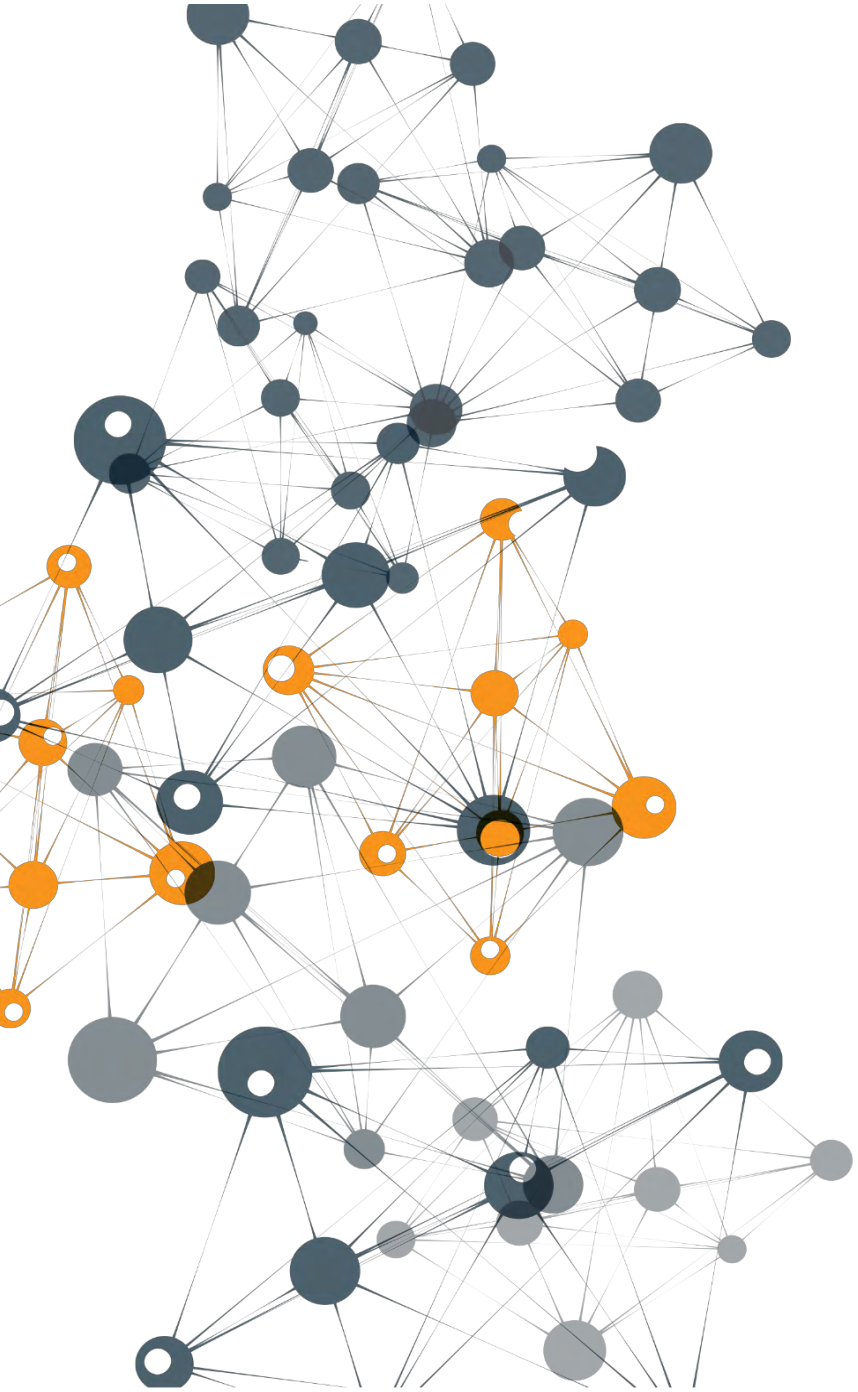


For Health that lasts a **lifetime!**

eubiologics

EuBiologics' update

WHO GTFCC OCV WG Meeting

Mombasa, Kenya

Rachel Park

7th Oct 2024

I. EuBiologics Introduction

II. OCV Availability

III. OCV Registration Status

IV. CTC and Pregnancy Study Progress

V. Euvichol-Plus Shaking Study

VI. Euvichol-S Phase III Clinical Study

I. EuBiologics_Introduction

- **EuBiologics is a publicly traded biopharmaceutical company based in South Korea focusing on vaccine development for global public health.**

Company Profile

Establishment	10th March, 2010
Business Place	HQ: Seoul, South Korea Facilities; - Two Manufacturing sites in Chuncheon - R&D Center in Chuncheon
No. of Employee	350
Market Capital	USD 400M Listed in KOSDAQ since Jan 2017
Business Area	- Vaccine Development, Manufacturing & Supply - CRMO(Contract R&D and Manufacturing Organization)

Plant

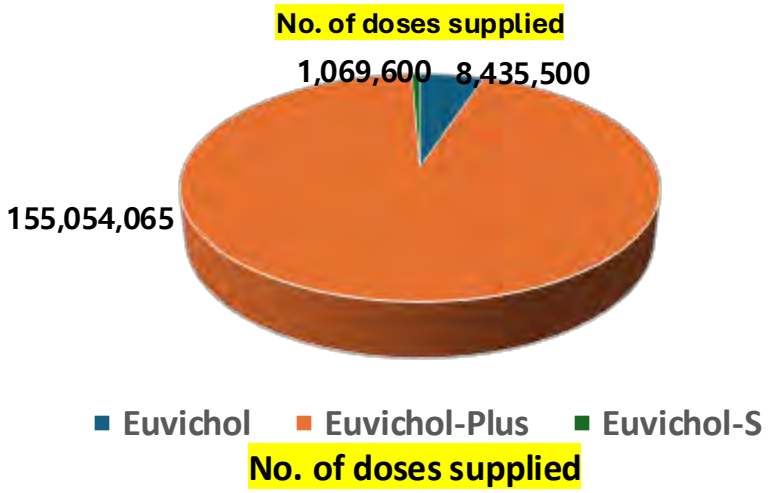
[C-Plant]

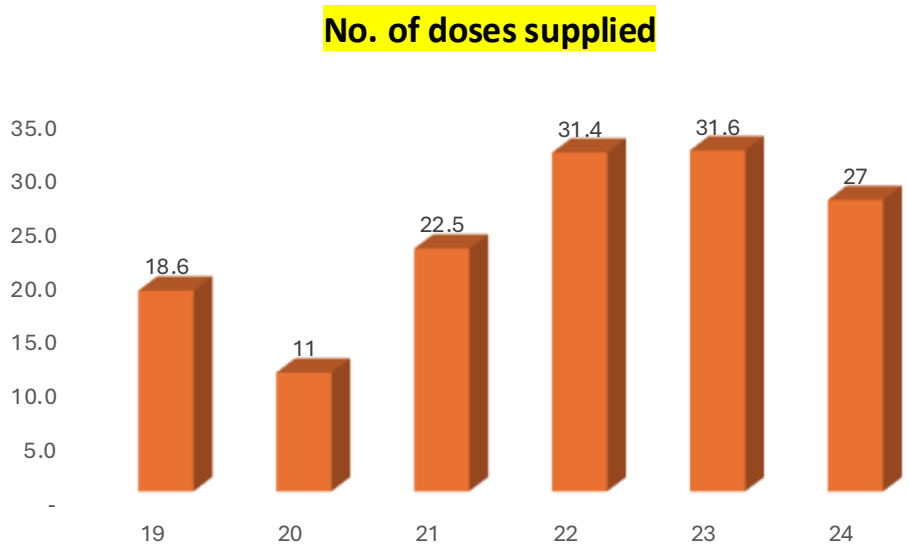
[V-Plant, R&D Center]

- **C Plant**
  : Oral Cholera Vaccine-DS & DP (45M doses/y)
  : Recombinant/subunit-DS (200M doses/y, 1,000L*2 lines of Animal cell culture line)
- **V Plant**
  : Bacterial fermentation, conjugation production line- DS(Total 200M doses/y)
  : Oral Cholera Vaccine-DS&DP (45M & 50M doses/y)
  *Expansion ongoing funded by BMGF
  : CMO for APIs ; Suite#4, 5 (50/100/200/500/1,000-L Lines)

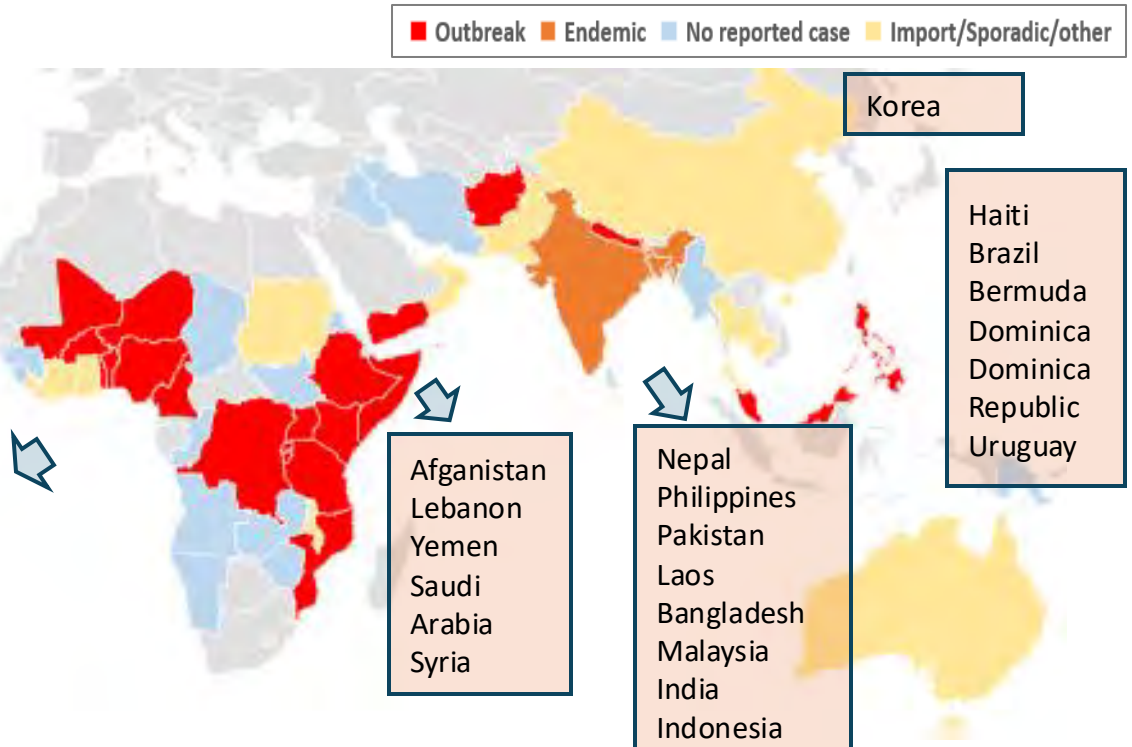
I. EuBiologics_OCV Supply

- **EuBiologics is currently the largest supplier of OCV to LMICs through UNICEF. We plan to fully switch the production from Euvichol-Plus to Euvichol-S from 2025.**
- **Until 2024 Q3, EuBiologics has supplied more than 164M doses to 48 countries.**





Malawi
Somalia
Zambia
Sierra Leone
South Sudan
Egypt
Uganda
Nigeria
Mozambique
Zimbabwe
DRC
Ethiopia
SNNP
Cameroon
Sudan
Niger
Burkina Faso
Burundi
Comoros
Haiti
Kenya
Syria
Yemen



Korea

Haiti
Brazil
Bermuda
Dominica
Dominica
Republic
Uruguay

Afganistan
Lebanon
Yemen
Saudi
Arabia
Syria

Nepal
Philippines
Pakistan
Laos
Bangladesh
Malaysia
India
Indonesia
Cambodia
Myanmmar
Thailand

II. OCV Availability in 2024

eubiologics

- **The total available quantity of OCVs from EuBiologics in 2024 is up to 45.8 million doses.**
  - Additional 19.9 million doses are available during 4Q 2024.

Product	Shipped (including POs) *	Oct **	Nov	Dec	Total (Unit: Million)
Euvichol-Plus	24.55	2.05			26.6
Euvichol-S	1.06	4.25	3.76	4.23	12.24
Euvichol	1.39	2.43	1.39	1.74	6.95
Total quantity	**27.00**	**8.73**	**5.15**	**5.97**	**45.79**

*POs for Bangladesh (Euvichol) and Niger (Euvichol-S) received but not shipped yet.
**Heads-up for Ethiopia (Euvichol-Plus, 1,265,100) have not been deducted from Oct quantity.

II. OCV Availability in 2025/2026

- **The total available quantity of OCVs from EuBiologics in 2025 is up to 72 million doses.**
  - Euvichol-S: 62.95 M (20.38M subject to PQ of Suite 3 expected in July 2025)
  - Euvichol: 8.36 M
  - Euvichol-Plus: 0.71 M

- **OCV availability goes up to 90 million doses from 2026 onwards.**

<Monthly availability of OCVs in 2025>

Month		Jan-25	Feb-25	Mar-25	Apr-25	May-25	Jun-25	Jul-25	Aug-25	Sep-25	Oct-25	Nov-25	Dec-25	Jan-26	TOTAL
Euvichol-S	C-Plant	3.76	3.53	3.53	3.53	3.53	3.53	3.53	3.53	3.53	3.53	3.53	3.53		42.57
	V-Plant	-	-	-	-	-	-	2.35	3.61	3.61	3.61	3.61	3.61	-	20.38
Euvichol-P	C-Plant	-	0.71	-	-	-	-	-	-	-	-	-	-		0.71
Euvichol	GCC	2.44	0.78	-	1.13	-	-	-	-	-	-	1.39	1.74	0.87	8.36
Total		6.20	5.02	3.53	4.66	3.53	3.53	5.88	7.13	7.13	7.13	8.53	8.87	0.87	72.01

III. Registration Status_Euvichol-Plus

eubiologics

- **Euvichol-Plus is registered in 12 countries including South Korea.**

No.	Country	Registration Date	Registration Number
1	Republic of Korea	Mar 2017	201701512
2	WHO PQ	Aug 2017	336.1
3	Caribbean Regulatory System(CARPHA/CRS)	Apr 2018	CRS/112017/193/022.1
4	Nepal	May 2018	8900
5	Nigeria	Jul 2018	N/A*
6	Mozambique	Sep 2019	J5814
7	Malaysia	Dec 2019	MAL19126001AZ
8	Zambia	Feb 2020	388/001
9	Myanmar	Mar 2020	2411AA5210
10	Pakistan	June 2021	107916
11	Philippines	Dec 2021	BR-1384
12	India	Jul 2023(Jul 2023/Import of Drug into Indi a)	IMP/BIO/23/000044 (RC/ BIO-000368)
13	Kenya	Aug 2024	H2024/CTD11328/24084
14	Thailand	Expected in May 2025	Ongoing
15	Egypt	Expected in Mar 2025	Ongoing
16	Saudi Arabia	Expected in Aug 2025	Ongoing

III. Registration Status_Euvichol-S

- **Registration is ongoing in Kenya, Ghana, Nigeria, Zambia, Ethiopia and Zimbabwe.**
- **We're engaging with potential agents in Bangladesh, Cameroon and Mozambique and distribution agreement expected by the end of 2024.**

No.	Country	Registration Date	Registration Number
1	Republic of Korea	Dec 2023	5
2	WHO PQ	Apr 2024	N/A
3	Kenya	Expected in Aug 2025	Ongoing
4	Ghana	Expected in May 2025	Ongoing
5	Nigeria	Expected in Oct 2026	Ongoing
6	Zambia	Expected in Oct 2025	Ongoing
7	Ethiopia	Expected in Oct 2025	Ongoing
8	Zimbabwe	Expected in Dec 2025	Ongoing
9	Philippines	Expected in Oct 2025	Ongoing

IV. Euvichol-S CTC Progress & Pregnancy Study

eubiologics

- **Expected to have a pre-consultation with PQ team in November 2024**
  - 7 batches of Euvichol-S have satisfied with criteria (4 clinical batches in addition to 3 commercial batches)

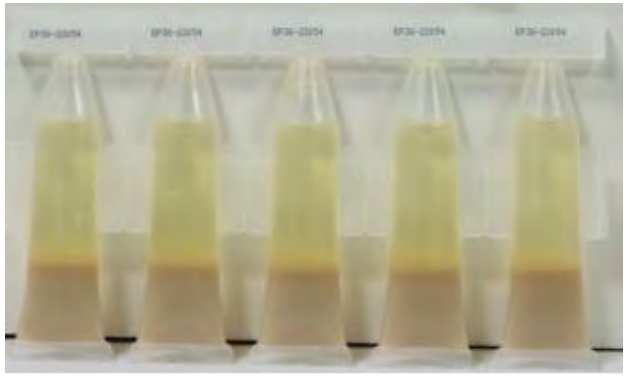
- **IVI expects to conduct a study in pregnant women given that funding from RF and Wellcome is secured.**

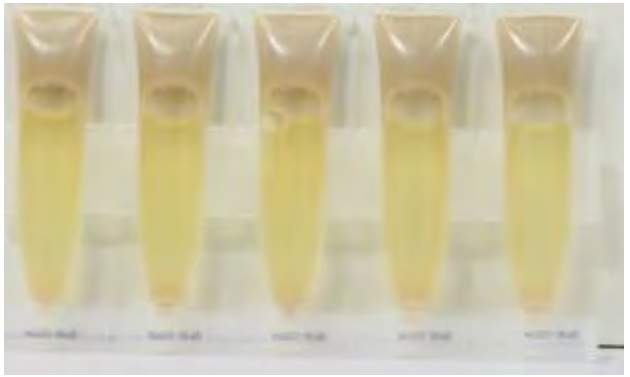
V. Shaking Study_Overview

- Euvichol-Plus is a plastic tube containing a yellow or yellowish suspension of inactivated *Vibrio* cholerae. Sedimentation can occur over time as shown in the picture below.

- The Instruction for Use in Package Insert, 'the vaccine is presented as a suspension, therefore, after the shaking the vaccine container rigorously, 1.5mL of the vaccine should be squirted in the mouth. However, this is not often followed during reactive campaigns in outbreak setting. Also, a guideline of shaking rigorously needs to be provided.

- Therefore, shaking study was conducted to evaluate the impact of shaking the tube by hand before oral administration of Euvichol-Plus on its protective efficacy.





V. Shaking Study_Testing Method

eubiologics

- **In the study, the LPS content results were analyzed based on the shaking method and frequency that Euvichol-Plus was shaken by hand.**

- **Sample Information:**

Product	Item	Content
Euvichol-Plus	Batch No.	EP36-22054
	Manufacturing date	Aug. 25, 2022
	Expiration date	Aug. 24, 2024

- **Testing Plan: Hand shaken up to 5 times (vertical and horizontal shaking)**

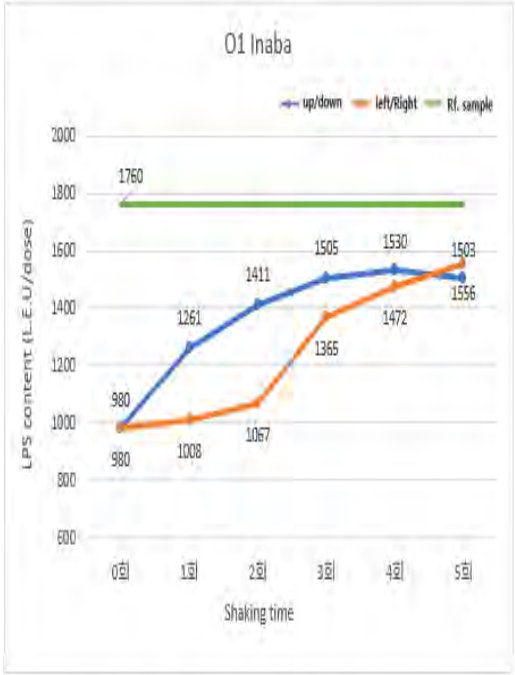
Shaking No.	Shaking Method					
	UP / Down (↓ ↑)			Left / Right (← →)		
	O1 Inaba	O1 Ogawa	O139	O1 Inaba	O1 Ogawa	O139
0	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose
1	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose
2	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose
3	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose
4	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose
5	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose	L.E.U/dose
Reference sample(*)	L.E.U/dose					

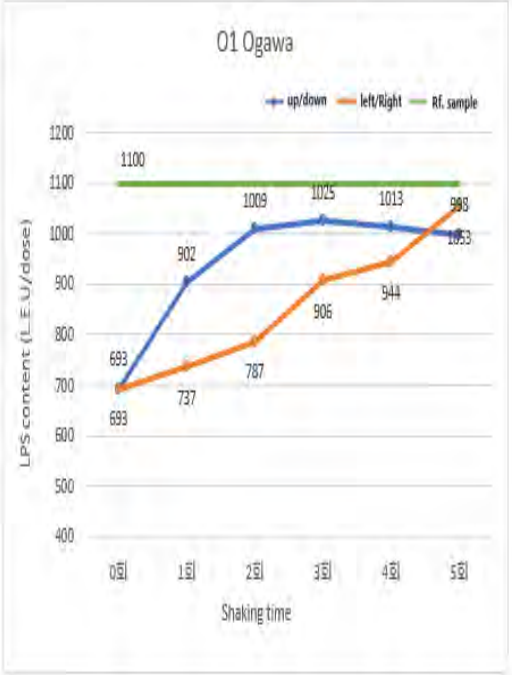
(*) Reference sample: the reference sample is not shaken by hand; it is a sample that has been automatically vortexed for 3 minutes in accordance with the SOP "LPS content testing method".

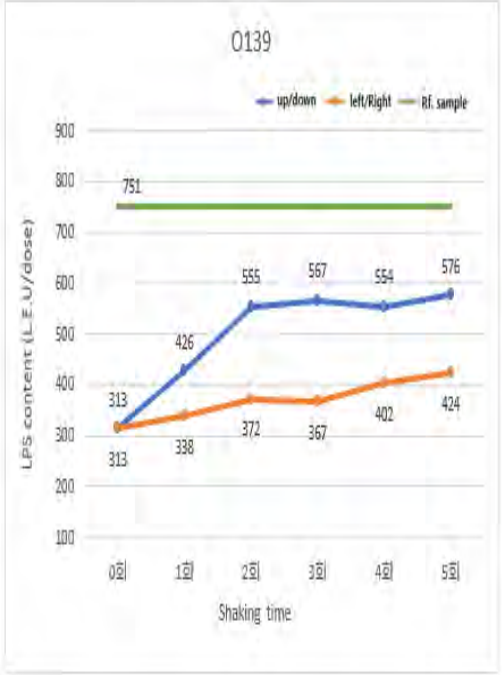
V. Shaking Study_Testing Results

eubiologics

- **LPS contents Results:**





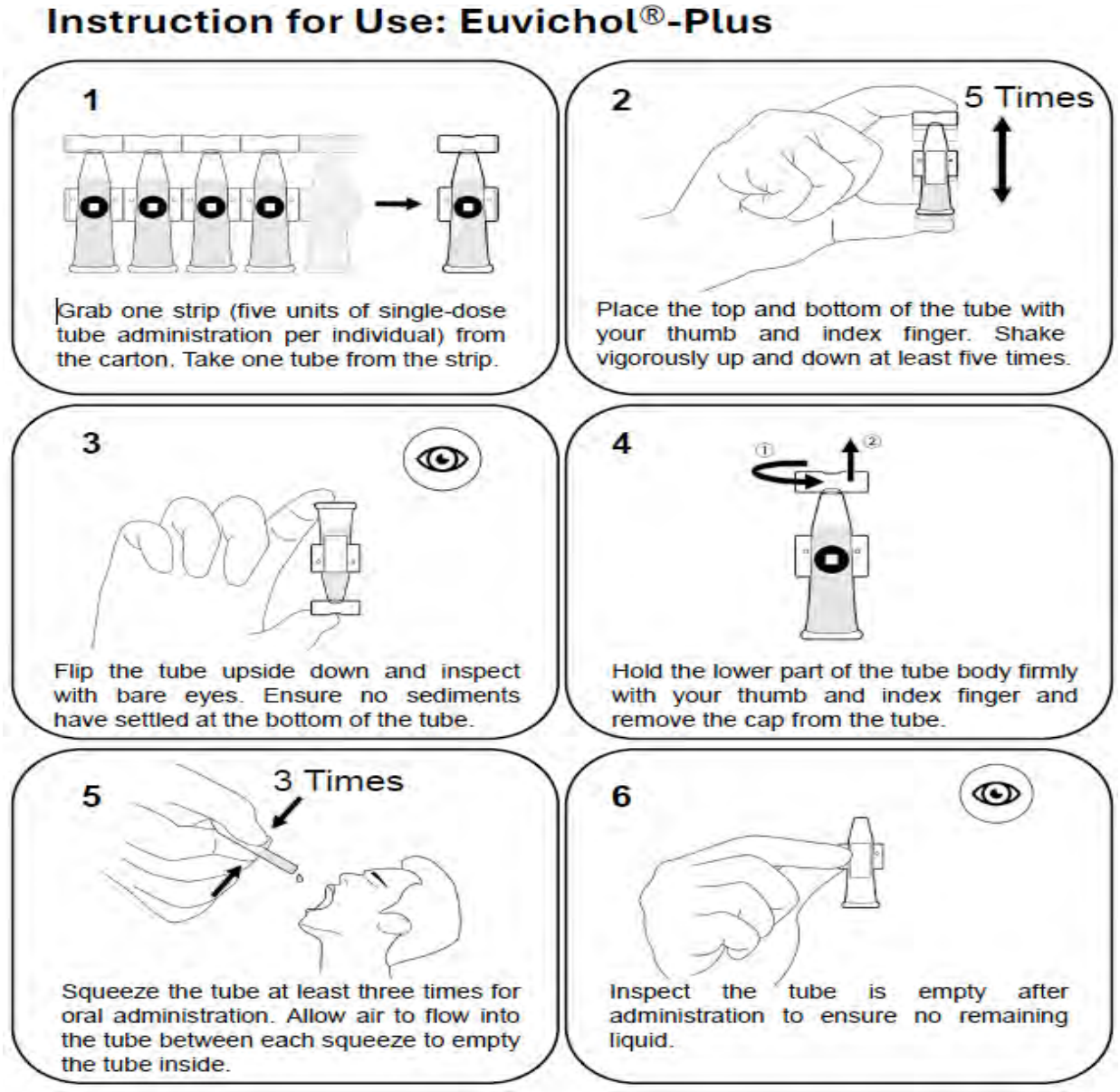


Strains	O1 Inaba		O1 Ogawa		O139	
Test criteria	≥ 800 L.E.U/dose		≥ 400 L.E.U/dose		≥ 400 L.E.U/dose	
Shaking conditions (frequency and method)	Up/Down	Left/Right	Up/Down	Left/Right	Up/Down	Left/Right
0	980		693		313	
1 time	1261	1008	902	737	426	338
2 times	1411	1067	1009	787	555	372
3 times	1505	1365	1025	906	567	367
4 times	1530	1472	1013	944	554	402
5 times	1503	1556	998	1053	576	424
Reference sample	1760		1100		751	

- As the number of shaking increases, the LPS contents showed a rising trend.
- Both O1 Inaba and O1 Ogawa were consistently maintained within a relative standard deviation (RSD) of 5% up to 5 shaking cycles, regardless of vertical and horizontal shaking. However, the O139 strain showed relatively lower LPS content when shaken horizontally.
- Based on the overall trend, vertical shaking is observed to be more effective than horizontal.
- Reference samples maintained higher LPS content values than hand-shaking up to 5 times, due to sufficient vortexing.

V. Shaking Study_Instruction for Use

- The higher LPS contents have been observed with a sufficient number of shakings, which suggests at least 5 shakings in up and down is needed to ensure protection before oral administration.
- We expect to revise the wording in Package Insert from shaking vigorously to shaking at least 5 times up & down before oral administration and include the instruction for use.
- Visual confirmation of the absence of sediment is recommended.



V. Euvichol-S Introduction

Euvichol®-Simplified

- Simplified Oral Cholera Vaccine(OCV-S) from Euvichol®-Plus
- WHO prequalified on April 12th, 2024*
- Supply is expected to increase by 38%
- Pricing reduction is expected
- Expect to achieve the Controlled Temperature Chain (CTC) with Euvichol-S
- First shipment expected to Niger in Oct 2024

Products	Euvichol® / Euvichol®-Plus	Euvichol®-S
Strain	**Quantity (Unit: L.E.U.)**	
V. cholerae O1 Inaba Cairo 48 (Heat, H)	300	-
V. cholerae O1 Inaba Phil 6973 El Tor (Formalin, F)	600	900
V. cholerae O1 Ogawa Cairo 50 (F)	300	600
V. cholerae O1 Ogawa Cairo 50(H)	300	-
V. cholerae O139 4260B (F)	600	-
Appearance	Yellow or slightly yellow, cloudy solution containing inactivated cholera bacteria	
Dosage and Administration	Administer orally twice at two-week intervals	
Indication	Prevention of cholera caused by Vibrio cholerae serogroup O1 in children, adolescents, and adults over 1 year of age.	
Storage temperature	2 to 8 ℃	
Shelf life	24 months	

***Reference:** https://extranet.who.int/prequal/vaccines/p/euvicholr-s

V. Euvichol-S Clinical Trial Design

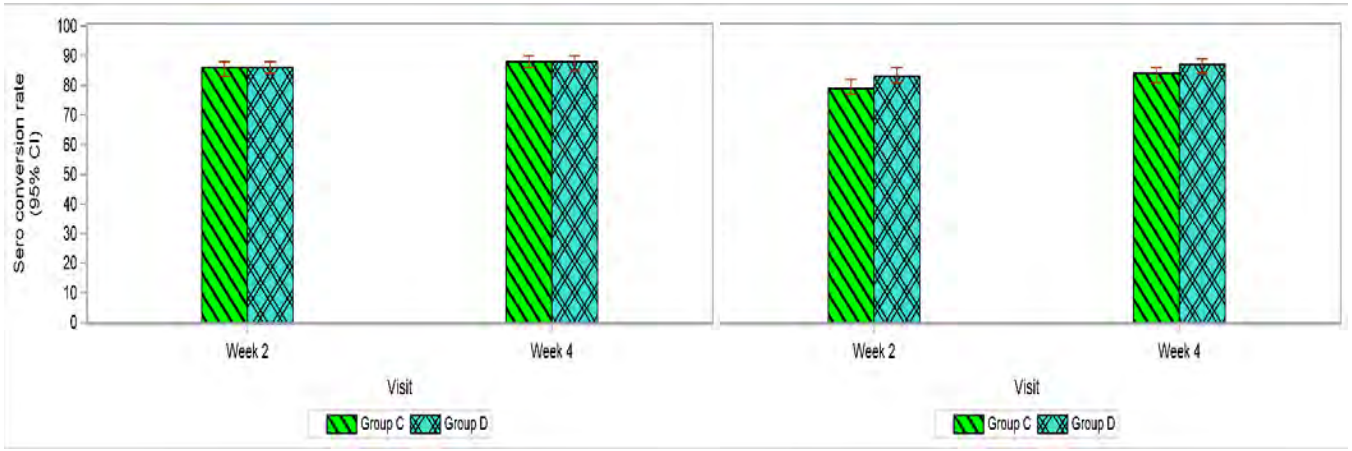
eubiologics

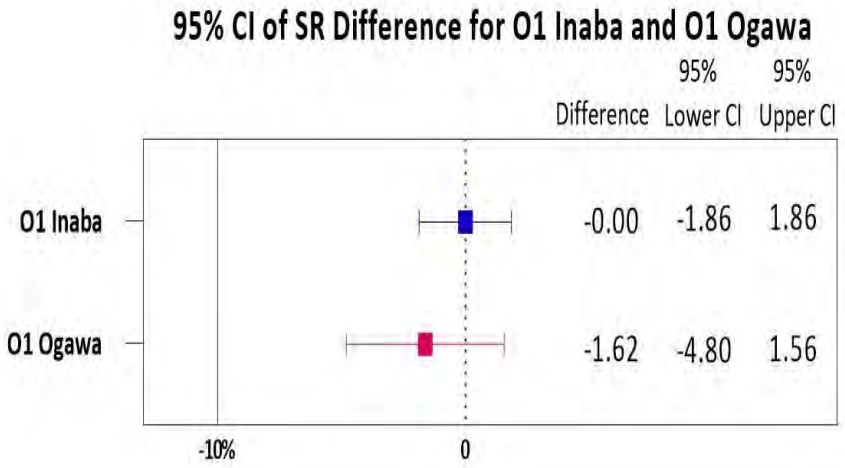
Clinical Trial	Phase 3
Protocol Number	OCV-S
ClinicalTrials.gov	NCT04760236
Endpoint	• **Primary:** Immune non-inferiority and safety profile • **Secondary and Exploratory:** Lot to Lot consistency and immunogenicity by age stratum, etc.
Country	Nepal
Enrollment Period	October 2021~August 2022
Participant Enrollment	**Overall: 2529 (Safety Set)** Euvichol®-S: 1595 participants Shanchol™: 934 participants **Age Group:** 1~5 yrs: 489 participants 6~17 yrs: 720 participants 18~40 yrs: 1320 participants
Age	1 year ~ 40 years
Administration	Two doses at two weeks apart
Safety Follow-up	Up to six months
Study Status	Completed
Publication*	The Lancet, published in May 2024

*** Reference:** https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(24)00059-7/fulltext

V. Euvichol-S Clinical Trial Result

- **The primary comparison to show the non-inferiority of Euvichol®-S compared to Shanchol™ is** Seroconversion rate of vibriocidal titers against *Vibrio cholerae* O1 Inaba and O1 Ogawa at 2 weeks after second dose of Euvichol®-S (Group C) is non-inferior to seroconversion rate at 2 weeks after second dose of Shanchol™ (Group D) using non-inferiority margin of -10%.
  - ✓ **Endpoints**: Seroconversion against *Vibrio cholerae* O1 Inaba and Ogawa
  - ✓ **Time Point**: 2 weeks after the second dose of Euvichol®-S and Shanchol™
  - ✓ **Age**: Ages 1 to 40 years old
  - ✓ **Analysis Population(Per Protocol Set):** Euvichol®-S (Group C) 904, Shanchol™ (Group D) 892
  - ✓ **Conclusion:** Both Euvichol®-S O1 Inaba and Ogawa vibriocidal titers at 2 weeks after the second dose for **overall ages fulfilled**





- **The safety profile:** Safety results confirmed satisfactory safety profile for Euvichol-S® in all age strata

Thank - you