For Health that lasts a **lifetime!**

eubiologics

EuBiologics's Vaccine Technologies for Equity

March 2023

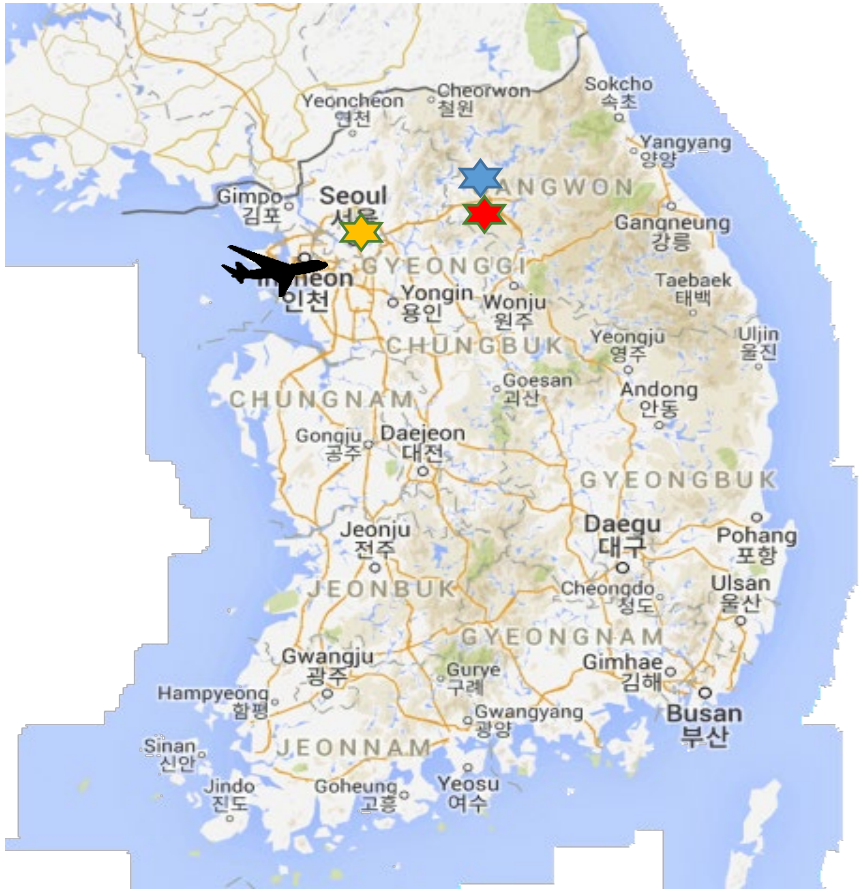
www.eubiologics.com

I. EuBiologics_Company Overview

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 Facility - Two Manufacturing sites in Chuncheon - R&D Center in Chuncheon
No. of Employee	323
Market Capital	USD 200M Listed in KOSDAQ since Jan 2017
Business Area	- Vaccine Development, Manufacturing & Supply - CRMO(Contract R&D and Manufacturing Organization)



I. EuBiologics_Company Overview

EuBiologics has two manufacturing sites in Chuncheon South Korea with a total capacity of up to 500M doses per annum.

Plant

[C-Plant]

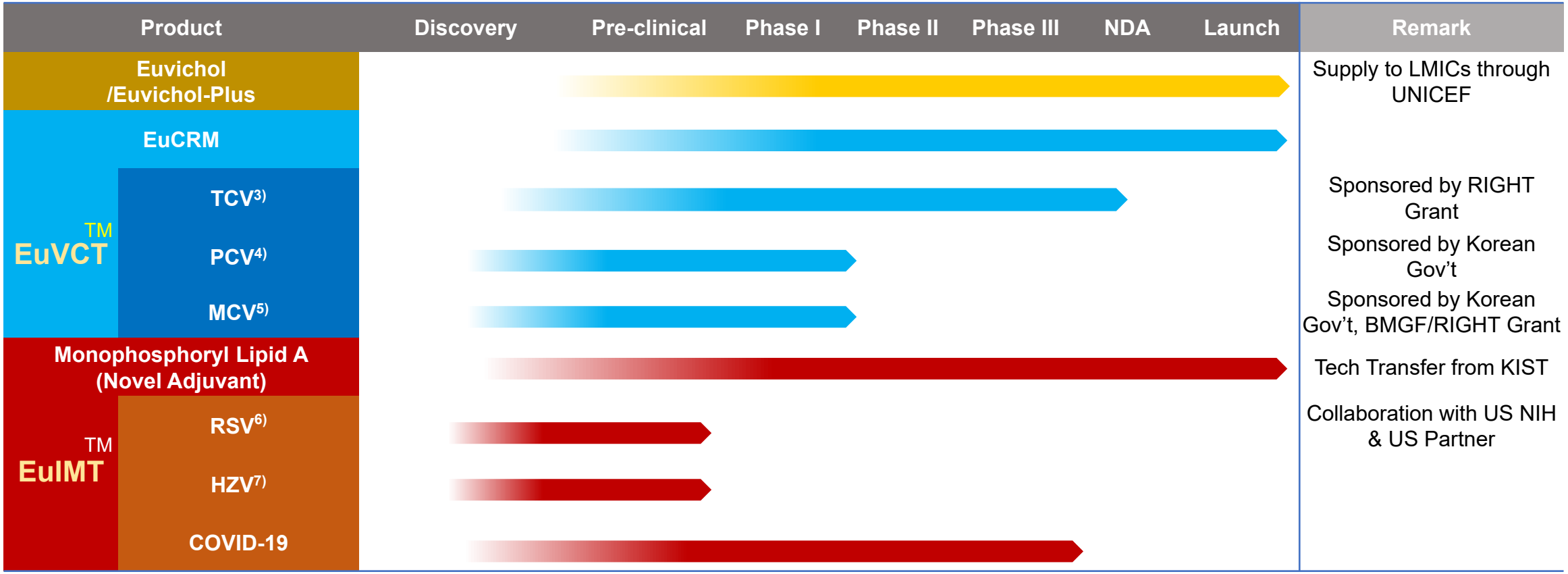
[V-Plant, R&D Center]

[Facility and Capacity]

- C Plant : Oral Cholera Vaccine-DS & DP (33M doses/y)
  EuCorvac-19 Vaccine-DS (200M doses/y, 1,000L*2 lines of Animal cell culture line)
- V Plant : Bacterial conjugation production line- DS(Total 200M doses/y) → rCRM197, TCV, MCV, PCV etc
  : Oral Cholera Vaccine-DS & DP (33M & 50M doses/y) expansion ongoing funded by BMGF
  : CMO for APIs ; Suite#4, 5 (50/100/200/500/1,000-L Lines)

I. EuBiologics_Pipeline

EuBiologics has a pipeline of vaccines leveraging its platform technologies, EuVCT™ 1) and EuIMT™ 2)



1) EuVCT: **Eu**Biologics **V**accine **C**onjugation **T**echnology
2) EuIMT: **Eu**Biologics **I**mmuno-**M**odulation **T**echnology
3) TCV: Typhoid Conjugate Vaccine
4) PCV: Pneumococcal Conjugate Vaccine
5) MCV: Multivalent Meningococcal Conjugate Vaccines
6) RSV: Respiratory Syncytial Virus
7) HZV: Herpes Zoster Virus

II. OCV_Cholera Overview

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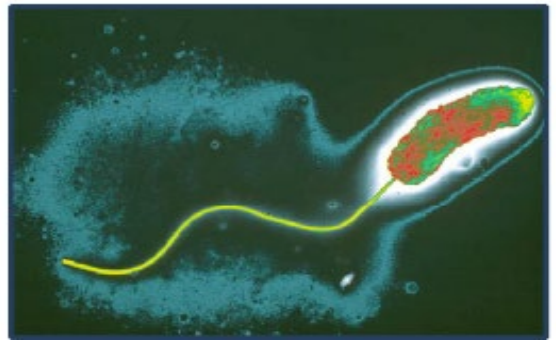
- Vibrio cholerae, highly pathogenic waterborne bacterium, causes outbreaks of acute diarrheal disease
  ; 3 million cases per year, mainly in Africa and Southeast Asia, 100,000 deaths

- Two types of oral cholera vaccine (OCV) available;
  - Killed (inactivated) bacterial cells
  - Live attenuated bacteria
  ; Reluctance to invest in vaccine development and scale-up



- A global stockpile of OCV created in 2013, to control cholera epidemics.
  ; 2~3 million doses in Stockpile, to convert the “vicious cycle” into “virtuous cycle” of vaccine availability and country adoption, as demand and/or supply stimuli are needed
  ; Initial Support for global stockpile up to USD 115M over 2014-2018 to trigger vaccine demand/supply

II. OCV_Development History

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- EuBiologics was awarded as the 2nd manufacturer of Oral Cholera Vaccine (OCV) through the Cholera Vaccine Initiative (CHOVI) program sponsored by Bill and Melinda Gates Foundation (BMGF), and has technology transferred by International Vaccine Institute in 2010
  - IVI and EuBiologics both based in Korea (ODA member country) creating synergies
  - Can serve as a stepping stone to develop vaccines for high income countries

<Targets for OCV Development>

- ✓ A low-cost vaccine;
  - → DS: Process optimization, Yield increase (fed-batch fermentation)
  - → DP: Plastic Tube Presentation
- ✓ High quality vaccine in compliance with global standards;
  - → In compliance with Korea GMP and WHO GMP
  - → Thimerosal free formulation
- ✓ Sufficient capacity more than 6 Million doses per annum targeted to global public market
  - → from 100L to 600L scale (up to 25 M per year)
  - → Easier administration (Plastic Tube Presentation)

II. OCV_Milestones

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- **Euvichol is the 2nd OCV developed by technology transfer from IVI and equivalent to Shanchol (Shantha Biotechnics, India) in terms of quality, safety and effectiveness**

  - Sep 2010 OCV License Agreement with IVI

  - Apr 2011 Non-clinical Trial for OCV in Korea (http://dx.doi.org/10.5487/TR.2012.28.4.225)

  - Oct 2012 Phase I Clinical Trial in Korea (http://synapse.koreamed.org/DOIx.php?id=10.3346/jkms.2014.29.4.494)

  - Aug 2014. Non-inferiority trial "A Randomized, Non-inferiority Trial Comparing Two Bivalent Killed, Whole Cell, Oral Cholera Vaccine (Euvichol vs Shanchol) in the Philippines (http://linkinghub.elsevier.com/retrieve/pii/S0264-410X(15)01228-1)

  - Jan 2015 Approval of Marketing Authorization from Korea MFDS

  - Dec 2015 Euvichol Prequalification from WHO (6M doses per annum)

  - Sep 2016 PQ variation approval (600L scale up allowing 25M doses & removal of thimerosal)

  - Aug 2017 PQ variation approval (Plastic Tube)

II. OCV_Drivers for Plastic-Tube Decision-Making

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- **In-house FF facility needed for OCV**
  - Outsourced DP production limiting a total capacity of OCV (DS Capa: 25M, Outsourced DP capa: 12M)
  - High cost associated

- **Differentiation from existing product needed as a late comer**
  - The competitor has the same formulation transferred from IVI
  - Plastic tube presentation can make a difference

- **Plastic tube offers a number of benefits over glass vial, lower production cost, easy administration, storage, wastage and transportation**
  - 30% reduction in volume, more than 50% reduction in weight
    (Savings from freight forward charges can be spent for procurement of additional doses for vaccine equity)
  - Pricing offered to UNICEF decreased by 23% in the first year attributed to the CoGs decline

External Box for export	Width (mm)	Length (mm)	Height (mm)	Quantity per carton	Volume /dose (㎤)	Weight/dose (g)
Euvichol	570	530	425	2,400	53.5	14.6
Euvichol-Plus	700	700	505	6,400	38.7	6.7

II. OCV_Drivers for Plastic-Tube Decision-Making

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- **Easier Administration**

	Euvichol	Euvichol-Plus	Note
Opening	Challenging	Simple	For Euvichol, field workers often complain about difficulty to remove caps & need tweezers/forceps
Administration	Upside down & hit the bottom	Squeeze	Exact AMT can be administered using plastic tube

<Euvichol>

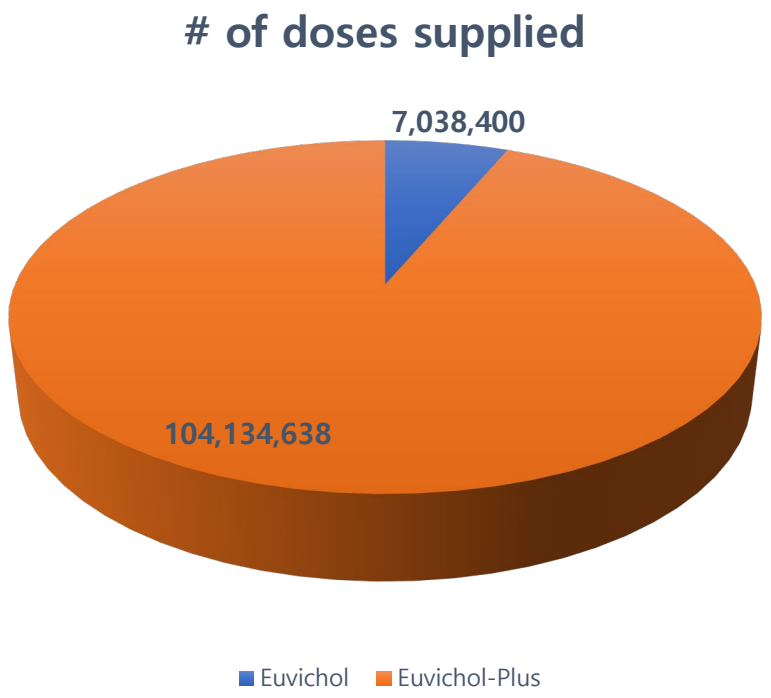
VS

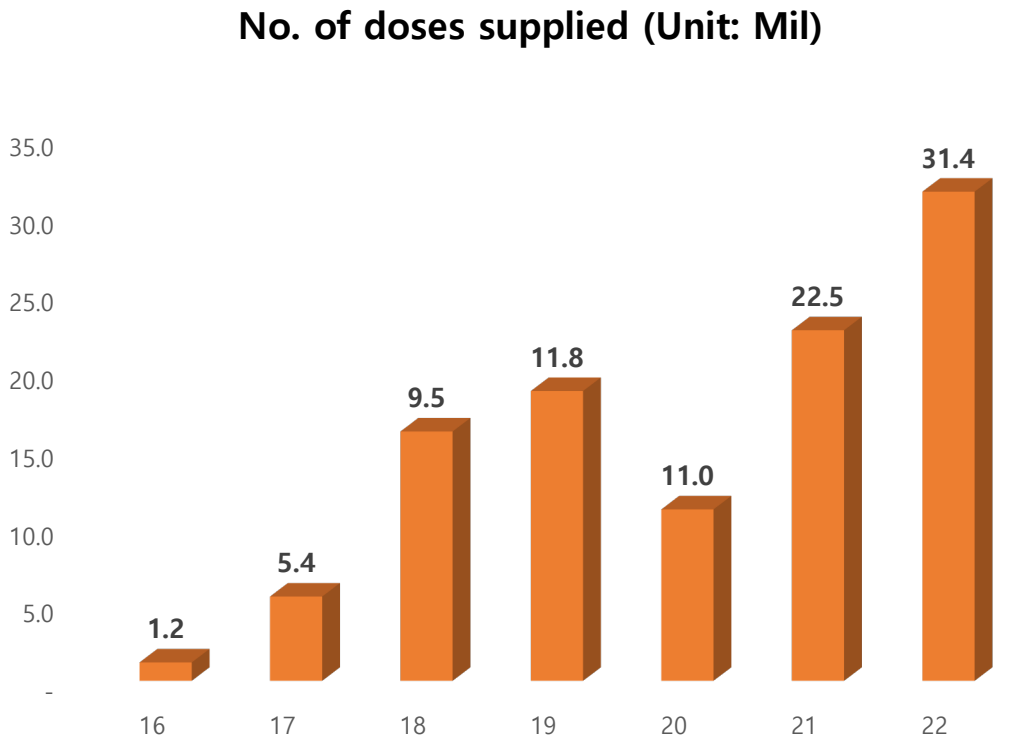
<Euvichol-Plus>

- **External funding available for Fill/Seal(FS) facility**
  - Global Health Investment Fund (GHIF) led investment for FS facility in consortium with Korean investors
  - Leachable/Extractable study was partly funded by DCVMN

II. OCV_No. of doses shipped

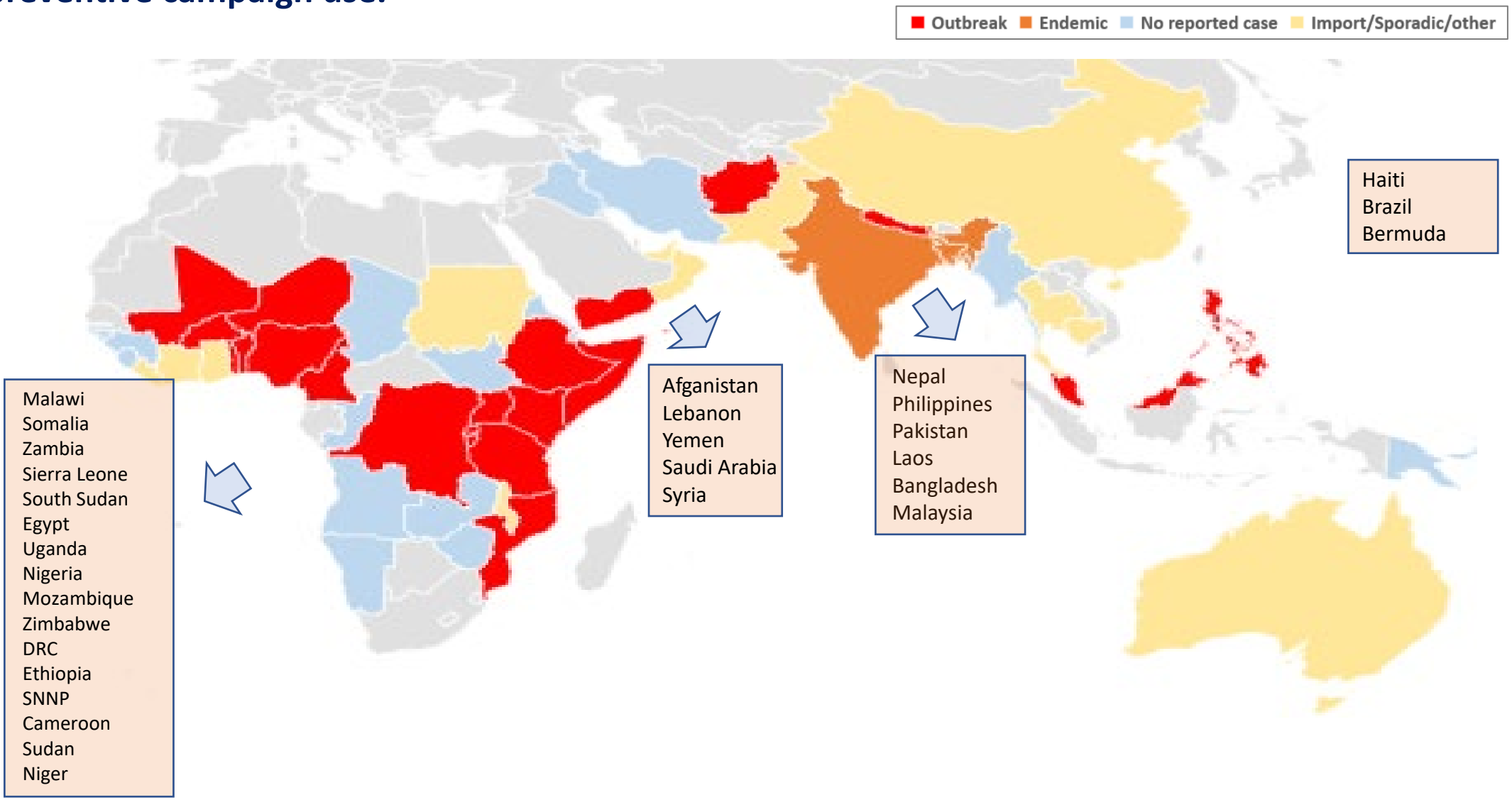
- EuBiologics phased out the production of Euvichol after prequalification of Euvichol-Plus in 2017.
- As of now, EuBiologics is the only supplier of oral cholera vaccine to LMICs through UNICEF.





II. OCV_Deliveries

EuBiologics has supplied more than 110M doses of its OCV to 31 countries for outbreak response or preventive campaign use.



II. OCV_Current Unmet Needs

- **Shortage of oral cholera vaccine**
  - Global trend is moving towards more numerous, widespread and severe outbreaks due to floods, droughts, conflict, population movements etc.
  - Current supply is not sufficient to serve demand for reactive campaigns to outbreaks

Development of Euvichol-S and expansion ongoing

- **Lower efficacy for children under 5 years of age**
  - OCV are limited to induce high level durable protective immunity in young children

Cholera Conjugate Vaccine (injectable) under development in collaboration with IVI and Massachusetts General Hospital

II. OCV_Euvichol-S development

- **Euvichol-Plus contains 5 distinct components. Euvichol-S contains only two current components, *O1 Inaba* (*Phil El Tor*) and *O1 Ogawa* (*classical Cairo 50*) and inactivated by a single method (formalin)**

Arms	O1 Inaba Cairo 48 Heat	O1 Inaba Phil 6973 (El Tor) Formalin	O1 Ogawa Cairo 50 Heat	O1 Ogawa Cairo 50 (Classical) Formalin	O139 Formalin
Euvichol-P	300 LEU	600 LEU	300 LEU	300 LEU	600 LEU
Euvichol-S		900 LEU		600 LEU	

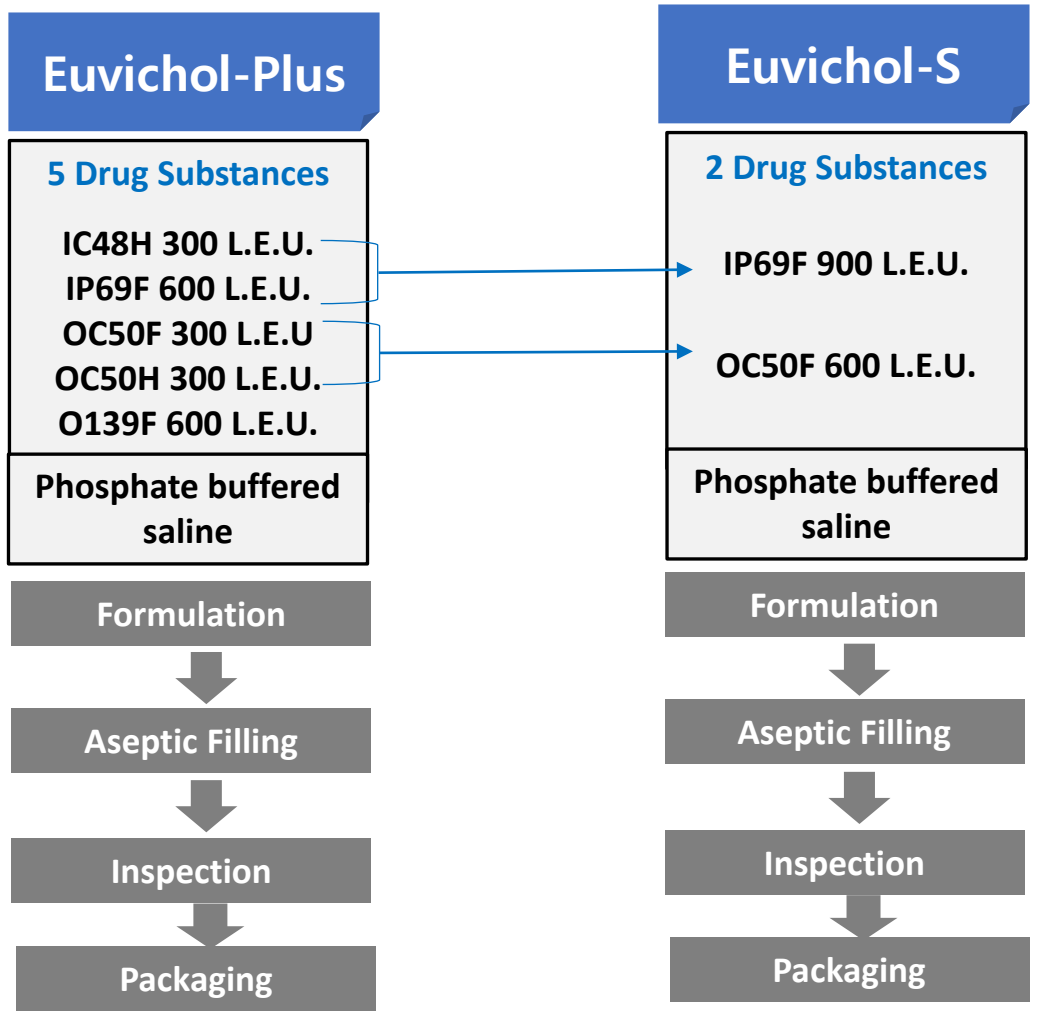
- **A Phase III, Multicenter, Observer-Blinded, Randomized, Active Controlled Trial to Evaluate Immune Non-Inferiority, Safety and Lot-to-Lot Consistency of Euvichol-S compared to Shanchol in 1 to 40 years old Healthy Nepalese Participants by IVI**
  - To demonstrate non-inferiority of Euvichol-S compared 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)

- **Immunogenicity response results:**
  - Primary immunogenicity results (non-inferiority) were fulfilled
  - Secondary immunogenicity results (lot to lot consistency) were fulfilled

- **Safety response results: Safety results confirmed satisfactory safety profile for OCV-S in all age strata.**

II. OCV_Euvichol-S

- Supply is expected to increase by 38% by switching from Euvichol-Plus to Euvichol-S.
- Pricing reduction is expected.
- We expect to submit our dossier to KMFDS in March 2023, anticipating an approval by year-end.
- PQ timeline will be subject to the feasibility of expedited review by PQ team.
- Expect to achieve the Controlled Temperature Chain (CTC) with Euvichol-S.



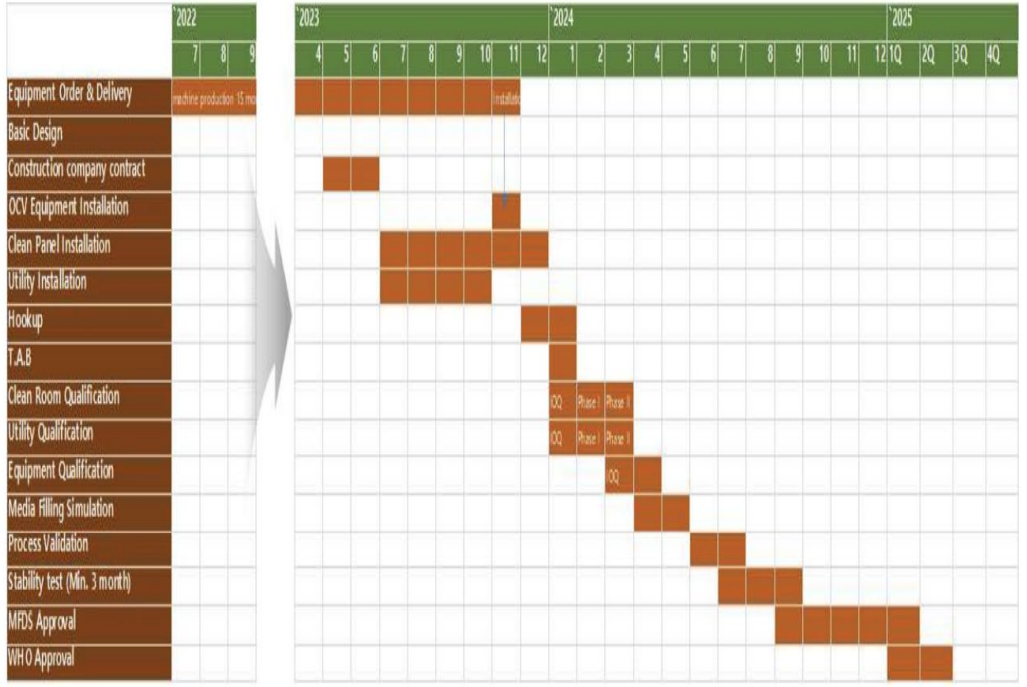
II. OCV_Expansion

- EuBiologics has been working on 2nd site to double the production capacity, 2nd site is expected to be prequalified in Jul 2024 by the support of BMGF
- EuBiologics expects to have an additional fill/finish facility in 2nd site to increase the capacity to be completed by June 2025 by the support of BMGF

<Drug Substance>

No.	Process Breakdown	Start	Finish	Duration (Month)
1	Design	Nov ‘19	Dec ‘19	2M
2	Construction	Jul ‘20	Dec ‘20	6M
3	**Equipment Purchase**	**Nov ‘19**	**Mar ‘22**	**29M**
4	Qualification	Apr ‘22	Dec ‘22	9M
5	Process Validation	Jan ‘23	Mar ‘23	3M
6	Comparability Study	Apr ’23	Jun ‘23	3M
7	Licensure by MFDS	Jul ‘23	Dec ’23	6M
8	Variation Approval by WHO	Jan ’24	Jun ‘24	6M
9	**GMP Production**	**Jul ‘24**		

<Drug Product>



II. OCV_Availability

- **OCV Availability assuming expansion (both DS and DP) and Euvichol-S (either Euvichol-Plus or Euvichol-S)**
  - In 2024, 41M doses are available (either Euvichol-Plus or Euvichol-S)
  - In 2025, 70M doses are available (Euvichol-S)
  - In 2026, 80M doses are available (Euvichol-S)

		2024	2025	2026	Note
Euvichol-Plus	DS	52	65	65	Currently 33md, increasing 65md by June 2024 when 2nd site is online
	DP	41	70	91	Currently 41md capacity, increasing 91md by June 2025 when 2nd site is online
Euvichol-S	DS	72	80	80	Assuming a 38% increase in antigen availability following PQ of Euvichol-S by the end of 2023 earliest (based on concurrent review) that we switch from Euvichol-P to Euvichol-S from 2024.
	DP	41	70	91	Currently 41md capacity, increasing 91md by June 2025 when 2nd site is online

II. CCV

- **EuBiologics is in collaboration with IVI and Massachusetts General Hospital for development of Cholera Conjugate Vaccine**

- **Phase I clinical study is ongoing at Gangnam St Mary's Hospital**

Cohort	IP	Progress
Cohort A	CCV 5μg	Enrollment: Dec 2022 Completion: Jan 2023
	CCV 5μg +AL	
Cohort B	CCV 10μg	Enrollment: March 2023 Completion: May 2023 2023년
	CCV 10μg +AL	
Cohort C	CCV 25μg	Enrollment: June 2023 (exp) Completion: July 2023 (exp)
	CCV 25μg +AL	

- **A CCV could have utility as an independent monovalent vaccine, as part of a prime-boost approach when combined with oral cholera vaccination to boost immune responses in young children and to consolidate long term protection, and/or as part of multivalent conjugate enteric vaccine that targets other intestinal pathogens, such as shigella and salmonella.**

III. Summary

- EuBiologics developed OCV technology transferred by IVI and introduced an innovative presentation, Euvichol-Plus in 2017.

- Euvichol-Plus has advantages over glass vial in terms of cost, administration, transportation, wastage and storage.

- EuBiologics is the only supplier of OCV to LMICs through UNICEF and shipped more than 110M doses since Oct 2016

- In order to meet the unmet needs, EuBiologics has been working on development of Euvichol-Simplified which will allow 38% increase of total capacity.

- In addition, EuBiologics' capacity of OCV is up to 80M doses in 2026 after expansion is completed.

- In collaboration with IVI and MGH, EuBiologics is under development of cholera conjugate vaccine to increase the efficacy on children under 5 years of age and considers the development of combo vaccine targeting enteric diseases.