Antimicrobial Resistance and Vaccines

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GVIRF Meeting

Bangkok, Thailand

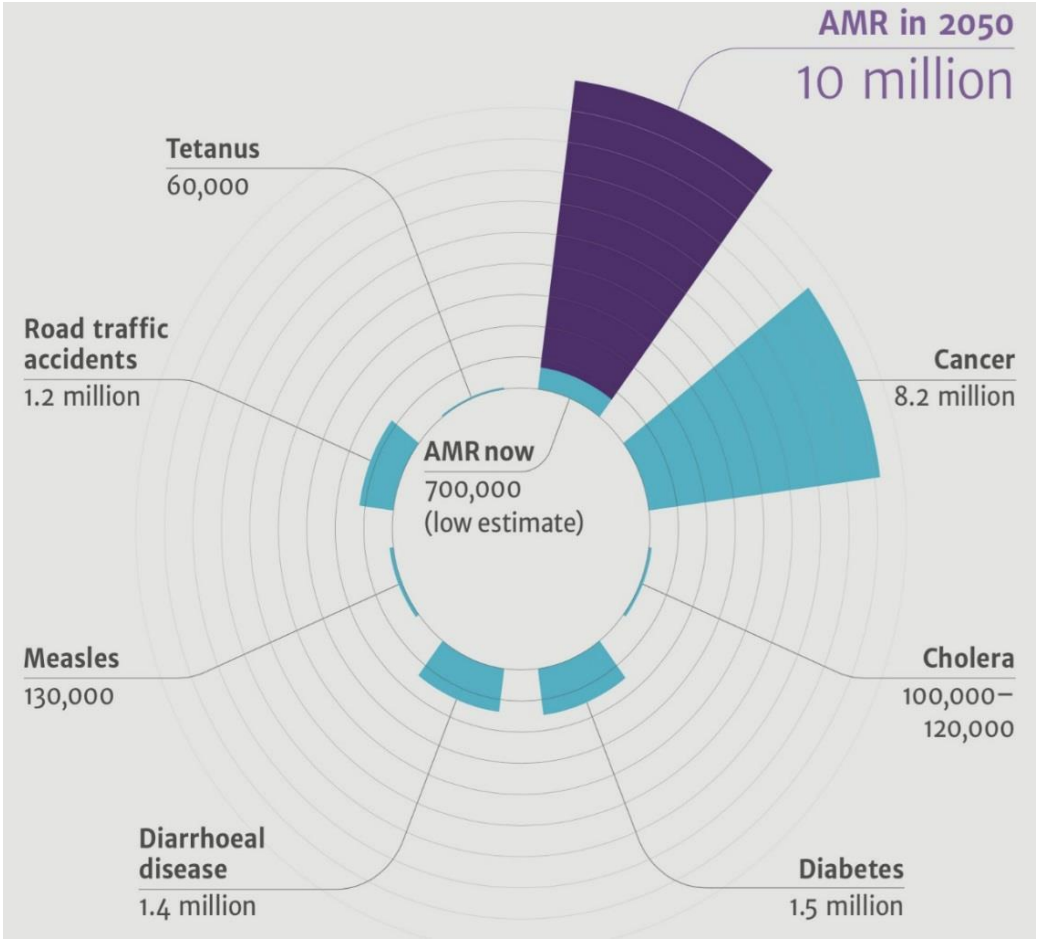
National Institute of Allergy and Infectious Diseases

AMR Has Moved from Scientific to Political Discussions

- **G7**
- **G20**
- **UN General Assembly**

… among others

Deaths Attributable to AMR Every Year



- **A continued rise in resistance by 2050 would lead to 10 million people dying every year globally.**
- **Antibiotic-resistant bacteria cause more than 2 million illnesses and at least 23,000 deaths each year in the US.**

The Review on Antimicrobial Resistance, Chaired by Jim O'Neill
http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf

NIH National Institute of Allergy and Infectious Diseases

2016 Global Vaccine & Immunization Research Forum (GVIRF)

15 – 17 March 2016, Johannesburg, South Africa

Chair	**Dennis Dixon (NIAID)**
Speakers	1. Martin Friede (WHO) and Bruce Gellin (NVPO, U.S. DHHS): The Role of Vaccines in AMR Strategies 2. Olaf Schneewind (University of Chicago, USA): Staphylococcal Vaccines 3. Magnus Unemo (Örebro University Hospital, Sweden): Gonococcal Vaccines 4. Jordi Rello (Vall d'Hebron University Hospital, Spain): Vaccines for Gram-Negative Healthcare Pathogens No ESKAPE

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2018 Global Vaccine & Immunization Research Forum (GVIRF)

20 – 22 March 2018, Bangkok, Thailand
W8: Vaccines and Antimicrobial Resistance

Chair	**Dennis Dixon (NIAID)**
Panel Moderator	**Johan Vekemans (WHO)**
Speakers	1. Dennis Dixon (NIH): Update since 2016 2. Edgar Brun (Norwegian Veterinary Institute): Salmon Vaccine 3. Scott Hultgren (Washington University, USA): *E. coli* Vaccine for UTIs
Panel Discussion	1. Visanu Thamlikitkul (Mahidol University, Thailand) 2. Suphot Wattanaphansak (Chulalongkorn University, Thailand) 3. Nithima Sumpradit (Food and Drug Administration, Thailand)

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Effectiveness of a Group B Outer Membrane Vesicle Meningococcal Vaccine Against Gonorrhea in New Zealand

- Retrospective case-control study of patients at sexual health clinics; aged 15–30; eligible to receive MeNZB
  - Compared rates of and gonococcal and chlamydial infection in vaccinated vs. unvaccinated individuals
  - Estimated efficacy against gonococcal infection of 31% vs. none for chlamydia

- **Interpretation:** "Exposure to MeNZB was associated with reduced rates of gonorrhoea diagnosis, the first time a vaccine has shown any protection against gonorrhoea."

- These results provide a proof of principle that can inform prospective vaccine development for gonorrhea.

Petousis-Harris H, et al. Lancet 2017; 390:1603-10
Seib K. Lancet 2017; 390:1567-69

A Randomized Placebo-controlled Phase II Study of a *Pseudomonas* Vaccine in Ventilated ICU Patients

Trial Design:

- 400 mechanically ventilated ICU patients; 34 sites (Europe and South America)
- Recombinant outer membrane protein IC43, 100ug and 200 ug, w/ and w/o Alum
- 2 doses in a 7-day interval, with 90 days follow-up

Results:

- No safety concerns
- Highly immunogenic
- No significant differences in *P. aeruginosa* infection rates – not powered as secondary endpoint

The vaccinated group has:

- Low rate of invasive infections (pneumonia or bacteremia)
- Low mortality rate by day 28, predicted by Ab titer on day 14
- Low immunogenicity when adjuvanted with Alum

Improved Clinical Outcome?

Rello J, et al. Critical Care 2017; 21:22

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FDA Advisory Committee Meeting 7 November 2017: Pfizer's SA4AG Study (B34510002) for Spinal Fusion Surgery

Trial Design:

- *Staphylococcus aureus* 4-antigen vaccine (SA4Ag)
- 6000 subjects at 278 sites in 10 countries
- Adults undergoing elective open posterior spinal fusion procedures with multilevel instrumentation

Primary Endpoint:

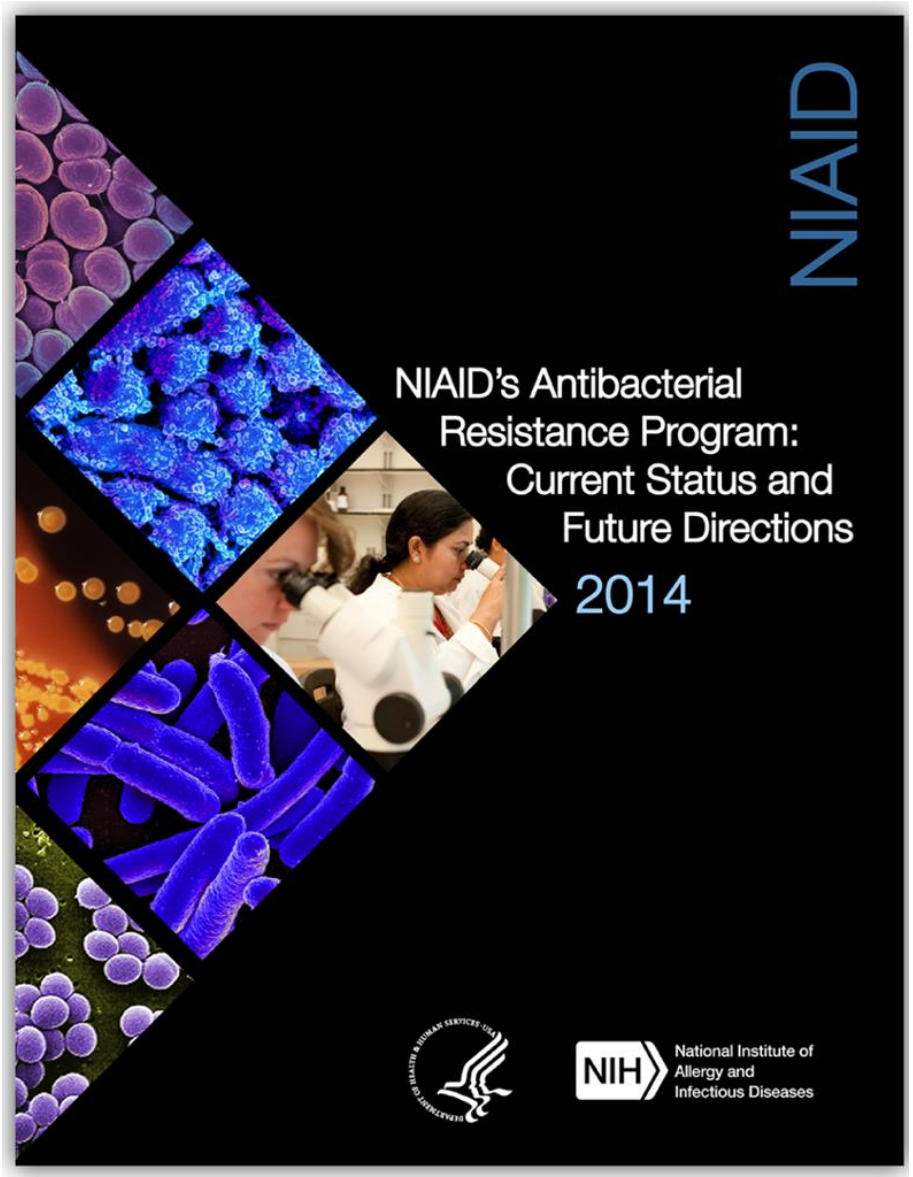
- Prevention of invasive disease caused by *S. aureus*

Discussion on Indication Label:

- Assuming that the ongoing study of SA4Ag achieves its pre-specified primary efficacy objective, please discuss the reasons why efficacy and safety should or should not be generalized to other elective orthopedic surgical populations.

Adapted from FDA Briefing Document (11/7/2017)
Vaccines and Related Biological Products Advisory Committee Meeting
FDA UCM583779.pdf

NIAID Antibacterial Resistance Program



- **Basic Research**
- **Translational Research/ Product Development**
- **Clinical Research**

Diagnosis, Prevention and Treatment

Web Search Term: **NIAID AR pdf**

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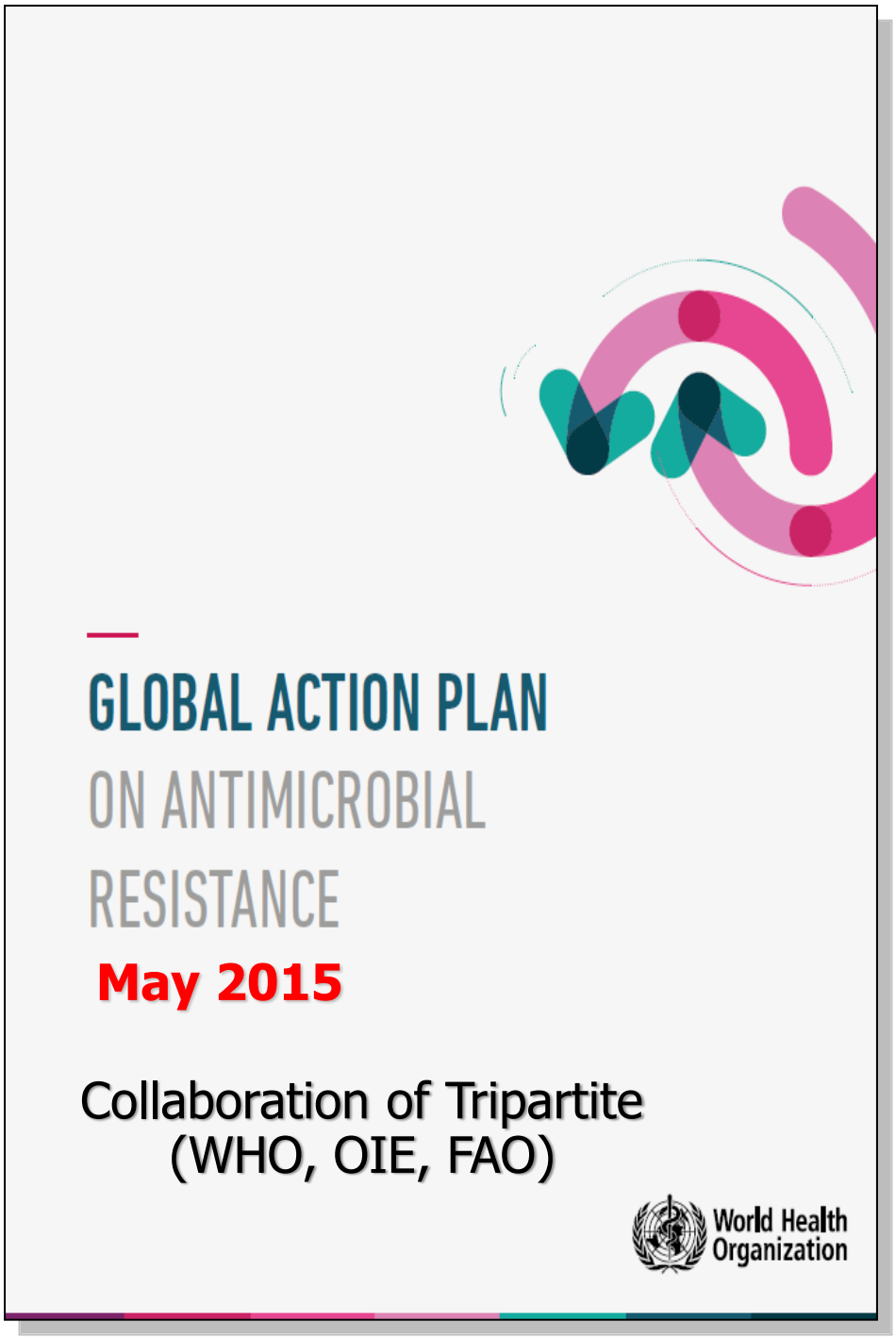
NIH/NIAID's New Initiative on AMR

RFA-AI-17-017:
Partnerships for the Development of Vaccines and Immunoprophylactics Targeting Multiple Antimicrobial-Resistant Bacteria (R01)

Funding Opportunity Purpose:

- The purpose of this FOA is to support milestone-driven projects focused on discovery, establishment of proof-of-concept for, and/or preclinical development of, lead candidate vaccines or immunoprophylactics that target multiple antimicrobial-resistant Gram-negative bacterial pathogens prevalent in nosocomial infections: carbapenem-resistant Enterobacteriaceae (CRE), multidrug-resistant (MDR) *Acinetobacter* and MDR *Pseudomonas aeruginosa*.

https://grants.nih.gov/grants/guide/rfa-files/RFA-AI-17-017.html

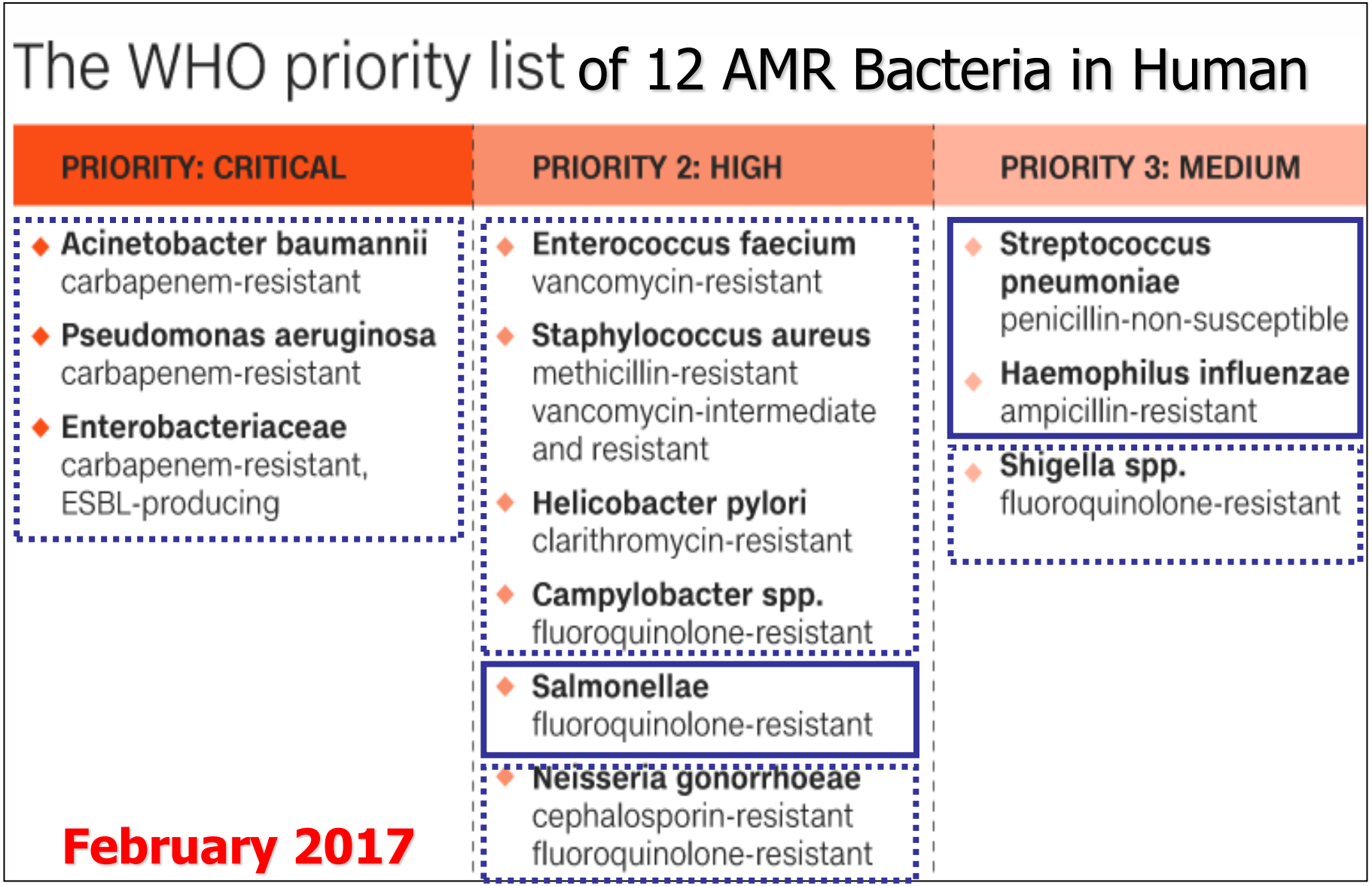


WHO Global Action Plan on AMR

- **5 Strategic Objectives**

1) Improve awareness and understanding of AMR
2) Strengthen AMR surveillance and research
3) Reduce incidence of infection
4) Optimize use of antimicrobials in human and animal health
5) Develop economic case for sustainable investment on AMR

Vaccine for AMR Bacteria in Human



Thank You

… for your interest