Cholera Program Update 2021

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GTFCC Meeting Dec 2021

International Vaccine Institute

IVI Cholera Program Strategy and Projects

Goals	Program Objectives	Current Projects
Ensure OCV Supply	Continue Supporting Manufacturers	• Critical Reagents • BIBCOL • **Reformulation of OCV (OCV-S)**
Improve Cholera Vaccine	Improve Vaccine Efficacy (Especially in <5 y.o.) And Flexibility of Use	• Euvichol-P CTC Label-> OCV-S CTC • **Pre-Clinical Development of Cholera Conjugate Vaccine (CCV)**
OCV Use & Introduction	Generate Evidence to Support Endemic Countries Introduction	• **ECHO-Nepal** • **ECHO-Mozambique** • **ECCP-Ethiopia** • Extended Analysis

Reformulation of OCV

Funded by BMGF
Conducted in collaboration with EuBiologics

- OCV contains 5 distinct components:
  - Redundant heat and formalin inactivated O1 Inaba and Ogawa
  - Vibrio cholera O139

➢ *Could a simplified formulation containing only two current components, O1 Inaba (El Tor) and O1 Ogawa (classical), and inactivated by a single method, be equally effective?*

- Anticipate ~20% reduction in costs and ~38% increase in production capacity

- Technical Expert Group Meeting Jan 2020 =>
  - Consensus that **two-component** vaccine should achieve an **equivalent protective immune response to O1** serotypes of *V. cholerae*
  - Agreed that the **O139 component** provides **no cross-protection to O1**, and little public health value as O139 has limited circulation

- Regulatory Consultations =>
  - Acceptable rationale for change, and acceptable clinical development plan

Reformulation of OCV

Funded by BMGF
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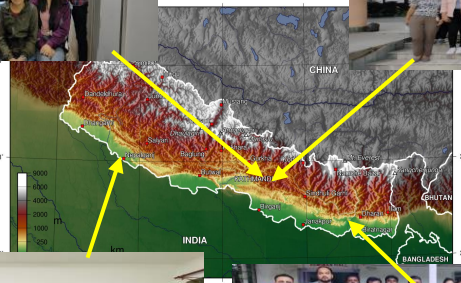
- A Phase III, Multicenter, Observer-Blinded, Randomized, Active Controlled Trial to Evaluate Immune Non-Inferiority, Safety and Lot-to-Lot Consistency of Oral Cholera Vaccine-Simplified (OCV-S) Compared to Shanchol in 1 to 40 years old Healthy Nepalese Participants
  - To demonstrate non-inferiority of OCV-S compared to Shanchol™ as measured by seroconversion rates of anti-*V. cholerae* O1 Inaba and anti-*V. cholerae* O1 Ogawa vibriocidal titer 2 weeks after second dose for all ages
  - 4 Sites in Nepal
  - N=2,530 subjects (age 1-40 y)
  - Enrollment began 4 October
- CSR expected 1Q 2023

Dhulikhel Hospital, Kavre

Kanti Children's Hospital, Kathmandu



Nepalgunj Medical College

BPKIHS: Dharan

Cholera Conjugate Vaccine

Funded by RIGHT Fund and Wellcome Trust
Conducted in collaboration with MGH and EuBiologics

- Approximately half of the cholera cases and deaths are estimated to occur in children five years of age and younger (WHO, 2017)
- Current pre-qualified two-dose OCV has reduced efficacy in children under 5 yrs; and a single dose has no efficacy
  - Not ideally suitable for delivery through EPI
  - In spite of reduced direct protection, young children may be protected from cholera by indirect effects in mass vaccination campaigns
- Current SAGE recommendations advocate re-dosing OCV every three years
- With the intent to encourage development of new and improved cholera vaccines, in 2017 the WHO Initiative for Vaccine Research (IVR) convened a Stakeholder Consultation on Preferred Product Characteristics for Next Generation Cholera vaccines, with the aim that these *will need to support a new sustainable implementation paradigm that will maintain cholera control;* these PPCs are:
  - Higher efficacy in infants and children under 5 years of age
  - Longer duration of protection
  - Lower cost
  - Single dose

Rationale for CCV

Funded by RIGHT Fund and Wellcome Trust
Conducted in collaboration with MGH and EuBiologics

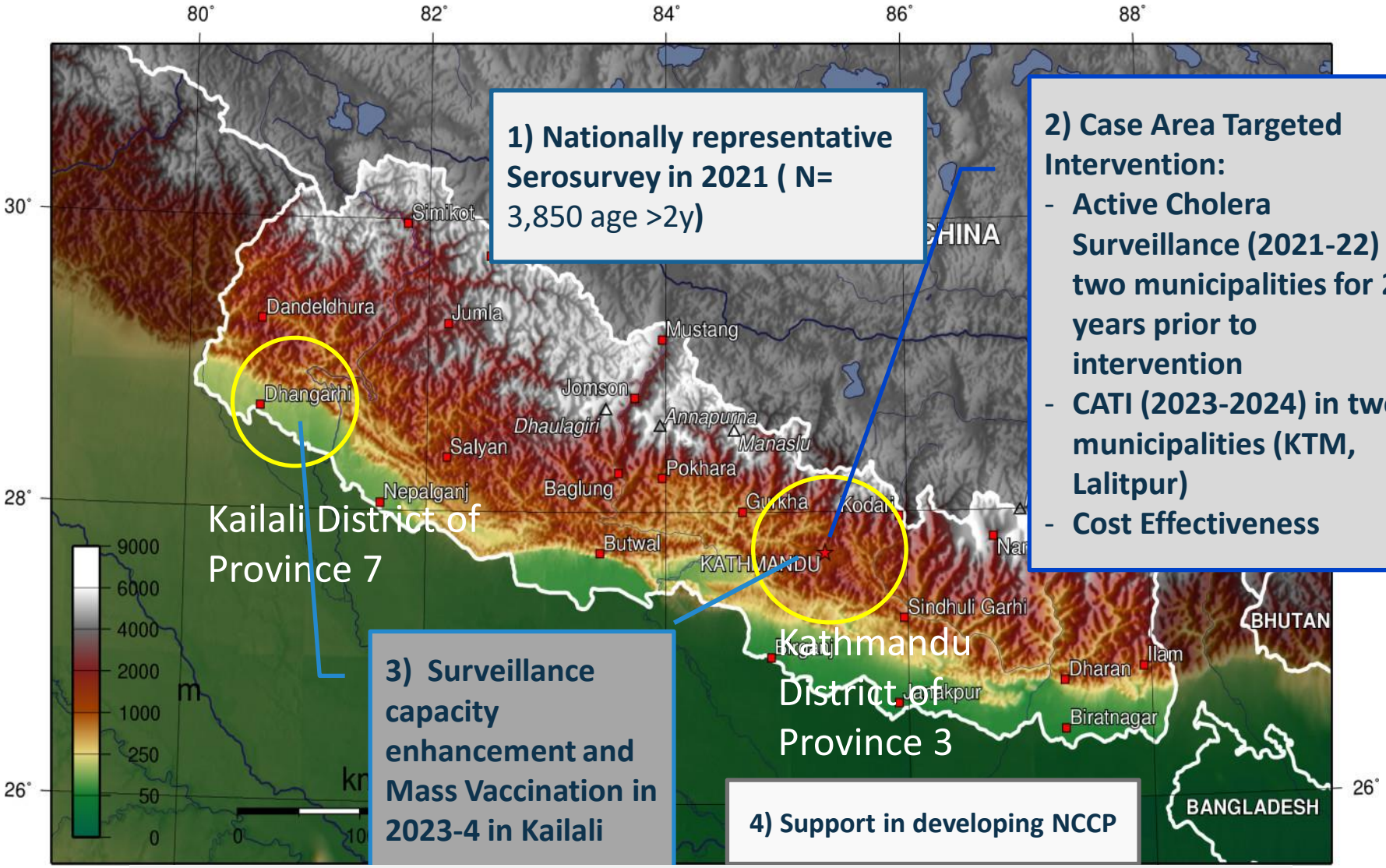
- Conjugate vaccines elicit long lasting T-cell dependent immune responses in young children, often with a single dose
- An injected vaccine with a long duration of protection can be cost effectively incorporated into EPI, reducing the burden of repeated vaccination campaigns, and building population immunity from infancy up
- CCV candidate vaccine developed by collaborators at MGH-Harvard, icddrb and US NIH
- The resultant product is protectively immunogenic in preclinical animal models
  - Scalable production and immunogenicity of a cholera conjugate vaccine. Vaccine. 2021 Oct 26:S0264-410X(21)01312-8. doi: 10.1016/j.vaccine.2021.10.005. Epub ahead of print. PMID: 34716040.
  - A COG analysis suggested a cost of 0.42 USD per dose

- ➢ Pre-clinical development is complete including toxicology studies
- ➢ IND application under review
- ➢ Grant application for Phase 1 trial conditionally approved by RIGHT Fund pending identification of co-funding

Enhancing CHOlera control (ECHO) in Nepal

Project Lead: Jacqueline Lim, PhD

Funded by KOICA
Conducted in collaboration with Nepal MOHP



1) Nationally representative Serosurvey in 2021 (N= 3,850 age >2y**)**

2) Case Area Targeted Intervention:

- **Active Cholera Surveillance (2021-22) in two municipalities for 2 years prior to intervention**
- **CATI (2023-2024) in two municipalities (KTM, Lalitpur)**
- **Cost Effectiveness**

3) Surveillance capacity enhancement and Mass Vaccination in 2023-4 in Kailali

4) Support in developing NCCP

Key Partners: Nepal MOHP, EDCD; National Public Health Laboratory (NPHL); Group for Technical Assistance (GTA); Good Neighbors International (GNI); Nepal Medical College (NMC); New Era

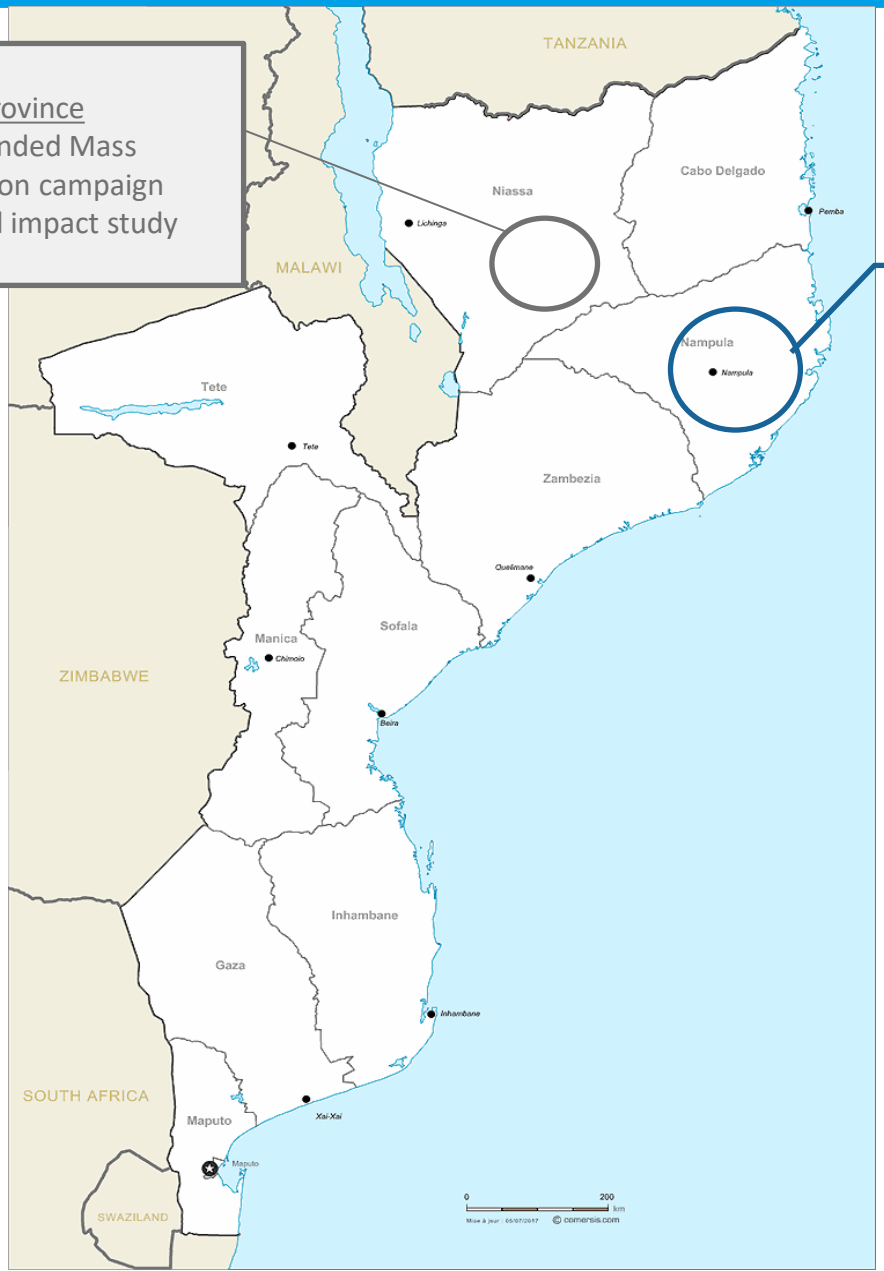
Enhancing Cholera Control in Mozambique: ECHO-Mozambique

Project Lead: Se Eun Park, PhD

Funded by KOICA

Conducted in collaboration with INS, MOPH

Niassa Province
KOICA funded Mass Vaccination campaign 2018 and impact study



Nampula Province

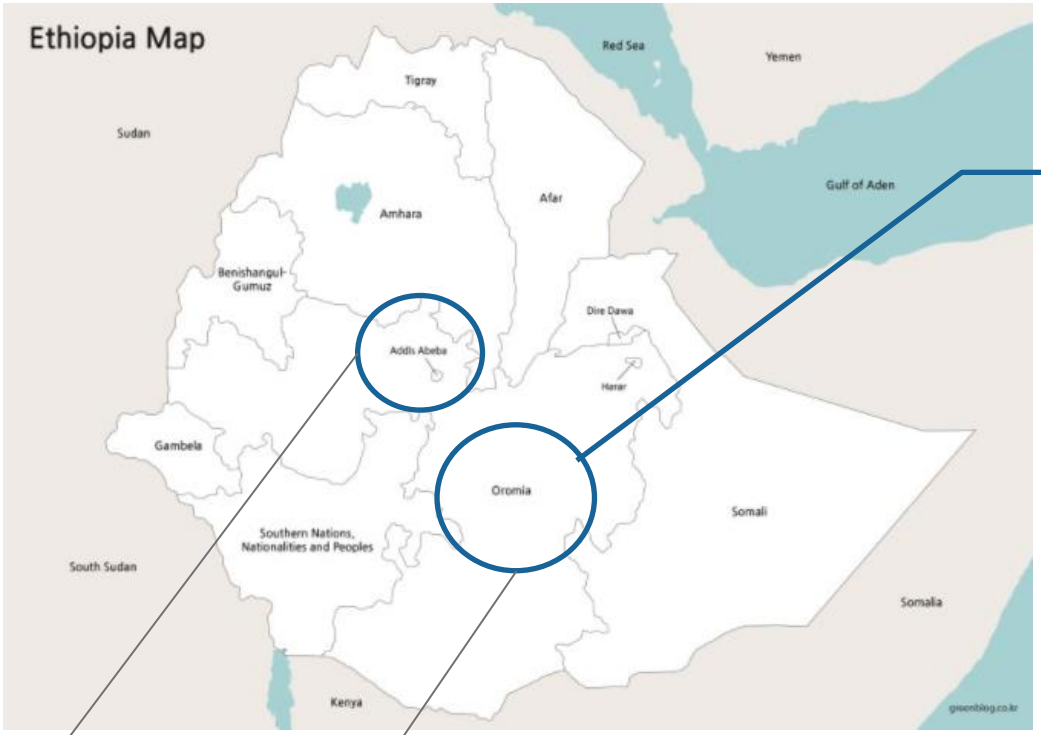
- Enhancement of sentinel-based surveillance in a rural and urban area of Nampula (2021)
- Conduct Community Health Utilization and Risk Factor Survey
- Mass Vaccination intervention of 150K (2023) with 3 years surveillance
- Cost Effectiveness analysis
- Strengthen government's cholera outbreak preparedness and rapid response
- Support development of national cholera control and prevention plan

Key Partners: INS; MOPH

Ethiopia Cholera Control and Prevention (ECCP)

Principal Investigator: Se Eun Park, PhD

Funded by KSC/LGE



Oromia region – Shashemene Town & Woreda

- Enhancement of sentinel-based cholera and diarrheal disease surveillance in rural and urban (cholera high priority) areas
- Conduct Community Health Utilization and Risk Factor Survey
- Mass Vaccination intervention of 100K (2022) with 2 years surveillance
- Vaccine effectiveness and impact assessment
- Ethiopian government stakeholder engagement on cholera control

Addis Ababa
AHRI laboratory

EPSA cold chain vaccine storage

Shashemene Town
Shashemene Specialized Hospital laboratory

Shashemene Town & Woreda
Sentinel healthcare facilities

Key Partners: AHRI, EPHI, EPSA, MOH

Thank you