WHO’s 2018 Product Development for Vaccines Advisory Committee meeting: A year in review

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What does PDVAC do?

PDVAC’s mission is to accelerate product development of vaccines and technologies that are urgently needed and ensure they are appropriately targeted for use in low and middle income contexts.

- Vaccine candidates
- Monoclonal antibodies
- Delivery technologies
What does PDVAC do?

- Horizon scanning of vaccine in early clinical development
- Evaluates probability of technical and regulatory success and a role for WHO
- Unmet public health need for a vaccine from an LMIC perspective and communicate priorities
What is the problem we are trying to solve?

- Translation gap
- Implementation gap

**Phase I-III:** Discovery, Preclinical, Phase I-III, Registration, WHO policy & PQ, Implementation studies, Financing & Procurement, Uptake
How does PDVAC work?

Preferred product characteristics and the global preferred product profile describe vaccine preferences.

Pathogen-specific guidance for LMIC use

**PPC:** Indication, target population, schedule, efficacy target, route of admin….

**gPPP:** Formulation, primary container, packaging

Roadmaps and pathway consultations facilitate how to achieve PPCs.

Considerations for product development pathways

Vaccine roadmap

Developed by PDVAC
Developed by Vaccine Presentation and Packaging Advisory Group (VPPAG)
### WHO PPCs seek to broaden the scope of Target product profiles (TPPs)* to incorporate LMIC market

<table>
<thead>
<tr>
<th>Parameter</th>
<th>WHO PPC</th>
<th>TPP</th>
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<tbody>
<tr>
<td>Focus</td>
<td>Pathogen-specific</td>
<td>Candidate (product) specific</td>
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<tr>
<td>Content</td>
<td>Describes preferences for LMICs</td>
<td>Sets minimal criteria for development</td>
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<tr>
<td>Audience</td>
<td>Any entity seeking eventual PQ/LMIC market</td>
<td>Stakeholders interested in return on investment</td>
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<td>Purpose</td>
<td>Encourage innovation, broaden vaccine target populations</td>
<td>Guide investment decision making</td>
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<td>Process of development</td>
<td>Public health stakeholder consultation</td>
<td>Within institutions</td>
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* TPPs are developed by other stakeholders and entities, typically private industry
Full Public Health Value Propositions (FPHVP)* for Vaccines

Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization, Geneva, 17-18 April 2018
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*Full public health value of vaccines (FPHVV)
What is the problem we are trying to solve?

Articulating the public health value, PPCs, roadmaps *early in product development* help to define the value proposition, encourage investment and mitigate against the implementation gap.
Human Immunodeficiency virus (HIV)

- Two HIV vaccine candidates are currently in late stage clinical trials in HIV-uninfected populations, as heterologous prime-boost approaches. mAb also in late stage.
- Data anticipated in 2020-21

2017 PDVAC recommendation:

- Facilitate scenario planning and development of communication strategies in preparation for HIV vaccine and monoclonal antibody study outcomes.
- Evaluate the development pathway beyond ongoing proof-of-concept studies. Identify gaps in guidelines to support licensure, availability and use in LMICs

✔ February 2018: From proof of efficacy to policy decision, access and use of product for passive and active immunization to prevent HIV infection: Prepare for Success
Tuberculosis (TB)

- Primary strategic public health goal: reduction of disease in adolescents and adults
- Seven tuberculosis vaccine candidates in phase II clinical studies, and one in phase III.

2017 PDVAC recommendation:
- Continue to facilitate and seek to accelerate development of vaccines for prevention of tuberculosis in adults and adolescents
- Development of a PPC for this indication.

- October 2017: WHO Initiative for Vaccine Research & Global Tuberculosis Program Consultation on Tuberculosis Vaccine Research and Development
- PPC published
Malaria

- Progress towards start of RTS,S/AS01 pilot implementation studies
- Fractional RTS,S/AS01 dose regimen with potential for increased protection: ongoing evaluation
- Progress in several areas of translational clinical development, including investigating IV administration of attenuated sporozoites
- Past WHO PPC and roadmap date back > 5 years. Warrants reconsideration for second generation malaria vaccines.
Influenza

- WHO Preferred Product Characteristics for Next-Generation Influenza Vaccines have been published.
- Several candidate vaccines designed to elicit antibodies to conserved epitopes on the hemagglutinin head or stem are advancing to early stage clinical development with the goal of achieving broad and durable immunity.

- BMGF meeting on Influenza Human Challenge Model for universal flu vaccine development
Enterotoxigenic *E.coli* (ETEC)

- According to the most recent IHME estimates, ETEC mortality has declined BUT causes 75 million episodes of diarrhea each year
- During VASE 2018, BMGF announced to phase out investment in ETEC vaccine development due to lower perceived burden and technical feasibility
- The leading ETEC vaccine candidate has advanced to a Phase IIb proof-of-concept field study in adult travelers; data expected 2019
- Same candidate has completed a phase II study in infants and children in Bangladesh

2017 PDVAC recommendation:

- Develop PPCs and clarity on development pathways for use in LMICs
- **October 2017:** ETEC Vaccine Preferred Product Characteristics (PPCs)
- **February 2018:** Joint WHO-NIAID-PATH Workshop on development and standardization of ETEC assays and antigens
Shigella

- According to IHME, Shigella is the second most deadly diarrhoeal disease.
- WHO AMR priority list
- Clinical pipeline of subunit, live and killed approaches
- Three next generation O-Ag based vaccines prioritized by BMGF, with a view to understanding how CHIM can accelerate licensure

2017 PDVAC recommendation:

- Develop PPCs and clarity on development pathways for use in LMICs

✓ **October 2017: Shigella Vaccine Preferred Product Characteristics (PPCs)**
✓ **May 2018: WHO Consultation on Product development and Policy pathways for O-antigen based conjugate Shigella vaccines**
Respiratory Syncytial Virus (RSV)

- Progress in vaccine indications for maternal immunization and monoclonal antibodies
- Lead candidate Ph3 evaluation progressing, having successfully passed a futility analysis
- Multiple gaps identified on the pathway to future implementation in LMICs
- Collaborative platform on maternal immunization, driven by RSV

- WHO R&D and technical roadmap and PPC available
- WHO AC set up, work expanding for preparing consideration for policy decision
Group B streptococcus (GBS)

- Currently two GBS vaccine candidates undergoing clinical evaluation, with several in preclinical development.
- Efforts to characterize the relationship between levels of antibodies and protection are continuing in parallel with consultations regarding an acceptable regulatory route to licensure and policy decision.

2017 recommendations:
- Pursue efforts to identify a correlate of protection.
- Evaluate the vaccine value proposition considering health, economic and societal dimensions.

- WHO PPC and Roadmap publically available
- December 2017: GBS vaccines: the role of correlates of protection in the pathway to licensure and policy
- February 2018: WHO Scientific Advisory Group to provide inputs to the development of a value proposition for Group B Streptococcus (GBS) Vaccine
Group A streptococcus (GAS)

- New burden estimates: An estimated 18 million people suffer from a serious GAS disease, and 1.8 million new cases and 517,000 deaths occur annually.
- The greatest burden is due to rheumatic heart disease, but invasive GAS diseases (including maternal and neonatal sepsis) also contribute significantly.
- 2018 WHA resolution on ‘Rheumatic Fever and Rheumatic Heart Disease’

2017 recommendations:
- Evaluate the vaccine value proposition considering health, economic and societal dimensions.

- WHO PPC and Roadmap publically available
- May 2018: WHO Consultation on GAS vaccine research and development
  - Renewed consensus development pathway, active collaborations on the value proposition
Herpes Simplex Virus (HSV)

- Prophylactic HSV2 vaccines are preferred for LMICs, but current clinical candidates being tested as therapeutic vaccines
- Therapeutic vaccines have demonstrated clinical POC, but have not progressed
- Therapeutic HSV2 candidates could have population impact in LMICS if able to reduce HSV2 transmission and/or HIV acquisition, as well as GUD
- Need to articulate strong value propositions for prophylactic and therapeutic HSV vaccines in LMICs

- HSV PPC drafted
- Several activities underway to strengthen the full public health value of HSV vaccines
  - Estimates of HSV GUD, HSV-2-associated HIV, HSV-1 outcomes
  - HSV economic burden
  - HSV vaccine impact modeling
Nucleic acid vaccine (NAVs) platforms

- Advances in the *in vivo* expression, stabilization and delivery of both RNA and DNA have improved the prospects for immunization by NAVs.
- Increasingly, NAV vaccines are considered to be a potential game changer for epidemic and pandemic response due to the expectation that they may be significantly faster and cheaper to manufacture, simpler to administer, and potentially more effective than conventional vaccines.
- WHO Consultation held to determine whether the existing DNA guidelines were due for revision or if they remained relevant with today’s status of nucleic acid vaccine development and maturity towards licensure

- **February 2018**: Product development and programmatic considerations for nucleic acid based vaccines
- & WHO Consultation on Nucleic acid vaccine guidelines
Microarray patch product development for MR vaccines

Recommendation by SAGE, October 2016:
SAGE acknowledged the importance of operational and technological research to address the barriers to achieving GVAP [Global Vaccine Action Plan] measles and rubella goals. In particular, SAGE recommended that the most expeditious clinical development and regulatory pathway to licensure of measles containing vaccines (MCV) micro-array patch (MAP) be determined, and that barriers to the development, licensure, and use of MAPs for measles and rubella vaccine delivery be identified and addressed urgently.

March 2018: Measles containing vaccines (MCV) Microarray Patch (MAP) product development
Novel approaches to prioritize vaccine innovations to improve coverage and equity

Vaccine coverage for routine vaccines has failed to reach the global targets of 90% using current delivery strategies.

Development and uptake of novel vaccines, delivery approaches and delivery technologies are needed to reach the immunization targets.
Novel approaches to prioritize vaccine innovations to improve coverage and equity

Gavi, WHO, Unicef, PATH and BMGF are working together to develop two new tools to identify and prioritise high impact innovations that meet the preferences and priorities of low and middle income countries.

**Total Systems Effectiveness (TSE)** is a holistic approach to evaluate and prioritize vaccine innovations, by considering their potential to increase the coverage and to inform novel vaccine innovations through **Vaccine Innovation Prioritization Strategy (VIPS)**.
WHO oversight and guidance of vaccine product development and introduction

Early-stage value proposition

- Discovery
- Preclinical
- Phase I
- Phase II
- Phase III

Late-stage value proposition

- Registration
- WHO policy & PQ
- Implement'n studies
- F&P
- Uptake

PDVAC: Early stage (pre-Phase II POC)
IVIR-AC: Policy preparation & decision-making
IPAC: Immunization Practices Advisory Committee
PQ: Prequalification
SAGE: Strategic Advisory Group of Experts on Immunization

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
Co-hosted by WHO, the National Institute of Allergy and Infectious Diseases, and the Bill & Melinda Gates Foundation.

All research aspects related to the Global Vaccine Action Plan (GVAP)

Pathogen and cross-cutting topics such as expanding and leveraging DCVMs, maternal and adolescent immunization platforms, innovating for equity

- Tracks progress, identifies gaps, creates alignment and coordinates activities to increase the efficiency and impact of activities and resources.

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/