# Cholera Program Update 2022

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GTFCC Meeting Jun 2022

International Vaccine Institute

# IVI Cholera Program Strategy and Projects

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

# 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 reduction in costs and ~35% increase in production capacity

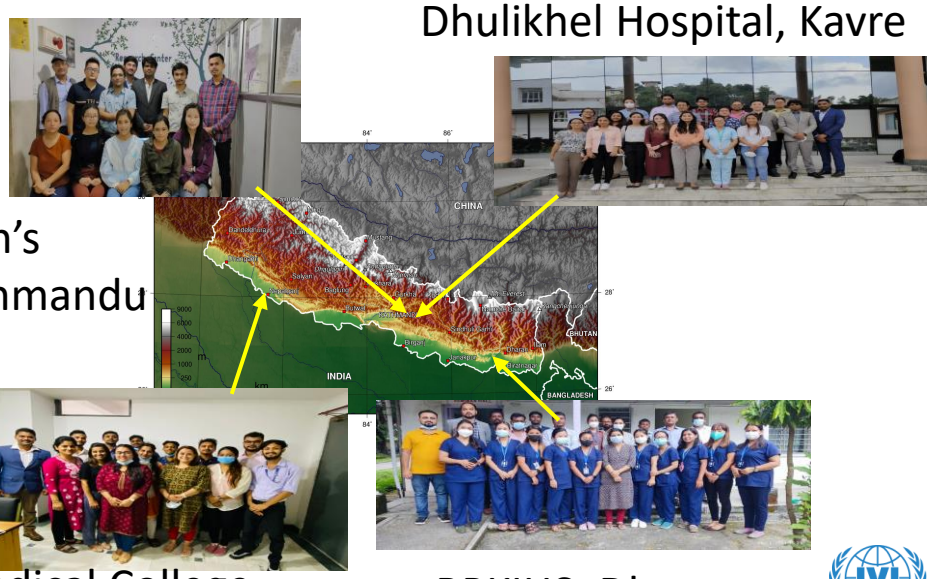
- Technical Expert Group Meeting Jan 2020 =>
  - Consensus that **two-component** vaccine should achieve an **equivalent protective immune response to O1** serotypes of *V. cholerae*
  - Agreed that the **O139 component** provides **no cross-protection to O1**, and little public health value as O139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

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

# Reformulation of OCV

*Funded by BMGF*
*Conducted in collaboration with EuBiologics*

- A Phase III, Multicenter, Observer-Blinded, Randomized, Active Controlled Trial to Evaluate Immune Non-Inferiority, Safety and Lot-to-Lot Consistency of Euvichol-Simplified (Euvichol-S) Compared to Shanchol in 1 to 40 years old Healthy Nepalese Participants
  - To demonstrate non-inferiority of Euvichol-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
- Results expected 1Q 2023



# Duochol

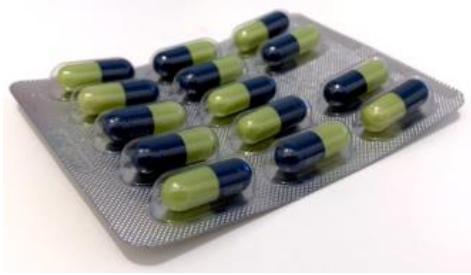
*Funded by Wellcome Trust, Govt of Sweden*
*Conducted in collaboration with Jan Holmgren, University of Gothenburg*

- Lyophilized mixture of formalin inactivated whole-cells of serotype O1 *V. cholerae* Inaba and Ogawa with cholera toxin B-subunit (rCTB) contained in an enterocoated capsule to be taken in two doses 2 to 6 weeks apart

➢ **Dukoral in a capsule**

**Advantages**

- 85% efficacy against cholera for 9 months in under 6y
- Protection against ETEC diarrhea for 6-9 months for all ages
- Cost similar to current OCV
- Thermostability demonstrated at 40 C for 6 months
- Weight/volume of product substantially reduced
  - Significantly lower product delivery costs
  - Significantly less waste



**Disadvantage**

- Children under 6y may not reliably swallow capsule
  - Will require dissolution in 3 ml liquid

# Duochol

*Funded by Wellcome Trust, Govt of Sweden*
*Conducted in collaboration with Jan Holmgren, University of Gothenburg*

- Completing pre-clinical development in 2022
- Proposals for funding Phase 1 and Phase 2 in progress
  - Phase 2 trial would explore feasibility and acceptability of dosing under 6 years of age
- Uptake Likelihood Analysis to be initiated in 2023 (funded)
  - Evaluate scenarios of use (feasibility, acceptability, cost/resources)

- General Use: Reactive or Preventive Campaign
  - → All Ages
  - → Mixed Delivery
    85% capsule/15% Liquid

- Special Settings: Forward outbreak stockpile

# 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, Open Philanthropy 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
- A COG analysis suggested a cost of 0.42 USD per dose

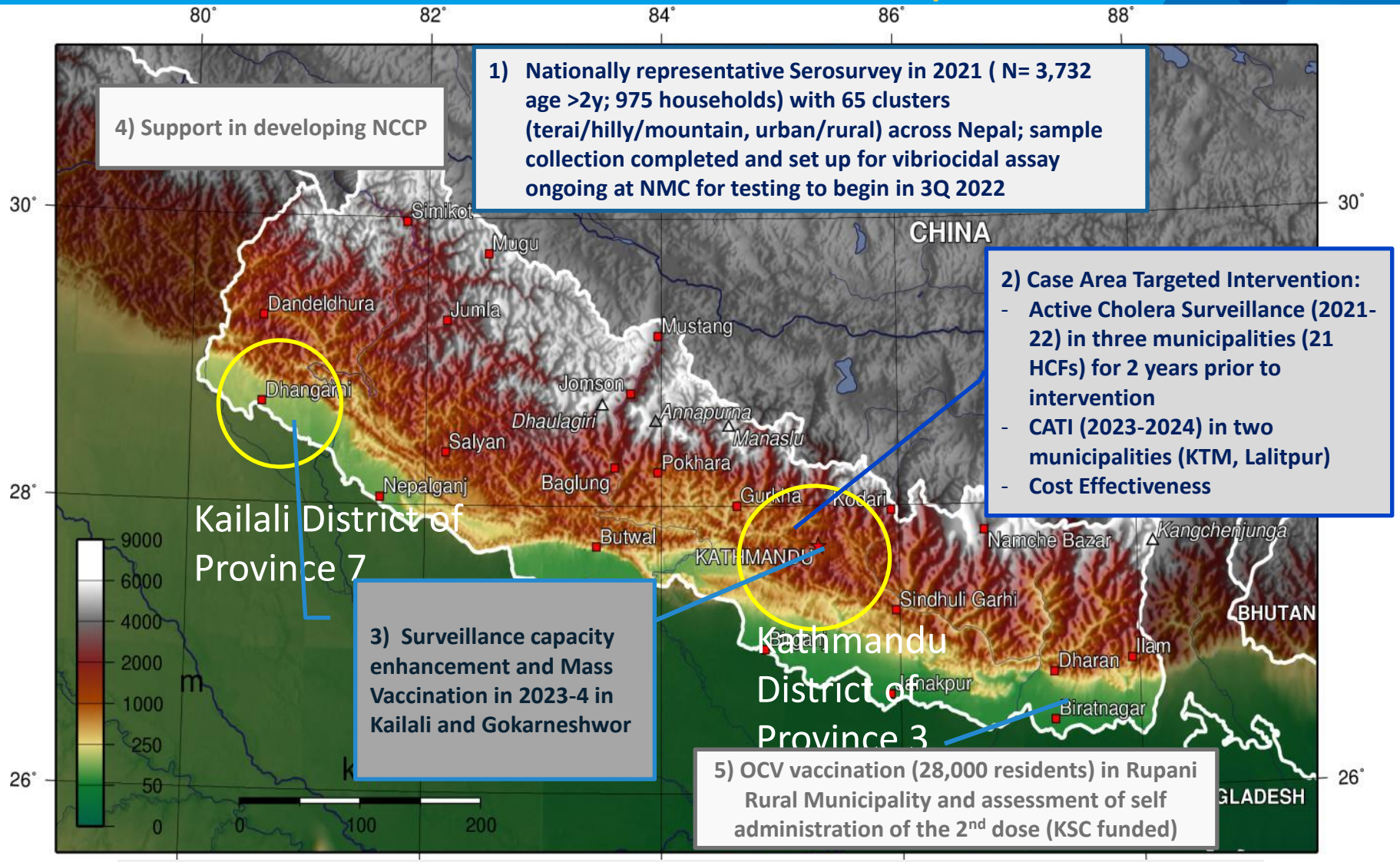
- Pre-clinical development is complete including toxicology studies
- Phase 1 trial in preparation with August 2022 start
  - South Korea
  - Results expected 1Q 2024

# Thank you


# 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= 3,732 age >2y; 975 households) with 65 clusters (terai/hilly/mountain, urban/rural) across Nepal; sample collection completed and set up for vibriocidal assay ongoing at NMC for testing to begin in 3Q 2022

2) Case Area Targeted Intervention:
- Active Cholera Surveillance (2021-22) in three municipalities (21 HCFs) 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 and Gokarneshwor

4) Support in developing NCCP

5) OCV vaccination (28,000 residents) in Rupani Rural Municipality and assessment of self administration of the 2nd dose (KSC funded)

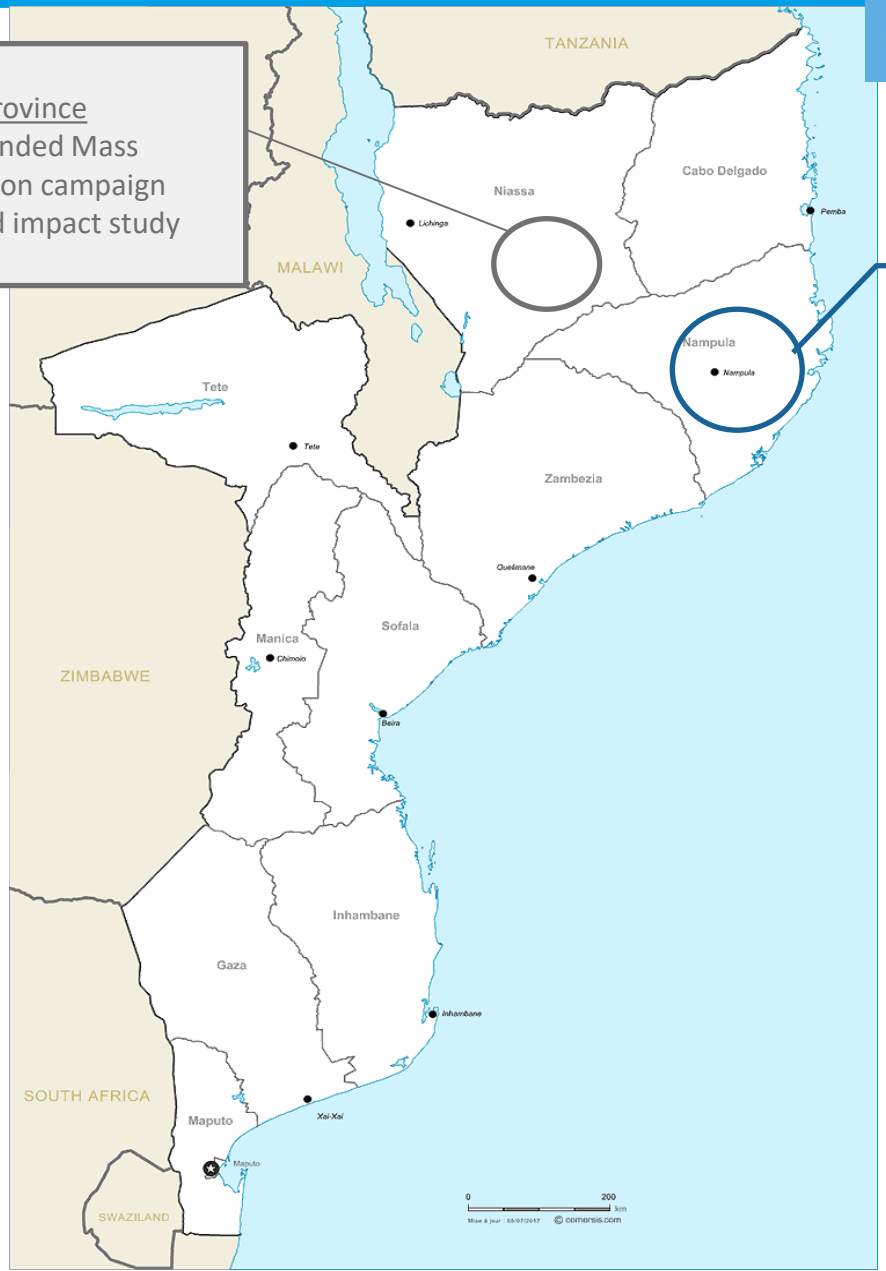
Key Partners: Nepal MOHP, EDCD; National Public Health Laboratory (NPHL); JHU; Group for Technical Assistance (GTA); Good Neighbors International (GNI); Nepal Medical College (NMC); icddr,b; New Era

# 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

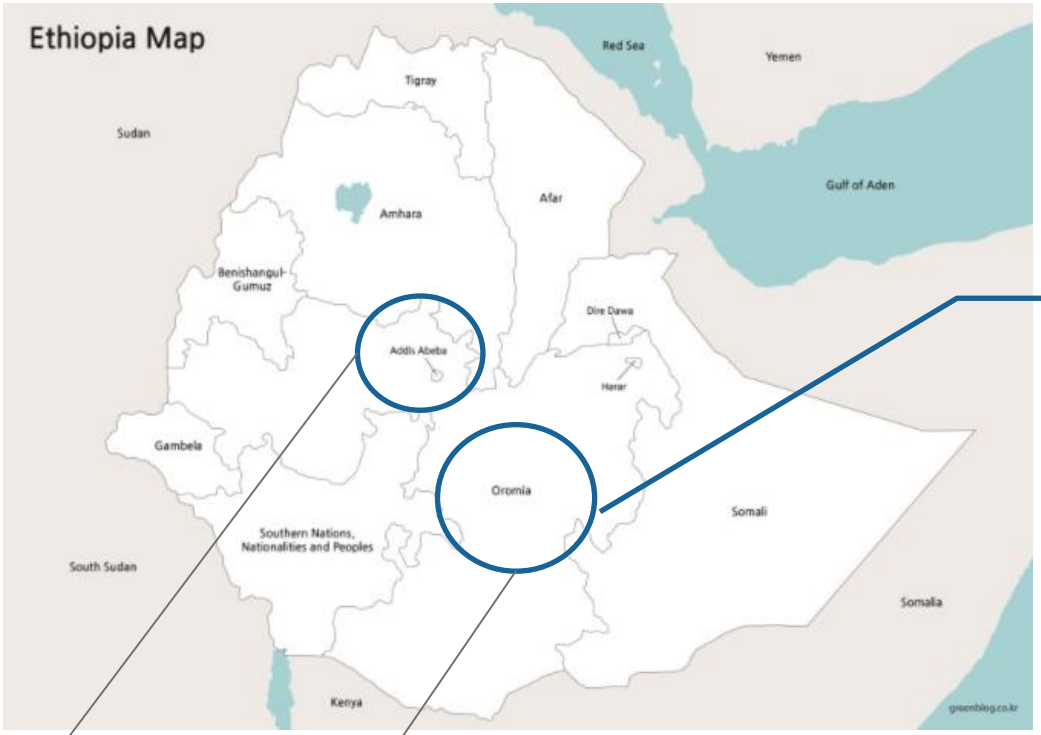
Key Partners: INS; MOPH

# Ethiopia Cholera Control and Prevention (ECCP)

**Principal Investigator: Se Eun Park, PhD**

***Funded by KSC/LGE***

***Key Partners: AHRI, EPHI, EPSA, MOH***




<u>Addis Ababa</u>
AHRI laboratory

EPSA cold chain vaccine storage

<u>Shashemene Town</u>
Shashemene Specialized Hospital laboratory

<u>Shashemene Town & Woreda</u>
Sentinel healthcare facilities

<u>Oromia region – Shashemene Town & Woreda</u>

- 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