Tetanus Toxoid Vaccines (TT)
WHO recommendations & general information

- Tetanus is a bacterial disease caused by the *Clostridium tetani* bacterium. Infection can result in case-fatality rates as high as 100%. Disease in humans results from production of the potent neurotoxin tetanospasmin, which manifests in symptoms such as muscle stiffness and spasms. In countries where the elimination target has not been reached, the WHO recommends using the ‘high-risk approach’, whereby all women of childbearing age are targeted through use of concerted campaigns and supplementary immunisation activities.

- Most tetanus cases occur in developing countries among newborns or in mothers after unhygienic births or poor postnatal hygiene. The WHO estimates that in 2010, 58,000 newborns died as a result of neonatal tetanus, and in 2011, 72,600 children under the age of five died from tetanus.

- Since 1999, the WHO has declared the goal of eliminating maternal and neonatal tetanus globally and achieving and sustaining high coverage of three doses of DTP to prevent tetanus in all age groups [see box, The Maternal and Neonatal Tetanus Elimination Initiative, page 91].

- In countries with a high prevalence of maternal and neonatal tetanus (MNT), all pregnant women are to be immunised with at least one dose of a TT-containing vaccine (usually dT); this is under the assumption that they have completed the childhood vaccination series. Pregnant women with unknown immunisation history are to receive two doses, the first as early as possible, and the second a minimum of four weeks later.

- It is recommended that districts with limited access to routine vaccination services and areas where the elimination target (fewer than one case per 1,000 live births) has not been achieved adopt the ‘high-risk approach’. Implementing this approach covers all women of child-bearing age with three doses of TT over a 12-month period, with an attempt to complete five doses overall if possible.

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**Vaccine** | **Age at 1st dose** | **Doses in primary series (interval between doses)** | **Booster**
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DTP, primary course | <1 year (doses to be given at 6, 10, 14 weeks) | 3 doses (4 weeks minimum between 1st and 2nd dose and between 2nd and 3rd dose) | 1st DTP booster at 1–6 years of age if aged 4–7 years, 1st booster administered as DT
|  |  |  | 2nd at 12–15 years (TT)
|  |  |  | 3rd booster (6th dose of tetanus vaccine overall) for women at time of first pregnancy (TT)
### Products & manufacturers

<table>
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<th>Product</th>
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<th>WHO PQ date</th>
<th>Form and presentation</th>
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</table>
| Tetanus toxoid vaccine      | BB-NCIPD                | May 2006    | Liquid, 10- and 20-dose vials* | N/A                              | VVM 14  
10-vial carton, 10-dose vials = 4.12 cm³  
10 vial carton, 20-dose vials = 2.05 cm³ |
10-vial box, 10-dose vials = 2.10 cm³  
10 vial box, 20-dose vials = 0.75 cm³ |
| Tetanus toxoid vaccine      | Bio Farma               | Oct 2003    | Liquid, 1-dose Uniject  | N/A                              | VVM 30  
Secondary packaging of 100 = 12 cm³ |
| Tetanus toxoid vaccine      | Biological E            | Dec 2009 (20-dose vial)  
Jul 2012 (1- and 10-dose vials) | Liquid, 1-, 10-*, and 20-dose vials | 10-dose: 0.070  
20-dose: 0.050          | VVM 30  
48-vial box, 1-dose vials = 14.70 cm³  
30-vial box, 10-dose vials = 3.90 cm³  
20-vial carton, 20-dose vials = 2.90 cm³ |
| Tetanus toxoid vaccine      | Sanofi Pasteur          | Jul 1997    | Liquid; 10- and 20-dose vials* | N/A                              | No VVM  
10 vials of 10 doses = 2.46 cm³ |
| Tetanus toxoid vaccine      | Serum Institute of India| Apr 1995    | Liquid, 1-dose ampoule  
Liquid, 10- and 20-dose vials* | 10-dose: 0.077  
20-dose: 0.053          | VVM 30  
50-ampoule carton, 1-dose ampoules = 15.71 cm³  
50-vial carton, 10-dose vials = 2.61 cm³  
25-vial carton, 20-dose vials = 2.43 cm³ |
| Shan TT                     | Shantha Biotechnics     | Aug 2007    | Liquid, 10- and 20-dose vials* | 10-dose: 0.080                  | VVM 14  
30-vial carton, 10-dose vials = 4.36 cm³  
30-vial carton, 20-dose vials = 2.57 cm³ |

**PIPELINE PRODUCTS**

The Chinese manufacturer Walvax has a TT vaccine in Phase III clinical trials.

**CHALLENGES**

Lack of adequate health infrastructure in countries with high MNT prevalence continues to be a challenge to improving routine immunisation and supplementary immunisation activities that address MNT.

Major funding gaps continue to exist for continuation of key immunisation activities targeting MNT, including strengthening of existing immunisation programmes, routine immunisation structures and supplementary immunisation activities.

*Opened multidose vials can be kept for use in subsequent immunisation sessions for up to a maximum of 28 days, provided certain conditions are met (WHO policy on use of opened multidose vials).* [172]
THE MATERNAL AND NEONATAL TETANUS ELIMINATION INITIATIVE

The first call to eliminate neonatal tetanus was made at the World Health Assembly in 1989; ten years later this was bolstered by the call to eliminate maternal tetanus (elimination is considered achieved when there is fewer than one case per 1,000 live births in every district of a country). However, both calls missed their initial target of eliminating neonatal tetanus by 1995 and maternal tetanus by 2005, and progress towards elimination has been slow. The Maternal and Neonatal Tetanus Elimination (MNTE) initiative was re-launched in 1999, and the current goal is to achieve global elimination by 2015.329,332 Cumulatively, 54 countries initiated or expanded TT Supplementary Immunisation Activities (TT-SIAs) between 1999 and 2012.330

Strategies to achieve MNTE focus on promoting clean delivery practices, routine immunisation of pregnant women, TT-SIAs in high risk areas, and surveillance.331 It is estimated that the cost of immunising women with three doses of TT through TT-SIAs is around US$1.80335 per woman. As of December 2013, 34 countries (out of the 59 identified countries that had not eliminated MNT in 1999) had achieved MNT elimination, leaving 25 countries where the disease is yet to be eliminated.331,330 The MNTE initiative is supported by the public and private sectors, with stakeholders including governments, civil societies, the Bill & Melinda Gates Foundation, Gavi, PATH, UNICEF, USAID, WHO, and others. Funding from Gavi has reached US$61.4 million, through funds received from the International Finance Facility for Immunization (IFFim) since 2007 and allocated to 32 countries.337 The association Kiwanis also partnered with UNICEF in 2010 through The Eliminate Project and has raised US$51 million to date (with a goal of reaching US$110 million before 2015).335

As more countries approach elimination, the current 2012–2015 strategic plan aims to achieve and maintain elimination. The estimated cost to achieve elimination, mainly through TT-SIAs, between 2012 and 2015, is US$227 million. One of the biggest challenges of the initiative is the availability of funds.332 Funds are especially hard to secure, as the initiative is competing against other global health priorities such as measles and polio eradication.336
As seen in Graph 24 below, the price of TT vaccines supplied to UNICEF is relatively low: between US$0.05–0.093 per dose in 2014.

However, despite the large manufacturer base and a generally low price, the lowest price available to UNICEF has increased by 127% between 2001 and 2014 (the lowest prices being US$0.22/dose for a vaccine by CSL Limited in a 20-dose vial in 2001 and US$0.50/dose for a vaccine by Biological E in a ten-dose vial in 2014).

A large supplier base and fierce competition on price can drive originator manufacturers out of the market. Crucell decided to leave the TT market after it could not compete with lower price offers to UNICEF from other suppliers.

**Notes:**
- For UNICEF, where agreements include a range of prices during a calendar year period or for different countries or groups of countries, the lowest price of the range was kept.
- Not represented on the graph: Intervax offered 10-dose and 20-dose presentations to UNICEF at US$0.037–0.043 per dose and US$0.024–0.027 (respectively) in 2001–2003; Sanofi Pasteur offered 10-dose and 20-dose presentations to UNICEF at US$0.08 per dose in 2003.
- Novartis has supplied TT to UNICEF but has not agreed to the publication of prices.
PRICES IN COUNTRIES

From Graph 25 below, it appears that the price of TT vaccines is low for international organisations, but goes up to US$7.74 in the private sector (Czech Republic).

Outside of government purchases, low prices seem to be available from emerging manufacturers. For instance, in hospitals in Tunisia, a TT vaccine by Serum Institute of India is available for US$1.98 per dose.

One study from Pakistan in 2004 showed that SIAs to prevent neonatal tetanus were cost-effective (at US$0.04 per dose of the vaccine, representing 11% of the total cost of immunisation, at US$0.40 per dose administered). The vaccine is available for close to this price through international organisations such as UNICEF.

Graph 25: Prices for Tetanus Toxoid (TT) vaccines in several countries, by income group and price type, 2013/2014*

Sources: PAHO Revolving Fund, UNICEF Supply Division, country price analysis.
*Annex A, Section C

Notes:
- Numbers in parentheses are number of doses per vial, when known.
- MSF price is with CPT Incoterm (see Annex C).
- The Philippines procures through UNICEF.
- Only the lowest price available to PAHO, UNICEF and MSF is presented in the graph.