

The World Health Organization Product Development for Vaccines Advisory Committee (PDVAC)

7-9 Sep 2015. Initial Summary. Full Meeting Report to follow.

The World Health Organization Product Development for Vaccines Advisory Committee (PDVAC) met from Sep 7 to 9 2015. The committee reviewed 22 pathogens for which specific read-ahead documents had been prepared. Each document provided a global pipeline analysis commissioned by WHO according to a standardised template which included the following sections: the pathogen, disease and unmet public health need focusing on low and middle income countries (LMICs); the status of the vaccine development pipeline; the pathway to licensure; suggested possible roles for WHO to advance the vaccine pipeline towards public health objectives. All of these documents will be made available in a supplement of the journal *Vaccine* by Q1 2016. WHO thanks the many individuals and organizations that contributed to this community effort to assess the global pipeline for these pathogens.

PDVAC's core role is to consider in which pathogen areas vaccines are likely to emerge in the short to medium term from the pipeline for diseases inflicting a substantial public health burden in LMICs, and in areas where WHO has a key role to play to increase the likelihood that the vaccines are used to reduce the disease burden in LMICs. Thus, PDVAC is not a vaccine prioritization committee, but rather the committee assesses the status of the vaccine pipeline for diseases for which new or improved vaccines are a priority. PDVAC does not generally assess the vaccine landscape for pathogens with licensed vaccines, unless there are major new technologies that could be brought to bear to develop second generation vaccines.

Following consideration of the 22 documents, and presentations by leaders in 13 of the pathogen fields, the following statements were made.

- RSV is highlighted as a pathogen for which there is major vaccine pipeline activity, high technical feasibility, and major disease burden in LMICs. RSV vaccine developments will therefore be reviewed at a specific "For information" SAGE session in April 2016.
- Two major manufacturers are engaged in Group B Streptococcal (GBS) vaccine development, technical feasibility appears good, and GBS is a major disease burden in LMICs, particularly those in Africa. PDVAC recommends that WHO develops guidance on the testing and development pathway for Group B Streptococcal vaccines. This would include agreement of strategic goals, trial design considerations and development of Preferred Product Characteristics (PPCs) for GBS vaccines.
- With regard to universal influenza vaccines, the committee advised WHO to develop strategic public health goals for improved seasonal influenza vaccines and PPCs for such vaccines to provide guidance on data that would need to be generated to establish improved performance of such vaccines.
- Group A Streptococcal causes a substantial disease burden, particularly in terms of rheumatic heart disease in some regions of the world, and the technical feasibility for developing a vaccine appears high. A WHO PPC document is in development. It is

recommended that two business/investment cases are developed by the GAS community – these would include a public sector investment case based on prevention of severe outcomes in resource poor settings such as southern Africa, parts of Asia and certain high risk communities, including those in Australasia. In addition, a business case should be developed for a dual market product for the indication of GAS Pharyngitis in high income countries, and for prevention of cardiac outcomes in LMICs. Once such a business case is developed PDVAC would be better able to advise on the next steps.

- PDVAC advised that WHO explore the possibility of addition of Norovirus surveillance to the WHO network for rotavirus surveillance. Norovirus vaccine development is proceeding, and filling in gaps related to disease burden estimation and strain surveillance in all regions of the world may be enabling to decision-making related to Norovirus vaccine development beyond the well-established high income setting indications.
- WHO should expand its capacity to be able to better support pipeline enteric vaccine development, including consensus building on the key design considerations for Phase 3 trials of ETEC and potentially Shigella vaccines. It will be essential that such guidance is available prior to the start of Phase 3 trials.

PDVAC notes the initiation of WHO's Blueprint for Emergency R&D Preparedness and Research Response. PDVAC will review vaccine-related elements that will feed into the Blueprint, understanding the need to ensure complementarity with guidance in development also related to drugs, diagnostics and non product-development related research as part of the emerging pathogen R&D focus of the blueprint. The first of these are the WHO Ebola Vaccine Target Product Profiles under public consultation in September 2015.

Very important and helpful presentations were given on HIV, malaria, tuberculosis, HSV, dengue, chikungunya and MERS. PDVAC endorsed the importance of the major ongoing product development activities in all these areas.

PDVAC noted that many important platform technologies, such as certain viral vectors, novel antigen design and broadly neutralising antibody approaches, are often being tested first in HIV and malaria. It is therefore very important that information on clinical portfolios is shared between communities. WHO will begin to collate summary information on the global portfolios across several pathogen fields, building on the existing experience in malaria vaccines.

PDVAC noted the major progress towards Phase 3 trials in HIV vaccines and will follow developments with great interest. PDVAC requested further information on the potentially promising developments (of interest beyond HIV alone) related to replication competent vectors and broadly neutralising antibody induction. It was noted that it was HIV clinical trial data that was available for a rVSV vector, which proved helpful in planning rVSV ebola vaccine trials.

PDVAC commended the consensus emerging in the TB vaccine field that development of vaccines to prevent pulmonary tuberculosis in adults and adolescents is now a significant focus for the field. Further work on development pathways for this indication was encouraged, noting that the TB vaccine field is at too early a stage to focus too much emphasis on any single approach. Basic and translational research should remain an important focus for TB vaccines, whilst establishing a development pathway towards an adult pulmonary TB vaccine in parallel.

For HSV it was recommended that a systematic review be conducted of age-specific seroprevalence data for HSV-1 and HSV-2 in different LMIC paediatric populations. This will be helpful to guide the important product development activities underway. PD VAC noted that a major incentive for the development of HSV vaccines, in addition to the public health burden directly accountable to these viruses, was their potential to reduce HIV infection rates. PDVAC would like to review the business case and modelling outcomes under development for HSV once they are available, and commends the HSV community for taking up this initiative. Finally, with regard to HSV it was recommended that the HSV data from the minimally invasive autopsy component of the large CHAMPS study is carefully assessed in better understanding the neonatal HSV mortality burden. PDVAC also notes and supports the broader sexually transmitted infection roadmap for vaccine development, and would like to be kept updated on progress.

In the cases of dengue and malaria vaccines, PDVAC noted that vaccine development for both both diseases are entering a critical stage whereby guidance on trial design and endpoints related to second generation vaccines will be needed, and recommended that WHO initiates development of such guidance. The promise of chimeric vaccine vectors has been highlighted from both Dengue and Ebola (yellow fever and VSV backbones respectively).

MERS and chikungunya vaccines will be further assessed as part of the WHO Blueprint discussions.

The next meeting of PDVAC is planned for June 8-10 2016.

A full meeting report will be published in a Vaccine journal supplements which will include each pathogen specific pipeline analysis