GVIRF 2014 Plenary Session 2: Regulatory and public health challenges for vaccines with modest efficacy	
Rapporteurs: Duncan Steele, BMGF and Cristina Cassetti, NIAID	
Session Outline	**Chair: David Salisbury** **Presentations:** Peter Smith, London School of Hygiene and Tropical Medicine **Discussants:** Marion Gruber, US Food and Drug Administration, Pieter Neels, Brad Gessner, Agence de Médecine Préventive
Objectives of the session	Discuss regulatory and public health issues related to authorisation and use of vaccines with modest efficacy, and with consideration of reducing disease burden (and possibly transmission) on a population basis.
Main outcome	More guidance is needed both for regulation and public health recommendations of vaccines of modest efficacy. Post-registration studies will be needed for proper benefit/risk and cost effectiveness assessments.
Summary	Future discussions will need to consider that not all vaccinees will be fully protected by modest efficacy vaccines, individuals may be only partially protected, and the protection may not be life-long. Vaccines that demonstrate modest efficacy in clinical trials can still have enormous public health impact in populations with high disease burden, and need to be carefully assessed for use. Acceptable levels of protection for each vaccine depend on the incidence and severity of the disease; target population; other control or therapeutic options; and the safety profile of the product. Several examples of vaccines with high public health impact, despite modest estimates of efficacy are available, such as rotavirus and malaria vaccines: the benefits of these vaccines are highest in settings where the disease incidence is high. The clearest example of this is the high public health impact of rotavirus vaccines in Malawi and Bangladesh, despite modest (42-49%) vaccine efficacy. Regulators specifically look at vaccine quality, safety and efficacy. Currently there is limited guidance from regulatory authorities in terms of how to evaluate vaccines with limited efficacy, but open dialogue with the regulators is encouraged early in clinical development. There is no statutory or regulatory requirement to demonstrate a specific efficacy. Study design is crucial and having clearly defined clinical endpoints and case definitions with defined lower bounds of efficacy, preferably in multi-site settings will all contribute to a better understanding of vaccine efficacy. Other important factors for public health interventions such as cost effectiveness of and any potential indirect (herd) effects may not be available at the time of licensure, and hence cannot inform policy and implementation decisions. Epidemiological modelling of the public health impact and cost effectiveness of modestly efficacious vaccines will be an important component in interpreting their true worth. Studies to monitor the impact of these vaccines post-introduction are also important functions to provide needed evidence of cost effectiveness and public health impact, to help address new or ongoing issues of risk/benefit, and to provide evidence for the continued or widespread use of the vaccines. Communication strategies will be important in the interpretation and understanding of the public health benefits of modestly efficacious vaccines, particularly in the absence of clear regulatory guidelines or less than complete protection.
Key references or quotes	• "The answers need to be Delphic, as there are no absolute values or standards for decision making in this arena" (David Salisbury) • "The regulatory perspective and the public health perspectives are different" (Marion Gruber) • FDA Guidance document (2008) – from M Gruber's presentation. • Madhi SA & Cunliffe NA, *et al*. Effect of human rotavirus vaccine on severe diarrhoea in African infants. *N Engl J Med* 2010; 362(4): 289-298 • Zaman K, *et al*. Efficacy of the pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in Asia. *Lancet* 2010; 376: 615-22)