GVIRF 2018 Plenary 1: Progress Towards and Commonalities in Vaccine Development Against HIV, TB, and Malaria	
Rapporteur: Mary Marovich (NIAID)	
Session Outline	**Chair:** Johan Vekemans (Medical Officer, WHO) **Presentations:** *Advanced Clinical Development of HIV Vaccines,* Kathy Mngadi (Site Investigator, HIV Vaccine Trials Network, CAPRISA ECRS) *Progress towards vaccines against TB,* Gerald Voss (Scientific Advisor, TuBerculosis Vaccine Initiative, Board Vice-President, Global HIV vaccine Enterprise) *Global Pipeline for Malaria Vaccines: Progress and Challenges to accelerate vaccine development,* Fred Binka (Professor, School of Public Health, University of Health and Allied Sciences, Ghana) **Discussants:** *Commonalities across vaccine development efforts,* Punnee Pitisittithum (Faculty of Tropical Medicine, Mahidol University) Willem Hanekom (Deputy Director, Tuberculosis, Bill & Melinda Gates Foundation) *Gaps in Malaria Vaccines,* J Kevin Baird (Professor, Eijkman Oxford Clinical Research Unit, Eijkman Institute of Molecular Biology, and University of Oxford)
Objectives of the session	*To discuss:* • Progress in the development of HIV, TB and Malaria vaccines • Cross-cutting issues and regional perspective
Main outcome	HIV, TB, and malaria vaccines carry implementation risks because of their complex regimens that extend well beyond the EPI schedule. A new paradigm is needed that addresses implementation science alongside safety and efficacy assessments and manages risk for all stakeholders on the value chain.
Summary	**HIV.** High HIV incidence, notably in young women (15-24yrs) in south and east Africa, underscores an urgent need for a vaccine. Two ongoing HIV vaccine efficacy trials, HVTN702 and HVTN705 are expected to provide efficacy signals around 2020. HVTN702, ongoing in South Africa, uses an ALVAC-C prime and ALVAC-C+ bivalent env protein/MF59 boost regimen and is 50% enrolled. Multiple P5-related Phase 1 studies testing different adjuvants and priming regimens are running in parallel to inform clinical development should a correlate be verified. HVTN705 consists of an Ad26 vector prime with an Ad26+env protein boost aiming for global, cross-clade protection. This newly-opened study focuses on women in 6 southern African countries, with all study participants offered PrEP. **TB.** There is a diverse pipeline of TB vaccines including subunit proteins, viral

	vectors, whole cell inactivated and live-attenuated candidates.[a, b] A recent study in adolescents tested two well-tolerated vaccines, H4:IC31 and BCG re-vaccination. Though neither vaccine prevented initial infection, BCG re-vaccination showed statistically significant prevention (VE 45%, p=0.01) of sustained quantiferon-conversion while the H4:IC31 gave a more modest signal (VE 30%, p=0.08). These results can be used to identify correlates of vaccine protection and de-risk development. A stage gating approach with critical decision points is being used to guide investment decisions and portfolio management. Priorities include developing a controlled human challenge model and identifying alternative clinical endpoints. **Malaria.** The first EMA-recommended malaria vaccine, RTS,S, is in pilot deployment. Data from evaluations in Ghana, Kenya, and Malawi are expected by 2022 and will inform the wider use of RTS,S. Current gaps include a vaccine with high and durable efficacy, suitable for use in older children and adults including pregnant women, able to impact transmission and contributing to malaria elimination; and vaccines effective against *P. vivax.* A diverse pipeline including pre-erythrocytic, blood and sexual stage candidate vaccines, aims to address many of these needs.[c] Monoclonal antibodies may provide new opportunities. Controlled malaria human challenge models contribute to guide product development. **Cross-cutting issues.** Robust correlates of protection are needed to progress rapidly from partially efficacious products to more highly efficacious and deliverable successors. Vaccine development should systematically explore correlates of protection and apply innovative tools such as antibody lineage evaluation and sequencing of breakthrough infections. Many new vaccines have complex regimens and new target populations that will create delivery challenges in low resource settings. Implementation research such as the RTS,S pilots will be required to inform policy decisions on new vaccines and to guide their successful delivery. A new paradigm is needed that addresses implementation science alongside safety and efficacy assessments and manages risk for all stakeholders on the value chain.[d] This is crucially important for vaccine manufacturers, which need to consider business risks and opportunity costs in addition to societal benefits.
Key references or quotes	a. WHO. Accessed 13 April 2018. Malaria Vaccine Rainbow Tables. http://www.who.int/vaccine_research/links/Rainbow/en/index.html b. Voss G, Casimiro D, Neyrolles O et al. Progress and challenges in TB vaccine development [version 1; referees: 2 approved]. F1000Research 2018, 7:199. (doi: 10.12688/f1000research.13588.1) c. Schrager L, et al. The Global Report on Tuberculosis Vaccines 2018. Available at http://www.tbvi.eu/wp-content/uploads/2018/02/Summary-SWRTV_Finalproof.pdf. d. O'Brien, Katherine L et al. Mind the gap: jumping from vaccine licensure to routine use. The Lancet, Volume 387, Issue 10031, 1887 – 1889.