

**Advance Market Committee (AMC) Independent Assessment Committee (IAC)  
Eligibility Determination Meeting  
Public summary of meeting  
9 August 2016 – Teleconference**

**Participants**

IAC members:

- Arthur Elliot, Senior Programme Manager, Vaccines and Anti Viral Agents, US Department of Health and Human Services, USA
- Bernard Fanget, CEO, Bernard Fanget Consulting; VP R&D and Pharmaceutical Development, Neovacs
- Claire Broome, Adjunct Professor Division of Global Health Rollins, School of Public Health Emory University Atlanta, Georgia, USA (Chair)
- George Amofah, Lecturer, School of Public Health, University of Ghana, Legon
- Halvor Sommerfelt, Professor of Epidemiology, Center for International Health, University of Bergen, Norway; Director, Centre for Intervention Science in Maternal and Child Health
- Mary Kitambi, Public Health Specialist Ministry of Health, Community Development, Gender, Elderly and Children, Tanzania
- Soonman Kwon, Chief of Health Sector Group (Tech. Advisor), Asian Development Bank, Philippines; Professor & Former Dean, School of Public Health, Seoul National Univ., Korea
- Vitaly Zverev, Director, I.I. Mechnikov Institute of Vaccine Sera under the RAMS, Russia

AMC Secretariat/Gavi:

- Sara Sá Silva, Vaccine Programme Manager
- Melissa Ko, Senior Programme Manager
- Jason Marett, Associate Legal Counsel

WHO:

- Drew Meek, Scientist, HIS/EMP/PQT

UNICEF Supply Division (Observer):

- J. Barral-Guerin, Senior Contracts Manager, New Vaccines, Vaccine Centre

### **Objective of meeting**

As per the AMC Procedures Memorandum, the objective of the meeting was to review Pfizer's application for AMC eligibility for PCV13 4 dose vials and determine if the candidate vaccine met the Target Product Profile (TPP) for the AMC.

### **Commencement**

The IAC met by conference call on 9 August 2016. Eight of nine members of the IAC attended the call and a minimum quorum was obtained as required in the IAC Charter and Bylaws. The meeting was chaired by Dr. Claire Broome, IAC Chairperson. The meeting started at 16:00 CEST.

### **Programme update**

Sara Sá Silva presented a brief update on the pneumococcal AMC programme implementation. 57 AMC-supported PCV introductions had taken place to date, with the latest introduction in Myanmar on 1st July 2016. The phased Nigeria introduction, which started in December 2014, was almost completed, with the remaining states expected to introduce in September 2016. The next PCV introductions to be funded by the AMC were Haiti and India; India was expected to start rolling out PCV in Q1 2017 in a few states (exact states still pending confirmation), with national roll-out expected in the future. Based on the WHO UNICEF immunisation coverage estimates released in July 2016, 2015 PCV third dose coverage was 35% in the Gavi 73 countries, short of the goal of 40% due to delayed roll out in large countries, such as Nigeria and Bangladesh. Discrepancies between DTP3 and PCV3 still existed in some countries, such as DRC, indicating PCV-specific bottlenecks, which the Gavi Alliance would look into and address through country assistance. It was also described that once the PCV13 4ds vial are deemed AMC eligible, roll out would start in 2017 in 15-17 countries; India would be one of these countries. Sara clarified that India's recent decision to access a multi-national PCV product through AMC support had been a result of many factors, including strong political will from the India Government and Gavi Alliance's decision to provide catalytic support to the country for a limited number of years; India was nonetheless planning to implement a locally produced PCV once it becomes available.

## Review of TPP criteria attributed to WHO prequalification

Drew Meek reviewed the TPP criteria attributed to WHO prequalification<sup>1</sup> for the IAC, as per the “WHO prequalification review” column in the table below. The IAC received WHO's written report outlining how the candidate vaccine met the criteria listed below prior to the meeting.

Attribute	Minimally Acceptable Profile
<b>A. Immunogenicity</b>	Immunogenicity should be demonstrated in accordance with WHO criteria, which are based on non-inferiority to a licensed pneumococcal vaccine as outlined in WHO <i>Recommendations for the production and control of pneumococcal conjugate vaccines</i> . (WHO Technical Report Series, No 927, 2005 and any subsequent published guidance).
<b>B. Safety, reactogenicity and contra-indications</b>	The safety and reactogenicity profile should be comparable to, or better than that of the currently licensed pneumococcal conjugate vaccine. Contra-indications should be restricted to known hypersensitivity to any of the vaccine components.
<b>C. Interference and co-administration with other vaccines</b>	There should be no clinically significant interaction or interference in relation to safety and immunogenicity with concurrently administered vaccines.
<b>D. Product presentation</b>	The vaccine must be available in mono-dose or low multi-dose presentations. Mono-doses must be either a single dose vial or a auto-disable compact pre-filled device. Low multi-dose presentations must be formulated and labelled in compliance with WHO policy or guidance.
<b>E. Storage and cold chain requirements</b>	The product must be stable at 2-8 °C with a shelf-life of at least 24 months and a vaccine vial monitor should be attached as outlined in <i>Making use of vaccine vial monitors. Flexible vaccine management for polio</i> (WHO/V&B/00.14).

<sup>1</sup> As per the AMC Procedures Memorandum, Schedule 2, Paragraph A.

<b>F. Packaging and labelling</b>	Name and labelling must be in accordance with WHO <i>Recommendations for the production and control of pneumococcal conjugate vaccines</i> . (WHO Technical Report Series, No 927, 2005). Packaging must ensure minimal storage space requirements as set out in <i>Guidelines on the international packaging and shipping of vaccines</i> (WHO/IVB/05.23).
<b>G. Product registration and prequalification</b>	The product must be WHO pre-qualified in accordance with <i>Procedures for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies</i> (WHO/IVB/05.19).  <i>Note: WHO indicated that this reference is obsolete. Should refer to WHP TRS 978, Annex 6.</i>
<b>H. Post marketing surveillance</b>	Post-marketing surveillance should be conducted in accordance with national regulatory authorities and WHO prequalification requirements as set out in <i>Guideline for preparation of the product summary file for vaccine prequalification</i> (WHO/IVB/06.16) , <i>Guidelines on clinical evaluation of vaccines: regulatory expectations</i> (WHO Technical Report Series, No 924, 2004) and any relevant published guidance.

### **IAC discussion on the TPP criteria attributed to WHO prequalification**

The IAC confirmed that they were comfortable with the conclusions from the WHO prequalification set forth in the “WHO prequalification review” column in the table above. The IAC was also appreciative of the immunogenicity data that became available upon request following the initial IAC meeting, which indicated immunogenicity of the 4 dose vial was comparable to that of the 1 dose vial. In addition, the IAC highlighted the following aspects of programmatic importance for the pneumococcal AMC implementation:

- **Wastage:** The IAC expressed strong interest in the wastage monitoring of the 4 dose vial, a concern that had also been expressed in the previous meeting. WHO EPI team had previously clarified, in a document provided to the IAC, that the wastage was likely to be similar to other low multi-dose vial presentations with preservative and that a PIE could be warranted in the first few countries switching to this vaccine for dissemination of any lessons learned.
- **Cost of goods:** The IAC also expressed concerns around the cost per dose in the 4 dose vial and the minimal difference in relation to the 1 dose vial, considering the presumed cost savings for the manufacturers. WHO EPI team had previously clarified, in a document provided to the IAC, that costs of delivery include training, logistics, and removal of PCV10 2 dose vial stickers but that cost savings could be obtained from a cold chain and transport perspective.

### Review of TPP criteria assessed by the IAC

The IAC assessed the vaccine using the TPP IAC assessment criteria<sup>2</sup>, set forth in the table below.

Attribute	Minimally Acceptable Profile
(a) <b>Vaccine serotypes</b>	The serotypes in the vaccine formulation must cover at least 60% of the invasive disease isolates in the target region, and must include serotypes 1, 5 and 14 which are the most frequent isolates in GAVI Eligible Countries
(b) <b>Target population/ target age groups</b>	The vaccine must be designed to prevent disease among children <5 years of age and in particular be effective in those <2 years of age.
(c) <b>Dosage schedule</b>	Vaccine scheduling must be compatible with national infant immunisation programmes and consist of not more than 3 doses in the first year of life. The first dose must be shown to be administrable at 6 weeks of life or earlier.

<sup>2</sup> As per the AMC Procedures Memorandum, Schedule 2, Paragraph B.

(d) <b>Route of administration</b>	Intramuscular or subcutaneous.
(e) <b>Product formulation</b>	Liquid formulation with a standard volume of 0.5 ml/dose.

### **IAC discussion on the TPP criteria assessed by the IAC**

Claire Broome highlighted that due to the prior determination of AMC eligibility of the single dose vial and the non-inferiority of the 4 dose vial in relation to the single dose vial in terms of immunogenicity and serotype coverage, there was sufficient evidence for the 4 dose vial to meet the IAC assessment criteria as per the TPP. It was also clarified that the PCV13 formulation covers 70-85% of the invasive disease isolates in different Gavi regions.

### **Determination**

The IAC members participating in the meeting unanimously determined that PCV13 4 dose vial vaccine presentation meets all of the TPP criteria and that the candidate vaccine is therefore eligible for purchase pursuant to the terms and conditions of the pneumococcal AMC.

### **Other issues and recommendations**

The IAC recommended the conduct of post-introduction surveillance and monitoring, with feedback to be provided to the IAC on a regular basis in the context of the annual reports from manufacturers. Particularly, the IAC highly recommended the monitoring of wastage of 4 dose vials during delivery through routine immunisation. The availability of the vaccine was emphasised to avoid shortage or delay to introduce vaccines.

The meeting was adjourned at 16.43 CEST.