GVIRF 2016: Regulatory Challenges and Constraints When Evaluating Vaccine Clinical Trials	
Rapporteurs: Kirsten Vannice	
Session Outline	**Chair:** Klaus Cichutek (PEI) **Opening remarks:** Klaus Cichutek (PEI) **Presentations:** William Wekwete (Medicines Control Agency of Zimbabwe): Regulatory Strengthening – status update Dick Akanmori (WHO): The African Vaccine Regulatory Forum Nelson L. Michael (MHRP/WRAIR): Good Participatory Practices for vaccine clinical trials Marco Cavaleri (EMA): Lessons learned from experience with vaccines and the EMAs Article 58 process **Discussants:** Helen Rees (U. Witwatersrand) Nicholas Perombelom (IFPMA) **Closing Remarks**: Klaus Cichutek (PEI)
Objectives of the session	*To discuss:* (1) To share information on status of WHO Regulatory Strengthening work and current challenges in the regulation of vaccines and how they are being addressed (2) To focus on the knowledge gap around community engagement in vaccine clinical trials, and obtain feedback from the community on the implications of introducing Good Participatory Practices as a tool to address this need (3) To share information on the procedure according to Article 58 to Regulation (EC) No. 726/2004 resulting in CHMP's scientific opinion in the context of cooperation with the WHO, lessons learned from recent reviews, and future directions
Main outcome	The latest information was provided on developments in the regulation of vaccines, particularly changes to the African Vaccine Regulatory Forum (AVAREF) and Article 58, including discussion of opportunities to improve regulatory processes for all stakeholders (regulators, developers, and policy makers).
Summary (400-500 words)	146 vaccine manufacturers are located in 44 vaccine-producing countries, although 90% of global production is concentrated in 25 countries. In Africa, only Senegal and Egypt had vaccine industry. Thirty manufacturers produce WHO-prequalified products. WHO had assessed National Regulatory Authorities in 114 out of 194 countries based on six key functions: marketing authorizations, regulatory inspections, clinical trial approvals and monitoring, vigilance, lot release, and laboratory access. NRAs that developed and implemented institutional development plans (IDPs) after the assessments were considered functional by WHO. Significant progress had been made in vaccine regulation over the previous decades. The standards of applications, reviews, timelines and participant protection had all greatly improved. However, there were still a number of areas for improvement, of which many were similarly faced by developed and developing countries. A number of challenges in the regulatory evaluation of clinical trials were identified, particularly a

	lack of resources in many countries. There was also limited capacity for ethics committees, especially for experts without potential conflicts of interest. The roles of regulatory authorities and ethics committees in some countries need to be clarified and transparency of processes improved. Pharmacovigilance and monitoring for counterfeit and substandard products must also be improved in many settings. There have been efforts to harmonize regulatory processes and timelines across countries in Africa through the African Vaccine Regulatory Forum (AVAREF) to promote clinical development in these settings. AVAREF was constituted in 2006 and has facilitated joint reviews of clinical trial applications, GCP inspections, and harmonization across NRAs. A new AVAREF strategy is being launched in 2016, the goal of which is to strengthen clinical trials regulatory authorization and oversight by increasing efficiency and building optimal infrastructure for regulatory review of clinical trial applications. The strategy will include monitoring and evaluation of review/approval timelines, expansion in scope to medicines, adoption of a regional approach, and capacity building. Good Participatory Practice (GPP) Guidelines are important standard practices that have been critical to the HIV/AIDS research field and could greatly benefit clinical trial participants through their adaptation to other diseases, especially in outbreak situations. An update of the current version of the UNAIDS document on Good Participatory Practices should explore their adaptation to biomedical intervention clinical trials in general. Article 58 was introduced in 2004 by the European Commission as a tool to help expand LMIC access to new medicines. It provides a scientific opinion of the CHMP/EMA on the quality, safety, and efficacy of a medical product through the same rigor used for an assessment that would lead to a marketing authorization in the EU. Experts and observers from WHO or regulators in non-EU countries participate in the assessment process. The result is a scientific opinion on use outside the EU taking into consideration the benefit/risk of the intended target population. In addition to a number of medicines for HIV and malaria, three vaccines have received a scientific opinion of the CHMP through the Article 58 process: Hexaxim, Tritanix HB, and Mosquirix. The need to improve communication of the process, in particular the relevance of Article 58 for non-EU authorities, increasing their involvement and highlighting WHO co-ownership of the process have been identified and will be part of an action plan to be taken forward in 2016 and 2017. To maximize product development for public health, it is important to engage with regulators (as well as manufacturers and other stakeholders) early, and proactive consultations on generic issues are helpful to build capacity and facilitate efficient reviews. Lessons learned from AVAREF should be applied to other regulatory networks in other regions, as standard and harmonized processes promote product development and access to medicinal products, including in times of public health emergencies.
Key references or quotes (up to 5)	http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000157.jsp http://www.who.int/immunization_standards/vaccine_regulation/africa_network/en/ http://www.unaids.org/en/resources/documents/2011/20110629_JC1853_GPP_Guidelines_2011%20OK