Product Development for Vaccines Advisory Committee (PDVAC):

Vaccine development highlights from 2016/17

Strategic Advisory Groups of Experts for Immunization
October 2017
David C. Kaslow, MD
Chair, PDVAC

World Health Organization

Scope of the 2017 PDVAC meeting

- Report progress in vaccine development and IVR/PDVAC activities across previously prioritized pathogens [HIV, TB, malaria, influenza, RSV, Group B Strep (GBS), Group A Strep (GAS), Enterotoxigenic *E. coli* (ETEC), *Shigella*, Herpes Simplex Virus (HSV)];

- Review the status of vaccine development for new pathogens, including cytomegalovirus (CMV) and gonorrhoea;

- Discuss the advances and challenges with respect to product development of platform technologies, for example nucleic acid vaccines and monoclonal antibodies;

- Evaluate cross-cutting issues/technologies that could impact the value proposition and development strategy for several vaccine candidates, for example anti-microbial resistance (AMR), passive immunization and nucleic acid vaccines.

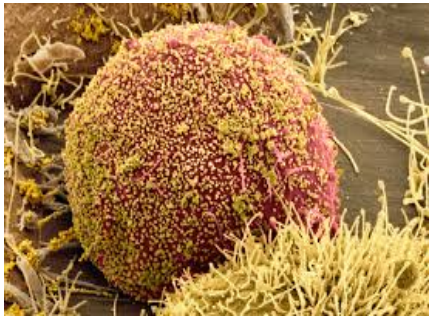
World Health Organization

Summary of vaccine development status, and outcomes from PDVAC **2017:GVAP pathogens**

Human Immunodeficiency virus:

— Two HIV vaccine candidates are in late stage clinical trials as heterologous prime-boost approaches. Ph III data expected 2021.

— Broadly neutralizing antibody approaches for HIV are in late stage (PhIIb) clinical development in adults. Data expected 2020.



PDVAC recommended:

➢ Evaluation of the development pathway for candidates beyond ongoing proof-of-concept studies,

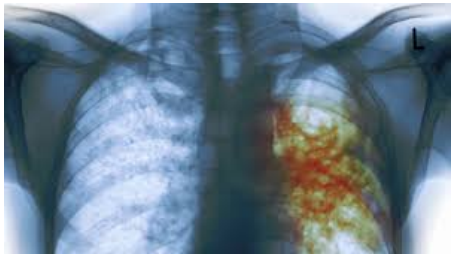
➢ Identification gaps in guidelines (i.e. heterologous prime-boost) to support licensure, availability and use in LMICs for both adult and infant populations

Tuberculosis:

— Three vaccine candidates in Ph IIb trials, and 1 in Ph III (China)

— Three candidates target adults and adolescents; one is an improved recombinant BCG

— Preferred product characteristics (PPCs) drafted and consultation ongoing for tuberculosis vaccines targeted to 1) adults and adolescents, and 2) improved BCG vaccines



World Health Organization

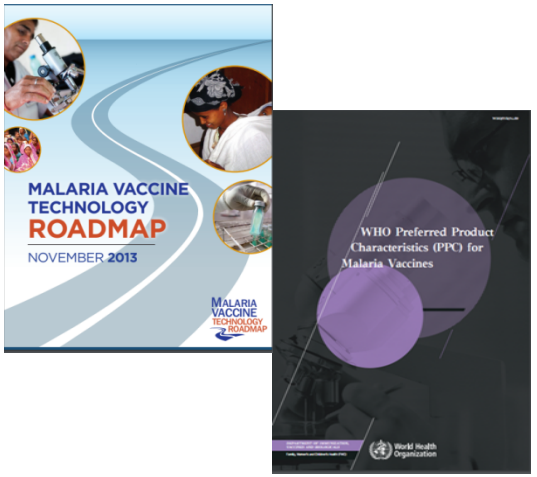
Summary of vaccine development status, and outcomes from PDVAC **2017:GVAP pathogens**

Malaria:

— RTS,S pilot implementation programme in preparation

— Development status of second generation malaria vaccines will be discussed in 2018 under purview of WHO MALVAC

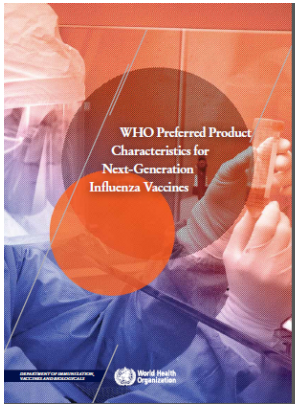
— Expected to include PPC and roadmap for 2nd generation malaria vaccines



Influenza:

— Several candidate vaccines designed to elicit antibodies to conserved epitopes on the hemagglutinin head or stem are advancing to clinical development

— WHO PPC for next-generation influenza vaccines available

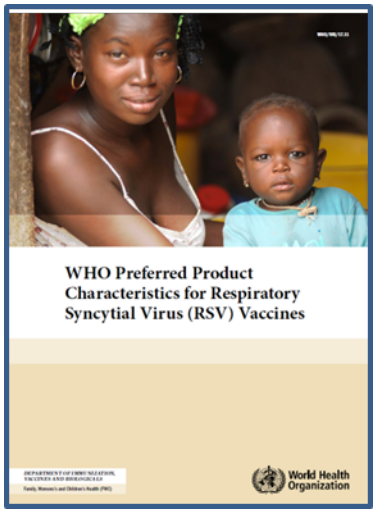


World Health Organization

Summary of vaccine development status, and outcomes from PDVAC 2017: **Maternal immunization approaches**

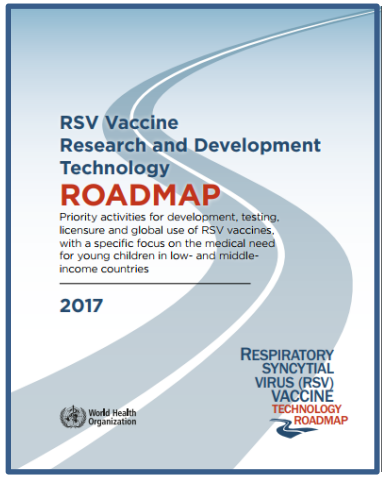
Respiratory Syncytial Virus:

- Two recombinant protein, post-fusion F-based vaccine candidates did not demonstrate efficacy in clinical proof-of-concept studies in the elderly
- An adjuvanted post-fusion F-based candidate is undergoing evaluation in pregnant women; data expected 2018
- Long-lived anti-F antigen mAbs in Ph IIb clinical development
- WHO PPCs and the Technical Roadmap for development of RSV vaccines are available
- RSV standardization work focusing on neutralization assays. A proposed international standard (IS) for anti-RSV antibody is under review by ECBS.



PDVAC recommended:

- Review the data from the late stage, clinical trials in the elderly of recombinant protein based post-fusion F-RSV vaccine candidates, and consider implications for product development of other F-antigen based approaches.

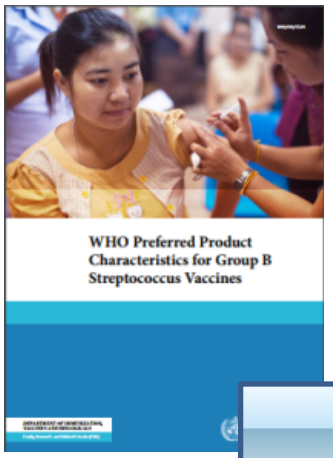


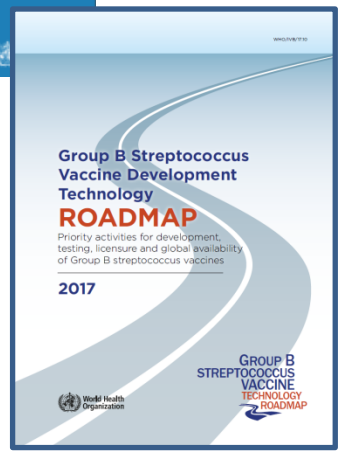
World Health Organization

Summary of vaccine development status, and outcomes from PDVAC 2017: **Maternal immunization approaches**

Group B Streptococcus:

- Two GBS vaccine candidates in the clinic; several in preclinical development
- WHO PPCs and Technical Roadmap for development of GBS vaccines are available
- BMGF-sponsored Imperial College-led collaborative initiative underway to develop standardized GBS antibody assays
- Co-ordinated efforts to establish a correlate of protection that may preclude the need for a field efficacy study.





PDVAC recommended:

- Pursue implementation of the priorities identified in the R&D technological roadmap, including efforts to identify a correlate of protection
- Evaluate the vaccine value proposition considering health, economic and societal dimensions

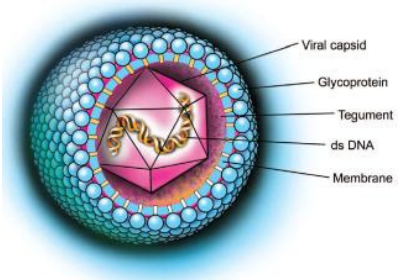
Summary of vaccine development status, and outcomes from PDVAC 2017: **Maternal immunization approaches**

Cytomegalovirus:

— Several live and recombinant vaccine approaches in clinical development, and may have utility in LMICs

PDVAC recommended:

➢ Undertake a vaccine landscape analysis of CMV vaccines, including the potential product development pathways and target populations for use in LMICs.



HCMV Human Cytomegalovirus

Summary of vaccine development status, and outcomes from PDVAC 2017: **Enteric and diarrheal diseases**

Enterotoxigenic *E.coli* (ETEC):

— The leading ETEC vaccine candidate has advanced to a Ph IIb proof-of-concept field study in adult travelers; licensure anticipated in 2022.
— WHO PPC development for infants and young children in LMICs, and assessment of accelerated clinical development is underway
— IVR plans an assay development workshop in early 2018

***Shigella*:**

— Several leading *Shigella* candidates in Ph I evaluation or controlled human infection model (CHIM) studies.
— Most advanced candidates are bioconjugates; POC in children demonstrated.
— Concerted effort to understand how CHIM can identify correlates of protection and inform product development pathways in infants and young children, including challenge-(heterologous challenge and endemic challenge
— WHO PPC development for infants and young children in LMICs, and assessment of accelerated clinical development is underway

World Health Organization

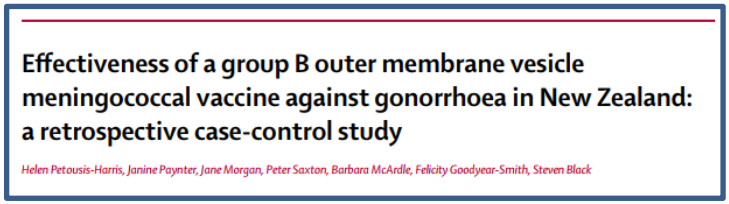
Summary of vaccine development status, and outcomes from PDVAC 2017: **Sexually transmitted infections**

Herpes simplex virus:

— Several therapeutic vaccine candidates are in late stage clinical development
— PPC development for therapeutic and prophylactic vaccines is underway
— Development of a value proposition for HSV vaccines is underway

Gonorrhea:

— First line therapy is failing due to antimicrobial resistance.
— No vaccine candidates are currently in clinical development, but recently published data demonstrates that outer membrane vesicle (OMV)-based Group B meningococcal vaccine provides some cross-protection.
— PDVAC landscape analysis drafted for publication



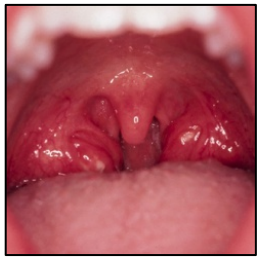
PDVAC recommended:

➢ WHO consultation on Gonorrhea vaccine development

World Health Organization

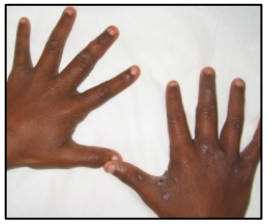
PDVAC Prioritized Pathogens: Group A Streptococcus (GAS)

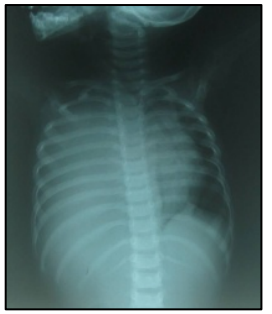
- Underestimated disease burden, causes very diverse disease syndrome
- Significant driver of antibiotic use
- WHO/IVI held a consultation on GAS investment case
- PPC and technical roadmap in advanced status



Antimicrobial resistance (AMR):

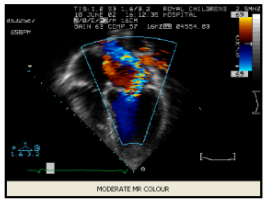
- WHO published its first ever list of antibiotic-resistant "priority pathogens'' that pose the greatest threat to human health.
- Both *Neisseria gonorrhoeae* and *Shigella spp.* listed





PDVAC recommended:

- Develop a quantitative framework through which the public health impact of vaccines to combat AMR can be evaluated, to inform the incremental value that these vaccines could offer over and above reduction of disease.

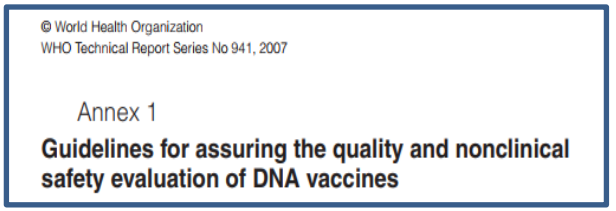


World Health Organization

Summary of vaccine development status, and outcomes from PDVAC 2017: **Platform and cross-cutting aspects**

Nucleic acid-based delivery technologies:

— A new generation of DNA and RNA-based vaccine candidates are in pre-clinical and early clinical development including for Zika and influenza



PDVAC recommended:

- Evaluation of the product development considerations for nucleic acid vaccine platforms, including the context of maternal and prime boost immunization strategies.
- Consider if WHO needs to update the current ECBS TRS for nucleic acid-based vaccines, to include RNA and considerations for use in maternal immunization.

Passive immunization:

— Monoclonal antibody products to prevent infection and disease are in development against an increasing number of pathogens, including HIV, RSV, *Staphylococcus aureus* and rabies

— Some (HIV, RSV) are in late stage, with neonates as the target population

PDVAC recommended:

- Evaluation of the technical, regulatory and commercial barriers to development, licensure and availability of monoclonal antibodies (mAb), specifically for use in low- and middle-income countries (LMICs)

World Health Organization

New directions for PDVAC since the last meeting

- Engaging with stakeholders across a greater number of pathogens and platforms
- Increased consideration of and focus on cross-cutting issues; leverage learning
- Diversification of scope to assess novel antigen delivery platforms and technologies
- Increased consideration of the need to define the value proposition for new products

For more information on PDVAC activities:

Including all slides presentations and executive summary:

http://www.who.int/immunization/research/committees/pdvac/en/