IVI Cholera Activities

5th Initiative Against Diarrheal and Enteric Diseases in Asia (IDEA)
Hanoi, March 6-9, 2017.

Dr. Julia Lynch
Deputy Director General
Development and Delivery

International Vaccine Institute

Outline

- **Introduce IVI**
- **Review OCV Development**
  - mORCVAX
  - Shanchol
  - Euvichol
  - Cholvax
- **Single Dose Study**
- **Campaigns and Demonstration projects**

IVI is a Vaccine R&D center with a Global Health mission

VISION	**Developing countries free of suffering from infectious diseases**
MISSION	**Discover, develop and deliver safe, effective and affordable vaccines for global public health**

International Organization

- UNDP initiative
- First international organization in Korea (1997)
- 35 countries and WHO as state parties

Global Vaccine Research Institute

- HQ and laboratory in Seoul
- Field programs in 29 countries: Asia, Africa, Latin America

IVI Full Spectrum: Bench to Delivery

DISCOVER

- Pathogen genotyping
- Novel antigens
- Novel adjuvants
- New delivery mechanisms
- New routes of administration

DEVELOP

- Laboratory process development
- Assay development
- Technology transfer for large-scale production
- Clinical development
- Regulatory expertise

DELIVER

- Epidemiological and Socioeconomic studies
- Vaccine feasibility/acceptance
- Field effectiveness studies
- Cost-effectiveness and impact analyses
- Dissemination to stakeholders

DCVM

Safe, effective, affordable and sustainable vaccine introduction

Development of Killed Oral WC Vaccine

- Technology transfer from University of Gothenburg, Professor Jan Holmgren to VABIOTECH in 1980s
  - Inactivated Whole Cell-only vaccine, without CTB component
  - Vaccine reformulated by VABIOTECH, proven safe and effective in Vietnamese people and licensed as ORC-Vax™ in 1997
- IVI engaged VABIOTECH to modify and reformulate vaccine to meet WHO standards (2004)
  - Modification of Strains, Production, Standardization & QC
  - A Safety and Immunogenicity Study of a 2-Dose Regimen of the Reformulated Bivalent Killed Oral Cholera Vaccine in Vietnamese Subjects (NIHE/IVI)
  - Licensed in Vietnam **(**mORCVAX™**)**

Cholera Vaccine (Inactivated Whole Cell Oral Cholera vaccine)

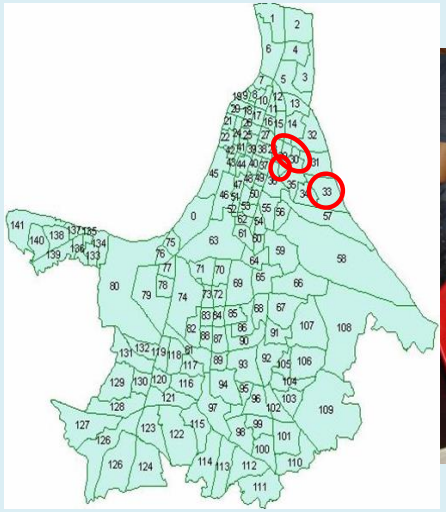
IVI Technology Transfers

Company	Partnership	Stage of development
Vabiotech (Vietnam)	IVI re-formulated, redeveloped process to meet WHO standards.	Licensed in Vietnam (mORCVAX™)
Shantha (India)	Technology transfer May 2008	Licensed in India (Feb 2009). WHO prequalified Sep 2011.

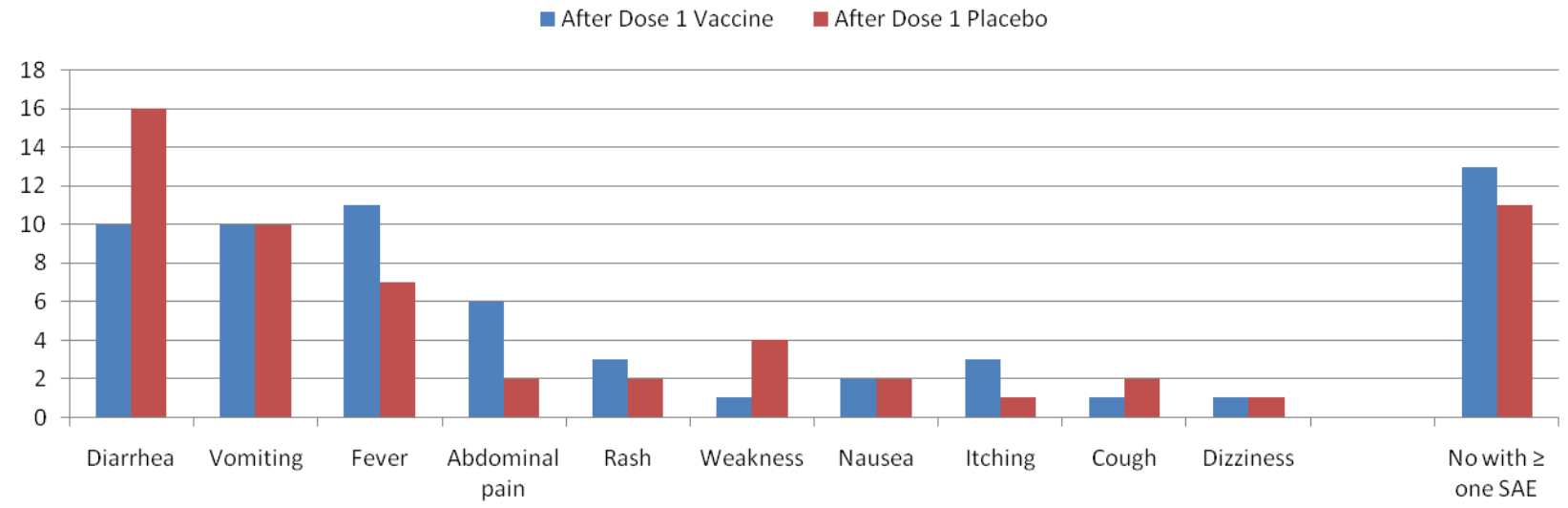
- Because NRA of Vietnam not recognized by WHO at that time, mORCVAX could not be WHO approved and made available on global PH market
- IVI Tech transferred the vaccine to Shantha in 2008 for production in India → Shanchol

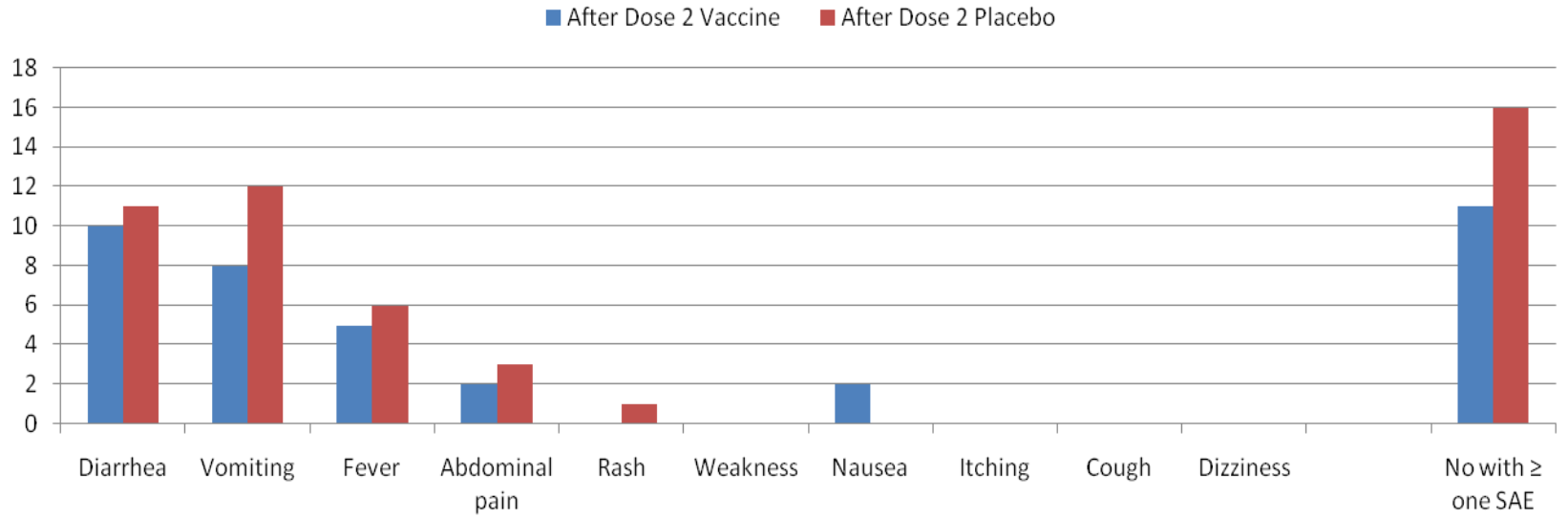
Shanchol Trial: Phase III Study of the Reformulated Bivalent Killed Oral Cholera Vaccine in Kolkata (NICED/IVI)

- **To assess the protection of a two-dose regimen of the reformulated oral killed WC cholera vaccine against episodes of cholera severe enough to require medical treatment**
- A cluster-randomised, double-blind, placebo-controlled trial
  - Cholera endemic urban slums of Kolkata, India
  - 65,000 subjects (3,478 clusters)
  - Age > 1 year (excluding pregnant women)
  - Two doses, 14 days apart



OCV Safety: Shanchol Common Adverse Events





Protective Efficacy during Three Years of Follow-up in Per Protocol Analyses, by Year of Follow-up

	Year of Follow-up					
	First Year		Second Year		Third year	
	Vaccine	Placebo	Vaccine	Placebo	Vaccine	Placebo
	n=31,932	*n=34,968*	*N=30,532*	*N=33,466*	*n=28,976*	*n=31,677*
Cholera Episodes	11	23	9	45	18	60
Incidence (per 100,000 person-days)	.10	.19	.08	.38	.17	.53
Protective Efficacy (95% CI lower boundary)						
Adjusted analysis	41% (-13%)		76%** (52%)		65%** (44%)	

*p<.05; **p<.01

5 year efficacy of a bivalent killed whole-cell oral cholera vaccine in Kolkata, India: a cluster-randomised, double-blind, placebo-controlled trial

Sujit K Bhattacharya, Dipika Sur, Mohammad Ali, Suman Kanungo, Young Ae You, Byomkesh Manna, Binod Sah, Swapan K Niyogi, Jin Kyung Park, Banwarilal Sarkar, Mahesh K Puri, Deok Ryun Kim, Jacqueline L Deen, Jan Holmgren, Rodney Carbis, Mandeep Singh Dhingra, Allan Donner, G Balakrish Nair, Anna Lena Lopez, Thomas F Wierzba, John D Clemens

Summary

Background Efficacy and safety of a two-dose regimen of bivalent killed whole-cell oral cholera vaccine (Shantha Biotechnics, Hyderabad, India) to 3 years is established, but long-term efficacy is not. We aimed to assess protective efficacy up to 5 years in a slum area of Kolkata, India.

Methods In our double-blind, cluster-randomised, placebo-controlled trial, we assessed incidence of cholera in non-pregnant individuals older than 1 year residing in 3933 dwellings (clusters) in Kolkata, India. We randomly allocated participants, by dwelling, to receive two oral doses of modified killed bivalent whole-cell cholera vaccine or heat-killed *Escherichia coli* K12 placebo, 14 days apart. Randomisation was done by use of a computer-generated sequence in blocks of four. The primary endpoint was prevention of episodes of culture-confirmed *Vibrio cholerae* O1 diarrhoea severe enough for patients to seek treatment in a health-care facility. We identified culture-confirmed cholera cases among participants seeking treatment for diarrhoea at a study clinic or government hospital between 14 days and 1825 days after receipt of the second dose. We assessed vaccine protection in a per-protocol population of participants who had completely ingested two doses of assigned study treatment.

Findings 69 of 31932 recipients of vaccine and 219 of 34968 recipients of placebo developed cholera during 5 year follow-up (incidence 2·2 per 1000 in the vaccine group and 6·3 per 1000 in the placebo group). Cumulative protective efficacy of the vaccine at 5 years was 65% (95% CI 52–74; p<0·0001), and point estimates by year of follow-up suggested no evidence of decline in protective efficacy.

Interpretation Sustained protection for 5 years at the level we reported has not been noted previously with other oral cholera vaccines. Established long-term efficacy of this vaccine could assist policy makers formulate rational vaccination strategies to reduce overall cholera burden in endemic settings.

Funding Bill & Melinda Gates Foundation.

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Introduction

Cholera is a serious global public health problem because clean drinking water and sanitation are not universally available, and appropriate case management is not accessible to many patients. In endemic countries alone, about 1·4 billion people are at risk of cholera and an estimated 2·8 million cases and 91000 deaths occur every year. More than half these cases and deaths occur in cholera-endemic countries in Asia and in Africa.[1] Furthermore, recent outbreaks in Cuba, Haiti, and Zimbabwe show the ability of this disease to spread rapidly to new areas and to produce outbreaks with substantial morbidity and mortality. Because of their capacity to spread rapidly, cholera outbreaks can overwhelm existing public health infrastructures and require substantial resources. The economic burden of cholera in African countries alone in 2005–07 ranged from US$39 million to $156 million per year, dependent on the estimate of average life expectancy used.[2] Additional preventive interventions are needed.

To complement improvements in access to water and sanitation and rehydration therapies, much attention has been given to development of a cholera vaccine. After several studies in the 1960s showed that injectable whole-cell cholera vaccines conferred only modest protection of short duration, often with significant side-effects, researchers focused on oral vaccines that could efficiently stimulate local immunity in the gut.[3] The first oral cholera vaccine to be prequalified by WHO for purchase by UN agencies contains a mixture of killed *Vibrio cholerae* O1 bacteria and the non-toxic B subunit of cholera toxin, and is marketed under the trade name Dukoral (Crucell, Netherlands). This vaccine was licensed largely on the basis of studies done more than 20 years ago in Bangladesh[4] and Peru[5] that showed 85% protection for the first 4–6 months and 60% protection for 2 years after a primary regimen of two or three doses. The protection declined substantially in the third year and was evident against *V cholerae* O1 El Tor only in the first year for individuals younger than 5 years.[6] The vaccine is used primarily by people travelling from

ocol)

mulative protective efficacy of

cacy(PE)	Adjusted protective efficac
ue)	y (95%CI; p-value)
·001)	65% (52-74%; <·001)*

ratified point estimates of efficacy
t statistically different between
ips, however, suggest reduced
for under 5yo

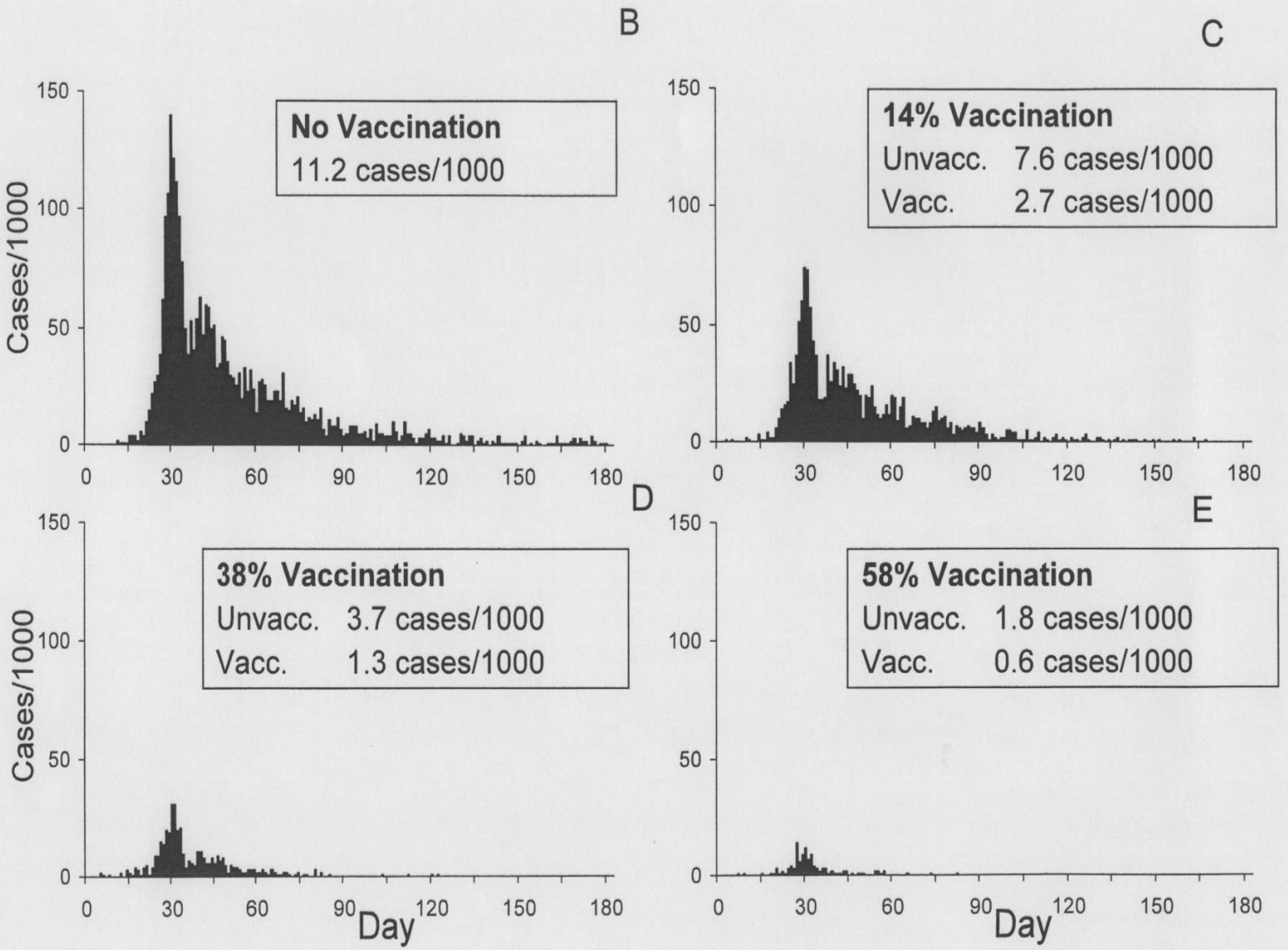
cases were prevented in children
than other age groups

Herd Effect:
Re-analysis of the Bangladesh Field Trial of Killed, Oral Cholera Vaccines (Ali, Lancet, 2005)

- A re-analysis of the 1985 trial of killed whole cell-based oral cholera vaccines found:

  -- Non-vaccinees were protected against cholera if they lived in neighborhoods with high levels of vaccine coverage

  -- Vaccinated persons had higher levels of protection if they lived in highly vaccinated neighborhoods


B
No Vaccination
11.2 cases/1000
C
14% Vaccination
Unvacc. 7.6 cases/1000
Vacc. 2.7 cases/1000
D
38% Vaccination
Unvacc. 3.7 cases/1000
Vacc. 1.3 cases/1000
E
58% Vaccination
Unvacc. 1.8 cases/1000
Vacc. 0.6 cases/1000
Cases/1000
Day
0
30
60
90
120
150
180
50
100

Cholera Vaccine (Inactivated Whole Cell Oral Cholera vaccine)

IVI Technology Transfers

Company	Partnership	Stage of development
Vabiotech (Vietnam)	IVI re-formulated, redeveloped proc ess to meet WHO standards.	Licensed in Vietnam (mORCVAX™)
Shantha (India)	Technology transfer May 2008	Licensed in India (Feb 2009). WHO prequalified Sep 2011.

2010, 85, 117–128 No. 13

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record

Relevé épidémiologique hebdomadaire

26 MARCH 2010, 85th YEAR / 26 MARS 2010, 85e ANNÉE

No. 13, 2010, 85, 117–128

http://www.who.int/wer

"OCV should be used in endemic areas and should be considered f or use in areas at risk for outbreaks in conjunction with other prevention and control strategies"

- **IVI engaged Eubiologics in a tech transfer Euvichol® Development Strategy**

-Tech Transfer of identical process and materials

-Conduct comparative biophysical and quality analysis

-Conduct clinical trials to evaluate safety and immunogenicity (non- inferiority) compared to Shanchol™

ORIGINAL ARTICLE
Infectious Diseases, Microbiology & Parasitology

JKMS

Safety and Immunogenicity Assessment of an Oral Cholera Vaccine through Phase I Clinical Trial in Korea

Young Ok Baik,* Seuk Keun Choi,† Jae Woo Kim,‡ Jae Seung Yang,‡ Ick Young Kim,‡ Chan Wha Kim,‡ and Jang Hee Hong‡

The safety, tolerability and immunogenicity of an oral cholera vaccine (OCV) was assessed in adult Korean male through an open-label, non-comparative clinical study. Two doses of vaccine with an interval of 2 weeks were given to 20 healthy subjects. A total of 7 adverse events occurred in 6 subjects. However, no clinically significant change was observed in electrocardiograms, vital signs, physical examinations, and clinical laboratory tests. The immunogenicity of OCV was evaluated by serum vibriocidal assay where anti-Vibrio cholerae O1 and O139 antibodies were measured at day 0, 14, and 28 of vaccine administration. The antibody titers ranged from < 2.5–5,120 for *V. cholerae* O1 Inaba, < 2.5–10,240 for *V. cholerae* O1 Ogawa and < 2.5–480 for *V. cholerae* O139. In addition, the fold increase in antibody titers ranged from 1–4,096 for O1 Inaba, 1–8,192 for O1 Ogawa, and 1–384 for O139. The seroconversion rate was 95% and 45% for O1 and O139 antibodies, respectively. Our study clearly shows that administration of two doses of OCV at a 2 week-interval increases an appropriate level of antibody titer in the serum of healthy Korean adult males (Clinical Trial Number, NCT01305317).

Keywords: Oral Cholera Vaccine; Safety; Immunogenicity; Vibriocidal Assay; Seroconversion Rate

INTRODUCTION

Cholera, a rapidly dehydrating diarrhoeal disease, is spread mainly by food and water contaminated through the fecal material of infected carriers or persons (1, 2). The main symptoms of cholera are acute and profuse watery diarrhea with vomiting for a period of one or few days. Within 3-4 hr of starting the symptoms, a healthy person may become severely dehydrated and may die within 24 hr if a proper treatment is not given immediately (1). Cholera is one of prevalent endemic diseases particularly in South-Eastern Asia and Africa. Approximately 3-5 million people are affected by this disease, and 100,000-130,000 deaths are reported in every year throughout the world (3). The rate of cholera in endemic areas varies from around 1 to 8 per 1,000 population and children aged of 2-9 yr are in high risk of infection (1, 2).

Cholera is caused by the ingestion of toxigenic serogroups of *Vibrio cholerae*, a Gram-negative, rod-shaped non-invasive motility noninvasive bacterium. There are more than 200 serogroups of *V. cholerae* available in nature. However, the disease is mainly caused by the serogroups O1 and O139 (1, 2). O1 strains are divided into two biotypes (e.g., classical and El Tor). The classical biotype has been discovered during the cholera outbreaks in India, and was responsible for the previous six pandemics in modern history. El Tor causes more asymptomatic cases as compared to the classical strain, and is responsible for the seventh pandemic that started in 1961 and continues till today. *V. cholerae* O1 strains are further divided into two serotypes (e.g., Ogawa and Inaba) based on their phenotypic differences in O1 antigen. In 1992, *V. cholerae* O139 strain was found that caused extensive epidemics in Bangladesh and India, and subsequently in other parts of South Asia. This strain, a genetic derivative of El Tor biotype in which the O1 biosynthetic genes were replaced by the O139 biosynthetic genes, appears to be associated with more severe cholera disease (1, 2).

Enteric vaccination has already been regarded as the most effective approach to control such illnesses as well as to prevent cholera in endemic countries with limited public health and sanitary facilities (4). Injectable vaccine is not recommended by the World Health Organization (WHO) mainly because of its limited efficacy and short duration of protection. To maximize the intestinal secretory antibody response and long-lived effi-

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A randomized, non-inferiority trial comparing two bivalent killed, whole cell, oral cholera vaccines (Euvichol vs Shanchol) in the Philippines

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Adults

ABSTRACT

Background: Currently, there are two oral cholera vaccines (OCV) that are prequalified by the World Health Organization. Both (Dukoral and Shanchol) have been proven to be safe, immunogenic, and effective. As the global supply of OCV remains limited, we assessed the safety and immunogenicity of a new low cost, killed, bivalent OCV (Euvichol) in the Philippines.
Methods: The randomized controlled trial was carried out in healthy Filipino adults and children. Two doses of either the current WHO prequalified OCV (Shanchol) or the same composition OCV being considered for WHO prequalification (Euvichol) were administered to participants.
Results: The pivotal study was conducted in total of 1263 healthy participants (777 adults and 486 children). No serious adverse reactions were elicited in either vaccine groups. Vibriocidal antibody responses to *V. cholerae* O1 Inaba following administration of two doses of Euvichol were non-inferior to those of Shanchol in adults (82% vs 76%) and children (87% vs 89%). Similar findings were observed for O1 Ogawa in adults (80% vs 74%) and children (91% vs 88%).
Conclusion: A two dose schedule with Euvichol induces a strong vibriocidal response comparable to those elicited by the currently WHO prequalified OCV, Shanchol. Euvichol will be an oral cholera vaccine suitable for use in lower income countries, where cholera still has a significant economic and public health impact.

1. Introduction

Cholera is a rapidly dehydrating diarrheal disease, which is preventable and treatable. It has a disease case burden of 2.8 million and kills approximately 100,000 people each year [1]. Prolonged and frequent outbreaks can be devastating and dramatically impact many countries throughout the Asian, African, and in Haiti and the Dominican Republic. Improvements to water quality, sanitation, and hygiene are mainstays of cholera prevention, but continue to be goals far out of reach for many affected countries. Safe and effective oral cholera vaccines (OCV) have been available since the mid-1980s, but have not been widely used due to concerns over low vaccine production capacity and possible diversion of traditional prevention and control efforts.

Considerable progress has been made during the last decade in the development of OCV. After technology was transferred for an efficacious, killed OCV from Sweden, the Vietnamese government used a local manufacturer to license and produce OCV for

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0264-410X/

Shanchol™

Each oral dose of 1.5mL contains

Vaccine Strain	Quantity
V. cholera 01 Inaba E1 Tor strain Phil 6973 formaldehyde killed	600 Elisa Units(EU) of lipopolysaccharide(LPS)
V. cholerae O1 Ogawa classical strain Cairo 50 heat killed	300 EU of LPS
V. cholerae O1 Ogawa classical strain strain Cairo 60 formaldehyde killed	300 EU of LPS
V. cholera O1 Inaba classical strain Cairo 48 heat killed	300 EU of LPS
V. cholerae O139 strain 4260B formaldehyde killed	600 EU of LPS
Thiomersal B.P.	Not more than 0.02%(w/v)
Buffer	q.s to 1.5mL
VVM	13

Euvichol

90mm*35mm*35m
=110cm³/10 vials

Each oral dose of 1.5mL contains

Description	V. Cholerae O1 and O139 bivalent inactivated vaccine	
Composition in 1.5ml	**Composition**	**Quantity**
	V. Cholerae O1 inaba 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 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
	Phosphate buffered saline(pH7.3)	20mM
	Thimerosal	0.15 mg
VVM	VVM 30	

Cholera Vaccine (Inactivated Whole Cell Oral Cholera vaccine)

IVI Technology Transfers

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Vabiotech (Vietnam)	mORCVAX	IVI re-formulated, redeveloped process to meet WHO standards.	Licensed in Vietnam (mORCVAX™)
Shantha (India)	Shanchol	Technology transfer May 2008	Licensed in India (Feb 2009). WHO prequalified Sep 2011.
Eubiologics (Korea)	Euvichol	Technology transfer 2010-11	Korean export license 2014 WHO prequalified Dec 2015

Euvichol® (Eubiologics, Korea)

Euvichol

100L Formulation

- Market authorization from Korean FDA Jan 2015
- **WHO PQ obtained Dec 2015**

600L/no-thimerosal variation → *capacity up to 25M doses/year*

Bridging trial (100L to 600L) in the Philippines May 5, 2016

442 participants : Age 1-40y

- **Variation Approval from WHO received Sept 2016**

Eubiologics expected to be the major supplier of OCV to the WHO stockpile

(Funder: BMGF)

Euvichol-P

Thermostability: currently VVM 30 (30 days at 37C)

Easier administration

Lower production cost

Lower cost of delivery

Cholera Vaccine (Inactivated Whole Cell Oral Cholera vaccine)

IVI Technology Transfers

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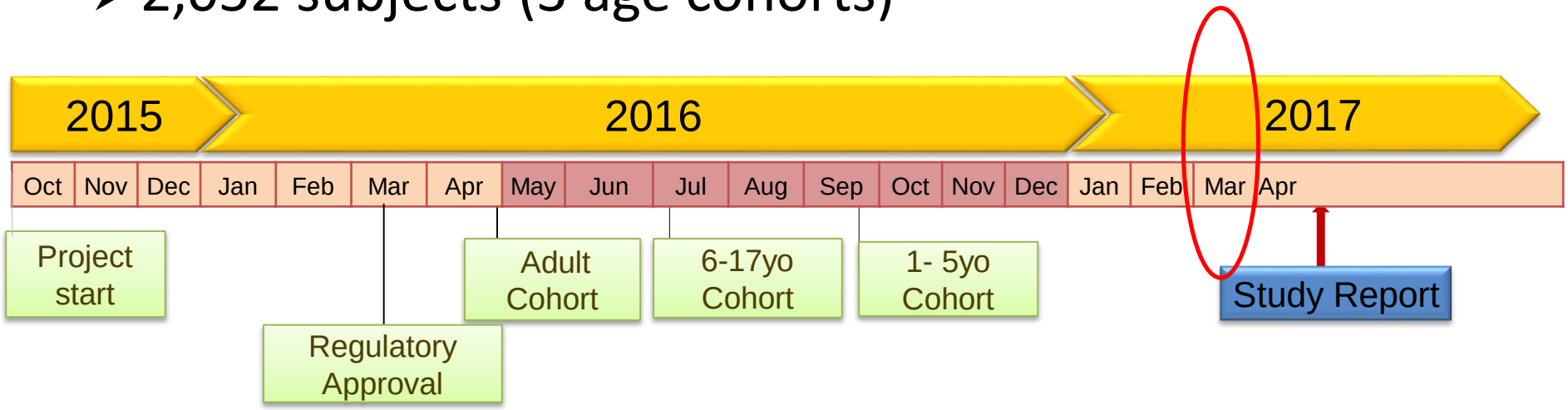
Vabiotech (Vietnam)	mORCVAX	IVI re-formulated, redeveloped process to meet WHO standards.	Licensed in Vietnam (mORCVAX™)
Shantha (India)	Shanchol	Technology transfer May 2008	Licensed in India (Feb 2009). WHO prequalified Sep 2011.
Eubiologics (Korea)	Euvichol	Technology transfer 2010-11	Korean export license 2014 WHO prequalified Dec 2015
Incepta (Bangladesh)	Cholvax	Technology transfer May 2014	IVI conducting clinical trials in Bangladesh, license in Bangladesh expected 2017/18.

Cholvax® (Incepta, Bangladesh) : Supply

- OCV Tech Transfer to Incepta 2014
- GMP Support (ongoing)

- Clinical Trial: Non-inferiority to Shanchol (icddr,b)
  - ➢Safety, Immunogenicity, lot-to-lot consistency
  - ➢2,052 subjects (3 age cohorts)



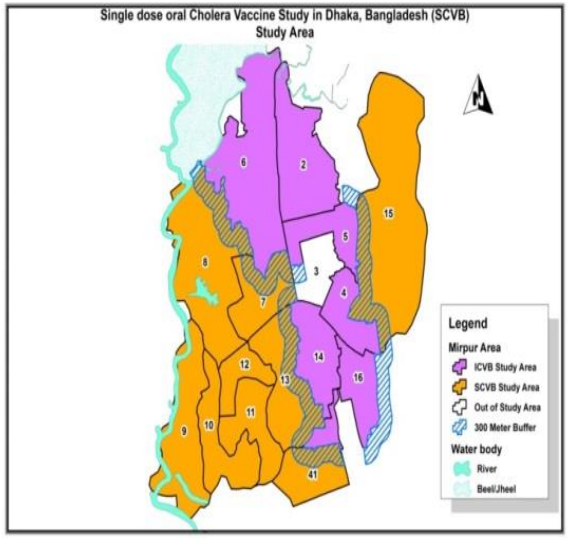
- Challenges to achieve WHO PQ
  - ➢ Recognition of NRA (~2020)

(Funder: BMGF)

Single Dose Study (icddr,b): Flexibility

An individually randomized, placebo controlled trial of a single dose of Shanchol in an endemic setting

205,000 subjects enrolled



- **Primary Objective:**

Protective efficacy of a single dose of Shanchol™ during initial 6 months following dosing

- **Secondary Objective:**

Protective efficacy of a single dose of Shanchol™ at 12, 18, and 24 months following dosing

6 Month vaccine protective efficacy (PE)

- 40% (95% CI lower-bound (LB)=16%; P=·006) against all cholera cases
- 63% (95% CI=24%-82%; P=.007) against severely dehydrating cholera cases
- *Efficacy only in >5 years of age*

2 Year follow-up being analyzed now

(Funder: BMGF)

Vaccination campaigns 2015/16

Demonstrate feasibility, cost effectiveness in different settings

Year	Location/Type	Target #	Coverage	Outcomes
2016 /17	Nepal Pre-emptive	25,000	90%	M&E In progress Expect Cost of Delivery and assessment of Choltool
2015	Nsanje, Malawi Reactive	160,000	1st 98% 2nd 68%	Acceptability, feasibility, Effectiveness (on going) Delivery and Cost of Illness (COI) Cost-Effectiveness Analysis
2015	Shashemene Ethiopia	~62,000	1st 76% 2nd 65%	Acceptability Feasibility
2015	Newakot and D hading, Nepal Pre-emptive	10,000	1st 105% 2nd 96%	Feasibility of delivering OCV in earthquake aff ected districts (during monsoon season) using government infrastructure

Expanding Use of OCV: Malawi Campaign 2015

- 10 February 2015 : 1st cholera case lab confirmed in Nsanje District
- 4 March 2015 : 72 cases, 2 deaths
- 50,000 person pre-emptive campaign became a 160,000 person reactive effort (collaboration with WHO, MoH)
  - ✓ Camps hosting the internally displaced populations and surrounding villages
- 320,000 doses
  - ✓ 110,000 redirected from planned pre-emptive campaign
  - ✓ 210,000 dispatched via the ICG Stockpile

Coverage : 1st dose 98%, 2nd dose 68%

Expanding Use of OCV: Malawi Campaign 2015

Cholera Surveillance in Malawi (CSIMA)

Goal: To determine the 2-year protective effectiveness of OCV delivered through a reactive campaign in Nsanje District and increase the capacity for diarrheal surveillance in Nsanje and Chikwawa Districts

-Vaccine Effectiveness (VE): case-control study design

-Vaccination campaign delivery costs (Choltool)

-Cost of illness: public and private expenditures for treatment and productivity losses associated with cholera

-Cost-effectiveness

-Capacity building and strengthening surveillance system: support of Nsanje/Chikwawa laboratories

(Funder: BMGF)

Rotary Nepal Project:
Cholera Prevention and Control (CCPC) in Nepal

Preemptive Campaign in rural "hot spot" in Nepal

Banke District, (Terai plain): 25,000 target population

2 doses of Euvichol®

Funders: Rotary International, IVI Korean Support Committee

Partners:

- Rotary Korea and Rotary Nagarjun Nepal
- JHUSPH-M&E
- GoN, MOH (EDCD)
- District Public Health Office

Outcomes:

- Feasibility
- Assessment of Choltool
  - comparison of the prediction of campaign costs with actual costs

Vaccination: Dec 2016 –Jan 2017

(~90% coverage)

M&E: ongoing

Thank You

IVI website
www.ivi.int

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Follow us
https://twitter.com/IVIHeadquarters

Signatories to IVI's Establishment Agreement


Bangladesh


Bhutan


Brazil


China


Ecuador


Egypt


India


Indonesia


Israel


Jamaica


Kazakhstan


Kyrgyzstan


Lebanon


Liberia


Malta

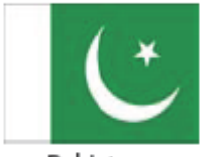

Mongolia


Myanmar


Nepal


Netherlands


Oman


Pakistan


Panama


Papua New Guinea


Peru


Philippines


Republic of Korea


Romania


Senegal


Sri Lanka


Sweden


Tajikistan


Thailand

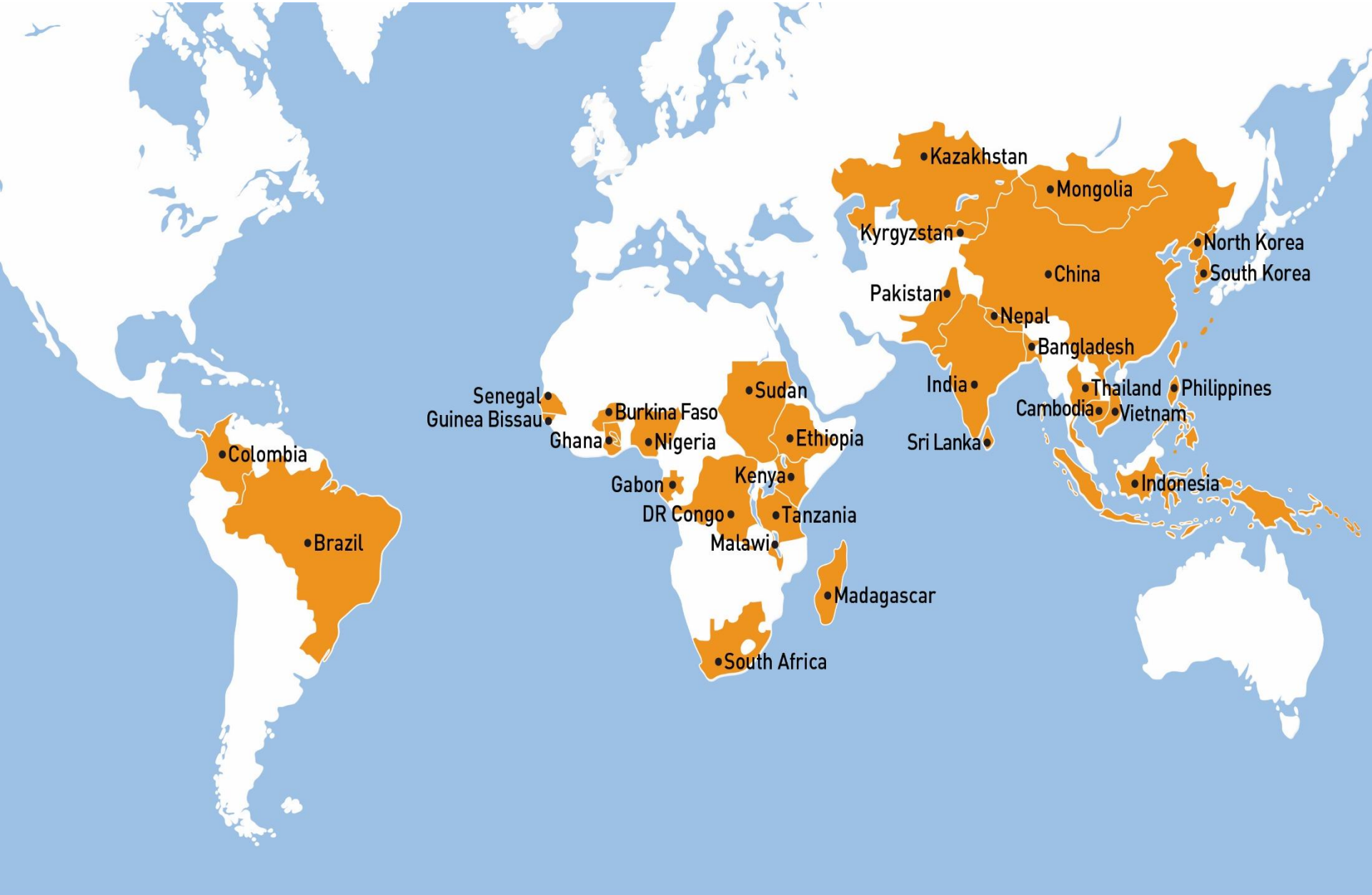

Turkey


Uzbekistan


Vietnam


World Health Organization

Global Footprint



IVI Cholera Vaccine Program Strategy 2008-2016

Development and Delivery

Strategic Goals	Program Objectives	Key Activities
OCV Supply	**Increasing the availability of OCV**	• Partnership with manufacturers for TT, GMP, GCP, Clinical Development • Two OCVs licensed and WHO-PQed • One more OCV (Cholvax) in development
Easier OCV Delivery	**Flexibility of Use**	• Alternative dosing schedule(14 vs 28) • Efficacy of a Single Dose of OCV
OCV Use & Introduction	**Expand the use of OCV and gather evidence for introduction**	• Vaccination Campaigns • Feasibility, Safety, Effectiveness of OCV • Delivery Costs and Cost of Illness • Cost-Effectiveness Analysis

Comparison of Reformulated vs Vietnamese Oral Killed WC Vaccines

Strain	Vietnamese Vaccine	Reformulated Vaccine
Formalin-Killed El Tor Inaba (Phil 6973)	5 x 10^{10} cells	600 EU LPS
Heat-Killed Classical Ogawa (Cairo 50)	2.5 x 10^{10} cells	300 EU LPS
Formalin-Killed Classical Inaba (569B)	2.5 x 10^{10} cells	-
Formalin-Killed Classical Ogawa (Cairo 50)	-	300 EU LPS
Heat-Killed Classical Inaba (Cairo 48)	-	300 EU LPS
0139 (4260B)	5 x 10^{10} cells	600 EU LPS

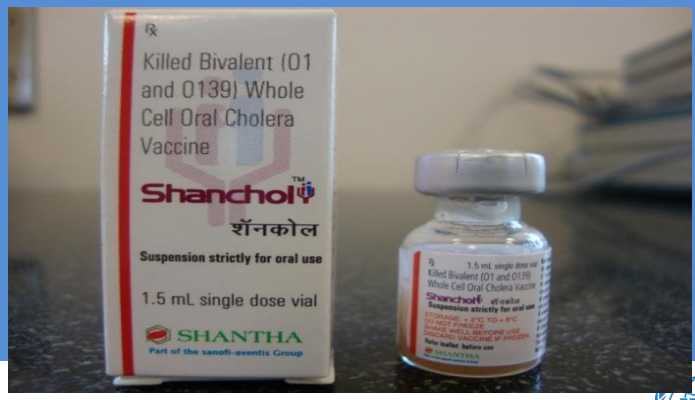
WHO pre-qualified and available OCVs 2010-11

Dukoral

- Killed whole cell vaccine + B (binding) subunit of cholera toxin
- Requires buffer (75-150 ml)
- 2 doses for age>5 yrs. and 3 doses for age 2-5 yrs.
- Vaccine efficacy of 60% sustained over 2 years
- High vaccine price, mainly for travelers
- Monovalent (O1)

Shanchol

- Killed whole cell vaccine (no cholera toxin subunit)
- Buffer is not required
- 2 doses for all age groups (1+ years)
- Efficacy of 66% for 3 years
- Low-cost
- Bivalent (both O1 and O139)



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Shanchol

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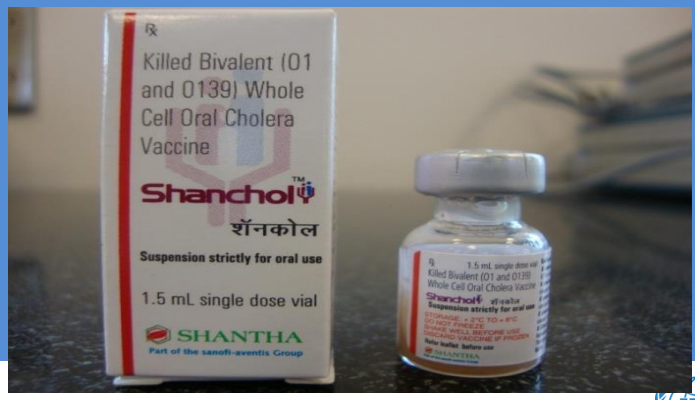
- Buffer is not required
- 2 doses for all age groups (1+ years)
- Efficacy of 66% for 5 years
- Low-cost
- Bivalent (both O1 and O139)



IVI's Cholera Program Activities Overview
(Supply, Flexibility of Use, Introduction)