Product Development for Vaccines Advisory Committee:

Highlights from the 2016 year of vaccine development

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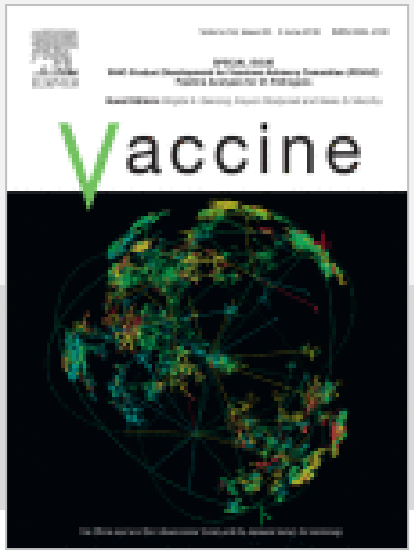
David C. Kaslow, MD

Chair, Product Development for Vaccines Advisory Committee



World Health Organization

Summary of the 2016 PDVAC meeting (June 2016)

- Reviewed progress since previous meeting, against 2015 recommendations for: RSV, ETEC , Shigella, norovirus, GBS, GAS, malaria, HIV, tuberculosis and improved influenza vaccines
- Seven additional pathogen areas reviewed:
  - second generation rotavirus
  - *Clostridium difficile*
  - *Helicobacter pylori*
  - *Staphylococcus aureus*
  - *Chlamydia trachomatis*
  - Enterovirus 71
  - Zika virus
- Cross-cutting issues discussed, such as how PDVAC effectively interfaces with the R&D Blueprint, the delivery technologies working group, WHO task force on the global action plan against anti-microbial resistance.

Recommendations and Outcomes from the 2016 PDVAC meeting

- Respiratory Syncytial Virus (RSV)

- Most advanced vaccine candidate for maternal immunization in phase III. Most advanced long acting antibody for newborn infants in phase IIb.
- All large vaccine manufacturers engaged.

WHO in active discussions to advance SAGE April 2016 recommendations on RSV vaccines, including:

- RSV surveillance to determine **seasonality and age-stratified RSV disease burden and community morbidity and mortality**, especially in Africa and south-east Asia
- assessment of the long term effects of RSV interventions and the potential **impact of vaccination on reducing recurrent wheeze**, to inform cost-effectiveness and impact data
- **strengthening of the maternal immunization platform** in collaboration with other maternal immunization vaccines
- establishing **a WHO prequalification pathway for monoclonal antibodies**
- initiate **early discussions with financing bodies**, and to align with the upcoming GAVI Vaccine Investment Strategy (VIS)

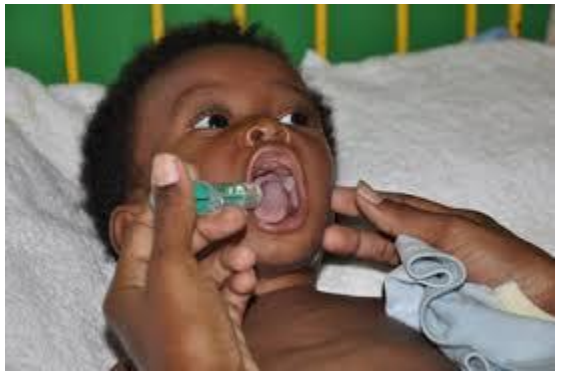
Recommendations and Outcomes from the 2016 PDVAC meeting
- Group B Streptococcus (GBS)

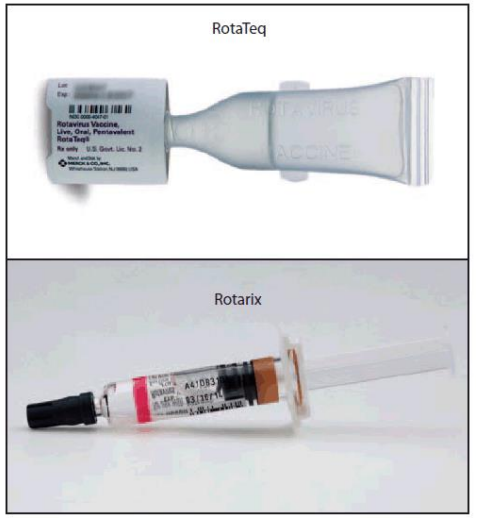
- Globally, GBS remains the **leading cause of sepsis and meningitis in young infants** less than 3mo of age
- GBS may be **an under-reported cause of stillbirth** and may impact estimate of the global public health need for vaccine; **better surveillance** is needed
- Two large **pharmaceutical companies engaged**, most advanced in phase IIb
- Prioritized by PDVAC in 2015
- First WHO consultation in April 2016
- PDVAC endorsed the consensus-based development of **a PPC and vaccine development technology roadmap**
- WHO considering developing **a business case for greater engagement** by industry and donors

Recommendations and Outcomes from the 2016 PDVAC meeting

- Enterotoxigenic *E.coli* (ETEC) and *Shigella*

- Lead candidates are oral inactivated whole cell ETEC (4 strains) and oral inactivated whole cell *Shigella* (3 strains)
- Existing **clinical proof-of-concept** data
- Formulation (+/- adjuvant), **dose selection in infants** and presentation optimization ongoing
- Approaching **efficacy trial in 2019 but several fundamental questions** with respect to burden of disease, single vs combination, presentation, programmatic suitability, clinical trial designs
- Scope of planned activity includes: **derivation of PPCs for single and combination vaccines, including consensus on clinical endpoints for phase III efficacy study;** and understanding data requirements for both regulatory and policy perspectives.





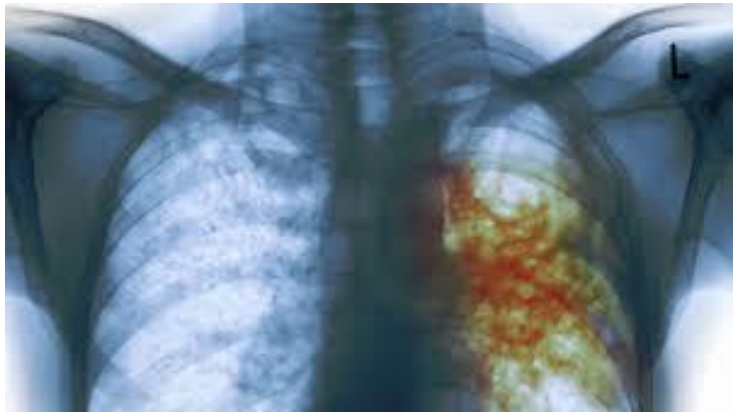
Recommendations and Outcomes from the 2016 PDVAC meeting
- Tuberculosis (TB)

- A better vaccine is imperative to achieving the End TB goals, particularly through preventing disease, and therefore transmission in **adolescents and adults**
- Several candidates are in clinical proof-of-concept studies, approaching key endpoints in the next 12-24 months

➢ **PDVAC recommended that WHO prioritize and facilitate consensus building with respect to the development of PPC(s) for vaccines targeted to adolescents and adults**

➢ **Issues with supply of legacy BCG are distinct from the development issues with new TB vaccines**

➢ **Concern than recombinant BCG may lead to higher prices than legacy BCG: clarity on added value will be critical**



Other 2015 PDVAC recommendations to IVB, and 2016 activities

Pathogen area	2015 PDVAC recommendation	2016 activity
Group A streptococcus (GAS)	WHO to support development of an investment case	• **Consultation planned** for December 2016 in collaboration with International Vaccine Institute (IVI), Seoul.
Herpes Simplex Virus (HSV)	Understand potential impact of HSV vaccines on broader range of outcomes including HIV incidence to help drive investment case	• WHO commissioned an **updated systematic review and meta-analysis** of the effect of **HSV-2 infection on HIV acquisition** • **First global estimates of HSV-1** published • **First global estimates** of **neonatal herpes** near completion (publication late 2016) • Secured resources to **initiate an HSV PPC**
Norovirus	WHO exploring the possibility of incorporating norovirus surveillance within the WHO global rotavirus surveillance network (RGSN)	• Performed an assessment of norovirus surveillance capability at sites within RGSN; **advocated for inclusion of norovirus genotype surveillance** in assessment of diarrheal pathogens • **Norovirus to be included in expanded diarrheal surveillance at selected RGSN sites**

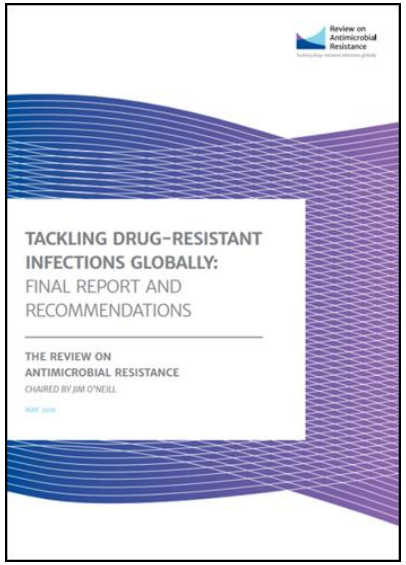
Other PDVAC/ vaccine development related activities in 2016

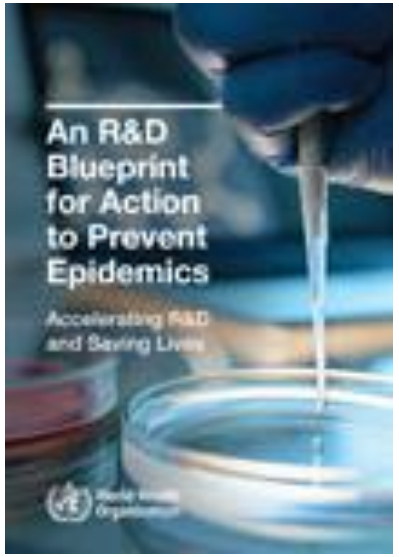
- Public consultation underway on **WHO multivalent filovirus vaccine TPP**
- A **WHO roadmap for research and product development in MERS-CoV published in Nature Medicine** – diagnostics and vaccine trials progress but resources constrained due to Zika virus
- WHO **MERS-CoV diagnostics and vaccine TPPs** in development
- In response to the PHEIC and through public consultation, WHO developed **a TPP for Zika virus vaccine**. Also held a WHO consultation on **regulatory considerations for emergency use vac**cines*
- Established the **delivery technology working group**, to consider innovative vaccine delivery devices earlier in development
- **R&D Blueprint will be transitioning to IVR** in 2017: PDVAC will continue to advise on vaccine-related elements for emerging infectious disease product development.
- Collaborated with the Reproductive Health Program to secure resources to **implement the STI (sexually transmitted infection) vaccine roadmap**
- PDVAC secretariat **published 25 pathogen specific vaccine pipeline analyses** in a special issue of Vaccine**

*http://www.who.int/immunization/research/development/zika/en/; ** http://www.sciencedirect.com/science/journal/0264410X/34/26

Looking ahead…

- Next PDVAC meeting is in June 2017
- In addition to progress in vaccine development in pathogen specific areas, meeting will focus on:
  - Vaccine development aspects of vaccines in the **anti-microbial resistance** agenda
  - Emerging **innovative delivery technologies** (MAPs)
  - Advances in **novel delivery platforms** (DNA, RNA)
  - Synergizing efforts to develop **vaccines against prioritized emerging pathogens** (CEPI/R&D blueprint agenda)





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