Product Development for Vaccines Advisory Committee:

Highlights from the 2016 year of vaccine development

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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 antimicrobial 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

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<tr>
<th>Pathogen area</th>
<th>2015 PDVAC recommendation</th>
<th>2016 activity</th>
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<tr>
<td>Group A streptococcus (GAS)</td>
<td>WHO to support development of an investment case</td>
<td>• Consultation planned for December 2016 in collaboration with International Vaccine Institute (IVI), Seoul.</td>
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| 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 vaccines***
- 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**

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)