IVI Cholera Program 2019

Future Vaccine Supply

Julia Lynch, MD
Cholera Program Director

International Vaccine Institute

IVI Cholera Program Strategy and Projects

Goals	Program Objectives	Current Projects	Future Projects
Ensure OCV Supply	Continue Supporting Manufacturers and Create New Supply	• Critical Reagents • **Cholvax** • **BIBCOL** • **Reformulation of OCV**	
Improve Cholera Vaccine	Improve Vaccine Efficacy (Especially in <5 y.o.) and Flexibility of Use	• Euvichol-P CTC Label • **Pre-clinical development of Cholera conjugate vaccine (CCV)**	• *Clinical evaluation of CCV*
OCV Introduction and Use	Generate Evidence to Support Endemic Countries Introduction and Use	• CSIMA (PAVE) • MOCA (PAVE) • Modeling Impact of Global Roadmap (PER) • Extended Analysis	• *ECHO- Nepal (2020)* • *ECHO- Mozambique (2020)*

OCV Supply

Cholvax - Technology Transfer of OCV to Incepta (Incepta, BMGF)

- Phase 3 met primary end-point of non-inferiority to Shanchol
- Technical issues have delayed registration in Bangladesh
  - Application for registration in Bangladesh (only) expected in 2020
- 4-6 M doses/yr initial capacity

BIBCOL-Technology Transfer of OCV to Government of India manufacturing facility (THSTI, BIBCOL, GOI-DBT)

– 3-5 years to reach 2-4 M doses/yr capacity

Goal

- Manufacturing OCV according to global GMP standards to meet domestic supply needs in support of national vaccine security
- Objectives

1. Successful transfer of OCV manufacturing technology to a manufacturing facility in India: **Bharat Immunologicals and Biologicals Corporation Limited** (BIBCOL)
2. Successful transfer of technology and know-how of SBA to **Translational Health Science and Technology Institute (**THSTI) to support clinical development and registration of the OCV in India
3. Support conduct of pre-clinical/clinical studies for registration of OCV in India

Reformulation of OCV

Composition	Quantity
V. Cholerae O1 inaba classical Cairo 48, Heat inactivated	300 L.E.U*
V. Cholerae O1 Phil 6973 El Tor, Formalin inactivated	600 L.E.U
V. Cholerae O1 Ogawa classical Cairo 50, Formalin inactivated	300 L.E.U
V. Cholerae O1 Cairo 50, Heat inactivated	300 L.E.U
V. Cholerae O139 4260B, Formalin inactivated	600 L.E.U

Rationale

- OCV contains 5 distinct components:
- Redundant heat and formalin inactivated O1 components
- Vibrio cholera O139 was included under concern that it might become a pandemic pathogen

➢ Could a simplified formulation containing only two current components, O1 Inaba (Phil El Tor) and O1 Ogawa (classical Cairo 50), and inactivated by a single method (formalin), be equally effective?

➢ Anticipate 25% reduction in costs and 38% increase in production capacity

- Technical and Regulatory Consultations
- Test formulations
- Production of CTM of simplified formulation
- Clinical trial
- Regulatory approvals

3 Years

New Cholera Vaccines

Cholera Conjugate Vaccine (CCV) (Ed Ryan- Mass General Hospital, Harvard University, IVI, Eubiologics) [RIGHT, IVI]

- Novel conjugation chemistry links key protective epitope (OSP) to carrier protein (rTTHC) in sunburst display
- Potential for a single dose injectable vaccine, durable immune response, improved immunogenicity in < 2 yo
  - Delivered through EPI to infants
  - Combinable with other antigens (shigella conjugate in earlier stage development)
  - Complementary to OCV used in mass vaccination by protecting or priming <5 yo
- Process development initially done at Paragon
- Technology transfer to Eubiologics as manufacturing partner for CTM
- Expect CTM available in 2021 for FIH