
# Next-Gen Cholera Vaccines

GTFCC OCV Working Group Meeting

Sourabh Sobti

December 5-6th 2018, Annecy, France

# HILLCHOL IS AN INNOVATIVE VACCINE WITH STREAMLINED MANUFACTURING PROCESS

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## PROBLEM STATEMENT

**Current prequalified vaccines effective but complex to manufacture:**

–3 or 4 different strains

–Two different inactivation methods

## APPROACH

**Single vaccine strain (Hikojima) incorporating desirable characteristics of the current Cholera vaccine:**

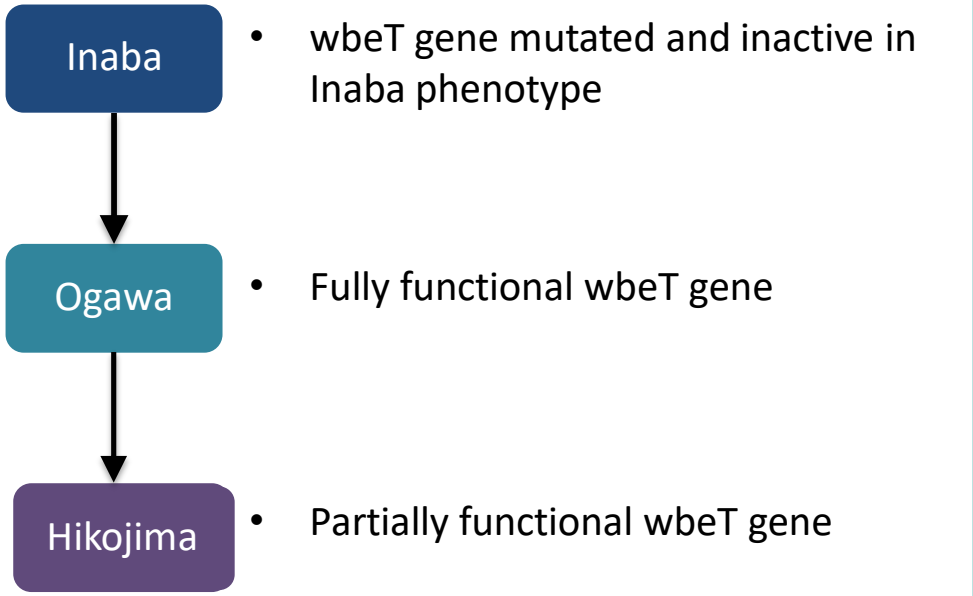
– Ogawa and Inaba dual expression

– Single fermentation run

– One inactivation method

– Efficient process results in lower COGs

## SCIENCE




**Co-expression of Inaba and Ogawa serotype antigens**

***However, no stable Hikojima strains exist in nature***

PLOS ONE, November 2014 | Volume 9 | Issue 11 | e108521

# HILLCHOL HAS BEEN PROVEN SAFE AND NON-INFERIOR IN PHASE I/II CLINICAL TRIALS CONDUCTED BY ICDDR,B IN BANGLADESH

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## Study Objective

- Evaluate and compare the safety following immunization with 2 dose of OCV using WHO-PQ Shanchol as comparator
- To establish Non inferiority of Hillchol vs Shanchol in terms of Vibrocidal response with ~ 840 patients
  - Adult (18-45 years): 360 subjects
  - Young Children and Adolescents (5-17 years): 240 subjects
  - Kids (1-4 years): 240 subjects

  Study cohorts for both test vaccine were powered to demonstrate Non-Inferiority to Shanchol

## Study Centre

- Mirpur field site of icddr,b, Bangladesh

## Study Endpoints

- Proportion of subjects receiving test vaccine or Shanchol with any AE/ SAEs
- Proportion of subjects demonstrating four fold rise vibriocidal response at 14 days after each dose

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## Study Design

- Active controlled randomized study
- Monitored for immunogenicity up to 2 weeks after each dose; for safety up to 1 month after second dose

## Study Results

**Analysis of safety and immunogenicity results from adult cohort indicate that:**

- HL 246 Formulation was safe, and the frequency and severity of adverse events as similar to that of Shanchol.
- The vibriocidal antibody response was elicited by HL 246 formulation, against both Ogawa and Inaba serotypes.
- Immune response elicited by HL246 was non-inferior to that of Shanchol in terms of GMT as evident from GMR & Reverse cumulative curves and also for sero-conversion rates.
- We observed a dose dependent response with high dose (HD) HL246 eliciting superior immune response to that of low dose HL246 (LD).

# HILLEMAN IS IN DISCUSSION WITH PARTNERS TO ACHIEVE WHO PQ BY 2021

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| MILESTONE | STATUS |
|---|---|
| • Technology Development at scale done in Hilleman Labs | ☑ |
| • Pre-clinical and Toxicity studies conduced in Korea | ☑ |
| • Technology Transfer to CMO | ☑ |
| • Phase I/II clinical trial in ~ 840 subjects completed at ICDDR, Bangladesh | ☑ |
| • In-discussion with DCVM to make GMP Phase III clinical trial material | In-Progress |
| • Phase III clinical trials to commence by Q3 2019 with licensure by Q4 2020 | ☐ |
| • WHO-PQ by 2021 | ☐ |

# HILLEMAN IS KEEN TO SUPPORT GTFCC IN ENDING CHOLERA AND HAS 2 CHOLERA VACCINES (HL 246, HL 445) IN DEVELOPMENT

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## Target Product Profiles

| Attribute | HL 246 | HL 445 |
|---|---|---|
| **Indication** | • Diarrhea caused by Vibrio Cholera | • Travelers diarrhea caused by Vibrio cholera and ETEC |
| **Active Ingredients** | • Whole cell inactivated Stable Hikojima<br>• expressing both *Inaba* and *Ogawa* LPS | • Whole cell inactivated Stable Hikojima+ recombinant cholera toxin B subunit (rCTB) |
| **Dosing** | • *2 Oral doses given 14 days apart* | • *2 Oral doses given 14 days apart* |
| **Minimum Age** | • 1 year | • 1 year |
| **Duration of Protection** | • ≥3 years | • ≥2 years |
| **Presentation** | • 2mL liquid in vial or BFS | • Oral tablet: blister pack of two<br>• Liquid Suspension: rCTB as microbeads and whole cell as liquid |
| **Current Status** | • Completed Phase II | • Pre-Clinical |
| **Notes** | • In-discussion with partner to commence Phase III clinical trials | • Similar to Dukoral<br>• Strong potential to gain US FDA Priority Review Voucher |

*#Thanks#*

# HILLEMAN LABS IS A GLOBAL VACCINE R&D ORGANIZATION COMMITTED TO DEVELOPING AFFORDABLE VACCINES FOR PEOPLE IN LOW & MIDDLE INCOME COUNTRIES

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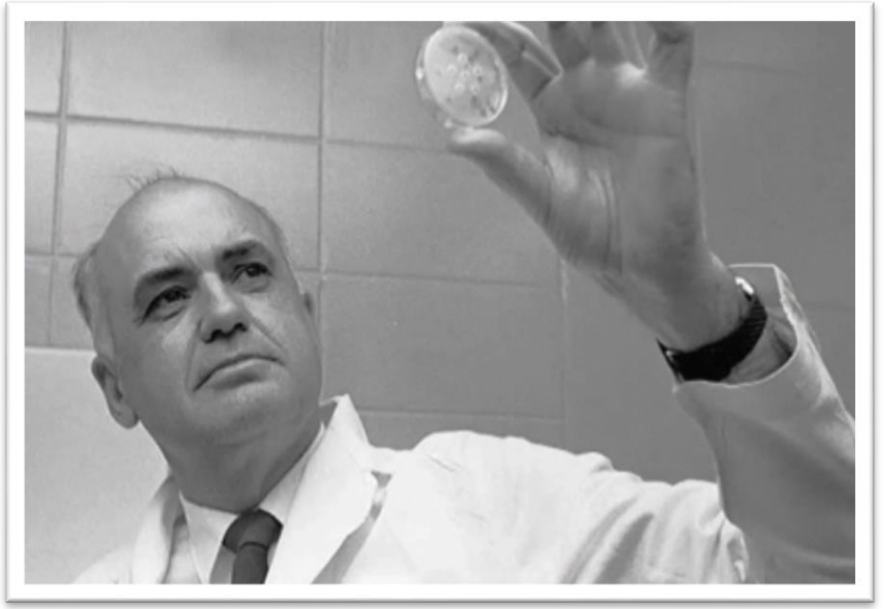
- We function as a biotech company translating our innovation into important vaccine products and technology platforms.
- Our focus is on transforming ideas into products and technologies through translational R&D and by building partnerships with vaccine manufacturers
- Sustainability for funding Hilleman Lab's R&D
  - Founding contribution from MSD and Wellcome Trust
  - Licensing and Royalty payments
  - Raising project specific funding
  - Grants & Innovative financing
- To date, our focus has been largely on **Vaccines and Infectious Disease, technologies** and opportunities that meet the unmet needs of the developing world



**Maurice Hilleman**