WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

SKYTyphoid Multi Inj. (Typhoid Vi Polysaccharide Conjugated to Diphtheria Toxoid)

SK bioscience Co., Ltd., Republic of Korea

What is SKYTyphoid Multi Inj. (Typhoid Vi Polysaccharide Conjugated to Diphtheria Toxoid) Vaccine?

SKYTyphoid Multi Inj. Vaccine is the SK bioscience Co., Ltd., trade name for purified Vi polysaccharide of *Salmonella* Typhi which is conjugated to carrier protein, Diphtheria Toxoid. The vaccine is a clear colorless liquid supplied as 2.5 mL multidose vial (0.5 mL x 5 doses) containing 2-phenoxyethanol (5 mg/dose) as preservative.

The SKYTyphoid Multi Inj. Vaccine consists of the following composition per 0.5mL dose:

Components	**Quantity (per 0.5 mL)**
Active ingredient	
Typhoid Vi polysaccharide conjugated to diphtheria toxoid	25 µg
Preservative: 2-Phenoxyethanol	5 mg
Diluent	
Water for injection	*q.s.*
Excipients	
Sodium chloride, Disodium hydrogen phosphate anhydrous, Sodium dihydrogen phosphate dihydrate	

The multi-dose (2.5-mL/5-doses/vial) is presented in a Type I borosilicate glass vial with 3 mL capacity, with pharmaceutical grade rubber stopper made out of Chlorobutyl rubber, with a 13 mm flip-off aluminium seals.

The shelf-life of the SKYTyphoid Multi Inj. Vaccine is 24 months at storage conditions 2 to 8°C.

The SKYTyphoid vial bears a Vaccine Vial Monitor (VVM) type 30 as part of the label.

The manufacturing of bulks, formulation, and filling occurs at the facilities of SK bioscience Co., Ltd. at L HOUSE, GMP facility in Andong, Korea

What is SKYTyphoid Multi Inj. (Typhoid Vi Polysaccharide Conjugated to Diphtheria Toxoid) Vaccine used for?

The SKYTyphoid Multi Inj. Vaccine is intended for prevention of typhoid fever caused by *Salmonella* Typhi in age of ≥ 6 months and ≤ 45 years.

How is SKYTyphoid Multi Inj. (Typhoid Vi Polysaccharide Conjugated to Diphtheria Toxoid) Vaccine used?

The SKYTyphoid Multi Inj. Vaccine (dose of 0.5mL) is administered intramuscularly in the deltoid region of subjects. For children aged ≥ 6 months to < 2 years, it can be given intramuscularly in anterolateral thigh.

What is SKYTyphoid Multi Inj. (Typhoid Vi Polysaccharide Conjugated to Diphtheria Toxoid) Vaccine characteristic?

The SKYTyphoid Multi Inj. Vaccine must be stored between 2 to 8°C. Under the recommended storage conditions, the vaccine is stable for 24 months from the date of manufacture.

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

The SKYTyphoid Multi Inj. Vaccine is manufactured and licensed in Republic of Korea by SK bioscience Co., Ltd., Republic of Korea. The Korea Ministry of Food and Drug Safety (MFDS) is the authority responsible for the continuing oversight of this WHO prequalified vaccine.

How has SKYTyphoid Multi Inj. (Typhoid Vi Polysaccharide Conjugated to Diphtheria Toxoid) Vaccine been studied from the clinical point of view?

The clinical program included four safety and immunogenicity clinical trials involving a total of 4,389 healthy individuals, including 3,330 subjects who received any formulation of SK-TCV[1] of whom 1,168 were young children aged 6 to 23 months. Study participants came from two countries, Philippines and Nepal.

Clinical trial "IVI-T001" was a Phase 1 study to assess the safety and immunogenicity of SK-TCV[1] conducted in 144 healthy individuals from May 2016 to June 2017, in Philippines. This randomized, observer-blinded trial was conducted in healthy adults and children aged 2 - 45 years.

Clinical trial "IVI T002" was a Phase 2 safety and immunogenicity study conducted in 285 healthy infants aged 6-23 months between April 2018 and October 2020 in Philippines. This randomized, observer-blinded study was designed to compare one and two doses of SK-TCV[1] vaccine.

Clinical trial "IVI T003" was a Phase 3, randomized, active-controlled, observer-blinded clinical trial to assess the immunogenicity and safety of SK-TCV[1] vaccine compared to Typbar TCV®. The study was conducted between November 2019 and December 2020 in 2,160 healthy infants, children and adults aged 6 months to 45 years old at four sites in Nepal.

Clinical trial "IVI T004" was a Phase 3, randomized, controlled, observer-blinded study to compare the safety and immunogenicity of the multi-dose (MD) and the single-dose (SD) formulation of SK-TCV[1]. The study was conducted from February 2020 to February 2021 in 1800 healthy individuals aged 6 months to 45 years in Philippines.

In this clinical development program, the Vi-DT[1] typhoid conjugate vaccine at a dose of 25 µg demonstrated an acceptable safety and immunogenicity profile for use in infants, children and adults from age 6 months to 45 years. Safety was demonstrated in 3,300 infant, children and adult vaccine recipients in two countries (Nepal and Philippines). Vi-DT[1] was immunogenic across all age groups, with higher responses than the comparator Vi polysaccharide typhoid vaccine (Typhim Vi®), and non-inferior to the licensed typhoid conjugate vaccine, Vi-TT (Typbar TCV®). The program demonstrated that a single dose of Vi-DT[1], using either a multi-dose or single-dose formulation, across 3 different lots is safe and immunogenic.
The Vi-DT[1] vaccine was immunogenic in all recipients across age groups from 2 years to 45 years, showing higher titers of binding antibody and bactericidal antibody than the comparator Vi polysaccharide vaccine (Typhim Vi®) in the Phase 1 study (IVI-T001). The immunogenicity data is particularly compelling in the immediate target population of infants and toddlers aged 6 to 23 months. The Vi-DT[1] vaccine induced high levels of seroconversion (> 99%) after a single dose, which persisted until week 28 in the Phase 2 (IVI-T002). A single dose was shown to be non-inferior to two doses, in terms of Anti-Vi IgG GMT, and Anti-Vi IgG GMTs were significantly greater than those observed in comparator vaccine recipients across all age strata. In the Phase 3 studies (IVI-T003 and IVI-T004), the Anti-Vi IgG GMTs of Vi-DT[1] achieved non-inferiority to Vi-TT (Typbar TCV®) in the combined age agroup of 6 months to 45 years old, and immune equivalence among 3 different lots and between single-dose (SD) and multi-dose (MD) formulations was demonstrated.

For the immediate target population of infants and toddlers aged 6-23 months, the program provided an adequate safety database. The safety profile of Vi-DT[1] was comparable to other licensed typhoid polysaccharide or conjugate vaccine. No patterns of concerning reactogenicity or adverse events (AEs) were identified. The clinical studies were conducted with appropriate local and national ethics and regulatory review and oversight, following ICH/GCP guidelines. Appropriate clinical study design, sample sizes and statistical analyses were used to evaluate safety, humoral immunogenicity, non-inferiority of immune responses, and immune equivalence. The concurrence of intention-to-treat (ITT) and per protocol immunogenicity analyses throughout the program strengthened the validity of immunologic findings, as did the use of a single clinical immunology lab across the four clinical trials reviewed in this report.

Other information about evaluation of SKYTyphoid Multi Inj. Vaccine:

As part of the prequalification process for SKYTyphoid Multi Inj. Vaccine, the Common Technical Document and the responses provided by the manufacturer to observations made by WHO have been reviewed for quality, safety, and efficacy by a team of WHO experts, and found to meet WHO requirements of WHO Technical Report Series WHO TRS 1030 (Annex 2), Recommendations to assure the quality, safety, and efficacy of typhoid conjugate vaccines.

The manufacturing facility was audited by a WHO team of experts and found to be in compliance with the WHO GMP requirements (WHO TRS 996, Annex 3 2016; TRS 961, Annexes 2, 3 and 6).

WHO has conducted independent testing of batches of the SKYTyphoid Multi Inj. Vaccine for critical release parameters in contracted laboratories qualified by WHO for the purpose, and results obtained were in compliance with the quality specifications of the product as specified in the WHO Technical Report Series WHO TRS 1030 (Annex 2)

This summary was last updated and published on 04 March 2024.

[1] SK-TCV and Vi-DT represent SKYTyphoid vaccine used in clinical trials.