MoF

WHO oversight and guidance of vaccine product development and introduction





PDVAC: Product Development for Vaccines Advisory Committee

IVIR-AC: Immunization and Vaccines-related Implementation Research Advisory Committee

IPAC: Immunization Practices Advisory Committee

SAGE: Strategic Advisory Group of Experts on Immunization

PSPQ: Prequalification

In summary...



FPHVPs are intended to support decision-making across the continuum of vaccine development and uptake with a line-of-sight to sustainable public health impact

The purpose of the FPHVP is to:

- > Create alignment across a range of stakeholders, with respect to public health priorities
- > Provide a resource to effectively advocate for development of vaccines
- ➤ Inform investment decisions at all stages of development
- > To accelerate suitability for and accessibility of vaccines to LMICs

....however significant resources will be needed to undertake them, through coordinated collaborations/consortiums

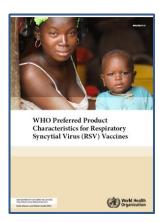


Back up slides

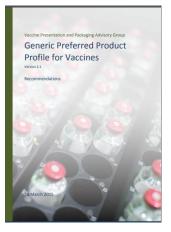


Example of how the PPC, gPPP and PSPQ complement each other

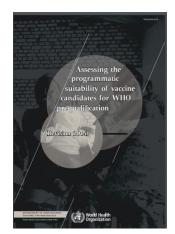




PPC for RSV: 'Indication: Active immunization of women during pregnancy, for prevention of severe RSV disease in offspring during the neonatal period and early infancy'



gPPP: 'Heat stability: Maximise vaccine heat stability to the extent possible to improve effectiveness, enable higher-temperature storage, and enable taking the vaccines beyond the cold chain (40°C target)'



PSPQ: Thermostability/storage:

- mandatory characteristic: The vaccine or any component presented for prequalification should not require storage at less than -20°C.
- preferred characteristic: Vaccines with data and licencing allowing for higher temperature storage. If feasible, use 40°C as the current target threshold temperature.

Policy questions drive valuation methods



Analysis	Policy question	Summary measures
Effectiveness study	How effective is vaccine in improving health outcome?	Clinical trial outcomes Health outcomes Summary measures
Costing study	What is the money value of resources consumed to develop/introduce a new vaccine?	Cost per dose Cost per capita Cost per infant in the target population Cost per fully immunized child
Cost-effectiveness analysis (CEA)	Is a vaccine or related activity economically justified according to the opportunity cost of health care spending?	Incremental cost-effectiveness ratio (ICER)
Extended cost- effectiveness analysis (ECEA)	With given cost, what is the effect of a vaccine on financial risk protection, health gains, and averted private expenditures across income quintiles?	Financial protection afforded per expenditure, distributional aspects of outcomes
Benefit-Cost analysis (BCA)	Is vaccine purchase economically justified according to individuals' willingness to pay for health gains?	Benefit-cost ratio (BCR) Positive net benefits

Analysis	Policy question	Summary measures
Cost of Illness Study (COI)	What is the economic burden that a vaccine-preventable disease imposes on the society?	Total direct and indirectalth cost of treatment for a case due to a vaccine preventable disease
Investment case	What is the return on investment for a vaccine or related activity?	Return on investment (ROI) Net present value (NPV) Internal rate of investment (IRR)
Economic surplus analysis	How is global welfare in dollar terms generated by the uptake of vaccines distributed between vaccine producers vs purchasers/target audience? Between HIC vs LMICs? Across countries?	Consumer surplus Producer surplus Total economic surplus
Budget Impact Analysis (BIA)	What will be the impact of adding a new vaccine on the budget of a stakeholder (i.e. annual budget of the Ministry of Health)?	Difference in the health system costs (with vs. without the intervention)
Optimization modelling	Given a constrained budget, what is the best possible set of interventions including vaccine that maximizes/minimizes the target outcome?	Minimization/maximizatio n of outcome variable(s) of interest
Fiscal impact modelling	What is the change in tax revenue and transfer payments attributable to changes in mortality and morbidity caused by a vaccine?	Net present value (NPV) Return on investment (ROI) Benefit-cost ratio (BCR)

References



Generic Preferred Product Profile for Vaccines (gPPP)

http://www.who.int/immunization/policy/committees/VPPAG_Generic_PPP_and_Workplan.pdf?ua=1

Assessing the programmatic suitability of vaccine candidates for WHO prequalification (Revision 2014) http://apps.who.int/iris/bitstream/10665/148168/1/WHO_IVB_14.10_eng.pdf?ua=1

IVR vaccine PPCs and Roadmaps:

http://www.who.int/immunization/research/ppc-tpp/preferred_product_characteristics/en/