The occurrence of diphtheria reflects inadequate coverage of the national childhood immunization programme. Therefore, obstacles to optimal vaccine delivery must be identified and forceful measures taken to improve immunization coverage.

Adequate quantities of diphtheria antitoxin should be available nationally or regionally for medical management of cases. Diphtheria antitoxin is not recommended for prophylaxis.

The freeze indicator is used to warn of freezing and is packed with vaccines that are sensitive to freezing temperatures: DTP, TT, DT, Td (freezing point of -6.5°C), hepatitis B (-0.5°C), liquid Hib and their combinations (DTP-HepB, and DTP-HepB+Hib vaccines) and JE. Every refrigerator storing vaccines should have a freeze indicator (Freeze Watch™). It is strongly recommended that one freeze indicator be placed in each cold box during vaccine transport and distribution. This is critical in places subject to low temperatures.
**Diphtheria**

### Vaccine Handling

Vaccines containing diphtheria toxoid should be stored at about +4 (2-8) °C. Vaccines that have been frozen should not be used.

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**Database ID** 52_5

**Year** 2006

Vaccines containing diphtheria toxoid should be stored at about +4 (2-8) °C. Vaccines that have been frozen should not be used.

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**Database ID** 81_1

**Year** 2006

The recommended conditions for storing vaccines used in immunization programmes are shown in Appendix 81_1. This diagram also indicates the maximum times and temperatures in each case. At the higher levels of the cold chain, i.e., at national (primary), and regional or province level, OPV must be kept frozen between -15°C and -25°C. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15°C to -25°C if cold chain space permits, but this is neither essential nor recommended. At other levels of the cold chain (intermediate vaccine stores and health facilities), these vaccines should be stored between +2°C and +8°C. All other vaccines should be stored at between +2°C and +8°C at all levels of the cold chain. Liquid formulations of vaccines containing diphtheria, pertussis, tetanus, hepatitis B, Haemophilus influenzae type b, IPV and their combinations should not be frozen.

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**Database ID** 81_2

**Year** 2006

WHO recommends that a policy permitting the use of vaccine outside the cold chain can be implemented either generally for all routine immunization activities or on a limited basis in certain areas or under special circumstances, such as:

- national immunization days;
- hard-to-reach geographical areas;
- immunizations provided in the home;
- cool seasons;
- storage and transportation of freeze-sensitive vaccines (DTP, TT, DT, Td, hepatitis B and Hib vaccines) where the risk of freezing is greater than the risk of heat exposure.

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Diphtheria

If it is suspected that adsorbed DTP, DT, or TT have been frozen they should be examined for physical changes. Where these are found the vaccines should be discarded. The amount of antigen in a non-homogeneous vaccine can vary greatly, and the administration of such a vaccine may be associated with a reduced immune response or an increased incidence of local reactions.

Temperature sensitivity of vaccines

Vaccines containing tetanus toxoid:
TT/DT/Td/DTP vaccines should never be frozen. The shake test will determine if the vaccine has been damaged by freezing. If the vaccine fails the shake test you must discard it.

Immunization in practice: a practical resource guide for Health workers – 2004 update Module 2: The vaccines

The “shake test” can help give an idea whether adsorbed vaccines (DTP, DT, Td, TT or hepatitis B) have been subjected to freezing temperatures likely to have damaged them. The test should be conducted for all boxes where freeze indicators are found to be activated or temperature recordings show negative temperatures. Identify and separate all vaccines that may have been frozen and ensure that none are distributed or used.


Check the freeze indicator in the refrigerator. If it warns of freezing or you suspect that a freeze-sensitive vaccine (DTP, DT, TT, Td, HepB, DTP-HepB, liquid Hib and DTP-HepB+Hib vaccines) has been frozen, you should perform the shake test.

Diphtheria

A policy permitting the use of vaccine outside the cold chain can be implemented either generally for all routine immunization activities or on a limited basis in certain areas or under special circumstances, such as:

- national immunization days;
- hard-to-reach geographical areas;
- immunizations provided in the home;
- cool seasons;
- storage and transportation of freeze-sensitive vaccines (DTP, TT, DT, Td, hepatitis B and Hib vaccines) where the risk of freezing is greater than the risk of heat exposure.

If it is suspected that adsorbed DTP, DT, TT or hepatitis B vaccines have been frozen they should be examined for physical changes. Where these are found the vaccines should be discarded.

Multi-dose Open Vials

See "Multi-Dose Open Vial" section of the "General" chapter in this catalogue for policies relevant for DTP, DT, TT, DTP-hepB, DTP-hepB-Hib, hepatitis B, liquid formulations of Hib and OPV.

27 June 2008
Diphtheria

Schedule

According to WHO requirements, the potency of diphtheria vaccine used for the immunization of children shall be no less than 30 IU per single human dose. Vaccines of lower potency are used for immunization of children aged ≈7 years and adults. This reduction of diphtheria toxoid potency minimizes reactogenicity at the injection site but is still sufficient to provoke an antibody response in older children and adults.

Database ID 52.4

The recommended schedule for vaccination against diphtheria varies considerably between countries. According to the WHO/EPI schedule, the primary series of DTwP- or DTaP-containing vaccines should be administered in 3 doses, starting as early as 6 weeks of age and given with a minimum interval of 4 weeks. Where resources permit, additional doses can be given after the completion of the primary series. Many national immunization programmes offer 1-2 booster doses, for example one at 2 years of age and a second at age 4-7 years.

Database ID 52.6

For previously un-immunized children aged 1-7 years, the recommended schedule (for diphtheria vaccine) is 2 doses 2 months apart, and a third dose after 6-12 months using DTwP or DTaP. The recommended schedule for primary immunizations of older children, adolescents and adults using the dT combination is 2 doses - months apart and a third dose after 6-12 months. People living in low-endemic or non-endemic areas should receive booster doses of DT approximately 10 years after completing the primary series and subsequently every 10 years throughout life. Special attention should be paid to immunizing health-care workers who may have occupational exposure to C. diphtheriae. Booster responses can still be elicited after intervals of 25-30 years, so repeat primary immunization is not required when boosters are delayed.

Database ID 52.7

27 June 2008
Diphtheria

Unfortunately, diphtheria infection does not always confer protective immunity. Individuals recovering from the disease should therefore complete active immunization with diphtheria toxoid during convalescence.

To compensate for the loss of natural boosting, industrialized countries should add childhood boosters of diphtheria toxoid to the primary immunization series of infancy. The optimal timing for and the number of such booster doses should be based on epidemiological surveillance as well as on immunological and programmatic considerations. Boosting at the age of 12 months, at school entry and just before leaving school are all possible options. In addition to these childhood immunizations, people living in low-endemic or non-endemic areas may require booster injections of diphtheria toxoid at about 10-year intervals to maintain lifelong protection.

To further promote immunity against diphtheria, diphtheria toxoid and tetanus toxoid rather than tetanus toxoid alone should be used when tetanus prophylaxis is needed following injuries.

In accordance with the recommendations in the previous position paper on diphtheria, use of diphtheria–tetanus vaccine is preferable to single-antigen tetanus toxoid vaccine. In future, the inclusion of other antigens, e.g. pertussis or Haemophilus influenzae type b (Hib), in booster doses should be considered.

Vaccines containing DT are used for children aged <7 years and dT-containing vaccines for individuals aged ≥7 years.
As a rule, vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated.

Both TT and dT can be used at any time during pregnancy.

See Appendix 83_18 for a summary table of immunizations with diphtheria–tetanus–pertussis (DTP) and diphtheria toxoid (Td) vaccines required to obtain long-term protection against tetanus.

Immunizing infants and children with DTP or DT and adults with Td prevents tetanus.

Because it contains high levels of diphtheria toxoid, (DT) should not be given to children older than six years old or adults.

Td, or tetanus-diphtheria toxoids adult dose vaccine, is the same vaccine as DT, but with a lower diphtheria toxoid dose. It is suitable for children older than six years old and adults, including pregnant women.
**Vaccine Administration**

Diphtheria toxoid is administered in fixed combination with other vaccines. For childhood vaccination, DTwP or DTaP is generally used, often in combination with other antigens administered at the same time, such as Haemophilus influenzae type b, poliomyelitis, and hepatitis B vaccines, in order to reduce the number of injections. This is a positive development as long as adverse events remain infrequent and the immunogenicity of the individual components is ensured.

**Contraindications**

Because it contains high levels of diphtheria toxoid, (DT) should not be given to children older than six years old or adults.

Td, or tetanus-diphtheria toxoids adult dose vaccine, is the same vaccine as DT, but with a lower diphtheria toxoid dose. It is suitable for children older than six years old and adults, including pregnant women.
**Diphtheria**

### Adverse Event

In most cases, diphtheria toxoid is administered in fixed combination with other vaccines. For childhood vaccination, DTwP or DTaP is generally used, often in combination with other antigens administered at the same time, such as Haemophilus influenzae type b, poliomyelitis, and hepatitis B vaccines, in order to reduce the number of injections. This is a positive development as long as adverse events remain infrequent and the immunogenicity of the individual components is ensured.

*Diphtheria vaccine (WHO position paper)*

With the increasing number of doses (of diphtheria toxoid) that are now recommended, reactogenicity is likely to increase. Although further purification of extraneous proteins residing in the toxoid may help to ameliorate this problem, optimal future diphtheria vaccines should provide protection of longer duration, with fewer injections.

*Diphtheria vaccine (WHO position paper)*

### Outbreak Control

For diphtheria:
- All outbreaks should be investigated immediately and case-based data should be collected.
- In countries achieving low incidence (usually where coverage is >85-90%), immediate reporting of case-based data of probable or confirmed cases is recommended from the peripheral level to the intermediate and central levels.

*WHO–recommended standards for surveillance of selected vaccine-preventable diseases*
Immunization Coverage

(Diphtheria) surveillance data can be used to monitor levels of coverage (target >90%) and disease as a measure of the impact of control programmes.

Surveillance of Vaccine Preventable Disease

Epidemiological surveillance ensuring early detection of diphtheria outbreaks should be in place in all countries, and all countries should have access to laboratory facilities for reliable identification of toxigenic C. diphtheriae.

Recommended types of surveillance for diphtheria:

- Routine monthly reporting of aggregated data on probable or confirmed cases is recommended from the peripheral level to the intermediate and central levels.
- Designated reporting sites at all levels should report at a specified frequency (e.g. weekly or monthly) even if there are zero cases (often referred to as “zero reporting”).
(W)ith the increasing number of doses (of diphtheria toxoid) that are now recommended, reactogenicity is likely to increase. Although further purification of extraneous proteins residing in the toxoid may help to ameliorate this problem, optimal future diphtheria vaccines should provide protection of longer duration, with fewer injections.