Accelerating Impact Through Mindful Management of Innovation

Jerome H. Kim, MD
13th Typhoid & Other Invasive Salmonelloses
6 December 2023
IVI supports vaccine development across the vaccine value chain

**Discover**
- Pre-Clinical Study & Support
  - Material production, test & release for toxicity studies
  - Protocol dev.
  - CMO/CRO identification
- Process & Analytical Dev.
  - Scalable & optimized processes for candidate Ag
  - Analytical methods for qual. testing
  - In vivo animal studies

**Develop**
- Assay Validation & Clinical Samples Evaluation
- Critical assay development & optimization
- Method validation according to ICH guidelines
- Clinical sample evaluation in GCLP lab
- Candidates & process transfer to CMOs & stability plan dev.
- Process scale-up & ensuring of commercial-scale mfg. & vaccine candidate supply
- IPDP & CDP development
- Clinical trial implementation & management in HIC & LMIC

**Deliver**
- Health Economic Study
- Field-based data collection incl. costing & willingness to pay
- Global/country analyses incl. invest., budget impact, cost-effectiveness, demand & disease burden
- Site preparedness for Ph.3 trial & effectiveness study
- AMR assessment & public database creation

**Epi. Surveillance**
- Epidemiology/Observational Study Support
- Protocol dev. incl. definition of endpoint, bio investigation, & database
- Prevalence & incidence est. of infection/disease severity
- Data for decision on vaccine introduction
- Site preparedness for Ph.3 trial & effectiveness study
- AMR assessment & public database creation

**Diseases**
- • iNTS
- • Group A strep
- • SFTSV
- • Shigella
- • Hepatitis A, B
- • Tuberculosis
- • HAdV-55
- • COVID-19
- • Paratyphoid A
- • Zika
- • Hantavirus
- • Pulmonary Syndrome (HPS)
- • Lassa fever
- • MERS
- • Invasive Non-typhoidal Salmonella (iNTS)
- • MERS-CoV
- • Chikungunya
- • Schistosomiasis
- • Typhoid
- • COVID-19
- • Cholera
- • Micro-needle array (MAP) Hep-B
- • Dengue fever
- • Cholera
- • Typhoid
- • AMR
- • GAS
- • iNTS
- • RSV
- • Schistosomiasis
- • Typhoid
- • Cholera
- • COVID-19
- • RSV
- • GAS
- • Shigella
- • AMR

**Cross-Functional Activities**
- IVI develops and supports:
  - Translational Hubs
  - Innovation Vaccine Research Centers
  - Training and Capacity building
  - Project Management
Managing Innovation to Impact

**DEMAND**
- Lives saved
- ↓ DALYs
- Healthier families
  - ↓ poverty
  - ↑ cognitive and physical development
  - ↑ education
  - ↑ Economic growth

**SUPPLY**

**VACCINE**

**DEVELOPMENT**
- WHO/SAGE
  - Gavi/UNICEF
  - ADVOCACY
  - NITAGs

**NATIONAL VACCINATION PROGRAMS**

**DELIVERY**
- Manufacturing Clinical Development
  - NRA approval
  - WHO PQ

**NEW GLOBAL HEALTH VACCINES**
- Developing Country Vaccine Manufacturer

**NEED:** A safe, effective typhoid conjugate vaccine

**PUB HEALTH, ACCESS & VACCINE EPI**
- Technology Transfer & Mfr Support
  - New vaccines

**LABORATORY**
- Development & Delivery
  - Pub Health
  - Access & Vaccine Epi

**DEVELOPMENT AGENCIES**
- KOICA, SIDA, DFID, USAID

**FOUNDATIONS / TRUSTS DONORS**

**Support for NRA / NITAGs**
- Burden data
- Cost Effectiveness
- Investment Cases
- Full Public Value of Vaccines Analyses
- Support for NRA / NITAGs

**Clinical Development and Regulatory**
- Biostatistics
- Data Management
- Support for PQ

**Drug-resistant S. Typhi in Pakistan**

**New global health vaccines**
Understanding the burden of disease from *Salmonella* Typhi

**DISEASE BURDEN**

- 5 years of typhoid fever surveillance in 10 countries (Lancet GH, 2018)
- 5 years of severe typhoid surveillance in 6 countries (under review, pre-print available)

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**TSAP**
Typoid Fever Surveillance in Africa Program

- 2010 - 2014

**SETA**
Severe Typhoid Surveillance in Africa Program

- 2015 - 2019

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2007 ViVA
- Global Risk Factor Mapping

Dr. Florian Marks
TCV Cost Effectiveness Analysis

- Small target scenario – base population in either urban slums or rural areas without improved water
- Large target scenario – base population includes the whole population of a nation

### Table

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<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
<th>Group 6</th>
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<tbody>
<tr>
<td>North Africa</td>
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<td>West Africa</td>
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### Vaccination strategy

<table>
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<tr>
<th>Strategy</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>Infant routine &amp; booster dose</td>
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<tr>
<td>2</td>
<td>Infant routine &amp; booster dose &amp; 1-14 catch-up</td>
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<tr>
<td>3</td>
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Technology Transfer and Clinical Development of Vi-DT

**2013**
- SK bioscience: Technology Transfer
- IVI as co-sponsor

**2021**
- Sub-study with MMR
- KMFDs approval and WHO PQ submission (MAY 2022)
- WHO PQ approval (expected)

**2022**
- Phase I: Philippines
- Phase II: Philippines
- Phase III: Nepal
- IVI as co-sponsor

**2023**
- Phase I: Indonesia
- Phase II: Indonesia
- BPOM approval (AUG 2023)
- WHO PQ submission

**2024**
- Phase III: Indonesia
- IVI as technical advisor

Dr. Sushant Sahastrabuddhe
TCV introduction and effectiveness evaluation

**SUPPORT TCV INTRODUCTION**

- Large Phase IV cluster randomized trial in Ghana.
- Mass vaccination → VE evaluation in DRC, Madagascar and Fiji island.
- Vaccine cost effectiveness analysis.

**Typhoid Vaccination in Madagascar (TyMA)**

- **Surveillance**
  - Sustained high typhoid disease burden in Imenvihafy Beatra (10 years of data)
  - Enhanced surveillance in Antsiranana district
- **Vaccinations**
  - Vaccinate children aged 1–16 years of age with Vi-CRM*3
  - Case-control study to determine effectiveness
- **Upcoming plans**
  - Vaccination ongoing, anticipated until January 2024

**Mozambique Typhoid Fever Surveillance Program (MOTIF)**

- **Scope**
  - Typhoid fever surveillance capacity setup in Pemba and Nampula study areas
  - Support potential Gavi application for national introduction
- **Current status**
  - Surveillance started in Nampula (Aug 2022; Pemba started in Mar 2023)
  - Nine typhoid cases identified to date
  - Donets QA-2023 (nasal survey and bled culture)

**THECA**

Typhoid conjugate vaccine effectiveness in Africa

2019 - 2025

**SETA+/STIA**

Severe Typhoid Surveillance in Africa Program

2020 – 2022 -> 2025

Dr. Florian Marks
Impacts: a decade of work on Salmonelloses in Africa

Data/Samples use
A decade of work for TCV vaccine introduction, other vaccine prioritization work, and use for other groups

- Sustained typhoid fever AND INTS burden identified in African countries
- TCVs used now through studies in Ghana, DR Congo, Madagascar, Burkina Faso and introduced in Liberia, Malawi, Zimbabwe (2024)
- Other groups using data for advanced analysis (typhoid prediction, AMR, others)
- Other pathogens identified (INTS -> stakeholder conference in 2024 in Kinshasa)

Capacity building
More than 1000 people employed, labs established, capacity-building. Use of sites for other diseases and by other groups

- Capacity built in African sites (>1,000 people funded through programs)
- Sites used by other partners; sites writing their own proposals
- Program platform for other work (HEV, GAS, HDSS site, climate change)
Opportunity: Typhoid in Fiji – Vaccination and Elimination (TyFIVE) & TySICS

TyFIVE/TySICS

Typhoid in Fiji

- Important public health problem
- High burden in Northern Division
- Sero-prevalence (measure of past exposure) is higher than what the incidence would suggest, hinting at:
  - Substantial under-reported burden
  - Presence of asymptomatic transmission

Updates

- Vaccination complete (October 2023); coverage ca. 50%
- Case-control study ongoing
New burden studies: S. Typhi & invasive non-typhoidal *Salmonella*

**Diseases:**
- S. Typhi present
- Intestinal significant burden
- Highest pathogen found:
  - S. Infantis
  - S. Typhimurium
  - S. Enteriditis

**Plan:**
- ISA/MDU in progress
- Two-tiered approach:
  - Y1: Multi-site assessment of burden using assay from Stanford/Harvard
  - Y2: Focusing on 1-2 sites to setup BC-based surveillance

**Latin America – Peru and Brazil**

**Africa - Ethiopia**

**Objectives**

**Primary**
- Estimate the seroprevalence/sero incidence of S. Typhi/Paratyphi among the indigenous population in Maués, Brazil

**Secondary**
- Compare the seroprevalence of S. Typhi and S. Paratyphi among the indigenous and non-indigenous population in Maués, Brazil
- Identify risk factors associated with seropositivity against S. Typhi/Paratyphi in both indigenous and non-indigenous population in Maués, Brazil.

**Site:** Brazil: Maués

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**Collaboration:** IV, Armauer Hansen Research Institute (AhRI), Center for Innovative Drug Development and Therapeutic Trials for Africa (COT-Africa)

- Estimate the seroprevalence, sero incidence and risk factors associated with seropositivity against S. Typhi and S. Paratyphi at selected districts in Ethiopia - ELISA IgG and IgG anti-Hemolysin E
- Identify clustering of S. Typhi and S. Paratyphi occurrence of cases – Household based

**TSAP and SETA projects: Lower incidence rate of blood-culture S. Typhi fever cases compared to other African countries**

**Surveillance**
- Household cross-sectional survey, Q3 2024

**Study report**

**Training and Capacity Building**
- ELISA IgG and anti-Hemolysin E
- SemiCalculator Workshop (December 8, 2023, in Kigali, Rwanda) tool designed to generate robust typhoidal incidence estimates from cross-sectional surveys.
• Burden studies – DOMI, ViVA, TSAP, SETA (SETA+, STIA) include epidemiology, risk factors, early investment case, work with SAGE/Gavi
• Vi-DT TCV vaccine development – technology transfers (Shantha, SK Bioscience, BioFarma, Incepta)
  – SKB approved by MFDS, WHO PQ submitted (SKB)
  – BioFarma approved by BPOM, WHO PQ submission anticipated
• Effectiveness
  – THECA (TyVEGHA, TyVECO, TyMA)
  – Cost effectiveness
  – Support for Gavi applications
• Implementation / Uptake
• New innovation
  – Trivalent TCV-iNTS?
  – TCV MAP?
Thank You

International Vaccine Institute

VACCINES FOR A HEALTHIER FUTURE