Frequently Asked Questions and Answers

Replacement of TT with Td vaccine for dual protection

1. Our national surveillance data does not show that we have many cases of diphtheria. Why should we change from TT to Td vaccine when there is no perceived threat or need?

WHO has recommended minimum surveillance standards\(^1\) for diphtheria (national, facility-based case-based and laboratory confirmed) but globally many countries are not implementing or achieving these standards. As a result, the sporadic cases that occur are being missed by the surveillance system in many places. It is well established that the protection against diphtheria from the infant primary series wanes over time. To avoid the accumulation of susceptibles, booster doses of diphtheria-containing vaccine are needed. Recent large diphtheria outbreaks in Bangladesh, Indonesia, Kenya, Philippines, South Africa, Venezuela and Yemen demonstrate how devastating and costly it can be when population immunity to diphtheria is low.


2. We have internal processes for review and approval within and between ministries (health, finance, planning) and immunization partners at country level. How can we convince them on the need for the replacement?

To avoid the threat of diphtheria outbreaks, since 1998 WHO has recommended that all countries replace TT with Td for vaccination of women of reproductive age (and/or pregnant women as per national immunization target), older children and adolescents to improve protection against diphtheria.

To support the implementation of this longstanding recommendation, WHO and UNICEF have prepared various technical materials, including a Joint Communique, a Guidance Note, and these Q&As. These materials, as well as WHO policy recommendations and position papers are available at the following links and collectively explain the rationale and importance of the replacement. UNICEF and WHO will provide any required technical support to the Ministry of Health to prepare a submission to NITAG and ICC.

[https://www.unicef.org/health/index_43509.html](https://www.unicef.org/health/index_43509.html)

3. Why have we not heard more from the Regional and National Immunization Advisory Committees (RITAGs and NITAGs) and ICCs about this replacement?

Although the global policy recommendation to replace TT with Td vaccine has existed since 1998, the advocacy to support implementation has been insufficient. A notable exception is in the Americas where the PAHO Revolving Fund mechanism has only provided Td vaccine for decades – consequently countries in AMRO/PAHO use Td instead of TT vaccine. Together WHO and UNICEF are now intensifying efforts to raise awareness about the replacement and informing countries that TT vaccine will no longer be available through UNICEF from January 2020.
4. The price of Td vaccine is higher than TT vaccine. Why are UNICEF and WHO encouraging countries to replace a cheaper vaccine?

The price difference between the two vaccines is nominal, especially considering the additional benefit of having a single vaccine (Td) that will protect against two diseases - tetanus and diphtheria. The table below gives a comparative analysis. More information on UNICEF prices can be found at the following link:

UNICEF vaccines prices: [https://www.unicef.org/supply/files/2018_03_01_Td.pdf](https://www.unicef.org/supply/files/2018_03_01_Td.pdf)

<table>
<thead>
<tr>
<th>Vaccine (vial size)</th>
<th>Price $US / dose</th>
</tr>
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<tbody>
<tr>
<td>TT (10 dose)</td>
<td>$0.080 - 0.13</td>
</tr>
<tr>
<td>Td (10 dose)</td>
<td>$0.10 - 0.13</td>
</tr>
<tr>
<td>TT (20 dose)</td>
<td>$0.0531 - 0.085</td>
</tr>
<tr>
<td>Td (20 dose)</td>
<td>TBC (forthcoming by end 2018 after UNICEF completes its current tender process)</td>
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5. What presentations of Td vaccine are available in the market, considering that countries have been using 10 and 20 dose vials of TT vaccine?

Td vaccine is WHO pre-qualified and available in liquid formulation and 1, 10 and 20 dose presentations. Countries procuring through UNICEF, should indicate their preferred presentation of Td vaccine to UNICEF SD, during the annual forecast exercise.

6. Will there be sufficient supply of Td vaccine to meet global demand?

Td vaccine in liquid formulation has been WHO pre-qualified and used in immunization programmes since 1995. There is sufficient supply of Td vaccine available in three different presentations (1, 10 & 20 doses), from four different producing manufacturers, to meet global demand.

The tetanus-containing vaccines market is a healthy market, with ample capacity and five WHO pre-qualified suppliers of Td vaccine, four of which are actively supplying and have in-house production of tetanus and diphtheria bulk, with an estimated capacity of approximately 330 million doses per annum and potential to further expand. UNICEF Supply Division holds long-term agreements for Td vaccine with four manufacturers; Bio Farma (P.T. Persero), Intervax, Biological E and Serum Institute of India Ltd. UNICEF vaccine prices can be found at the following link:


There are also several (9) Td vaccine products non-prequalified and various other Td combination products (Tdap, Td-IPV and Tdap-IPV), for an additional capacity of about 80 million and potential to expand further. More information here: [http://www.who.int/immunization/MI4A](http://www.who.int/immunization/MI4A)

The current global demand for tetanus toxoid containing vaccines is approximately 250 million doses, of which 160 million doses are supplied through UNICEF. Therefore, there is sufficient supply of Td vaccines for all countries to replace TT with Td in their immunization schedule.
7. **What if my country self-procures TT vaccine?**

Available supply and opportunity for expansion can also serve self-procuring countries. A full list of all supply available (both prequalified and non-prequalified) for Td and other combination Td-containing products, is available at: [www.who.int/immunization/MI4A](http://www.who.int/immunization/MI4A).

Pricing prospects for self-procuring countries are provided in the table below based on country reported information:

<table>
<thead>
<tr>
<th>Vaccine (vial size)</th>
<th>Self-procuring countries median price $USD/dose (2017)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (20 dose)</td>
<td>0.05</td>
</tr>
<tr>
<td>Td (20 dose)</td>
<td>--</td>
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<tr>
<td>TT (10 dose)</td>
<td>0.25</td>
</tr>
<tr>
<td>Td (10 dose)</td>
<td>0.62</td>
</tr>
<tr>
<td>TT (2 dose)</td>
<td>0.10</td>
</tr>
<tr>
<td>Td (2 dose)</td>
<td>0.08</td>
</tr>
<tr>
<td>TT (1 dose)</td>
<td>2.46</td>
</tr>
<tr>
<td>Td (1 dose)</td>
<td>4.43</td>
</tr>
</tbody>
</table>

² Source: MI4A. Self-reported by countries to WHO through the V3P/MI4A mechanism.

Median prices for self-procuring MICs (excluding HICs) are considerably lower for the 10 dose (TT: $0.31, Td: $0.36) and 1 dose (TT: $1.93, Td: $0.86) presentations.

8. **Td is not a registered product in my country. What do I need to do before importing it?**

As the country is likely already using both tetanus and diphtheria vaccines in various formulations (e.g. DTP, Pentavalent, DT, TT, etc.), and Td vaccine is WHO prequalified, it is not anticipated that the registration process will be complex. The Ministry of Health can initiate registration of the product at the earliest, and if required, obtain importation waiver from National Regular Authority of the country as an interim arrangement. Additionally, countries are encouraged to use the WHO Collaborative procedure, which is the procedure for expedited review of imported prequalified vaccines for use in national immunization programmes. Further information on the Collaborative procedure between the WHO Prequalification of Medicines Programme and national medicines regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines, can be found here: [http://www.who.int/immunization_standards/vaccine_quality/expedited_review/en/](http://www.who.int/immunization_standards/vaccine_quality/expedited_review/en/)

9. **The country has queued up new vaccine introductions with Gavi support in 2019 and 2020 (competing priorities) and hence this change to Td vaccine is not possible at this point in time.**

This is just a replacement of TT with Td vaccine that has no implication on schedule, target population or cold chain requirement. This should not detract from programme efforts to introduce new vaccines. In fact, new vaccine introductions already planned in country can be leveraged as opportunities to include Td vaccine in revision of recording and reporting tools, and trainings can be used to sensitize health workers on the replacement.

10. **In the past, we have received vaccine introduction grants for Penta, PCV, Rota, IPV, etc. Will there be funding available to support this vaccine replacement?**

Td is not a new vaccine. It is combination of tetanus and diphtheria antigens that will directly replace the use of TT vaccine in the immunization schedule. There is a very small difference in vaccine cost and no programmatic impact on schedule, target group or cold chain capacity. However, the replacement will require orientation of health workers and revision of recording and reporting tools, these costs should be minimal and can be easily accommodated in national budget with available funds and by leveraging other opportunities such as planned health worker trainings.
11. Will there be an additional cold chain storage capacity requirement?
There will not be any requirement for additional cold chain storage capacity to accommodate Td vaccine when the same vial sizes (10 or 20 dose vials) are used to replace what the country is currently using for TT vaccine.

12. Will the replacement of TT with Td vaccine impact the immunization schedule?
Absolutely not. This is just change in formulation to include a second antigen, for dual protection – tetanus plus diphtheria. Same target population and same schedule.

13. What should be done with the remaining balance of TT vaccine in the country after shifting to Td vaccine?
If remaining stock of TT vaccine still meets all validity requirements, it should continue to be used first and then begin using Td vaccine. There is no need to discard or recall stocks of available TT vaccine.

14. Are there any safety concerns with use of Td vaccine during pregnancy?
Both tetanus and diphtheria toxoid containing vaccines are considered safe for use in pregnancy. These vaccines have been used for decades and there is no evidence of adverse pregnancy outcomes or risk to the fetus from the vaccination during pregnancy. However, local reactions at the site of injection are common.

For more information, see:

15. Is there a need for heightened AEFI monitoring for Td than already in place for other antigens?
There is always need for good AEFI monitoring for all vaccines. However, nothing specific or additional is required for Td vaccine.

16. If a woman or adolescent has received TT vaccine in the past, can Td be used for the next dose(s)? What will be the validity of previous TT doses? Should I repeat previous doses?
Yes, Td vaccine can be given as a subsequent dose following TT, and all previous TT doses will remain valid. There is no need to re-start the series.

17. The replacement of TT with Td vaccine may need a clear communication strategy and training of health workers. How can this be handled?
The replacement of TT with Td vaccine does not require a wide scale communication strategy as it should not have significant impact on the programme. The replacement will simply be an exchange of one vaccine product for another in the programme, with no change in targets population or schedule. Therefore, a simple orientation of health workers will be sufficient (e.g. an information circular and job aid).

18. How should the public/community be informed about this change?
As this is not a new vaccine introduction, a wide community engagement strategy is not necessary. However, health workers should be sensitized on how to explain and raise awareness of the benefits of Td vaccine among recipients. It is important to emphasize in all communications that this vaccine will offer the same protection against tetanus as TT with the added benefit of protection against a second disease (diphtheria).

19. What have been the experiences from countries that have replaced TT with Td vaccine?
All of the over 130 countries that have replaced TT with Td vaccine have had a seamless experience. Fourteen countries (Angola, Côte d’Ivoire, Guinea Bissau, Malawi, Mali, Nepal, Nigeria, Cabo Verde, Cameroon, DRC, Guinea, Myanmar, Niger and Uganda) have recently changed to Td vaccine. None have reported any problem with the replacement.
20. How many countries are still using TT vaccine?
As of June 2018, 133 out of 194 member states have already replaced TT with Td vaccine in their routine immunization programme, 61 countries are still using TT. 8 out of the 14 remaining high risk countries for maternal and neonatal tetanus are still using TT for campaign activities. However, as of 2019 all campaigns will be conducted with Td vaccine.

21. Will TT vaccine remain available in the global market?
UNICEF and WHO have a joint target to complete replacement of TT with Td vaccine in routine immunization programmes and in SIAs by January 2020. As of January 2019, UNICEF will no longer fund the supply of TT vaccine, and will only support access to Td vaccine for use in immunization programmes. Further as of January 2020, all countries supplied through UNICEF, can only access Td vaccine through UNICEF procurement services.
For countries, self-procuring TT vaccine, we do expect that TT vaccine will remain available on the global market. However, as a result of decreased demand through UNICEF and market evolution towards production of Td vaccine, the cost may increase, as well as the lead times required to fill orders.

FOR FURTHER INFORMATION
See attached guidance note and contact:
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