

Report from the World Health Organization's Third Product Development for Vaccines Advisory Committee (PDVAC) meeting, Geneva, 8-10th June 2016

Executive Summary

(full meeting report is available)

WHO's Product Development for Vaccines Advisory Committee (PDVAC) was convened for the third time in June 2016. Their remit was to revisit the pathogen areas where there has been significant progress since recommendations from the 2015 meeting, as well as to consider new advances in the development of vaccines against other pathogens. There have been several significant developments in the nine months since the previous meeting:

- the first Dengue and Malaria vaccines have been licensed or achieved the equivalent of licensure, respectively ,
- the first phase III trials of a Respiratory Syncytial Virus (RSV) vaccine candidate have commenced in the elderly and pregnant women. As an RSV vaccine could be licensed within the next 5 years, the status of RSV vaccine and monoclonal antibody development was presented to WHO's Strategic Advisory Group of Experts (SAGE) on Immunization in April 2016, for information,
- the most advanced HIV vaccine candidate met its endpoints in the interim analysis of a Phase II study, and preparations to commence an efficacy study are underway,
- Phase IIb trials of a number TB vaccine candidates are approaching key data points, and there is increased consensus on the importance of preventing of pulmonary disease in adolescents and adults as a priority public health need to reduce transmission,
- drafting of strategic goals and preferred product characteristics (PPCs) for improved influenza vaccines is underway and will be presented at a global conference in August 2016,
- WHO has increased its activity in the enteric pathogen arena and is preparing to initiate development of PPCs for Shigella and ETEC vaccines,
- the leading Norovirus candidate has entered a Phase IIb efficacy study,
- WHO convened its first consultation on group B streptococcus (GBS) and PPC development is underway,
- WHO supported a systematic review/meta-analysis of herpes simplex virus-2 (HSV-2) and the associated risk of HIV acquisition, expected to be published in late 2016. Improved global estimates of neonatal herpes burden have also been generated and will be published imminently. The most advanced therapeutic HSV-2 vaccine candidate demonstrated significant reduction in recurrent lesions and viral shedding of HSV-2 in HSV-1/HSV-2 double seronegative recipients over 12 months,
- WHO convened the MERS-Coronavirus R&D community, and a Phase 1 clinical study is now underway,
- Ebola virus vaccines are under WHO Emergency Use Assessment and Listing (EUAL) and have progressed to the point of consideration for licensure in record time,
- Zika has been declared a Public Emergency of International Concern (PHEIC), and there are co-ordinated efforts to develop a vaccine as expeditiously as possible. PDVAC is contributing significantly through a PDVAC working group which is overseeing development of a Zika vaccine target product profile (TPP), and regulatory considerations towards phase I and emergency use authorization,
- a delivery technologies working group (DTWG) has been established to evaluate R&D in novel delivery technologies and devices, with application to both existing vaccines and vaccines in development,
- WHO has established and maintains an online 'Vaccine Pipeline Tracker' in which information regarding all current clinical studies in several different pathogen areas can be found,
- landscape analyses for 25 pathogens from the 2015 meeting have been collated into a special issue in the journal 'Vaccine' and all are available through open access.

At the 2016 meeting, 18 pathogens were presented and discussed, 7 of which had not been previously reviewed by PDVAC. The agenda also included consideration of a number of cross-cutting vaccine development related issues, such as the development of novel delivery technologies. Specific recommendations that emerged from the pathogen-specific sessions include:

- development of strategic goal(s) and PPCs for TB vaccines targeted to adolescents and adults, in the first instance. There are several candidates and platforms in the pipeline against tuberculosis in these age groups,, and other important target populations. PDVAC acknowledged the significant need for development for these vaccines in parallel, as well as continued efforts to understand the biological mechanism of disease in order to support the immunological rationalization of candidates,
- PDVAC recommended that development of 2nd generation malaria vaccines should continue in parallel to the pilot implementation programme for RTS,S, and proposed that the current version of the vaccine roadmap be updated, potentially in 2018, in light of the impacts/proposed next steps following pilot RTS,S implementation,
- PDVAC commended the advances in HIV vaccine development, and requests to be kept informed about progress of the vaccine trial HVTN702. Currently, there are no known intentions for global studies with the P5 candidate vaccine, or to seek WHO prequalification. PDVAC encourages the P5 partners and the South African HIV vaccine development community to keep WHO fully informed about progress with the trial,
- PDVAC concurs with the SAGE recommendation that, in addition to the safety and efficacy data that are needed to support RSV vaccine licensure, implementation research must be undertaken to inform assessment of cost-effectiveness to support vaccine recommendation and reduce the timeline to vaccine implementation and public health impact following licensure,
- Group A streptococcus has been prioritized by PDVAC previously, however it has been very difficult to engage stakeholders in this area. PDVAC recommends that WHO convenes a consultation to examine the value proposition for GAS vaccines, considering their potential impact across both high income and lower income settings – including the consideration of how current treatment regimens may contribute to increased antimicrobial resistance,
- PDVAC recommended WHO actively collaborate and support development of PPCs for HSV vaccines,
- As in 2015, PDVAC recommended increased surveillance of circulating norovirus genotypes in low and middle income countries (LMICs), and in children under 5 years, in order to assess the level of protection that might be offered by the leading vaccine candidate. In addition, assessment of vaccine programmatic suitability and applicability for prequalification is needed, prior to Phase III trials in order to ensure the vaccine is appropriate for use in low and middle income countries, assuming it is demonstrated to offer coverage over circulating genotypes within LMICs,
- PDVAC encouraged the development of a target product profile for a second generation Ebola virus vaccine that will likely cover several valencies, and will need to demonstrate long duration of protection,
- PDVAC was supportive of the DTWG and encouraged continued communication between vaccine and device/delivery technology development to identify potential opportunities for novel combination product development.
- the urgent need to establish a prequalification pathway for monoclonal antibodies was identified and will be a priority for WHO going forward.

In addition to these significant advances in vaccine development, the UK government commissioned and published in May 2016 a report on 'Tackling Drug- Resistant Infections Globally' in collaboration with the Wellcome Trust.. The report supports the WHO's 2015 Global Action Plan on Antimicrobial Resistance, and highlights the urgent need to reduce reliance on currently available antimicrobials. Development of vaccines against pathogens that are currently controlled by antimicrobials has become an imperative, as they have the potential to reduce the prevalence and spread of drug resistance, as well as to reduce the use, and cost, of

antimicrobials more broadly. As such, WHO is developing an integrated strategy that will include assessment of the public health impact of vaccines, and will likely support the value proposition for vaccines against diseases for which there is currently little private, or public, financial incentive for development.

In the wake of the 2014-15 Ebola virus disease outbreak, and at the request of its 194 Member States, WHO convened a broad global coalition to develop the R&D Blueprint to improve R&D preparedness and response to emerging pathogens which are likely to be the greatest global threat. WHO has defined its priority list of pathogens within the published Blueprint, and PDVAC has, and will continue to have a contributory role within this framework. For example, the current status of Ebola virus vaccine and Middle Eastern Respiratory Syndrome coronavirus (MERS-CoV) vaccine development was reviewed by PDVAC at this and previous meetings. A PDVAC Working Group has developed a WHO Zika virus vaccine Target Product Profile and convened a consultation on regulatory considerations for emergency use vaccines.

The Decade for Vaccines' Global Vaccine Action Plan (GVAP) is approaching its mid-term review, requiring an assessment of progress against objectives since its inception in 2011, and strategic planning to achieve the stated targets within the remaining 5 years. During the remaining timeframe, some vaccines could reach licensure, and WHO needs to ensure early engagement with policy makers regarding potential vaccine implementation, as well as alignment with GAVI's Vaccine Investment Strategy.

WHO's Immunization, Vaccine and Biologicals (IVB) department is now actively working in several pathogen areas on the recommendation of PDVAC, as well as continuing the horizon scanning for advances in vaccine development that may benefit low and middle income countries, such as the recent licensure of the enterovirus 71 (EV71) vaccine in China. On the basis of its continued interaction with SAGE, PDVAC will increasingly look beyond licensure and consider data needs for vaccine recommendation and implementation to reduce the delay between vaccine approval and vaccine impact.