### BCG

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### Thermostability of vaccines

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### WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

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Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

Reconstituted BCG vaccine is very unstable, must be kept cold, and must be discarded within six hours of reconstitution. The reasons for these precautions are as follows:
1. There is a risk of contamination because BCG vaccine, like other lyophilized live vaccines, does not contain any bacteriostatic agent. For this reason, WHO recommends that reconstituted lyophilized vaccine should be kept cold and discarded at the end of six hours.
2. There is a loss of potency.

Once reconstituted, all BCG vaccines should be kept cold and discarded within six hours, regardless of how many doses remain in the vial or ampoule.
Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15C and -25C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2C and +8C. All other national immunization service vaccines should be stored between +2C and +8C at all levels of the cold chain.

Temperature sensitivity of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be protected from light when used.

Cold Chain Equipment

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Ten key criteria for effective vaccine store management were agreed at a meeting of experts, which took place at WHO Geneva in December 2001. These criteria form the policy foundation for the effective vaccine store management initiative and are listed below. Satisfactory performance is set as the vaccine store meeting at least 80% of each criterion.

Over a period of twelve months:
1. Pre-shipment and arrival procedures have ensured that all shipments were in satisfactory condition when received in the primary stores.
2. All vaccines have been stored within WHO recommended temperature ranges.
3. The capacity of cold storage has been sufficient to meet the demand.
4. The buildings, equipment and transport available to the programme have enabled the cold store to function effectively.
5. All buildings, equipment and transport have been correctly maintained.
6. Stock management has been effective.
7. Deliveries of vaccine to the next level have been timely, sufficient and correct.
8. Minimal damage has occurred to the vaccine during distribution.
9. The facility has followed standard operating procedures.
10. Human and financial resources have been sufficient.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO and UNICEF strongly recommend that all countries adopt the EVSM (effective vaccine store management) initiative and conduct the necessary assessments and improvements leading to high quality management of their vaccine stores starting with the primary.
**DPT**

**Thermostability of vaccines**

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.

**Getting started with vaccine vial monitors**

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.

**Introduction of Haemophilus influenzae type b vaccine into immunization programmes**

If more than one type of DTP is being stored, DTP that is not approved for reconstitution should not be stored where there is any chance of confusion with the DTP that is approved for reconstitution.

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO recommended vaccine storage conditions (Appendix 17_3).

**Temperature sensitivity of vaccines**

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.
Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

The shake test should NOT be conducted under following circumstances and vials should be discarded immediately, without the need for any confirmatory test:
1. When a solid frozen vaccine vial(s) has been found
2. With a vial for which a homogeneous solution CANNOT be obtained after vigorous shaking. In such cases, the white lump/sediment cannot be separated from the walls of the glass vial. This happens only with DTP vials that are exposed to subzero temperatures without freezing.

Temperature sensitivity of vaccines

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

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product

Diphtheria

Thermostability of vaccines

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.
Getting started with vaccine vial monitors

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.

Diphtheria vaccine (WHO position paper)

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

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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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- 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.
Temperature sensitivity of vaccines

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.

General

Proper handling and reconstitution of vaccines avoids programme errors

WHO recommendations for diluents:
  _ To ensure the correct quantities of each are available, diluents should be shipped and distributed together with the vaccine vials they will be used to reconstitute.
  _ Diluents must NOT be frozen. They must, however, be cooled to below 8°C before reconstitution. This avoids thermal shock of the vaccine (which would occur if the diluent were warm).
  _ Only that diluent provided for the specific vaccine should be used.
  _ Distilled water for injection should NOT be used as a vaccine diluent.
  _ Oral vaccine diluents should never be injected. Such diluents should be marked as suitable for oral use only.

Proper handling and reconstitution of vaccines avoids programme errors

(F)reezing (of diluents) must be avoided so the vial does not crack.

Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

Proper handling and reconstitution of vaccines avoids programme errors

Some newly introduced vaccines also require diluents, and all reconstituted vaccines should be discarded before the time limit indicated in the manufacturers leaflet, or not longer than 6 hours after reconstitution, whichever is the shorter.

Proper handling and reconstitution of vaccines avoids programme errors

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20°C. Instead, they may be refrigerated at +2 to +8°C.
Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20C. Storing them at 20C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8C.

Proper handling and reconstitution of vaccines avoids programme errors

Oral polio vaccine (OPV) is the only vaccine that still needs to be kept deep-frozen at 20C at central and at provincial store levels whenever possible. However, OPV may be stored at +2 to +8C for up to 6 months. So, in any emergency or for polio national immunization days (NIDs), it may be possible to store OPV at this temperature relying on the vaccine vial monitors (VVMs) to warn of its condition.

Proper handling and reconstitution of vaccines avoids programme errors

Diluents should be handled with the same care as vaccines, and vaccination staff should be trained to know the proper way to reconstitute each of the vaccines they are using.

Proper handling and reconstitution of vaccines avoids programme errors

Special care must be taken in opening ampoules to avoid loss of the dry vaccine. Reconstitution should be carried out as recommended by WHO, away from direct sunlight and the vaccine stored under a protective covering in the foam pad of a vaccine carrier or wrapped in paper or foil. This minimizes exposure of the reconstituted vaccine to harmful ultraviolet rays.

Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted vaccine should be kept on ice to preserve its potency (by maintaining the maximum possible number of live organisms in each dose).

Proper handling and reconstitution of vaccines avoids programme errors

Vaccinators and store keepers should always:
_ Include diluents in stock control and ensure adequate supplies.
_ Check that the vaccines have been supplied with the right diluent. If any error is noted, the vaccine should not be used and the supervisor must be notified immediately.
_ Ensure the volume of diluent used is correct so that the proper number of doses per vial is obtained.
Thermostability of vaccines

Stabilized meningococcal vaccines in the lyophilized state can be stored at refrigerator temperatures for two years.

Thermostability of vaccines

Despite its relative stability, reconstituted meningococcal vaccine should be kept at refrigerator temperatures and should be discarded if not used during the day on which it is reconstituted.

Thermostability of vaccines

Reconstituted monovalent Hib vaccine or reconstituted Hib vaccine combined with other vaccines (DTP, DTPHB, or DTP-IPV) should be destroyed after an immunization session or within six hours.

Thermostability of vaccines

The Vi polysaccharide (typhoid) vaccine is highly stable and does not require a cold chain even in tropical conditions. This is a distinct advantage compared with the other two typhoid vaccines in use (attenuated Salmonella typhi strains used as live oral vaccines and inactivated whole cell oral vaccines.)

Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in a ice bath during the immunization session and should be discarded at the end of the session.

Thermostability of vaccines

The dogmatic approach to the cold chain causes resources to be wasted and places unnecessary restrictions on field operations.

The VVM can be seen as a catalyst for much-needed changes in strategies of vaccine distribution via the cold chain. It should eventually allow immunization programmes to exploit the stability of each vaccine to the greatest possible extent, minimize distribution costs, and increase flexibility in the handling of vaccines in the field, thus helping to make operations more effective.

Introducing hepatitis B vaccine into national immunization services

The storage temperature for HepB vaccine is the same as for DTP vaccine, from 2C to 8C. HepB vaccine should never be frozen.
Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

The currently available pentavalent vaccine requires the reconstitution of lyophilized Hib conjugate vaccine with liquid DTP-hepatitis B vaccine. In this instance, the Hib vaccine should be reconstituted only with the DTP-hepatitis B vaccine produced by the same manufacturer. Similarly, there is at least one DTP-Hib combination that requires the reconstitution of the lyophilized Hib conjugate vaccine with liquid DTP vaccine, and the Hib vaccine should be reconstituted only with the DTP vaccine produced by the same manufacturer.

Thermostability of vaccines

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.

Thermostability of vaccines

Adsorbed toxoids should never be frozen.

Thermostability of vaccines

HB vaccine should always be protected from being frozen, especially at the end of the cold chain when it is transported in cold boxes and may come into close contact with cold packs. HB vaccine thought to have been frozen should not be used.

Thermostability of vaccines

Although HB vaccine is extremely heat stable, there are not yet enough data to recommend using it entirely outside the cold chain. There is, however, scope for developing a management instruction that would allow removal of the vaccine from the cold chain in emergencies, or in outreach activities of short duration, provided that a high temperature indicator was attached to each vial.

Thermostability of vaccines

Measles vaccine in lyophilized form is quite stable. It is stable in temperatures below zero and it is not damaged by freezing and refreezing.

Thermostability of vaccines

Reconstituting (measles) vaccine with a warm diluent may be harmful.
Thermostability of vaccines

Reconstituted measles vaccine must be used in the same immunization session. There is a serious risk when reconstituted measles vaccine is stored at any temperature for longer than six hours or above 8°C for any period.

When used, measles vaccine should be protected from elevated temperature and from light.

Thermostability of vaccines

Yellow fever vaccine can safely be stored at -20°C or +4°C for two years or more.

Thermostability of vaccines

Lyophilized yellow fever vaccine can be safely stored at -20°C or +4°C for two years.

Thermostability of vaccines

Yellow fever vaccine should be quickly administered after reconstitution (up to one hour). If the reconstituted vaccine is kept continuously in an ice bath, it can be used within one immunization session but must be discarded at the end of the session.

Thermostability of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be packed in ampoules made from a substance of low light transmittance, such as amber glass, and should be protected from light when used.

Thermostability of vaccines

Reconstituted BCG vaccine is very unstable and should be used during one working session of five to six hours. Residual vaccine should be discarded at the end of the session.

Thermostability of vaccines

Oral poliomyelitis vaccine is unstable except when held at very low temperatures (frozen). When distribution is not imminent, it is advisable to store the vaccine at temperatures of -20°C or less, since this halts deterioration in vaccine potency.

Thermostability of vaccines

WHO management recommendation is that OPV should not be kept at refrigerator temperatures (0°C to 8°C) at health centres for more than one month, nor transported at these temperatures for more than one week.
**Introduction of Haemophilus influenzae type b vaccine into immunization programmes**

Hib vaccine should be stored between 2-8C. Liquid Hib vaccine must never be frozen. Lyophilized vaccine may be frozen until reconstitution, but since the most commonly used diluent, DTP, cannot be frozen, it is recommended to also store lyophilized Hib at 2-8C, to avoid errors.

The shelf life of Hib vaccines is two years from the date of manufacture if stored between 2 and 8C.

**Getting started with vaccine vial monitors**

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.

(There is no) limit to the number of times an unopened vial can be taken for outreach (or used in an NID), as long as the colour of the VVM indicates that excessive heat damage has not occurred.

For the initial period when there may be vials with and without VVMs in health centre stocks, vaccines with VVMs should be sent to the areas with the poorest cold chains. Once this has been done the vials without VVMs must be used first.

Vials with VVMs should not be used as proxy indicators of heat exposure for vials without VVMs, which should be handled as previously.
Getting started with vaccine vial monitors

VVMs must be monitored and vaccines must be used until the discard point is reached.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

Liquid Hib vaccine must never be frozen.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

The quadrivalent and pentavalent DTP+Hib and DTP-HepB+Hib formulations with lyophilized Hib are supplied in two separate vials (liquid DTP-HepB and lyophilized Hib) that are not packaged together. Lyophilized Hib vaccine can be stored either frozen at -20C or refrigerated between 2C and 8C; however, liquid DTP or DTP-HepB vaccine MUST NOT BE FROZEN. To ensure that Hib is correctly reconstituted with DTP-HepB it is recommended that both vials of the pentavalent DTP-HepB+Hib formulation are stored together between 2C and 8C, and both vials should be shipped and distributed together.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

If more than one type of DTP is being stored, DTP that is not approved for reconstitution should not be stored where there is any chance of confusion with the DTP that is approved for reconstitution.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Ten key criteria for effective vaccine store management were agreed at a meeting of experts, which took place at WHO Geneva in December 2001. These criteria form the policy foundation for the effective vaccine store management initiative and are listed below. Satisfactory performance is set as the vaccine store meeting at least 80% of each criterion. Over a period of twelve months:
1. Pre-shipment and arrival procedures have ensured that all shipments were in satisfactory condition when received in the primary stores.
2. All vaccines have been stored within WHO recommended temperature ranges.
3. The capacity of cold storage has been sufficient to meet the demand.
4. The buildings, equipment and transport available to the programme have enabled the cold store to function effectively.
5. All buildings, equipment and transport have been correctly maintained.
6. Stock management has been effective.
7. Deliveries of vaccine to the next level have been timely, sufficient and correct.
8. Minimal damage has occurred to the vaccine during distribution.
9. The facility has followed standard operating procedures.
10. Human and financial resources have been sufficient.
WHO and UNICEF strongly recommend that all countries adopt the EVSM (effective vaccine store management) initiative and conduct the necessary assessments and improvements leading to high quality management of their vaccine stores starting with the primary.

WHO recommended vaccine storage conditions (Appendix 17_3).

Diluents for vaccines are not sensitive to storage temperatures as the vaccines with which they are used. They are normally stored at ambient temperature, unless the diluent is packed with the vaccine. In this case they should be kept in the cold chain at between +2oC to +8oC. Diluent vials must never be frozen.

The earliest-expiry-first-out (EEFO) principle should generally be observed for deliveries. However, store keepers should be able to set aside the EEFO rule whenever vaccine vial monitor (VVM) status indicates heat exposure. Under such circumstances heat-exposed vaccines should be distributed first, regardless of expiry date.

At the higher levels of the cold chain, i.e., at primary, and regional intermediate stores oral polio vaccine (OPV) must be kept frozen between -15oC and -25oC.

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.
WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

If there is any doubt about the correct temperature for a particular vaccine, it must be stored in a cold room, and not in a freezer room or vaccine freezer.

Diluent must never be frozen.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Diluents must always be used with the vaccine for which they are manufactured.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Heat-exposed vaccine may have to be issued ahead of its EEFO (early expiry - first out) sequence, and in such cases the reason for doing so should be recorded. However, "promoting" vaccine in this way should be done with care because it may cause a displaced batch to reach its expiry date before it can be used.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Expired vials, heat damaged vials or vials with VVMs beyond the discard point should not be kept in the cold store, refrigerator or freezer, as they may be confused with good quality vaccines. If unusable vaccines have to be kept for a period before disposal, for example, until accounting or auditing procedures have been completed, such vials should be kept outside the cold chain, separated from all usable stocks and clearly labeled "Damaged/expired vaccine" - do not use" to avoid mistaken use.

Hepatitis B vaccines (WHO position paper)

Two types of hepatitis B vaccines are available: plasmaderived vaccines and recombinant vaccines. The two vaccines show no differences in terms of reactogenicity, efficacy or duration of protection. Their thermostability is also similar: both should be shipped and stored at 2-8 C; freezing must be avoided as it dissociates antigen from the alum adjuvant.

Measles vaccines (WHO position paper)

The (measles) vaccine is also very sensitive to sunlight, hence the need to keep it in coloured glass vials; following reconstitution, the vaccine must be stored in the dark at 2-8 C and used within 6 hours.

Rubella vaccines (WHO position paper)

The (rubella) vaccine should be stored at 2C-8 C and protected from light.
Typhoid vaccines (WHO position paper)

Recommended storage temperature (for Vi polysaccharide typhoid vaccine) is between +2 C and +8 C.

Diphtheria vaccine (WHO position paper)

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

Mass measles immunization campaigns: Reporting and investigating adverse events following immunization

To avoid programme errors (involving measles vaccine):
- vaccines must only be reconstituted with the diluent supplied by the manufacturer
- reconstituted vaccines must be discarded at the end of each immunization session and never kept longer than 6 hours.
- no other drugs or substances should be stored in the refrigerator of the immunization centre
- immunization workers must be adequately trained and closely supervised to ensure that proper procedures are being followed

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Ensuring the quality of vaccines at country level: Guidelines for health staff

Recommended storage conditions for national immunization service vaccines (Appendix 31_15.)

Ensuring the quality of vaccines at country level: Guidelines for health staff

Any expired vials, heat-damaged vials or vials with VVMs beyond the discard point should not be kept in a cold store, refrigerator or freezer, as they may be confused with vaccines of good quality. If unusable vaccines have to be retained for a period before disposal, until, for example, accounting or auditing procedures have been completed, the vials should be kept outside the cold chain, separated from all usable stocks and carefully labelled in order to avoid mistaken use.
Ensuring the quality of vaccines at country level: Guidelines for health staff

(V)ials of diluent must never be frozen. This would risk cracking the glass and contaminating the contents. Consequently, vials of diluent must never be kept in a freezer or placed in contact with a frozen surface.

Freeze-dried vaccines and their diluents should always be distributed together in matching quantities. The vaccines must be kept in the cold chain between +2°C and +8°C at all times, or, optionally, between -15°C and -25°C if there is sufficient space in the cold chain. For each distribution link the cold chain normally comprises cold boxes or vaccine carriers with ice packs. The diluents do not need to be kept in the cold chain unless they are to be used for reconstituting vaccines within the next 24 hours. However, diluents must travel with the vaccine at all times, and the diluent must always be of the correct type and from the same manufacturer as the vaccine that it is accompanying.

The reconstitution of freeze-dried vaccine must be carried out using only the specific diluent provided by the manufacturer for each type and batch of vaccine.

VVMs must be checked before reconstitution to ensure that the vaccine has not been exposed to excessive heat. After reconstitution, when the part where the VVM is located has been removed, the VVM cannot and should not be referred to because it no longer gives valid information.

Reconstituted vaccines must be discarded at the end of each immunization session or within six hours, whichever occurs first.

Pneumococcal vaccines (WHO position paper)

Pneumococcal polysaccharide vaccine . . . Does not tolerate freezing and should be stored at 2.8°C.

Typhoid vaccines (WHO position paper)

(Ty21a typhoid vaccine) requires storage between +2°C and +8°C.
Yellow fever vaccine (WHO position paper)

The lyophilized (YF) vaccine requires proper storage under cold-chain conditions, and reconstituted vaccine must be kept on ice and used within six hours.

Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

The shake test should NOT be conducted under following circumstances and vials should be discarded immediately, without the need for any confirmatory test:
1. When a solid frozen vaccine vial(s) has been found
2. With a vial for which a homogeneous solution CANNOT be obtained after vigorous shaking. In such cases, the white lump/sediment cannot be separated from the walls of the glass vial. This happens only with DTP vials that are exposed to subzero temperatures without freezing.

Temperature sensitivity of vaccines

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

The freezing temperature of HepB vaccine is -0.5 °C and freezing destroys potency, a result of destruction of the aluminum lattice. HepB vaccine should be protected from being frozen; vaccine thought to have been frozen should not be used.

Temperature sensitivity of vaccines

Despite its relative stability, reconstituted (meningococcal vaccine) vaccine should be kept at refrigerator temperatures and should be discarded if not used during the day on which it is reconstituted.

Temperature sensitivity of vaccines

However, it should be noted that in most cases lyophilized (Hib) vaccine should not be maintained past six hours after reconstitution.

Temperature sensitivity of vaccines

The only currently licensed pneumococcal conjugate vaccine, a 7-valent vaccine produced by Wyeth, is formulated with aluminum adjuvant, is a liquid, and should be protected from freezing as for other aluminum adjuvanted vaccines. For long term storage it should be stored at 2-8°C.

Temperature sensitivity of vaccines

Reconstituted BCG vaccine is very unstable, must be kept cold, and must be discarded within six hours of reconstitution. The reasons for these precautions are as follows:
1. There is a risk of contamination because BCG vaccine, like other lyophilized live vaccines, does not contain any bacteriostatic agent. For this reason, WHO recommends that reconstituted lyophilized vaccine should be kept cold and discarded at the end of six hours.
2. There is a loss of potency.

Once reconstituted, all BCG vaccines should be kept cold and discarded within six hours, regardless of how many doses remain in the vial or ampoule.

Temperature sensitivity of vaccines

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product.
Temperature sensitivity of vaccines

There is a serious risk when reconstituted (measles, mumps, and rubella vaccines and their combinations are) stored at any temperature for longer than six hours or above 8°C for any period. This is not only because of the lack of potency, but also because of the possibility of contamination of the product, which could cause serious adverse consequences in those being vaccinated. When used, measles vaccine should be protected from elevated temperature and from light (light may inactivate the virus). Reconstituted vaccines must be discarded at the end of each immunization session and should NEVER be kept for use in subsequent sessions.

After reconstitution, measles and MMR vaccine rapidly lose their potency when kept at temperatures above 2-8°C. Reconstituted measles and MMR vaccines should be kept cold during immunization procedures, must be discarded at the end of each immunization session and must never be kept for use in subsequent sessions.

Temperature sensitivity of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be protected from light when used.

Temperature sensitivity of vaccines

Regardless of stability of a reconstituted vaccine (including yellow fever), because of the risk of contamination, such products should be kept cold after reconstitution and discarded at the end of a 6-hour immunization session.

Temperature sensitivity of vaccines

Yellow fever vaccine should be quickly administered after reconstitution, maintained at 2-8°C, and discarded at the end of the session, not only to preserve potency, but to minimize risk of contamination of this lyophilized vaccine once reconstituted.

Temperature sensitivity of vaccines

Current recommendations (for OPV) require that, for maintenance of potency, the vaccine must be stored and shipped at low temperatures (-20°C).

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Temperature sensitivity of vaccines

Live attenuated influenza vaccines have been used for several decades in Russia and have recently been developed in the USA, for intranasal application.

It must be stored frozen (-15°C to -25°C), and thawed for up to 60 hours at +2°C to +8°C before use, but it should not be refrozen. Because temperature cycling could affect product stability, it should be stored in a frost-free freezer. A refrigerator stable formulation (to be kept at +2°C to +8°C) is in development.

Temperature sensitivity of vaccines

The lyophilized form (of varicella vaccine) can be stored at refrigerator temperature for 1.5 years or more, but manufacturers suggest it is better stored frozen. It should not be refrozen.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

HepB vaccine is sensitive to low temperatures and can be damaged by freezing. On the other hand, it is quite heat stable and use with a vaccine vial monitor (VVM) allows greater flexibility in transportation and storage.

Mumps virus vaccines (WHO position paper)

The (mumps) vaccines are cold-chain dependent, and should be protected from light both before and after reconstitution. Reconstituted vaccine must be discarded if not used within 6 hours.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

The storage temperature for Hib conjugate vaccines is the same as for DTP and hepatitis B vaccines, from 2°C to 8°C.
Temperature sensitivity of vaccines

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product.

Temperature sensitivity of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be protected from light when used.

Tetanus vaccine (WHO position paper)

Tetanus toxoid-containing vaccines should be stored at +4 (2-8) C; vaccines that have been frozen should not be used.

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery. The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18C.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

(PCV-7) does not tolerate freezing and should be stored at 2-8 C.

Getting started with vaccine vial monitors

(Vaccine vial monitors) enable the health worker to:
- use vaccine selectively so that, for instance, vials with minimal heat exposure can be selected for use in outreach sessions or mobile services;
- estimate the remaining shelf-life of vaccines and rotate inventories, so that the vials with the greatest heat exposure can be selected for use before the others (rather than adopting the earliest expiry- first out (EEFO) );
- identify cold chain problems or confirm problems suggested by VVMs or refrigerator thermometers; each significant exposure to heat produces a colour change on the VVM; in some cases it may be possible to investigate where this exposure has happened;
- reduce wastage by selecting the vials on which the VVMs are nearest to the end-point and in which the vaccine is still usable.

In larger stores, however, where vaccines are kept in their cartons and the VVMs are not visible, the EEFO policy may still be the most appropriate management option.
**Hepatitis B**

*Introducing hepatitis B vaccine into national immunization services*

The storage temperature for HepB vaccine is the same as for DTP vaccine, from 2C to 8C. HepB vaccine should never be frozen.

*Thermostability of vaccines*

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.

*Thermostability of vaccines*

HB vaccine should always be protected from being frozen, especially at the end of the cold chain when it is transported in cold boxes and may come into close contact with cold packs. HB vaccine thought to have been frozen should not be used.

*Thermostability of vaccines*

Although HB vaccine is extremely heat stable, there are not yet enough data to recommend using it entirely outside the cold chain. There is, however, scope for developing a management instruction that would allow removal of the vaccine from the cold chain in emergencies, or in outreach activities of short duration, provided that a high temperature indicator was attached to each vial.

*Getting started with vaccine vial monitors*

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.

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO recommended vaccine storage conditions (Appendix 17_3).
Hepatitis B vaccines (WHO position paper)

Two types of hepatitis B vaccines are available: plasmaderived vaccines and recombinant vaccines. The two vaccines show no differences in terms of reactogenicity, efficacy or duration of protection. Their thermostability is also similar: both should be shipped and stored at 2-8 °C; freezing must be avoided as it dissociates antigen from the alum adjuvant.

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

The freezing temperature of HepB vaccine is -0.5 C and freezing destroys potency, a result of destruction of the aluminum lattice. HepB vaccine should be protected from being frozen; vaccine thought to have been frozen should not be used.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

HepB vaccine is sensitive to low temperatures and can be damaged by freezing. On the other hand, it is quite heat stable and use with a vaccine vial monitor (VVM) allows greater flexibility in transportation and storage.
Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

Thermostability of vaccines

Reconstituted monovalent Hib vaccine or reconstituted Hib vaccine combined with other vaccines (DTP, DTPHB, or DTP-IPV) should be destroyed after an immunization session or within six hours.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

Hib vaccine should be stored between 2-8°C. Liquid Hib vaccine must never be frozen. Lyophilized vaccine may be frozen until reconstitution, but since the most commonly used diluent, DTP, cannot be frozen, it is recommended to also store lyophilized Hib at 2-8°C, to avoid errors.

The shelf life of Hib vaccines is two years from the date of manufacture if stored between 2 and 8°C.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

Types and formulations of Hib vaccines can be interchanged, so vaccines from different manufacturers can be used for each dose that a child receives.

Diluents, both in saline form and made from other vaccines, are produced to go with specific Hib vaccines and are not interchangeable.

Getting started with vaccine vial monitors

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.
**Introduction of Haemophilus influenzae type b vaccine into immunization programmes**

Liquid Hib vaccine must never be frozen.

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO recommended vaccine storage conditions (Appendix 17_3).

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.

**Temperature sensitivity of vaccines**

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

**Temperature sensitivity of vaccines**

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.

**Temperature sensitivity of vaccines**

However, it should be noted that in most cases lyophilized (Hib) vaccine should not be maintained past six hours after reconstitution.
Temperature sensitivity of vaccines

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

The storage temperature for Hib conjugate vaccines is the same as for DTP and hepatitis B vaccines, from 2C to 8C.

Temperature sensitivity of vaccines

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product.

Influenza

Temperature sensitivity of vaccines

Live attenuated influenza vaccines have been used for several decades in Russia and have recently been developed in the USA, for intranasal application.

It must be stored frozen (-15oC to -25oC), and thawed for up to 60 hours at +2oC to +8oC before use, but it should not be refrozen. Because temperature cycling could affect product stability, it should be stored in a frost-free freezer. A refrigerator stable formulation (to be kept at +2oC to +8oC) is in development.

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery . . . The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18C.

MMR

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).
Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

There is a serious risk when reconstituted (measles, mumps, and rubella vaccines and their combinations are) stored at any temperature for longer than six hours or above 8°C for any period. This is not only because of the lack of potency, but also because of the possibility of contamination of the product, which could cause serious adverse consequences in those being vaccinated. When used, measles vaccine should be protected from elevated temperature and from light (light may inactivate the virus). Reconstituted vaccines must be discarded at the end of each immunization session and should NEVER be kept for use in subsequent sessions.

After reconstitution, measles and MMR vaccine rapidly lose their potency when kept at temperatures above 2-8°C. Reconstituted measles and MMR vaccines should be kept cold during immunization procedures, must be discarded at the end of each immunization session and must never be kept for use in subsequent sessions.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.
### Measles

**Proper handling and reconstitution of vaccines avoids programme errors**

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

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page 1

**Proper handling and reconstitution of vaccines avoids programme errors**

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20°C. Instead, they may be refrigerated at +2 to +8°C.

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**Proper handling and reconstitution of vaccines avoids programme errors**

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.

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**Thermostability of vaccines**

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in an ice bath during the immunization session and should be discarded at the end of the session.

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**Thermostability of vaccines**

Measles vaccine in lyophilized form is quite stable. It is stable in temperatures below zero and it is not damaged by freezing and refreezing.

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**Thermostability of vaccines**

Reconstituting (measles) vaccine with a warm diluent may be harmful.

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**Thermostability of vaccines**

Reconstituted measles vaccine must be used in the same immunization session. There is a serious risk when reconstituted measles vaccine is stored at any temperature for longer than six hours or above 8°C for any period.

When used, measles vaccine should be protected from elevated temperature and from light.
WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20°C. Storing them at -20°C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2°C to +8°C.

Measles vaccines (WHO position paper)

The (measles) vaccine is also very sensitive to sunlight, hence the need to keep it in coloured glass vials; following reconstitution, the vaccine must be stored in the dark at 2-8°C and used within 6 hours.

Mass measles immunization campaigns: Reporting and investigating adverse events following immunization

To avoid programme errors (involving measles vaccine):
- vaccines must only be reconstituted with the diluent supplied by the manufacturer
- reconstituted vaccines must be discarded at the end of each immunization session and never kept longer than 6 hours.
- no other drugs or substances should be stored in the refrigerator of the immunization centre
- immunization workers must be adequately trained and closely supervised to ensure that proper procedures are being followed

Temperature sensitivity of vaccines

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.
Temperature sensitivity of vaccines

There is a serious risk when reconstituted (measles, mumps, and rubella vaccines and their combinations are) stored at any temperature for longer than six hours or above 8°C for any period. This is not only because of the lack of potency, but also because of the possibility of contamination of the product, which could cause serious adverse consequences in those being vaccinated. When used, measles vaccine should be protected from elevated temperature and from light (light may inactivate the virus). Reconstituted vaccines must be discarded at the end of each immunization session and should NEVER be kept for use in subsequent sessions.

After reconstitution, measles and MMR vaccine rapidly lose their potency when kept at temperatures above 2-8°C. Reconstituted measles and MMR vaccines should be kept cold during immunization procedures, must be discarded at the end of each immunization session and must never be kept for use in subsequent sessions.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.

Meningococcal

Thermostability of vaccines

Stabilized meningococcal vaccines in the lyophilized state can be stored at refrigerator temperatures for two years.

Thermostability of vaccines

Despite its relative stability, reconstituted meningococcal vaccine should be kept at refrigerator temperatures and should be discarded if not used during the day on which it is reconstituted.
Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

Temperature sensitivity of vaccines

Despite its relative stability, reconstituted (meningococcal vaccine) vaccine should be kept at refrigerator temperatures and should be discarded if not used during the day on which it is reconstituted.

Mumps

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.
Temperature sensitivity of vaccines

There is a serious risk when reconstituted (measles, mumps, and rubella vaccines and their combinations are) stored at any temperature for longer than six hours or above 8°C for any period. This is not only because of the lack of potency, but also because of the possibility of contamination of the product, which could cause serious adverse consequences in those being vaccinated. When used, measles vaccine should be protected from elevated temperature and from light (light may inactivate the virus). Reconstituted vaccines must be discarded at the end of each immunization session and should NEVER be kept for use in subsequent sessions.

After reconstitution, measles and MMR vaccine rapidly lose their potency when kept at temperatures above 2-8°C. Reconstituted measles and MMR vaccines should be kept cold during immunization procedures, must be discarded at the end of each immunization session and must never be kept for use in subsequent sessions.

Mumps virus vaccines (WHO position paper)

The (mumps) vaccines are cold-chain dependent, and should be protected from light both before and after reconstitution. Reconstituted vaccine must be discarded if not used within 6 hours.

Pentavalent

Thermostability of vaccines

Reconstituted monovalent Hib vaccine or reconstituted Hib vaccine combined with other vaccines (DTP, DTPHB, or DTP-IPV) should be destroyed after an immunization session or within six hours.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

The currently available pentavalent vaccine requires the reconstitution of lyophilized Hib conjugate vaccine with liquid DTP-hepatitis B vaccine. In this instance, the Hib vaccine should be reconstituted only with the DTP-hepatitis B vaccine produced by the same manufacturer. Similarly, there is at least one DTP-Hib combination that requires the reconstitution of the lyophilized Hib conjugate vaccine with liquid DTP vaccine, and the Hib vaccine should be reconstituted only with the DTP vaccine produced by the same manufacturer.
Introduction of Haemophilus influenzae type b vaccine into immunization programmes

The quadrivalent and pentavalent DTP+Hib and DTP-HepB+Hib formulations with lyophilized Hib are supplied in two separate vials (liquid DTP-HepB and lyophilized Hib) that are not packaged together. Lyophilized Hib vaccine can be stored either frozen at -20C or refrigerated between 2C and 8C; however, liquid DTP or DTP-HepB vaccine MUST NOT BE FROZEN. To ensure that Hib is correctly reconstituted with DTP-HepB it is recommended that both vials of the pentavalent DTP-HepB+Hib formation are stored together between 2C and 8C, and both vials should be shipped and distributed together.

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

Pneumococcal

Pneumococcal vaccines (WHO position paper)

Pneumococcal polysaccharide vaccine . . . Does not tolerate freezing and should be stored at 2.8 C.

Temperature sensitivity of vaccines

The only currently licensed pneumococcal conjugate vaccine, a 7-valent vaccine produced by Wyeth, is formulated with aluminum adjuvant, is a liquid, and should be protected from freezing as for other aluminum adjuvanted vaccines. For long term storage it should be stored at 2-8C.

Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

(PCV-7) does not tolerate freezing and should be stored at 2-8 C.
Proper handling and reconstitution of vaccines avoids programme errors

WHO recommendations for diluents:
- To ensure the correct quantities of each are available, diluents should be shipped and distributed together with the vaccine vials they will be used to reconstitute.
- Diluents must NOT be frozen. They must, however, be cooled to below 8°C before reconstitution. This avoids thermal shock of the vaccine (which would occur if the diluent were warm).
- Only that diluent provided for the specific vaccine should be used.
- Distilled water for injection should NOT be used as a vaccine diluent.
- Oral vaccine diluents should never be injected. Such diluents should be marked as suitable for oral use only.

Proper handling and reconstitution of vaccines avoids programme errors

(F)reezing (of diluents) must be avoided so the vial does not crack.

Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

Proper handling and reconstitution of vaccines avoids programme errors

Some newly introduced vaccines also require diluents, and all reconstituted vaccines should be discarded before the time limit indicated in the manufacturers leaflet, or not longer than 6 hours after reconstitution, whichever is the shorter.

Proper handling and reconstitution of vaccines avoids programme errors

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20°C. Instead, they may be refrigerated at +2 to +8°C.

Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20°C. Storing them at 20°C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8°C.
Proper handling and reconstitution of vaccines avoids programme errors

Oral polio vaccine (OPV) is the only vaccine that still needs to be kept deep-frozen at 20C at central and at provincial store levels whenever possible. However, OPV may be stored at +2 to +8C for up to 6 months. So, in any emergency or for polio national immunization days (NIDs), it may be possible to store OPV at this temperature relying on the vaccine vial monitors (VVMs) to warn of its condition.

Proper handling and reconstitution of vaccines avoids programme errors

Diluents should be handled with the same care as vaccines, and vaccination staff should be trained to know the proper way to reconstitute each of the vaccines they are using.

Proper handling and reconstitution of vaccines avoids programme errors

Special care must be taken in opening ampoules to avoid loss of the dry vaccine. Reconstitution should be carried out as recommended by WHO, away from direct sunlight and the vaccine stored under a protective covering in the foam pad of a vaccine carrier or wrapped in paper or foil. This minimizes exposure of the reconstituted vaccine to harmful ultraviolet rays.

Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted vaccine should be kept on ice to preserve its potency (by maintaining the maximum possible number of live organisms in each dose).

Proper handling and reconstitution of vaccines avoids programme errors

Vaccinators and store keepers should always:
  _Include diluents in stock control and ensure adequate supplies.
  _Check that the vaccines have been supplied with the right diluent. If any error is noted, the vaccine should not be used and the supervisor must be notified immediately.
  _Ensure the volume of diluent used is correct so that the proper number of doses per vial is obtained.

Thermostability of vaccines

Stabilized meningococcal vaccines in the lyophilized state can be stored at refrigerator temperatures for two years.
Thermostability of vaccines

Despite its relative stability, reconstituted meningococcal vaccine should be kept at refrigerator temperatures and should be discarded if not used during the day on which it is reconstituted.

Thermostability of vaccines

Reconstituted monovalent Hib vaccine or reconstituted Hib vaccine combined with other vaccines (DTP, DTPHB, or DTP-IPV) should be destroyed after an immunization session or within six hours.

Thermostability of vaccines

The Vi polysaccharide (typhoid) vaccine is highly stable and does not require a cold chain even in tropical conditions. This is a distinct advantage compared with the other two typhoid vaccines in use (attenuated Salmonella typhi strains used as live oral vaccines and inactivated whole cell oral vaccines.)

Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in a ice bath during the immunization session and should be discarded at the end of the session.

Thermostability of vaccines

The dogmatic approach to the cold chain causes resources to be wasted and places unnecessary restrictions on field operations.

The VVM can be seen as a catalyst for much-needed changes in strategies of vaccine distribution via the cold chain. It should eventually allow immunization programmes to exploit the stability of each vaccine to the greatest possible extent, minimize distribution costs, and increase flexibility in the handling of vaccines in the field, thus helping to make operations more effective.

Introducing hepatitis B vaccine into national immunization services

The storage temperature for HepB vaccine is the same as for DTP vaccine, from 2C to 8C. HepB vaccine should never be frozen.
Introducing *Haemophilus influenzae* type b (Hib) conjugate vaccine into national immunization services

The currently available pentavalent vaccine requires the reconstitution of lyophilized Hib conjugate vaccine with liquid DTP-hepatitis B vaccine. In this instance, the Hib vaccine should be reconstituted only with the DTP-hepatitis B vaccine produced by the same manufacturer. Similarly, there is at least one DTP-Hib combination that requires the reconstitution of the lyophilized Hib conjugate vaccine with liquid DTP vaccine, and the Hib vaccine should be reconstituted only with the DTP vaccine produced by the same manufacturer.

**Thermostability of vaccines**

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.

**Thermostability of vaccines**

Adsorbed toxoids should never be frozen.

**Thermostability of vaccines**

HB vaccine should always be protected from being frozen, especially at the end of the cold chain when it is transported in cold boxes and may come into close contact with cold packs. HB vaccine thought to have been frozen should not be used.

**Thermostability of vaccines**

Although HB vaccine is extremely heat stable, there are not yet enough data to recommend using it entirely outside the cold chain. There is, however, scope for developing a management instruction that would allow removal of the vaccine from the cold chain in emergencies, or in outreach activities of short duration, provided that a high temperature indicator was attached to each vial.

**Thermostability of vaccines**

Measles vaccine in lyophilized form is quite stable. It is stable in temperatures below zero and it is not damaged by freezing and refreezing.

**Thermostability of vaccines**

Reconstituting (measles) vaccine with a warm diluent may be harmful.
Thermostability of vaccines

Reconstituted measles vaccine must be used in the same immunization session. There is a serious risk when reconstituted measles vaccine is stored at any temperature for longer than six hours or above 8°C for any period.

When used, measles vaccine should be protected from elevated temperature and from light.

Thermostability of vaccines

Lyophilized yellow fever vaccine can be safely stored at -20°C or +4°C for two years.

Thermostability of vaccines

Yellow fever vaccine should be quickly administered after reconstitution (up to one hour). If the reconstituted vaccine is kept continuously in an ice bath, it can be used within one immunization session but must be discarded at the end of the session.

Thermostability of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be packed in ampoules made from a substance of low light transmittance, such as amber glass, and should be protected from light when used.

Thermostability of vaccines

Reconstituted BCG vaccine is very unstable and should be used during one working session of five to six hours. Residual vaccine should be discarded at the end of the session.

Thermostability of vaccines

Oral poliomyelitis vaccine is unstable except when held at very low temperatures (frozen). When distribution is not imminent, it is advisable to store the vaccine at temperatures of -20°C or less, since this halts deterioration in vaccine potency.

Thermostability of vaccines

WHO management recommendation is that OPV should not be kept at refrigerator temperatures (0°C to 8°C) at health centres for more than one month, nor transported at these temperatures for more than one week.
**Introduction of Haemophilus influenzae type b vaccine into immunization programmes**

Hib vaccine should be stored between 2-8°C. Liquid Hib vaccine must never be frozen. Lyophilized vaccine may be frozen until reconstitution, but since the most commonly used diluent, DTP, cannot be frozen, it is recommended to also store lyophilized Hib at 2-8°C, to avoid errors.

The shelf life of Hib vaccines is two years from the date of manufacture if stored between 2 and 8°C.

**Types and formulations of Hib vaccines can be interchanged, so vaccines from different manufacturers can be used for each dose that a child receives.**

Diluents, both in saline form and made from other vaccines, are produced to go with specific Hib vaccines and are not interchangeable.

**Getting started with vaccine vial monitors**

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.

(There is no) limit to the number of times an unopened vial can be taken for outreach (or used in an NID), as long as the colour of the VVM indicates that excessive heat damage has not occurred.

For the initial period when there may be vials with and without VVMs in health centre stocks, vaccines with VVMs should be sent to the areas with the poorest cold chains. Once this has been done the vials without VVMs must be used first.

Vials with VVMs should not be used as proxy indicators of heat exposure for vials without VVMs, which should be handled as previously.
Getting started with vaccine vial monitors

VVMs must be monitored and vaccines must be used until the discard point is reached.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

Liquid Hib vaccine must never be frozen.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

The quadrivalent and pentavalent DTP+Hib and DTP-HepB+Hib formulations with lyophilized Hib are supplied in two separate vials (liquid DTP-HepB and lyophilized Hib) that are not packaged together. Lyophilized Hib vaccine can be stored either frozen at -20C or refrigerated between 2C and 8C; however, liquid DTP or DTP-HepB vaccine MUST NOT BE FROZEN. To ensure that Hib is correctly reconstituted with DTP-HepB it is recommended that both vials of the pentavalent DTP-HepB+Hib formation are stored together between 2C and 8C, and both vials should be shipped and distributed together.

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

If more than one type of DTP is being stored, DTP that is not approved for reconstitution should not be stored where there is any chance of confusion with the DTP that is approved for reconstitution.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Ten key criteria for effective vaccine store management were agreed at a meeting of experts, which took place at WHO Geneva in December 2001. These criteria form the policy foundation for the effective vaccine store management initiative and are listed below. Satisfactory performance is set as the vaccine store meeting at least 80% of each criterion.

Over a period of twelve months:
1. Pre-shipment and arrival procedures have ensured that all shipments were in satisfactory condition when received in the primary stores.
2. All vaccines have been stored within WHO recommended temperature ranges.
3. The capacity of cold storage has been sufficient to meet the demand.
4. The buildings, equipment and transport available to the programme have enabled the cold store to function effectively.
5. All buildings, equipment and transport have been correctly maintained.
6. Stock management has been effective.
7. Deliveries of vaccine to the next level have been timely, sufficient and correct.
8. Minimal damage has occurred to the vaccine during distribution.
9. The facility has followed standard operating procedures.
10. Human and financial resources have been sufficient.
WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO and UNICEF strongly recommend that all countries adopt the EVSM (effective vaccine store management) initiative and conduct the necessary assessments and improvements leading to high quality management of their vaccine stores starting with the primary.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).

Diluents for vaccines are not sensitive to storage temperatures as the vaccines with which they are used. They are normally stored at ambient temperature, unless the diluent is packed with the vaccine. In this case they should be kept in the cold chain at between +2oC to +8oC. Diluent vials must never be frozen.

The earliest-expiry-first-out (EEFO) principle should generally be observed for deliveries. However, store keepers should be able to set aside the EEFO rule whenever vaccine vial monitor (VVM) status indicates heat exposure. Under such circumstances heat-exposed vaccines should be distributed first, regardless of expiry date.

At the higher levels of the cold chain, i.e., at primary, and regional intermediate stores oral polio vaccine (OPV) must be kept frozen between -15oC and -25oC.

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.
Vaccine Handling

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

If there is any doubt about the correct temperature for a particular vaccine, it must be stored in a cold room, and not in a freezer room or vaccine freezer.

Diluent must never be frozen.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Diluents must always be used with the vaccine for which they are manufactured.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Heat-exposed vaccine may have to be issued ahead of its EEFO (early expiry - first out) sequence, and in such cases the reason for doing so should be recorded. However, "promoting" vaccine in this way should be done with care because it may cause a displaced batch to reach its expiry date before it can be used.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

Expired vials, heat damaged vials or vials with VVMs beyond the discard point should not be kept in the cold store, refrigerator or freezer, as they may be confused with good quality vaccines. If unusable vaccines have to be kept for a period before disposal, for example, until accounting or auditing procedures have been completed, such vials should be kept outside the cold chain, separated from all usable stocks and clearly labeled "Damaged/expired vaccine" - do not use" to avoid mistaken use.

Hepatitis B vaccines (WHO position paper)

Two types of hepatitis B vaccines are available: plasmaderived vaccines and recombinant vaccines. The two vaccines show no differences in terms of reactogenicity, efficacy or duration of protection. Their thermostability is also similar: both should be shipped and stored at 2-8 C; freezing must be avoided as it dissociates antigen from the alum adjuvant.

Measles vaccines (WHO position paper)

The (measles) vaccine is also very sensitive to sunlight, hence the need to keep it in coloured glass vials; following reconstitution, the vaccine must be stored in the dark at 2-8 C and used within 6 hours.

Rubella vaccines (WHO position paper)

The (rubella) vaccine should be stored at 2C-8 C and protected from light.
Typhoid vaccines (WHO position paper)

Recommended storage temperature (for Vi polysaccharide typhoid vaccine) is between +2 C and +8 C.

Diphtheria vaccine (WHO position paper)

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

Mass measles immunization campaigns: Reporting and investigating adverse events following immunization

To avoid programme errors (involving measles vaccine): vaccines must only be reconstituted with the diluent supplied by the manufacturer.
reconstituted vaccines must be discarded at the end of each immunization session and never kept longer than 6 hours.
other drugs or substances should be stored in the refrigerator of the immunization centre.
immunization workers must be adequately trained and closely supervised to ensure that proper procedures are being followed.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Ensuring the quality of vaccines at country level: Guidelines for health staff

Recommended storage conditions for national immunization service vaccines (Appendix 31_15.)

Ensuring the quality of vaccines at country level: Guidelines for health staff

Any expired vials, heat-damaged vials or vials with VVMs beyond the discard point should not be kept in a cold store, refrigerator or freezer, as they may be confused with vaccines of good quality. If unusable vaccines have to be retained for a period before disposal, until, for example, accounting or auditing procedures have been completed, the vials should be kept outside the cold chain, separated from all usable stocks and carefully labelled in order to avoid mistaken use.
Ensuring the quality of vaccines at country level: Guidelines for health staff

(V)ials of diluent must never be frozen. This would risk cracking the glass and contaminating the contents. Consequently, vials of diluent must never be kept in a freezer or placed in contact with a frozen surface.

Ensuring the quality of vaccines at country level: Guidelines for health staff

Freeze-dried vaccines and their diluents should always be distributed together in matching quantities. The vaccines must be kept in the cold chain between +2°C and +8°C at all times, or, optionally, between -15°C and -25°C if there is sufficient space in the cold chain. For each distribution link the cold chain normally comprises cold boxes or vaccine carriers with ice packs. The diluents do not need to be kept in the cold chain unless they are to be used for reconstituting vaccines within the next 24 hours. However, diluents must travel with the vaccine at all times, and the diluent must always be of the correct type and from the same manufacturer as the vaccine that it is accompanying.

Ensuring the quality of vaccines at country level: Guidelines for health staff

The reconstitution of freeze-dried vaccine must be carried out using only the specific diluent provided by the manufacturer for each type and batch of vaccine.

Ensuring the quality of vaccines at country level: Guidelines for health staff

VVMs must be checked before reconstitution to ensure that the vaccine has not been exposed to excessive heat. After reconstitution, when the part where the VVM is located has been removed, the VVM cannot and should not be referred to because it no longer gives valid information.

Ensuring the quality of vaccines at country level: Guidelines for health staff

Reconstituted vaccines must be discarded at the end of each immunization session or within six hours, whichever occurs first.

Pneumococcal vaccines (WHO position paper)

Pneumococcal polysaccharide vaccine . . . Does not tolerate freezing and should be stored at 2.8°C.

Typhoid vaccines (WHO position paper)

(Ty21a typhoid vaccine) requires storage between +2°C and +8°C.
Yellow fever vaccine (WHO position paper)

The lyophilized (YF) vaccine requires proper storage under cold-chain conditions, and reconstituted vaccine must be kept on ice and used within six hours.

Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

The shake test should NOT be conducted under following circumstances and vials should be discarded immediately, without the need for any confirmatory test:
1. When a solid frozen vaccine vial(s) has been found
2. With a vial for which a homogeneous solution CANNOT be obtained after vigorous shaking. In such cases, the white lump/sediment cannot be separated from the walls of the glass vial. This happens only with DTP vials that are exposed to subzero temperatures without freezing.

Temperature sensitivity of vaccines

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

The freezing temperature of HepB vaccine is -0.5°C and freezing destroys potency, a result of destruction of the aluminum lattice. HepB vaccine should be protected from being frozen; vaccine thought to have been frozen should not be used.

Temperature sensitivity of vaccines

However, it should be noted that in most cases lyophilized (Hib) vaccine should not be maintained past six hours after reconstitution.

Temperature sensitivity of vaccines

The only currently licensed pneumococcal conjugate vaccine, a 7-valent vaccine produced by Wyeth, is formulated with aluminum adjuvant, is a liquid, and should be protected from freezing as for other aluminum adjuvanted vaccines. For long term storage it should be stored at 2-8°C.

Temperature sensitivity of vaccines

Reconstituted BCG vaccine is very unstable, must be kept cold, and must be discarded within six hours of reconstitution. The reasons for these precautions are as follows:
1. There is a risk of contamination because BCG vaccine, like other lyophilized live vaccines, does not contain any bacteriostatic agent. For this reason, WHO recommends that reconstituted lyophilized vaccine should be kept cold and discarded at the end of six hours.
2. There is a loss of potency.

Once reconstituted, all BCG vaccines should be kept cold and discarded within six hours, regardless of how many doses remain in the vial or ampoule.

Temperature sensitivity of vaccines

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product.
Temperature sensitivity of vaccines

There is a serious risk when reconstituted (measles, mumps, and rubella vaccines and their combinations are) stored at any temperature for longer than six hours or above 8°C for any period. This is not only because of the lack of potency, but also because of the possibility of contamination of the product, which could cause serious adverse consequences in those being vaccinated. When used, measles vaccine should be protected from elevated temperature and from light (light may inactivate the virus). Reconstituted vaccines must be discarded at the end of each immunization session and should NEVER be kept for use in subsequent sessions.

After reconstitution, measles and MMR vaccine rapidly lose their potency when kept at temperatures above 2-8°C. Reconstituted measles and MMR vaccines should be kept cold during immunization procedures, must be discarded at the end of each immunization session and must never be kept for use in subsequent sessions.

Temperature sensitivity of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be protected from light when used.

Temperature sensitivity of vaccines

Regardless of stability of a reconstituted vaccine (including yellow fever), because of the risk of contamination, such products should be kept cold after reconstitution and discarded at the end of a 6-hour immunization session.

Temperature sensitivity of vaccines

Yellow fever vaccine should be quickly administered after reconstitution, maintained at 2-8°C, and discarded at the end of the session, not only to preserve potency, but to minimize risk of contamination of this lyophilized vaccine once reconstituted.

Temperature sensitivity of vaccines

Current recommendations (for OPV) require that, for maintenance of potency, the vaccine must be stored and shipped at low temperatures (-20°C).
Temperature sensitivity of vaccines

Live attenuated influenza vaccines have been used for several decades in Russia and have recently been developed in the USA, for intranasal application.

It must be stored frozen (-15oC to -25oC), and thawed for up to 60 hours at +2oC to +8oC before use, but it should not be refrozen. Because temperature cycling could affect product stability, it should be stored in a frost-free freezer. A refrigerator stable formulation (to be kept at +2oC to +8oC) is in development.

Temperature sensitivity of vaccines

The lyophilized form (of varicella vaccine) can be stored at refrigerator temperature for 1.5 years or more, but manufacturers suggest it is better stored frozen. It should not be refrozen.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15C and -25C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15C and -25C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2C and +8C. All other national immunization service vaccines should be stored between +2C and +8C at all levels of the cold chain.

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

HepB vaccine is sensitive to low temperatures and can be damaged by freezing. On the other hand, it is quite heat stable and use with a vaccine vial monitor (VVM) allows greater flexibility in transportation and storage.

Mumps virus vaccines (WHO position paper)

The (mumps) vaccines are cold-chain dependent, and should be protected from light both before and after reconstitution. Reconstituted vaccine must be discarded if not used within 6 hours.

Introducing Haemophilus influenzae type b (Hib) conjugate vaccine into national immunization services

The storage temperature for Hib conjugate vaccines is the same as for DTP and hepatitis B vaccines, from 2C to 8C.
## Vaccine Handling

### Temperature sensitivity of vaccines

Liquid Hib should never be frozen, especially in combinations with DTP, as freezing may damage the immunogenicity of the product.

### Temperature sensitivity of vaccines

Freeze-dried BCG vaccines, regardless of their substrain, are sensitive to ultraviolet and fluorescent light. They should be protected from light when used.

### Tetanus vaccine (WHO position paper)

Tetanus toxoid-containing vaccines should be stored at +4 (2-8) C; vaccines that have been frozen should not be used.

### State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intranasal spray delivery. The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18°C.

### Pneumococcal conjugate vaccine for childhood immunization (WHO position paper)

(PCV-7) does not tolerate freezing and should be stored at 2-8 C.

### Getting started with vaccine vial monitors

(Vaccine vial monitors) enable the health worker to:
- use vaccine selectively so that, for instance, vials with minimal heat exposure can be selected for use in outreach sessions or mobile services;
- estimate the remaining shelf-life of vaccines and rotate inventories, so that the vials with the greatest heat exposure can be selected for use before the others (rather than adopting the earliest expiry- first out (EEFO));
- identify cold chain problems or confirm problems suggested by VVMs or refrigerator thermometers; each significant exposure to heat produces a colour change on the VVM; in some cases it may be possible to investigate where this exposure has happened;
- reduce wastage by selecting the vials on which the VVMs are nearest to the end-point and in which the vaccine is still usable.

In larger stores, however, where vaccines are kept in their cartons and the VVMs are not visible, the EEFO policy may still be the most appropriate management option.
**Polio**

**Proper handling and reconstitution of vaccines avoids programme errors**

Oral polio vaccine (OPV) is the only vaccine that still needs to be kept deep-frozen at 20°C at central and at provincial store levels whenever possible. However, OPV may be stored at +2 to +8°C for up to 6 months. So, in any emergency or for polio national immunization days (NIDs), it may be possible to store OPV at this temperature relying on the vaccine vial monitors (VVMs) to warn of its condition.

**Thermostability of vaccines**

Oral poliomyelitis vaccine is unstable except when held at very low temperatures (frozen). When distribution is not imminent, it is advisable to store the vaccine at temperatures of -20°C or less, since this halts deterioration in vaccine potency.

**Thermostability of vaccines**

WHO management recommendation is that OPV should not be kept at refrigerator temperatures (0°C to 8°C) at health centres for more than one month, nor transported at these temperatures for more than one week.

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

WHO recommended vaccine storage conditions (Appendix 17_3).

**WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4**

At the higher levels of the cold chain, i.e., at primary, and regional intermediate stores oral polio vaccine (OPV) must be kept frozen between -15°C and -25°C.

**Ensuring the quality of vaccines at country level: Guidelines for health staff**

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.
Temperature sensitivity of vaccines

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.

Temperature sensitivity of vaccines

Current recommendations (for OPV) require that, for maintenance of potency, the vaccine must be stored and shipped at low temperatures (-20°C).

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.

Program Management

Proper handling and reconstitution of vaccines avoids programme errors

Vaccinators and store keepers should always:
  _ Include diluents in stock control and ensure adequate supplies.
  _ Check that the vaccines have been supplied with the right diluent. If any error is noted, the vaccine should not be used and the supervisor must be notified immediately.
  _ Ensure the volume of diluent used is correct so that the proper number of doses per vial is obtained.
Rubella vaccines (WHO position paper)

The (rubella) vaccine should be stored at 2C-8 C and protected from light.

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

Temperature sensitivity of vaccines

There is a serious risk when reconstituted (measles, mumps, and rubella vaccines and their combinations are) stored at any temperature for longer than six hours or above 8C for any period. This is not only because of the lack of potency, but also because of the possibility of contamination of the product, which could cause serious adverse consequences in those being vaccinated. When used, measles vaccine should be protected from elevated temperature and from light (light may inactivate the virus). Reconstituted vaccines must be discarded at the end of each immunization session and should NEVER be kept for use in subsequent sessions.

After reconstitution, measles and MMR vaccine rapidly lose their potency when kept at temperatures above 2-8C. Reconstituted measles and MMR vaccines should be kept cold during immunization procedures, must be discarded at the end of each immunization session and must never be kept for use in subsequent sessions.

Schedule

State of the art of new vaccines: research and development

A trivalent live cold-adapted vaccine (Flumist) has been developed for intra-nasal spray delivery . . .
The vaccine has been licensed in the USA for vaccination of persons from 5-49 years of age, in view of side effects in younger children (wheezing, nasal congestion) and absence of data in the elderly. The vaccine is safe, effective, and shows remarkable genetic stability, but it has to be kept at -18C.
Tetanus

Thermostability of vaccines

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.

Getting started with vaccine vial monitors

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.

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

Temperature sensitivity of vaccines

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;
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- 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.
Temperature sensitivity of vaccines

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.

Tetanus vaccine (WHO position paper)

Tetanus toxoid-containing vaccines should be stored at +4 (2-8) C; vaccines that have been frozen should not be used.

Typhoid

Thermostability of vaccines

The Vi polysaccharide (typhoid) vaccine is highly stable and does not require a cold chain even in tropical conditions. This is a distinct advantage compared with the other two typhoid vaccines in use (attenuated Salmonella typhi strains used as live oral vaccines and inactivated whole cell oral vaccines.)

Typhoid vaccines (WHO position paper)

Recommended storage temperature (for Vi polysaccharide typhoid vaccine) is between + 2 C and + 8 C.

Typhoid vaccines (WHO position paper)

(Ty21a typhoid vaccine) requires storage between + 2 C and + 8 C.

Vaccine Administration

Introduction of Haemophilus influenzae type b vaccine into immunization programmes

Types and formulations of Hib vaccines can be interchanged, so vaccines from different manufacturers can be used for each dose that a child receives.

Diluents, both in saline form and made from other vaccines, are produced to go with specific Hib vaccines and are not interchangeable.
## Varicella

### Temperature sensitivity of vaccines

The lyophilized form (of varicella vaccine) can be stored at refrigerator temperature for 1.5 years or more, but manufacturers suggest it is better stored frozen. It should not be refrozen.

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## Yellow Fever

### Proper handling and reconstitution of vaccines avoids programme errors

Reconstituted BCG, measles and yellow fever vaccines must be kept cooled and must be discarded after 6 hours after reconstitution.

### Proper handling and reconstitution of vaccines avoids programme errors

It is no longer necessary to ship and store freeze-dried vaccines (measles, yellow fever and BCG) at 20C. Instead, they may be refrigerated at +2 to +8C.

### Proper handling and reconstitution of vaccines avoids programme errors

WHO no longer recommends that freeze-dried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at 20C. Storing them at 20C is not harmful but is unnecessary and uses up valuable storage space in the deep-freeze. Instead, they should be kept in refrigeration and transported at +2 to +8C.

### Thermostability of vaccines

Reconstituted vaccines against measles, yellow fever and tuberculosis (BCG) are unstable vaccines; they should be used as soon as possible after reconstitution, be kept in ice bath during the immunization session and should be discarded at the end of the session.

### Thermostability of vaccines

Yellow fever vaccine can safely be stored at -20C or +4C for two years or more.

### Thermostability of vaccines

Lyophilized yellow fever vaccine can be safely stored at -20C or +4C for two years.
Thermostability of vaccines

Yellow fever vaccine should be quickly administered after reconstitution (up to one hour). If the reconstituted vaccine is kept continuously in an ice bath, it can be used within one immunization session but must be discarded at the end of the session.

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO recommended vaccine storage conditions (Appendix 17_3).

WHO-UNICEF effective vaccine store management initiative: Modules 1 - 4

WHO no longer recommends that freezedried vaccines (measles, yellow fever, Hib and BCG) be shipped and stored at -20C. Storing them at -20C is not harmful but is unnecessary. Instead, these vaccines should be stored and transported at +2C to +8C.

Yellow fever vaccine (WHO position paper)

The lyophilized (YF) vaccine requires proper storage under cold-chain conditions, and reconstituted vaccine must be kept on ice and used within six hours.

Temperature sensitivity of vaccines

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 -15oC and -25oC. Freeze-dried vaccines (i.e., BCG, measles, MMR and yellow fever) may also be kept frozen at -15oC to -25oC 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 +2oC and +8oC. All other vaccines should be stored at between +2oC and +8oC 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.

Temperature sensitivity of vaccines

Regardless of stability of a reconstituted vaccine (including yellow fever), because of the risk of contamination, such products should be kept cold after reconstitution and discarded at the end of a 6-hour immunization session.
Temperature sensitivity of vaccines

Yellow fever vaccine should be quickly administered after reconstitution, maintained at 2-8°C, and discarded at the end of the session, not only to preserve potency, but to minimize risk of contamination of this lyophilized vaccine once reconstituted.

Ensuring the quality of vaccines at country level: Guidelines for health staff

At the higher levels of the cold chain, i.e. at the national (central) and regional or provincial levels, OPV must be kept frozen between -15°C and -25°C.

Freeze-dried vaccines, i.e. BCG, measles, MMR and yellow fever vaccines, may also be kept in this temperature range (-15°C and -25°C) if there is sufficient space in the cold chain, but this is neither essential nor recommended. At other levels of the cold chain these vaccines should be stored between +2°C and +8°C. All other national immunization service vaccines should be stored between +2°C and +8°C at all levels of the cold chain.