

# Typhoid Vaccine

## Information Paper

*A licensed vaccine developed by DoD and its partners*



**Product name:** Oral live typhoid vaccine  
**Commercial name:** Vivotif Berna  
**Date of licensure:** December 1989  
**Type of product:** attenuated live oral enteric-coated vaccine based on Ty21A strain  
**Company of manufacture:** Berna Products

**Target microorganism/associated disease:** Typhoid fever, an acute generalized illness caused by infection with the bacterium commonly referred to as *Salmonella typhi*, is characterized by fever, headache, abdominal pain, mild rash, and bowel movement and mental changes. The word "typhoid" is derived from the Greek "typhos", which means "smoke" because the disease is associated with mental confusion. *Salmonella typhi*, which causes infection only in humans, is acquired by ingestion of contaminated food or water or finger-to-mouth contact with contaminated feces. The infection can be spread by a healthy carrier of the bacterium ("typhoid Mary"). Typhoid fever is primarily a disease of adolescents and young adults, and may be fatal in untreated susceptible persons.

**Reasons for development:** During the Spanish-American War, one-fifth of U.S. troops (mostly U.S. Army) had typhoid fever, and over 1500 persons died of the disease. In the Anglo-Boer War the British army lost more men to typhoid (8225 deaths) than it did to wounds (7582 deaths). Development of a typhoid vaccine became a priority for both nations.

**Role of Department of Defense in product development:** Observational studies dating back to the Civil War had revealed that some typhoid fever survivors were not susceptible to repeat bouts of this illness. This evidence of natural immunity prompted efforts to develop vaccines to prevent typhoid fever. The first typhoid vaccines were created in Britain in 1896 by Wright; Leishman then created a more potent and less toxic version. After Captain Frederic Russell of the U.S. Army modified Leishman's vaccine to create a subcutaneous form and conducted volunteer studies demonstrating safety and efficacy, typhoid immunization was required of all U.S. service members beginning



*Typhoid fever remains a problem in countries that lack clean water and well-functioning sanitation systems.*

30 September 1911. The U.S. Army became the first military organization in the world to make typhoid vaccination mandatory, and had the lowest typhoid fever incidence of any major combatant in World War I. The first typhoid vaccine was licensed in the U.S. in 1914.

Levine and others conducted large scale studies in the 1980's in collaboration with the Ministry of Health in Chile with DoD funding which demonstrated 67% efficacy of an enteric-coated form of an attenuated Ty21a strain of *S. typhi* in conditions of moderate typhoid fever transmission in Chile. Later that decade, Simanjuntak and others at the Naval Medical Research Unit in Jakarta (NAMRU-2) and the Indonesian Ministry of Health demonstrated 42% efficacy of this vaccine in a setting of intense transmission of typhoid fever in Jakarta. The licensed version of Ty21A (Vivotif Berna) -- four enteric-coated capsules taken every other day -- helps protect against the disease, but other preventive measures such as hygiene are advised (as is the case with all typhoid vaccines, whether given by mouth or by injection).

The U.S. military has contributed to control of typhoid fever in other ways. (1) Identification of pathological bowel findings (such as enlarged intestinal lymphoid follicles or "Peyer's patches") during autopsies by U.S. Civil War surgeons were eventually linked to typhoid infection. (2) In 1899, during the Spanish-American War, the Reed-Vaughan-Shakespeare Typhoid Board was established. This board, with Major Walter Reed, Major Victor C. Vaughan, and Major Edward O. Shakespeare, carried out epidemiological investigations focusing on typhoid fever and noted that (1) either sick or healthy human carriers of typhoid bacilli were important sources of typhoid infection; and (2) the U.S. Army had failed to undertake established sanitary measures to prevent typhoid fever during the Spanish-American War. MAJ Carl Darnall developed a method of water purification in 1910, and MAJ William Lyster developed a water purification system using calcium hypochlorite in a linen bag (Lyster bag) in 1915.

The U.S. military has also contributed to improved treatments for typhoid fever patients. In 1948, Joseph Smadel, Ted Woodward, Herb Ley and Charles Wissman of The Walter Reed Army Institute of Research noted a patient given chloramphenicol for scrub typhus had typhoid fever responsive to chloramphenicol. Subsequently, investigators at NAMRU-2 and NAMRU-3 have demonstrated the utility of other antimicrobial agents for typhoid fever. Stephen Hoffman and others revealed the usefulness of the corticosteroid dexamethasone in reducing mortality from severe typhoid fever in 1984

## **Typhoid Fever Vaccine References:**

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