WHO PUBLIC ASSESSMENT REPORT (WHOPAR)			
Euvichol®-S Inactivated Oral Cholera Vaccine			
EuBiologics Co., Ltd., Republic of Korea.			
Ref. no. PQ-FVP-2023-0492-WHOPAR-03			
Effective date: 17 April 2024	**Published: 29 Jan 2025**	**Last Update: 29 Jan 2025**	**Version: 1**

What is Euvichol®-S?

Euvichol®-**S** is an oral cholera vaccine (OCV) containing inactivated whole cells (WCs) of *V. cholerae* O1 as the drug substance. The *V. cholerae* strains used for this OCV are the O1 Inaba Phil 6973 El Tor (formalin-inactivated) and O1 Ogawa Cairo 50 (formalin-inactivated).

As an oral suspension, the plastic tube of 1.5 mL should be shaken vigorously before the oral administration of its total content (1.5 mL). The vaccine is non-preserved and a non-adjuvanted oral suspension, ready to use after thorough agitation.

Each dose of vaccine (1.5 mL) contains:

Active components and quantity per dose	
Vibrio cholerae O1 Inaba Phil 6973 El Tor (formalin inactivated)	900 Lipopolysaccharide ELISA Unit (L.E.U.)
Vibrio cholerae O1 Ogawa Cairo 50 Classical (formalin inactivated)	600 Lipopolysaccharide ELISA Unit (L.E.U.)
Excipients	
The formulation system is complemented with a sodium-phosphate buffer in water for injection (q.s). These excipients are in compliance with the European Pharmacopoeia and other recognized pharmacopeial compendiums (e.g., USP).	

Euvichol®-S comes in a pack of 5 strips of 10 plastic tubes each, for a total of 50 oral vaccine Euvichol®-S mL.

Euvichol® is filled in a plastic tube as primary container. The plastic tubes made of low-density polyethylene (LDPE) conform to the specifications of the European Pharmacopoeia. The compatibility of the container closure system of Euvichol®-S was evaluated in terms of protection, compatibility, safety, packaging components, and system performance.

The stability data submitted by the prequalification holder supports a shelf life of 24 months when the vaccine is stored between 2°C to 8°C. The vaccine should be shipped and stored at this recommended temperature, and it should not be frozen. The data provided support the use of a Vaccine Vial Monitor (VVM) Type 30.

WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

Euvichol®-S Inactivated Oral Cholera Vaccine

EuBiologics Co., Ltd., Republic of Korea.

Ref. no. PQ-FVP-2023-0492-WHOPAR-03

Effective date: 17 April 2024	Published: 29 Jan 2025	Last Update: 29 Jan 2025	Version: 1

Euvichol®-S is manufactured and licensed by Eubiologics Co., Ltd., at 8F Seongdo Building, 207 Dosan-daero Gangnam-gu, Seoul, Republic of Korea.

What is Euvichol®-S used for?

Euvichol®-S is recommended for the prevention of cholera caused by *Vibrio cholerae* serogroup O1 in children aged 1 year and older, adolescents and adults.

How is Euvichol®-S used?

Euvichol®-S should be administered orally in a two doses of 1.5 mL schedule, at an interval of two weeks between the two doses.

The vaccine is presented as an oral suspension. Therefore, after a vigorous shaking of the plastic tube, the 1.5 mL content should be squirted into the mouth. A sip of water can be taken, if necessary.

Vaccines for which there is evidence that they have been frozen, should not be used.

As it is practice for other vaccines, appropriate medical treatments should always be readily available in case of rare events of anaphylactic reactions following the administration of the vaccine. Therefore, it is advisable to remain under medical supervision (e.g., at the immunization center) for at least 30 minutes after vaccination.

The vaccine contains traces of formaldehyde. Caution should be taken in subjects with known hypersensitivity to this substance.

Euvichol®-S should not be administered parenterally.

What are the vaccine characteristics?

Euvichol®-S must be stored as recommended by manufacturer, between 2°C to 8°C. Under these recommended storage conditions, the vaccine is stable for 24 months from the date of manufacture.

The vaccine is ready to use and does not contain preservative.

Cold chain volume per dose is 7.8 cm^3/dose in secondary packaging.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

Ministry of Food and Drug Safety (MFDS) of the Republic of Korea is the regulatory authority of record for the WHO prequalification procedure. The Marketing Authorization (MA) for Euvichol®-S was issued by the MFDS in December 2023.

How has Euvichol®-S been studied from the clinical point of view?

Considering that neither a new antigen nor a new process was added, and that only removal of antigens was carried out for the development of this simplified vaccine formulation, there was consensus among the expert group that phases I and II clinical studies were not required in the clinical development programme (CDP). This group of experts also agreed that the clinical benefit of Euvichol®-S be inferred from a non-inferiority immunogenicity study comparing Euvichol®-S to Shanchol™, a pre-qualified OCV that demonstrated efficacy in an efficacy trial using clinical endpoints.

Therefore, the clinical development program of Euvichol®-S was based on one randomized, controlled safety and immunogenicity phase III study designed to demonstrate non inferiority compared to Shancol™.

The **Phase III study -Primary Efficacy study** was a multicenter, observer-blinded, randomized, active controlled trial to evaluate immune non-inferiority, safety and lot-to-lot consistency of Oral Cholera Vaccine-Simplified compared to Shanchol ™ in 1 to 40 years old healthy Nepalese participants.

The phase 3 trial was appropriately designed and powered to demonstrate non-inferior immunogenicity of Euvichol®-S compared to Shanchol™ and clinical lot to lot consistency, using vibriocidal antibody response against *V. cholerae* O1 Inaba and *V. cholerae* O1 Ogawa strains.

In the overall population, as per the per-protocol analysis set, the seroconversion rates to *V. cholerae* O1 Ogawa at 2 weeks post second dose were 81.96% (95% CI: 79.64, 84.28) in the

Test group and 83.51% (95% CI: 81.00, 86.01) in the Comparator group, showing a non-inferiority difference between Test group and Comparator group of -1.54 (-4.77, 1.68).

The secondary immunogenicity endpoint(s) showed that in the overall ages, the GMT of vibriocidal antibodies against *V. cholerae* O1 Inaba at 2 weeks post second dose were comparable among the participants who received test and comparator. The GMT ratios were 1.01 (95% CI: 0.88, 1.17). The GMT of vibriocidal antibodies against *V. cholerae* O1 Inaba at 2 weeks post second dose were comparable among the three age groups who received test and comparator.

Non-inferiority was demonstrated using both endpoints, post-dose 2 seroconversion rate and post dose 2 GM of vibriocidal antibody titers in the overall study population and within each age stratum.

The safety data from this phase 3 clinical trial indicate that Euvichol®-S has a safety and reactogenicity profile that appears acceptable and similar to Shancol™.

Other information about evaluation of Euvichol®-S

The evaluation of Euvichol®-S prequalification application was based on the review of the information submitted to WHO by Eubiologics Co. Ltd., of the Republic of Korea, the availability of the Good Manufacturing Practice (GMP) certificate issued by the MFDS, which is a WHO-Listed Authority (WLA) that complies with all the indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking and performance evaluation process.

The vaccine prequalification dossier was submitted in a CTD format. The vaccine meets WHO Technical Report Series (e.g., TRS 924, Annex 3, 2004 “Guidelines for the production and control of inactivated oral cholera vaccine”. In addition, the vaccine was found in compliance with WHO programmatic suitability criteria, the Cholera vaccines: WHO position paper – August 2017, and general monograph for Vaccines of Human Use (04/2022:0153) of the European Pharmacopoeia 11.0.