

WHO prequalifies Bharat Biotech's typhoid conjugate vaccine

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Bharat Biotech's Typhbar TCV, the world's first clinically proven Typhoid Conjugate Vaccine against typhoid fever has received prequalification from World Health Organisation (WHO). This enables the procurement and supplies of this life saving vaccine to UNICEF, Pan-American Health Organization (PAHO) and GAVI supported countries. Typhbar TCV has been evaluated in Human Challenge Studies at Oxford University and typhoid conjugate vaccines have been recommended by WHO's Strategic Advisory Group of Experts on Immunization (WHO-SAGE).

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International Health Metrics and Evaluation (IHME) estimates that in 2016, there were approximately 12 million cases of typhoid fever resulting in around 130,000 deaths. Typhoid fever is caused by the bacterium *Salmonella Typhi* (*S. Typhi*), which infects humans due to contaminated food and beverages from sewage and other infected humans. Currently a third of the global population is at risk of typhoid fever, which results in reduced school attendance, loss of work and wages, lowered pregnancy outcomes and impaired physical and cognitive development of children. In most developing countries the cost of a course of treatment for typhoid fever ranges from \$50 to \$5000 for outpatient and inpatient treatments.

Typhbar TCV is a result of dedicated product development at Bharat Biotech since 2001, where all aspects of the product profile were studied and evaluated in human clinical trials. With 5 years of follow up data for seroconversion, Typhbar TCV at 25µg / dose has proven long term protection for children and adults alike, and can be administered to children from 6 months of age. Bharat Biotech is thankful to Dr. John Robbins, who in 1999 trusted the team to deliver the promise of vaccines against typhoid fever.

Enlightening the importance of WHO prequalification for an effective typhoid vaccine that is also safe for infants Dr. Krishna Ella, Chairman and Managing Director of Bharat Biotech said "Typhbar TCV is the first typhoid conjugate vaccine, clinically

proven to be administered to children from 6 months of age to adults and confers long term protection against typhoid fever. When we started this project, Typhoid fever was a neglected tropical disease. This success is a true reflection of Team Bharat Biotech's, ability to develop novel vaccines and sustain long term product development for fighting infectious diseases. It demonstrates the power of global partnerships to achieve novel breakthroughs."

WHO-SAGE recommended the use of typhoid conjugate vaccines for use in infants between 6 and 23 months of age and catch up vaccinations for children between 2 and 15 years of age. This recommendation paves the way for countries to introduce the vaccine into their immunization programs.

"With the recent Gavi Board approval of an US\$ 85 million funding window to make the typhoid conjugate vaccine available in Gavi-supported countries, we now expect the first introductions to take place as soon as the first half of 2019," said Dr Seth Berkley, CEO of Gavi, the Vaccine Alliance. "One of the main barriers to controlling typhoid has been the availability of a vaccine that is effective in young children, so this vaccine will be a game-changer for millions of the most vulnerable. This vaccine will not only save lives but considering the growing spread of drug resistant strains of typhoid, it will also prove to be a valuable weapon against antimicrobial resistance."

Revealing the go-to-community strategy for its affordable global typhoid fever vaccine in the global markets Dr. Ella said; "For Typbar TCV to reach vulnerable populations, we are pleased to announce the price of \$ 1.50/ dose for procurement for GAVI supported countries. Also, recognizing the importance of sustained vaccine procurement for low income and low-middle income countries, and in the interest of global public health, we announce a further price reduction to around \$ 1.0 or below / dose, post procurement of 100 million doses for LIC's and LMIC's."

The threat of antimicrobial resistance due to the overuse of antibiotics has resulted in multi drug resistant typhoid, similar to the reports from several parts of the world, and especially from Hyderabad Pakistan, where ceftriaxone-resistant typhoid was detected during 2016. Bharat Biotech has partnered with Aga Khan University Hospital in Hyderabad, Pakistan to introduce Typbar TCV to vulnerable populations in Pakistan. Towards this endeavor Bharat Biotech had generously donated 50,000 doses and agreed to supply an additional 200,000 doses at highly subsidized rates.

"India's leadership in developing this new typhoid vaccine reinforces a national commitment to improving the health of children around the world. For too long, typhoid, which invariably affects the world's poorest people, has been neglected in efforts to improve global health," said Dr. Anita Zaidi, the director of the Vaccine Development, Surveillance, and Enteric and Diarrheal Diseases teams at the Bill & Melinda Gates Foundation, which supported efforts that helped generate data for prequalification. "With this new vaccine – the first-ever to be useful for preventing typhoid in young children – countries will finally be able to protect millions of children who are most vulnerable to this deadly disease."

Oxford University conducted a human challenge study with Typbar TCV at 25µg / dose, where the subjects were challenged with live *S. Typhi* proving a protective efficacy of 87% against typhoid fever.

"The WHO prequalification of Typbar TCV marks an important milestone in the global effort to rid the world of typhoid fever and improve health for some of the most vulnerable populations in the world." said Prof Andrew Pollard, University of Oxford.

With the aim to accelerate the introduction of new typhoid conjugate vaccines as part of an integrated approach to reduce the burden of typhoid disease, Bharat Biotech has partnered with the Typhoid Vaccine Acceleration Consortium (TyVAC), a union between the Center for Vaccine Development at the University of Maryland, the Oxford Vaccine Group at Oxford University, and PATH. The consortium is conducting effectiveness studies for typhoid conjugate vaccines in Nepal, Malawi, and Bangladesh. Bharat Biotech has donated 50,000 doses of Typbar TCV, towards the conduct of these studies.

"The prequalification of the first typhoid conjugate vaccine is a major advancement for child health," said Dr. Kathy Neuzil, director of the Center for Vaccine Development at the University Of Maryland School Of Medicine. "Typbar TCV can be incorporated into routine vaccination schedules, giving us the best chance to reach children most at risk for this devastating disease."

In its efforts to become a comprehensive health care solutions provider for vaccine preventable infectious diseases, Bharat Biotech has partnered with the University of Maryland and the Wellcome Trust to develop and evaluate vaccines for non typhoidal salmonella (NTS) against the serovars Typhimurium and Enteritidis. The burden of disease from NTS is highest in sub Saharan Africa and a successful vaccine will result in a major impact on the disease burden from salmonellosis in Africa. Further, to develop a Salmonella Paratyphi A vaccine with the aim of providing future combination vaccines towards complete protection against salmonellosis, Bharat Biotech has an ongoing partnership with the University of Maryland.

Bharat Biotech has also partnered with the Navi Mumbai Municipal Corporation and the Centers for Disease Control USA, to

evaluate the effectiveness of Typbar TCV in Navi Mumbai. Dr. Krishna Ella, has generously donated 100,000 doses and agreed to supply an additional 300,000 doses at highly subsidized rates towards the conduct of these effectiveness studies.

Dr. M. K. Bhan, Former Secretary, Department of Biotechnology, Govt of India, said “Typbar TCV is a weapon against the high but under appreciated burden of Typhoid fever in children and adults. Immunisation will reduce use of antibiotics in acute febrile illnesses and antibiotic resistance.”

To provide global access to Typhoid Conjugate Vaccines, to save lives of populations in low income countries, Bharat Biotech is collaborating with the Clinton Health Access Initiative (CHAI). Bharat Biotech is able to supply up to 50 million doses / year and is actively working on expanding its manufacturing capacity to reach ~ 200 million doses. This will truly fulfill its mission to develop novel vaccines, manufacture and supply high volumes of high quality vaccines at affordable prices for low income countries and low-middle income countries.

Mr. Ira C. Magaziner, Chief Executive Officer at CHAI stated, “This significant price reduction for the typhoid conjugate vaccine will help save thousands of lives, particularly of the most vulnerable children. With its promise of an even lower price in the future, Bharat Biotech is making an important contribution to enable sustainable access to this vaccine in low-income countries.

Registrations for Typbar TCV are in process in more than 30 countries globally. With the vaccine already registered in India, Nigeria, Cambodia, Nepal, etc signaling assured global access to this life saving vaccine and delivering it to the populations that need it the most.