Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Vaccine 34 (2016) 2865–2869

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Report from the World Health Organization's Product Development for Vaccines Advisory Committee (PDVAC) meeting, Geneva, 7–9th Sep 2015☆

Birgitte K. Giersing[a], Kayvon Modjarrad[b], David C. Kaslow[c], Vasee S. Moorthy[a,*], WHO Product Development for Vaccines Advisory Committee[1]

[a] Initiative for Vaccine Research, World Health Organization, CH-1211 Geneva 27, Switzerland
[b] US Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD 20910, USA
[c] PATH, Seattle, WA 98109, USA

ARTICLE INFO

Article history:
Available online 15 March 2016

Keywords:
Vaccine
Candidate
Product development
PPC
LMIC

ABSTRACT

There are more vaccines in development, against a greater number of pathogens, than ever before. A challenge with this exceptional level of activity and investment is how to select and resource the most promising approaches to have the most significant impact on public health. The WHO Product Development for Vaccines Advisory Committee (PDVAC) was established in 2014 to provide strategic advice and recommendations to WHO for vaccines in clinical development that could have a significant impact on public health in low and middle income countries. On 7–9th September 2015, PDVAC was convened for the second time, when the committee reviewed vaccine developments in 24 disease areas. This report summarises the key recommendations from that consultation.

1. An introduction to PDVAC and its remit

The most recent publication of the Jordan Report provides a comprehensive summary of the vaccines that were in development in 2012: 577 vaccine candidates were identified, against 110 human pathogens [1]. PDVAC's remit is to consider how to accelerate vaccine candidates at the Phase 2 stage of clinical evaluation or earlier, for disease areas where there is substantial disease burden in low and middle income countries (LMICs), but where no vaccines currently exist, and where there is some ongoing product development activity which may benefit from guidance from WHO [2]. One of the potential key outputs from PDVAC review is the recommendation to generate a WHO guidance document describing the preferred product characteristics (PPCs) for a vaccine against a particular pathogen. These PPC documents describe WHO preferences for vaccines to be used in LMICs; in particular its indications, target groups and features of desirable clinical data related to safety and efficacy. They are intended to provide early guidance to developers at least 5–10 years from vaccine approval, and to ensure that, once licensed, data are available to enable decision-making on use of the vaccine in the populations that need it most.

2. The scope and objectives of the 2015 PDVAC meeting

The WHO convened its second PDVAC meeting in Geneva, in September 2015, involving subject matter experts from vaccine industry, academia and public private partnerships. In the 12 months since its first meeting, the vaccine research and development landscape had shifted significantly, with a renewed focus

* Corresponding author at: World Health Organization, Initiative for Vaccine Research, 20 Avenue Appia, 1211-CH Geneva 27, Switzerland. Tel.: +41 22 791 4760.
E-mail address: moorthyv@who.int (V.S. Moorthy).

[1] WHO Product Development for Vaccines Product Development Advisory Committee: Ashish Bavdekar (Kem Hospital and Research Center, Pune, India). Klaus Cichutek (Paul-Ehrlich-Institut, Langen, Germany). Alejandro Cravioto (Global Evaluative Sciences Inc., Seattle, WA, USA). Bernard Fritzell (Independent Consultant, Bordeaux, France). Barney S. Graham (National Institutes of Health, Bethesda, MD, USA). Ruth Karron (Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA). Claudio F. Lanata (Instituto de Investigacion Nutricional, Lima, Peru; and US Naval Medical Research Unit No. 6, Callao, Peru). Mair Powell (Medicines and Healthcare Products Regulatory Agency, London, United Kingdom of Great Britain & Northern Ireland). Yiming Shao (Chinese Center for Disease Control and Prevention, Beijing, People's Republic of China). Peter Smith (London School of Hygiene and Tropical Medicine, London, United Kingdom of Great Britain & Northern Ireland).

http://dx.doi.org/10.1016/j.vaccine.2016.02.078

on preparedness for emerging infectious diseases in the wake of the 2014–2015 Ebola emergency. For this reason, the 2015 agenda included an overview of the unprecedented process and timeline to interim efficacy data for Ebola vaccines, reports from the ongoing Phase III study, as well as a Target Product Profile that is now finalised and publically available [3]. In addition, the committee was informed of efforts to establish a WHO Blueprint for Emergency R&D Preparedness and Research Response. Middle Eastern Respiratory Syndrome-coronavirus (MERS-CoV) was reviewed as an ongoing case study of an emerging pathogen, under the auspices of this recently formed initiative.

Prior to the meeting, the committee reviewed 24 pathogen-specific landscape analyses that outline the unmet public health need, current vaccine development status and product development challenges. All of these documents are included in this special vaccine supplement on pipeline vaccines, and are on the WHO PDVAC website. For 13 of these 24 pathogens, subject matter experts described the status of vaccine development in presentations to the committee. PDVAC's remit is to consider which vaccines are likely to have clinical proof of concept data within the next 3 years and to identify areas where WHO has a clear role to play in increasing the likelihood that these vaccines will be used to reduce the disease burden in LMICs. PDVAC is not a vaccine prioritisation committee, but rather a committee to assess the vaccine pipeline and determine what activities or guidance may best accelerate vaccines for diseases that are most prevalent in LMICs.

This report summarises the conclusions and recommendations from the meeting. It is not intended to be an in depth summary of the product development status for each pathogen (for this, please refer to the individual landscape analyses and meeting presentations on the WHO website [2]). Also, many pathogens not discussed by PDVAC remain an important priority for vaccine research and development.

3. New vaccines for maternal immunisation on the horizon

Both Respiratory Syncytial Virus (RSV) and Group B Streptococcus (GBS) are pathogens for which there is major unmet public health need, particularly for neonates and infants in LMICs. For both pathogens, maternal immunisation could reduce the risk of neonatal infection and death by passive placental transfer of maternal antibodies. Although new vaccines against these conditions may establish a precedent for maternal immunisation as the initial indication, other existing vaccines such as those against influenza and tetanus have been recommended by the WHO for immunisation of pregnant women. Indeed, in the case of influenza, WHO highlighted pregnant women as the highest priority target group for vaccination.

3.1. RSV

RSV was highlighted at the inaugural PDVAC meeting as a pathogen for which there is significant clinical pipeline activity, and likelihood of a candidate emerging for licensure in the near term. Novavax's RSV F-protein based nanoparticle vaccine remains the most advanced candidate, with a Phase III study in pregnant women that started at the end of 2015, following the demonstration in a Phase II study [5] that palivizumab-competing antibody and RSV neutralising antibody were elicited and transferred to infants. In addition, recent preliminary data in the elderly demonstrated efficacy, and a phase III trial has been initiated in that target population (NCT02608502). GSK and J&J also have RSV F vaccines in clinical development that target pregnant women, and MedImmune is developing an RSV F vaccine for use in the elderly. A number of groups have RSV F vaccines in preclinical development, including NIAID. An RSV subunit vaccine containing the SH protein (Immunovax) is also currently being evaluated in adults. A number of live vaccines are in clinical development for active immunisation of infants and young children, including native RSV candidates from which nonessential genes have been deleted, and an adenovirus vector containing the RSV F gene. Passive prophylaxis with a long-half life monoclonal antibody developed by Medimmune is currently being evaluated in a dose-escalation/pharmacokinetics trial in healthy preterm infants (NCT02290340).

Following the 2014 PDVAC meeting, WHO convened a consultation to provide guidance on clinical endpoints and development pathways for maternal and paediatric RSV vaccine candidates, with a focus on considerations in LMICs [4]. In addition, WHO, PATH and National Institute for Biological Standards and Control (NIBSC) are collaborating to develop reference reagents, with a view to establishing International Standards. Efforts to develop PPCs, as well as to propose a roadmap for RSV vaccines, are underway and will be discussed during a WHO consultation in 2016. Given the significant progress in RSV vaccine development, a specific RSV update will be provided "For information" to WHO's Strategic Advisory Group of Experts (SAGE) in April 2016.

3.2. GBS

GBS is a significant cause of infant mortality particularly in the neonatal period, with most deaths occurring in LMICs, where treatment with intrapartum antibiotic prophylaxis (IAP) is not generally used. High levels of maternal anti-capsular polysaccharide (CPS) IgG correlate with reduced neonatal disease risk, and a vaccine against 5 of the 10 circulating serotypes may protect against up to 90% of disease. Two large pharmaceutical companies are currently engaged in GBS vaccine development, with Glaxo SmithKline considering Phase III study designs for their candidate. The proposed approach is to identify specific anti-CPS IgG thresholds as clinical correlates of protection, based on estimation of disease risk reduction, rather than conventional clinical disease end-points. With this in mind, PDVAC recommended that WHO develop guidance on the testing and development pathway for GBS vaccines, including consensus on strategic goals, clinical trial design considerations and development of PPCs. Key development considerations include ethical issues in conducting a vaccine efficacy study in a population with high GBS incidence, such as parts of Africa, where IAP is not the standard of care.

4. Advances in enteric vaccines

4.1. *Shigella and enterotoxigenic* Escherichia coli *(ETEC)*

Globally, there are nearly 1.7 billion cases of diarrhoeal disease every year, many with acute and chronic effects. The Global Enteric Multicenter Study (GEMS) was a large multi-country case-control study of the aetiology of cases of moderate-to-severe diarrhoea [6]). Molecular reanalysis of randomly selected samples collected in the study, using qPCR rather than culture, confirmed that ETEC and Shigella are two of the most significant pathogens that cause moderate-to-severe diarrhoea among children <5 years old in Africa and South Asia, accounting for around 40% of diarrhoea episodes in 12–23 month olds. In addition to diarrhoeal disease, ETEC and Shigella infections result in an estimated 4.6 million children with moderate or severe stunting due to malnutrition, accounting for an additional 31,000 deaths annually.

Killed (ETVAX [8]) or live attenuated (ACE527 [9]) whole vaccine approaches, in combination with the adjuvant Double Mutant Heat Labile Toxin (dmLT), are the most advanced ETEC vaccine candidates. Several Shigella vaccine candidates, based on live attenuated or sub-unit approaches, are also in clinical studies. Trials of

these vaccines are facing similar challenges to those for ETEC with respect to requiring multi-valent approaches, assay standardisation and identifying correlates of protection, as well as in defining appropriate clinical trial end-points and clinical trial design for field trials in endemic areas. In addition, it is uncertain whether a stand-alone ETEC or Shigella vaccine would be implemented, or whether developers should prioritise development of a combination ETEC/Shigella vaccine. The WHO intends to expand its current capacity to support consensus building, guidance and decision-making in this area, in readiness for the Phase III studies.

4.2. Norovirus

The recently published MAL-ED study, that documented the occurrence of community-associated non-severe diarrhoeal episodes in 7 sites in different countries, identified Norovirus, specifically the G.II strain, as having the highest attributable fraction [7]. Norovirus causes an estimated 200,000 deaths per year, globally. Takeda has the leading vaccine candidate, for which clinical proof of concept was demonstrated in a human challenge model. This vaccine is entering Phase IIb clinical studies in adults and paediatrics imminently. This bivalent candidate vaccine is based on a combination of GI.1 and GII.4 VLPs and is designed to offer cross-protection against the 25 human genotypes. However, ongoing and expanded surveillance is needed to monitor circulating strain replacement and to ensure that the candidate is able to protect against any emerging genotypes, as well as to better document the disease burden. With this in mind, PDVAC advised that WHO explore the possibility of incorporating Norovirus surveillance within the WHO rotavirus surveillance network.

5. The Global Vaccine Action Plan (GVAP): vaccine development efforts in HIV, malaria, TB and Universal Influenza

The GVAP is a framework approved by the World Health Assembly in 2012 to achieve the Decade of Vaccines vision in which all individuals and communities live free from vaccine preventable diseases [10]. Within this framework is a specific objective on research and development, with indicators related to progress towards vaccines against HIV, malaria, tuberculosis and a universal vaccine against influenza. According to the GVAP monitoring & evaluation framework, progress towards R&D related objectives is conducted every second year. PDVAC scrutinises the progress towards the R&D indicators and issues recommendations for the GVAP assessment report. As such, development efforts for these vaccines are 'standing items' for PDVAC review.

5.1. Human Immunodeficiency Virus (HIV)

Four HIV vaccine concepts have been tested in six efficacy trials in the last 30 years. One of these, the RV144 study, evaluated a heterologous prime boost regimen and demonstrated a modest level of efficacy (31%). The P5 partnership was established in the wake of the RV144 trial to further optimise the ALVAC/protein heterologous prime/boost approach with a different adjuvant. A Phase I/II study with this new regimen is underway in South Africa, with agreed go/no-go decision criteria to proceed to a phase III, based on interim data expected in early 2016. The final efficacy read out is expected in early 2020, following 2 years of follow up. PDVAC commended the major progress towards Phase 3 trials in HIV vaccines. It was acknowledged that novel approaches in the HIV field had advanced vaccine development against other pathogens.

5.2. Tuberculosis (TB)

The WHO post-2015 global TB strategic goals aim for a 95% reduction in TB mortality by 2035 worldwide and a 90% reduction in TB incidence (compared with 2015 levels). It is acknowledged that these reduction targets are not achievable without the development of novel tools for TB control. With the failure of the MVA-85A TB vaccine to show efficacy, the TB vaccine community has refocused on early stage, translational research and experimental medicine studies to evaluate a more diverse candidate portfolio with respect to both antigens and delivery platforms. To accelerate evaluation and to reduce costs, novel clinical study designs are being used to collect clinical proof of concept data in targeted, high incidence populations. Recent modelling data indicates that targeting vaccines to adolescents and adults may have the highest and earliest public health impact and cost-effectiveness, and consensus is emerging that development of vaccines to prevent pulmonary tuberculosis in this age population should be a significant focus. PDVAC noted the complexities from the policy perspective with "improved BCG vaccines", including issues related to non-specific beneficial effects ascribed to BCG vaccination. The committee encouraged work on development pathways for the adolescents/adult indication, noting that basic and translational research should remain an important focus.

5.3. Malaria

The progress of the most advanced candidate, RTS,S/AS01, was reviewed, noting that the European Medicines Agency issued a positive scientific opinion on the vaccine in July 2015. While the next steps with RTS,S/AS01 are explored there remains interest in second generation malaria vaccines. WHO has published a malaria vaccine PPC document outlining WHO's preferences for second generation malaria vaccines in two classes; firstly highly effective vaccines to reduce morbidity and mortality, and secondly vaccines to prevent transmission for the purpose of enabling malaria elimination [11]. Progress with transmission blocking vaccine trials in Mali and whole parasite vaccine development was highlighted.

While not included as one of the two highest priorities, a few groups are now exploring progression of vaccines designed to prevent pregnancy-associated malaria. The pathways to licensure and use of such vaccines are not yet well characterised. It was noted that *Plasmodium vivax* remains neglected for vaccine research activities, despite the very substantial disease burden due to this malaria parasite, especially in Asia. It was noted that the "Controlled Human Malaria Infection" model remains an important approach for initial screening of potential malaria vaccine candidates.

5.4. Universal influenza

PDVAC considered the case for an improved seasonal influenza vaccine approach, which optimises the currently available vaccines to improve the magnitude, quality and duration of the protective response and potentially offers protection for more than one influenza season. However, licensure of seasonal vaccines is based, in many jurisdictions, on achieving an established hemagglutination inhibition (HAI) threshold. Development of improved seasonal vaccines may represent lower hanging fruit in terms of regulatory acceptability, compared to the timelines for a truly universal influenza vaccine. The committee advised WHO to develop strategic public health goals and PPCs for improved seasonal influenza vaccines, and to provide guidance on data that would be needed to establish improved performance of such vaccines. In addition, the WHO is convening its eighth meeting on development of influenza

vaccines that induce broadly protective and long-lasting immune responses in August, 2016.

6. The first generation vaccine against dengue

There are four dengue serotypes, and all are capable of causing the full spectrum of disease. Life-long homotypic protection is conferred after initial infection but heterotypic protection against other serotypes is short-lived. A second infection with a different serotype is more likely to cause severe dengue disease, presumably through antibody-dependent enhancement (ADE). There two vaccine candidates soon to begin Phase 3 trials, and one candidate, Sanofi Pasteur's CYD-TDV, which requires 3 immunizations over six month intervals, has recently been approved for use in those 9–45 years of age living in endemic areas. Overall this vaccine offered around 60% protection against dengue disease, with variable efficacy by serostatus and age of vaccinee, infecting serotype, and severity of disease [12]. It will be reviewed by SAGE in 2016.

PDVAC considered the issue of trials of second generation vaccines, and whether or not there would be a need for comparability studies with the existing vaccine. It was noted that there are circumstances in which randomised, placebo controlled studies may be justified even when an efficacious vaccine exists, depending on a number of factors [13]. Related to this, WHO is planning to initiate a process in 2016 on trial design considerations for second generation dengue vaccines and their path to licensure.

7. Pipeline vaccines that may be biologically feasible, but for which a robust investment case needs to be developed to catalyse R&D

7.1. Group A Streptococcus (GAS)

GAS causes a substantial disease burden, with approximately 18 million people suffering from a serious GAS disease, 1.8 million new cases each year and 517,000 deaths annually [14]. The greatest mortality burden is due to rheumatic heart disease, but invasive GAS diseases such as maternal sepsis also contribute significantly. Previous human challenge studies, as well as vaccine trials, suggest that it is biologically feasible to develop a vaccine, however vaccine development has been impeded by safety concerns regarding the potential for induction of GAS-mediated autoimmune diseases such as acute rheumatic fever (ARF) and acute post-streptococcal glomerulonephritis (APGN). Although a number of recombinant, multivalent vaccine candidates have been developed, they are struggling to secure investment beyond early stage clinical studies.

PDVAC recommended that two separate investment cases be developed by the GAS community to target investment from (i) the public sector, 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, and (ii) the private sector, incorporating both the high income country (HIC) market for prevention of pharyngitis due to GAS, and the LMIC market for prevention of cardiac disease. The outcomes of these 2 investment cases will assist the GAS scientific community, PDVAC and funding agencies in determining the optimal product development strategy for GAS vaccines.

7.2. Herpes simplex virus (HSV)

Herpes simplex virus type 2 (HSV-2) is an extremely common sexually transmitted infection (STI), affecting over 400 million people aged 15–49 years globally, with lifelong recurrence of genital lesions. HSV type 1 (HSV-1), which infects the majority of the world's population, typically causes oral lesions but is also an increasingly important cause of genital infection. Control of HSV-2 infection is of particular concern for LMICs because it increases both acquisition and transmission of HIV infection. Previous development efforts for a prophylactic HSV vaccine did not show efficacy against HSV-2 but did demonstrate some efficacy against HSV-1 [15], suggesting that a vaccine against this class of viruses is biologically feasible. Currently, therapeutic vaccine candidates are more advanced than those with prophylactic indications, with one candidate demonstrating a 55% reduction in viral shedding.

PDVAC noted that development of a robust investment case, including updated morbidity and mortality data on the global burden of HSV-1, neonatal herpes, HSV-2 and HSV-associated HIV infection, may help to catalyse further vaccine development. Updated global estimates of prevalent and incident HSV-2 infection were recently published [16], as have the first WHO global and regional estimates of HSV-1 (including HSV-1 prevalence and incidence, in those aged 0–49 years, and genital HSV-1, in ages 15–49 years [17]. Neonatal herpes estimates are underway. PDVAC also recommended efforts to generate better primary data on neonatal herpes in LMICs, in particular through including HSV infection in the minimally invasive autopsy assessments to be undertaken by the Child Health and Mortality Prevention Surveillance Network (CHAMPS).

PDVAC noted that a major incentive for the development of HSV vaccines, in addition to the public health burden directly attributable to these viruses, is their potential to reduce HIV infection rates. In order to better understand the potential impact that a prophylactic or therapeutic vaccine may have on HIV transmission and disease, the WHO is commissioning an updated systematic review of the effects of HSV-2 infection on subsequent HIV incidence. In addition, the WHO and others in the HSV community have collaborated to develop an STI vaccine roadmap (most recent update included in this issue) and the elements required to formulate an HSV vaccine investment case, in order to incentivize funding and pharmaceutical company engagement in development of these vaccines.

8. Emerging infectious diseases, and the WHO Vaccine Preparedness Blueprint

The objective of the WHO Vaccine Preparedness Blueprint is to formulate a strategic roadmap and implementation plan that enables circumvention of obstacles that typically impede preemptive vaccine development prior to the onset of a public health emergency, and to facilitate a timely and effective R&D response when the inevitable future emergencies occur.

Some of the emerging pathogen areas presented to PDVAC, such as MERS, Nipah and chikungunya viruses will be further assessed as part of the WHO Blueprint discussions. PDVAC will review vaccine-related elements for these pathogens prior to Blueprint review, whilst ensuring complementarity with guidance in development related to drugs, diagnostics and non product-development related research as part of the holistic R&D focus on emerging pathogens. The first of these, the WHO Ebola Vaccine Target Product Profiles, was finalised in December 2015. A draft PPC, and a consultation meeting to initiate work on a roadmap towards a MERS vaccine and emergency response occurred in December 2015.

9. Looking ahead – PDVAC in 2016

The pathogens to be reviewed in 2016 will focus on those for which vaccines are most likely to enter clinical proof-of-concept studies within the next three years, such as *Clostridium difficile*. The recently published Phase III trials for the *Helicobacter pylori* [18] and Enterovirus 71 [19] (EV71) candidates, both of which were performed in China will also be discussed.

In addition to the evaluation of new vaccines, PDVAC has a role where first generation vaccines are licensed but development of improved second generation products are needed for an ongoing unmet public health need in LMICs. In keeping with this remit, the product development efforts ongoing for second generation pneumococcal vaccines, as well as for rotavirus will likely be discussed. In the cases of dengue and malaria vaccines, PDVAC noted that vaccine development for 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.

In general, PDVAC noted that many important platform technologies, such as novel viral vectors, innovative antigen design and broadly neutralising antibody approaches, often emerge from HIV and malaria vaccine R&D. It is therefore imperative that information on these potentially cross-cutting clinical portfolios is communicated between fields. WHO has begun to collate summary information on the global vaccines portfolios across several pathogen fields, including HIV, TB, malaria, respiratory and enteric pathogens available at: http://who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/.

The PDVAC review process offers a mechanism to 'deep dive' into the product development issues and opportunities across a range of pathogens, and solicits guidance from experts in the vaccine field. There have been several exciting developments in the last year, and the vaccine community looks forward to progress in all of the disease areas discussed. The next meeting of PDVAC is planned for June 8–10, 2016.

Acknowledgements

We gratefully acknowledge the pathogen specific landscape analyses that were prepared by the following individuals (in some cases the individuals acted as liaisons for a larger group within their institution): Mark Alderson, David Beasley, Coreen M. Beaumier, Ashley Birkett, Maria Elena Bottazzi, Louis Bourgeois, Jonathan Carapetis, Jane Cardosa, Charles B. Chesson, James Dale, Sana S. Dastgheyb, Brian E. Dawes, Hansi J. Dean, John J. Donnelly, Anna P. Durbin, Sami L. Gottlieb, Luiza Guilherme, Jesse H. Erasmus, Thomas Evans, Patricia E. Fast, John Fraser, Lisa Gieber, Portia M. Gillespie, Michael Good, Tara Hayward, Paul Heath, Deborah Higgins, Joachim Hombach, Peter J. Hotez, Christine Johnston, Cheryl Keech, Imran Khan, Hester Kuipers, Wayne C. Koff, Calman A. MacLennan, Sachin Mani, Laura B. Martin, Maureen Merrifield, Gregg N. Milligan, Nicole Moreland, Kim Mulholland, Mark S. Riddle, Jeffrey T. Safrit, Sushant Sahastrabuddhe, Benjamin A. Satterfield, Lewis Schrager, Francesco Berlanda Scorza, Raphael Simon, Claire Smalley, Pierre Smeesters, Andrew Steer, Ulrich Strych, Zarifah H. Reed, Sharon M. Tennant, Jelle Thole, Carrie Trujillo, Vadim Tsvetnitsky, Kirsten S. Vannice, Anna Wald, Richard I. Walker, and Thomas F. Wierzba, as well as the pathogen specific vaccine updates that were presented by the following individuals: David Beasley, Carolyn Deal, Patrick Duffy, Anna Durbin, Barney Graham, Glenda Gray, Mark Hatherill, Judith Kallenberg, Ruth Karron, Immaculada Margarit, Duncan Steele and Andrew Steer.

We thank the US Military HIV Research Program at Walter Reed Army Institute of Research for secondment of Kayvon Modjarrad to the World Health Organization.

This report contains the collective views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization, of the Department of the Navy, Department of Defence, nor of the U.S. Government.

KM and CFL are employees of the U.S. Government. This work was prepared as part of their official duties. Title 17 U.S.C. §105 provides that 'Copyright protection under this title is not available for any work of the United States Government.'

Conflict of interest: None declared.

References

[1] http://www.niaid.nih.gov/topics/vaccines/Documents/JordanReport2012.pdf.
[2] http://www.who.int/immunization/research/meetings_workshops/pdvac/en/
[3] http://apps.who.int/immunization/research/target-product-profile/WHO_Ebola_vaccine_TPP_version_final.pdf?ua=1.
[4] Modjarrad K, Giersing B, Kaslow DC, Smith PG, Moorthy VS, WHO RSV Vaccine Consultation Expert Group. WHO consultation on Respiratory Syncytial Virus Vaccine Development Report from a World Health Organization Meeting held on 23–24 March 2015. Vaccine 2015, pii: S0264-410X(15)00767-7.
[5] http://ir.novavax.com/phoenix.zhtml?c=71178&p=irol-newsArticle&ID=2091286.
[6] Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. Lancet 2013;382(9888):209–22.
[7] Platts-Mills JA, Babji S, Bodhidatta L, Gratz J, Haque R, Havt A, et al. Pathogen-specific burdens of community diarrhoea in developing countries: a multisite birth cohort study (MAL-ED). Lancet Glob Health 2015;3(September (9)):e564–75.
[8] Lundgren A, Bourgeois L, Carlin N, Clements J, Gustafsson B, Hartford M, et al. Safety and immunogenicity of an improved oral inactivated multivalent enterotoxigenic *Escherichia coli* (ETEC) vaccine administered alone and together with dmLT adjuvant in a double-blind, randomized, placebo-controlled Phase I study. Vaccine 2014;32(52):7077–84.
[9] Darsley MJ, Chakraborty S, DeNearing B, Sack DA, Feller A, Buchwaldt C, et al. The oral, live attenuated enterotoxigenic *Escherichia coli* vaccine ACE527 reduces the incidence and severity of diarrhea in a human challenge model of diarrheal disease. Clin Vaccine Immunol 2012;19(12):1921–31.
[10] http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/.
[11] http://apps.who.int/iris/bitstream/10665/149822/1/WHO_IVB_14.09_eng.pdf.
[12] Hadinegoro SR, Arredondo-García JL, Capeding MR, Deseda C, Chotpitayasunondh T, Dietze R, et al. Efficacy and long-term safety of a dengue vaccine in regions of endemic disease. N Engl J Med 2015;373(13):1195–206.
[13] Rid A, Saxena A, Baqui AH, Bhan A, Bines J, Bouesseau MC, et al. Placebo use in vaccine trials: recommendations of a WHO expert panel. Vaccine 2014;32(37):4708–12.
[14] http://apps.who.int/iris/bitstream/10665/69063/1/WHO_FCH_CAH_05.07.pdf.
[15] Belshe RB, Leone PA, Bernstein DI, Wald A, Levin MJ, Stapleton JT, et al. Efficacy results of a trial of a herpes simplex vaccine. N Engl J Med 2012;366:34–43.
[16] Looker KJ, Magaret AS, Turner KM, Vickerman P, Gottlieb SL, Newman LM, et al. Global estimates of prevalent and incident herpes simplex virus type 2 infections in 2012. PLOS ONE 2015;10(1):e114989.
[17] Looker KJ, Magaret AS, May MT, Turner KM, Vickerman P, Gottlieb SL, et al. Global and regional estimates of prevalent and incident herpes simplex virus type 1 infections in 2012. PLOS ONE 2015;10(10):e0140765.
[18] Zeng M, Mao XH, Li JX, Tong WD, Wang B, Zhang YJ, et al. Efficacy, safety, and immunogenicity of an oral recombinant *Helicobacter pylori* vaccine in children in China: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2015;386(10002):1457–64.
[19] Liang Z, Wang J. EV71 vaccine, an invaluable gift for children. Clin Transl Immunol 2014;3(10):e28.