

**GRADE TABLE 2****Population:** Immunocompetent individuals.**Intervention:** Tetanus Toxoid Containing Vaccine (TTCV).**Comparison:** No vaccine or control.**Outcome:** Serious adverse events following immunization.

<b>PICO Question:</b> <i>In immunocompetent individuals, is there an increase in the incidence of serious adverse events following immunization with any dose of TTCV vaccine compared to not giving a TTCV vaccine?</i>				
			Rating	Adjustment to rating
<b>Quality Assessment</b>	No. of studies/starting rating		20 RCT <sup>1</sup>	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	<b>Final numerical rating of certainty of evidence</b>			4
<b>Summary of Findings</b>	<b>Statement on certainty of evidence</b>		Evidence supports a high degree of confidence that the true effect lies close to that of the estimate of effect on health outcome.	
	<b>Conclusion</b>		Severe adverse events are extremely rare. TTCV using various presentations have demonstrated to be safe to use in immunocompetent individuals of various age and population groups including infants, children, adolescents, adults and pregnant women. <sup>2</sup>	

**References:**

[1] Bar-On ES, Goldberg E, Hellmann S, Leibovici L. Combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines for primary prevention of diphtheria, tetanus, pertussis, hepatitis B and Haemophilus influenzae B (HIB). *Cochrane Database Syst Rev* 2012;(4):CD005530.

[2] Zepp F, Knuf M, Heininger U, et al. Safety, reactogenicity and immunogenicity of a combined hexavalent tetanus, diphtheria, acellular pertussis, hepatitis B, inactivated poliovirus vaccine and Haemophilus influenzae type b conjugate vaccine, for primary immunization of infants. *Vaccine* 2004 Jun 2;22(17-18):2226-33.

[3] Zhou W, Pool V, Chen R (2004). Reports of brachial neuritis in the vaccine adverse event reporting system (VAERS), United States 1991 – 2003 (Abstract 557). 20th International Conference on Pharmacoepidemiology and Therapeutic Risk management. Bordeaux.

<sup>1</sup> Bar-on et al. [1] performed a meta-analysis with pooled results from 20 RCTs and 5232 participants for a reactogenicity analysis. They reported that TTCVs are well tolerated and severe adverse events are rare.

<sup>2</sup> Supporting evidence includes [2] 1 study assessing the safety of TTCVs used in a combined hexavalent tetanus, diphtheria, acellular pertussis, hepatitis B, inactivated polio vaccine and Haemophilus influenza type B conjugate vaccine for primary immunization of infants. The combination vaccine was found to be safe and well tolerated. Another study [3] assessed the reports of brachial neuritis, an extremely rare adverse event. The rate of reported cases of brachial neuritis occurring 0 to 60 days after vaccination was 0.69 cases for 10 million doses.