GVIRF 2018 Workshop 8: Vaccines and Antimicrobial Resistance (AMR)	
Rapporteurs: Claire Schuster (NIAID), Angela Hwang (Consultant)	
Session Outline	**Chair:** Dennis M. Dixon (Chief, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Diseases, NIAID) **Panel Moderator:** Johan Vekemans (Medical Officer, WHO) **Presentations:** *Antimicrobial Resistance and Vaccines,* Dennis M. Dixon (Chief, Bacteriology and Mycology Branch, Division of Microbiology and Infectious Diseases, NIAID) *Vaccination against bacterial diseases in farmed Atlantic salmon – experience and global applicability,* Edgar Brun (Head of Section, Norwegian Veterinary Institute) *Uropathogenic E. coli vaccines: basic and translational research approaches,* Scott Hultgren (Professor, Washington University) **Panelists:** Visanu Thamlikitkul (Director, WHO Collaborating Centre for AMR Prevention and Containment; Faculty of Medicine Siriraj Hospital, Mahidol University) *The principle and process of autogenous vaccine*, Suphot Wattanaphansak (Faculty of Veterinary Sciences, Chulalongkorn University) Nithima Sumpradit (AMR focal point, Thai FDA)
Objectives of the session	*To discuss* • vaccination strategies to reduce the use of antibiotics • areas where active immunization could limit the incidence and impact of resistant bacterial infections • scientific innovations for further development • challenges in the development and commercialization of immunization measures to address antimicrobial resistance
Main outcome	To combat AMR, new tools are needed beyond the development of novel therapeutics. Vaccines offer an innovative approach to prevent infections, reduce antimicrobial use, and promote antibiotic stewardship. While progress is being made for vaccines to combat AMR in human and animal health, awareness and acceptance of this approach remains a challenge. It is important to define and communicate the value of vaccines to combat AMR, identify populations who would benefit most, and consider affordability and accessibility in low and middle-income countries.
Summary	AMR has generated global interest as a growing threat. Vaccines have game-changing potential in addressing AMR. Examples of progress in vaccine R&D targeting frequently resistant pathogens were discussed. **Gonococcus**. A retrospective case-control study at sexual health clinics showed that individuals vaccinated with a group B meningococcal vaccine were 31%

	less likely to be diagnosed with gonorrhoea, providing proof of principle for prospective vaccine development for gonorrhoea.[a] ***Pseudomonas*.** A randomized, placebo-controlled Phase 2 study in ventilated ICU patients showed that a *Pseudomonas* vaccine was highly immunogenic, with no safety or mortality concerns. Although the study was not powered for efficacy, lower mortality was correlated with antibody titer.[b] ***Staphylococcus aureus*.** Pfizer is conducting a Phase 2 trial of a 4-antigen *S. aureus* vaccine in adults undergoing elective open posterior spinal fusion procedures. They are seeking input from FDA on whether the resulting efficacy and safety data are generalizable to other elective orthopaedic surgical populations.[c] **Uropathogenic *E. coli* (UPEC).** Urinary tract infections (UTIs) drive substantial antibiotic consumption, amounting to more than 10% of antibiotic prescriptions in the US. UPEC causes the majority of UTI cases, and multidrug-resistant strains are spreading globally. Preventive strategies are targeting the host-pathogen interface.[d] A FimH pilus adhesin protein vaccine (Sequoia Sciences) reduced recurrent UTIs in a Phase 1A/B trial and has received emergency use authorization on the strength of that data. A Phase 2 trial is in preparation. Orally bioavailable mannosides that bind to FimH can block colonization of the urinary tract. If effective, these strategies could dramatically reduce the use of antibiotics. **Aquaculture vaccines.** Fish diseases have devastating consequences for aquaculture. In Norway, consumption of antibacterials in salmon production decreased sharply in the mid-1990's with the introduction of vaccines against major fish diseases. Today, efficient multicomponent adjuvanted vaccines are available and the average annual antibiotic use in Norway is below 1 mg/kg fish produced. Given the vast scale of the industry, small benefits in survival or growth can be cost effective. Success requires epidemiology, diagnostic capability, and a focus on reducing antibiotic consumption. Additional impact can be achieved through public-private partnerships for new vaccine development, efficient licensure procedures, and better delivery systems. Biosecurity measures and antibiotics remain important because vaccines are not yet available for all the species in culture and to contain emerging pathogens. **Vaccines to combat AMR in Thailand**. Thailand's national action plan for AMR emphasizes the need to reduce AMR morbidity and decrease antimicrobial consumption. [e] Vaccines, an important approach for achieving these goals, are available for 3 of the 12 AMR pathogens prioritized by WHO. However due to vaccine costs none are included in the Thai national immunization program. To impact AMR, vaccines need to be affordable and added to Thailand's Essential Medicines List. Agricultural vaccines are preventing disease in pigs. Outbreaks of new diseases are being addressed using "autogenous" vaccines: pathogens isolated during outbreaks are propagated, inactivated, and administered on farms still experiencing the outbreak. Vaccination has correlated with 10-20% reductions in antimicrobials in feed and 30-40% reductions in injected antimicrobials while improving productivity through lower mortality and faster growth.

Key references or quotes	a. Petousis-Harris, H et al. Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study. The Lancet, Volume 390, Issue 10102 , 1603 – 1610 b. Rello J, Krenn C-G, Locker G, et al. A randomized placebo-controlled phase II study of a Pseudomonas vaccine in ventilated ICU patients. Critical Care. 2017;21:22. doi:10.1186/s13054-017-1601-9. c. *FDA Briefing Document (11/7/2017) Vaccines and Related Biological Products Advisory Committee Meeting FDA UCM583779.pdf* d. O'Brien VP, Hannan TJ, Nielsen HV, Hultgren SJ. Drug and Vaccine Development for the Treatment and Prevention of Urinary Tract Infections. Microbiology spectrum. 2016;4(1):10.1128/microbiolspec.UTI-0013-2012. doi:10.1128/microbiolspec.UTI-0013-2012. e. Ministry of Public Health, Ministry of Agriculture and Cooperatives. National strategic plan on antimicrobial resistance 2017-2021 http://www.fda.moph.go.th/sites/drug/Shared%20Documents/AMR/04.pdf