

1.10 TRANSPORT, STORAGE AND HANDLING OF VACCINES

Introduction

The 'cold-chain' is the system of transporting and storing vaccines within the temperature range of 2°C to 8°C from the place of manufacture to the point of administration. This temperature range is recommended because outside this range vaccines may (very quickly) lose their potency. **Immunisation service providers should maintain their vaccine refrigerators as close as possible to 5°C, as this gives a safety margin of + or – 3°C.** Maintenance of the cold-chain system requires that processes are in place to ensure that a potent vaccine reaches recipients.

The World Health Organization's Expanded Program on Immunization (EPI) has developed detailed guidelines on the maintenance of an effective cold-chain.²⁸ The guidelines here are based on the EPI recommendations, and on research and experience in Australia.^{29,30}

Purpose-built vaccine refrigerators

Purpose-built vaccine refrigerators are the preferred refrigerators for vaccine storage. It is recommended that if possible purpose-built refrigerators are used by larger vaccination services, including hospitals, pharmacies, larger community health centres and larger general practices. It is also recommended that they be used in remote settings in central and northern Australia.

There are several manufacturers and/or distributors of purpose-built vaccine refrigerators in Australia. Although they are considerably more expensive than domestic refrigerators, they have the advantage of not having to be modified for vaccine storage (see below). Also, they are programmed to maintain an internal temperature between 2°C to 8°C, they automatically defrost, they have an external temperature reading display and a maximum/minimum temperature continuous display, and an alarm for deviations outside the programmed temperature range. Information about these products can be obtained from most medical equipment wholesalers or distributors.

Safe vaccine storage when using a domestic refrigerator

'Frost-free' rather than cyclic type domestic refrigerators are recommended for storage of vaccines. Cyclic refrigerators are not recommended because they produce wide fluctuations in the internal temperatures, with regular internal heating. Frost-free refrigerators do not have heating cycles but remain frost-free with low levels of frequent warming temperatures.

Do not use 'multi-flow' refrigerators that direct air from the freezer compartment to the main cabinet. These types of refrigerators can easily be recognised by the presence of 2 thermostat controls.²⁹

Domestic refrigerators and many industrial refrigerators are designed only for the storage of food and drink and usually have several temperature zones to meet the requirements of different foods. They are not designed for the special temperature needs of vaccines. Domestic refrigerators that have a separate freezer compartment are recommended for vaccine storage.

Safe vaccine storage is possible in most refrigerators if the following procedures or modifications are carried out (see Figure 1.10.1):

- follow storage guidelines;
- store vaccine in a dedicated refrigerator if possible. **Do not store food or drink in vaccine refrigerators.** It is more difficult to maintain correct vaccine storage temperatures in 'Bar' refrigerators;
- store vaccines only on the middle and upper shelves in the refrigerator;
- allow air to circulate within the refrigerator, by not crowding or overfilling the refrigerator with the vaccines. A gap of at least 4 cm from all walls and between large packages of vaccine vials is recommended;
- rotate stock so that shortest date vaccines are used first;
- maintain a space between vaccine packages and the evaporation plate, to prevent the vaccines from freezing through contact with the plate;
- place plastic bottles containing salt water in the lower drawers and the door of the vaccine refrigerator. The salt water bottles help to stabilise the internal temperature quickly and reduce warming after the door is opened. Allow space between the bottles for air circulation. To make the

salt water for the bottles, add enough salt to make the water undrinkable (about 1-2 tablespoons per litre) and label 'Warning salt water. Do not drink'.

- open the door only when necessary and close it as soon as possible;
- check and record temperatures daily;
- give one person responsibility for adjusting the refrigerator control (it is important that other staff are also trained to ensure continuous monitoring);
- prevent ice build up in the freezer of non 'frost-free' refrigerators by defrosting regularly.
- ensure the power source is secured in a way to prevent the refrigerator from being accidentally unplugged or turned off. Tape in power plug and over switch to prevent accidental disconnection.

If a dedicated vaccine fridge is not available, store the vaccines in a (pre-cooled) Styro foam container with lid closed and place in the middle of the refrigerator. Ensure the vaccines inside the container are monitored and place a label on the outside stating 'Vaccines – keep refrigerated'.

Thermostat overrides have not been recommended due to the lack of published testing data on their performance when fitted to available refrigerator brands available in Australia. The temperature of the vaccine refrigerator must be recorded daily even if a thermostat override has been fitted.

When preparing ice packs or freezer blocks for transport, cool the thawed ice packs on the lower shelf of the refrigerator during the day before placing in the freezer. Place these ice packs in the freezer at the end of the day for freezing overnight and allow a minimum of 2 days for complete freezing before using these ice blocks for transporting vaccines. Do not stack ice packs on top of each other in the freezer but set them on their edge and allow space between them.

Maintaining and monitoring refrigerator temperatures

Refrigerators used for vaccines should have a minimum/maximum thermometer placed on a middle shelf and temperatures should be checked and recorded daily. The most effective minimum/maximum thermometer is a digital type with a probe.

If using a digital thermometer with a probe, place the probe directly in contact with a vaccine vial or package. Do not put the probe into fluid. The recommendation of keeping the vaccine storage temperature at between 2°C to 8°C is based on air, not fluid temperatures.

The refrigerator temperature should be read around the same time each day, preferably prior to each working day. One person only should be responsible for adjusting the refrigerator to maintain the temperature in the recommended range of 2°C to 8°C.

Refrigerators used for vaccine storage should have an uninterrupted power supply and door openings should be kept to a minimum.

During a power failure of 4 hours or less, the refrigerator door should be left closed. If the power fails for more than 4 hours, store vaccines in a pre-cooled, insulated container with ice packs to keep them cool (see 'Transporting vaccines in insulated containers' for more information).

Maintenance of the vaccine refrigerator

Refrigerator breakdowns should be repaired immediately. The door seals should be in good condition so that the door closes securely. Refrigerators that are not 'frost free' should be defrosted regularly to prevent ice build-up. Ice build-up can reduce the efficiency and performance of a refrigerator.

During defrosting or cleaning of the refrigerator, move the vaccines to a second refrigerator. This temporary storage refrigerator must also be monitored to ensure the correct temperature is maintained. Alternatively the vaccines can be stored in a pre-cooled insulated container with ice packs or ice until the normal vaccine refrigerator is ready for use again (see 'Transporting vaccines in insulated containers').

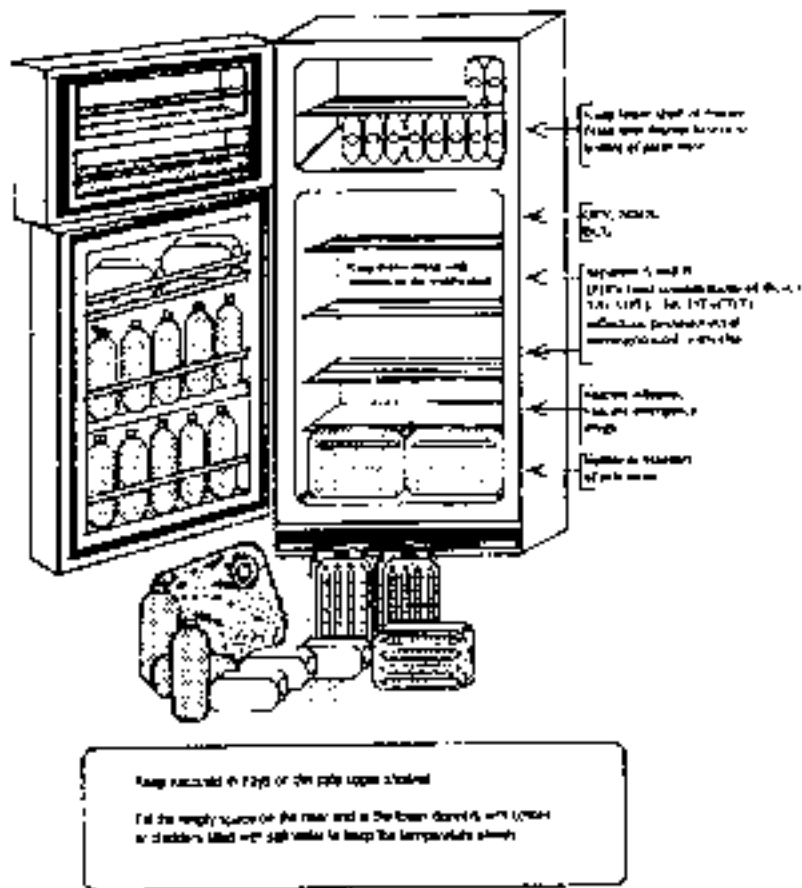
Unpacking vaccines after transport

Do not remove vaccines from their packaging regardless of their bulkiness. Removal from original packaging exposes vaccines to room temperature and/or lighting. Check cold-chain monitors when the vaccines arrive to ensure they have not been exposed to temperatures above 8°C or below 0°C.

If cold-chain monitors have not been included, check that the ice packs are still partially frozen; if they are completely thawed, the vaccines have not been kept sufficiently cold and may not be effective.

Do not discard any vaccines until you discuss the necessary actions with your State/Territory vaccine distribution centre, vaccine supplier, hospital pharmacy or local public health unit.

Figure 1.10.1: Thermal lag modification and storage patterns in a domestic refrigerator



Cold-chain monitors^{28,30}

Cold-chain monitors (CCM) include time-temperature (heat monitors) and freeze monitors. The CCM should accompany all vaccines during any long distance vaccine transport. A minimum/maximum thermometer is an acceptable alternative for monitoring temperature inside cold boxes during transport to outreach settings.

The CCM should not be removed from the (cold box) container until all vaccines have been removed for either use or storage. The index on the time-temperature or freeze monitor (or alternatively, the minimum/maximum thermometer if working in an outreach setting) should be checked when a vaccine is removed from the cold box. Any changes should be recorded. If possible, the CCM that arrived with the vaccines should remain with a portion of the vaccines during storage in the refrigerator until the vaccines have been used or discarded.

Always contact the State/Territory vaccine distribution centre, vaccine supplier, hospital pharmacy or the local public health unit for more information if required. See Appendix 1 for contact details.

CCMs work by showing colour change on an indicator strip when the temperature reaches or exceeds a threshold for a set period of time. The indicator strip should be attached to a card on which instructions for use are printed, in accordance with World Health Organization (WHO) format.

Time-temperature monitors (for monitoring exposure to heat over time)

There is one time-temperature monitor available that has 2 separate temperature thresholds.

- The Monitor Mark™ (Model 10N/34AA) manufactured by 3M; with +10°C, irreversible colour change (14 days to full scale colour change at +12°C); plus 34°C, irreversible colour change (3 hours to full scale colour change at 37°C).

If an equivalent monitor to this one recommended by the WHO becomes available in Australia, it should also be considered for use.

An Australian vaccine manufacturer/distributor uses an in-house time-temperature monitor, Bulls Eye™. This is a heat-sensitive monitor and the manufacturer claims that it changes colour from 'satisfactory' to 'unsatisfactory' at 30 hours at 21°C, and 10 days at 12°C. It is more heat sensitive than the Monitor Mark™ and this might mean that, if the monitor activates, vaccines could be discarded even though they are still potent. If the Bulls Eye™ monitors activate, vaccine providers should always seek advice from their State/Territory vaccine distribution centre before vaccines are discarded. There is currently insufficient evidence to assess the manufacturer's claims about this monitor's performance under various temperature conditions.

Freeze indicators

Freeze indicators work by a colour spot change at threshold temperatures at or below freezing. There are different models available in Australia made by different manufacturers. Activation is shown by staining of the indicator paper from the solution in the bulb.

- Freeze Watch™ (freeze) indicator (Berlinger or 3M). There are 2 models available: one is set to activate at 0°C and the other activates at -5°C. The model that activates at 0°C is recommended for use in Australia.
- ColdMark™ (freeze) indicator (IntroTech™). There are 2 models available: one is set to activate at 0°C and the other activates at -3°C. The model that activates at 0°C is recommended for use in Australia.

Procedures to be observed when using vaccines

Vaccines should remain in the refrigerator until they are required and all unused vaccines should be immediately returned to the refrigerator. The expiry date on the vial or container should be checked before use.

BCG vaccine that has been taken in and out of refrigeration during a clinic session should be discarded at the end of the clinic day. Reconstituted BCG is very unstable and should be discarded after one working session of 5 to 6 hours.

OPV can be stored either in the refrigerator at 2°C to 8°C or in a freezer at below -20°C. Frozen OPV will not lose potency if it is quickly thawed and then refrozen. The freeze-thaw cycle can occur until the vial is empty as long as the vaccine is stored in a freezer capable of achieving temperatures below -20°C. Most domestic refrigerators (with freezer compartments) are not capable of achieving this temperature. A minimum/maximum thermometer should be used to check the freezer temperature.

If storing OPV in a refrigerator at 2°C to 8°C, opened multidose vials of OPV can be used in subsequent sessions if the following three conditions are met:³¹

- the expiry date has not passed;
- the cold chain is maintained between 2°C to 8°C;
- the vaccine has not been taken away from the health centre (eg. outreach immunisation setting).

NB: In contrast to OPV, which can be kept frozen, IPV must *not* be frozen.

Transporting vaccines in insulated containers

Refrigerated transport is the best way to distribute vaccines from the central (usually State/Territory) vaccine centre to the door of the immunisation provider (clinic or surgery). This transport should include appropriate temperature control and monitoring equipment. When this is not feasible, other methods can be used to achieve an effective cold chain.

Containers specifically designed for transporting vaccines should be used if available. If such a container is not available, the following guidelines for packing vaccine for transport in an insulated container should be observed.

- Before packing ice packs with vaccines, remove the ice packs from the freezer at least 30 minutes prior to packing and allow them to 'sweat'. A 'sweated' ice brick is one that has been removed from the freezer for about 30 minutes. This action reduces the risk of freezing vaccines since the ice brick temperature is about -20°C when it is first taken out of the freezer.
- Place vaccines (and time-temperature monitors and freeze monitor as required) in a small Styrofoam container ('six-pack' container). Close the lid and secure with tape. Pack the small Styrofoam container inside a larger insulated container (a 'cooler' such as the EskyTM) and surround it with ice packs. Close and secure the lid of the large container. The vaccines must not be in direct contact with the ice packs because of the risk of freezing.
- If the vaccines are not packed using the above technique, an alternative method is to pack the vaccines inside a pre-cooled cold box (eg. EskyTM). Place the ice packs on top of the vaccines, ensuring they are separated from the vaccines by a layer of polystyrene foam, shredded paper or bubble-wrap plastic. Ensure the vaccines, CCM, ice packs and 'filler' material are packed to ensure they do not move around during transport. Vaccines must be packed to ensure the ice packs do not come into direct contact with the vaccines or CCM, and the cold air can circulate freely around the vaccines.
- Remove vaccines only as they are required, making sure the lids are replaced on both the small and large containers each time (if this is the method of transport). If the time-temperature monitors and/or freeze indicators (or alternatively, the min/max thermometer in an outreach situation) are used, they should be checked before administering the vaccine. If the time-temperature monitor indicates that vaccine is being subjected to temperatures above 10°C while being transported, use more freezer blocks to reduce and maintain the internal temperature at the correct level.

Stability of vaccines at different temperatures³¹

High temperatures affect all vaccines whereas freezing damages only some vaccines. In Australia, freezing has been shown to be the major cause of vaccine damage in both tropical and temperate areas. If concerned that vaccines may have been exposed to excessively high or low temperatures, contact your State/Territory immunisation coordinator.

The following vaccines are unstable at room temperature:

- BCG (Bacille Calmette-Guérin) vaccine
- Measles-mumps-rubella (MMR) vaccine
- Oral poliomyelitis vaccine (OPV)
- Varicella-zoster vaccine
- Yellow fever vaccine
- All reconstituted vaccines

Do not freeze the following vaccines:

- Diphtheria-tetanus-pertussis containing vaccines
- *Haemophilus influenzae* type b (the exception being the lyophilised PRP-T vaccines)
- Hepatitis B-containing vaccines
- Hepatitis A-containing vaccines
- Influenza vaccine
- Pneumococcal (polysaccharide and conjugate) vaccines
- Meningococcal C conjugate vaccines
- Japanese encephalitis vaccine
- All reconstituted vaccines
- All combinations of these vaccines
- Vaccine diluents

Note: Several other less frequently used vaccines (eg. rabies and typhoid) are also damaged by freezing. If the vaccines listed above have been exposed to temperatures 0°C and below, do not use.

The following vaccines must not be exposed to light:

- BCG (Bacille Calmette-Guérin) vaccine
- Reconstituted measles-mumps-rubella (MMR) vaccine

- Monovalent rubella vaccine
- Oral poliomyelitis vaccine (OPV)
- Varicella-zoster vaccine (VZV)
- Most DTPa-containing vaccines
- Meningococcal C conjugate vaccine
- Yellow fever vaccine.

Table 1.10.1: Information on vaccines exposed to different temperatures³¹

Vaccine (3) (4)	Stability at different temperatures (1) (2)				
	< 0°C	2°C to 8°C	22°C to 25°C	35°C to 37°C	over 37 °C
BCG (freeze-dried or lyophilised vaccine) (3) (4)	Can be stored at up to -20°C. Do not expose to light (ultraviolet and/or fluorescent).	Safe storage for 12 months. Do not expose to light (ultraviolet and/or fluorescent). Diluent – do not freeze (5) Store between 2°C and 8°C.	Stability varies. Some BCG vaccine may lose 25% to 40% of original potency after 2 months. Do not expose to light (ultraviolet and/or fluorescent).	Loses potency rapidly. Do not expose to light (ultraviolet and/or fluorescent).	Rapid loss of potency. Up to 73% loss of potency after 3 days. Do not expose to light (ultraviolet and/or fluorescent).
BCG (Reconstituted with diluent) (3) (4)	DO NOT FREEZE.	Very unstable. Protect from all forms of light (inactivates vaccine). Keep at between 2°C and 8°C when vial is not being used. Discard all unused vaccine at the end of the vaccination session (8 hours).	Very unstable. Protect from all forms of light (inactivates vaccine). Keep between 2°C and 8°C when vial is not being used.	Very unstable. Protect from all forms of light (inactivates vaccine). Keep at between 2°C to 8°C when vial is not being used.	Very unstable. Protect from all forms of light (inactivates vaccine). Keep at between 2°C to 8°C when vial is not being used.
Diphtheria, tetanus and/or acellular pertussis- containing vaccines Includes DTPa, DTPa-hepB, DTPa-Hib, DTPa-IPV, DTPa-hepB-IPV, DTPa-IPV-Hib, DTPa-IPV/Hib, DTPa-hepB-IPV-Hib, dTpa, DT (CDT), dT (ADT).	DO NOT FREEZE. Vaccines loses significant potency when stored at -5°C to -10°C. NB: Some vaccines may still remain as a liquid at <0°C. As little as 24 hours at <0°C or >25°C may cause antigens to fall from suspension and be very difficult to resuspend. Freezing point of tetanus is between -5°C to -10°C. The freezing point of pertussis is not known. Discard if exposed to temperatures of 0°C or below.	Safe to store at 2°C to 8°C for 24 months in spite of continuous slow decrease in potency of the pertussis component.	The DT components are stable for 4, possibly 6 months; the limiting factors are some of the other components. Some vaccines containing pertussis are stable for only 2 weeks at this temperature.	The DT components are stable for weeks but the stability of the other components vary with different vaccines. Some vaccines containing pertussis lose 50% of potency after one week.	DT components: stable for 2 weeks at 45°C but much less at higher temperatures. The other components are (where known) very unstable at high temperatures.
Freeze dried (lyophilised) monovalent PRP-T Hib vaccine	Freeze-dried or lyophilised vaccine PRP-T can be frozen.	Diluent – do not freeze (5) Store between 2°C and 8°C.	Not available.	Not available.	Not available.
Reconstituted monovalent PRP-T Hib vaccine	Reconstituted vaccine must NOT be frozen.	Store all components of the vaccine between 2°C and 8°C.	Not available.	Not available.	Not available.
Other Hib-containing vaccines (PRP-OMP, HbOC, Hib (PRP-OMP)-hep B	DO NOT FREEZE. The precise freezing point is not established. Manufacturers state freezing temperature of HbOC is -1.0°C. Discard if exposed to temperature of 0°C or below.	Store between 2°C and 8°C.	Stable for at least 24 months when stored at 25°C.	Not available.	Not available.

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Monovalent hepatitis A vaccine	DO NOT FREEZE. Discard if vaccine has been exposed to temperature of 0°C or below.	Store between 2°C to 8°C for many months (up to 36 months for some brands).	Stable for 15 months.	Stable for 15 months.	Not available.
Monovalent hepatitis B vaccine	DO NOT FREEZE. Freezing point of hepatitis B vaccine is – 0.5°C and vaccine is destroyed at this temperature. Discard if exposed to temperature of 0°C or below.	Retains satisfactory potency for 2 years.	Retains satisfactory potency for 30 days.	Stable for 1 week	Stable for 3 days.
Inactivated poliomyelitis vaccine (IPV)	DO NOT FREEZE. Discard if exposed to temperature of 0°C or below.	Store for up to 2 years between 2°C to 8°C.	Loses significant potency after 20 days.	Destroyed after 20 days.	Not available.
Influenza vaccine	DO NOT FREEZE. Discard if exposed to temperatures of 0°C or below.	Store between 2°C to 8°C	Not available.	Not available.	Not available.
Measles-mumps-rubella (MMR) (freeze-dried or lyophilised vaccine) (4)	May be stored in freezer at 0°C or below. Protect from light, which may inactivate virus.	Safe storage for 2 years at 2°C to 8°C. Diluent – do not freeze. (5) Store between 2°C and 8°C.	Retains satisfactory potency for 1 month.	Retains satisfactory potency for at least 1 week	50% loss of potency after 2 to 3 days at 41°C: 80% loss of potency after 1 day at 54°C.
Reconstituted measles-mumps-rubella (MMR) (3) (4)	DO NOT FREEZE. Protect from light.	Can be stored between 2°C to 8°C. Protect from light, which may inactivate the vaccine virus. Should be used in one vaccination session (8 hours) if kept cool and protected from sunlight. If not, discard after 1 hour.	Unstable: 50% loss of potency after 1 hour, 70% loss after 3 hours. Protect from light.	Very unstable: titre may be below acceptable level after 2 to 7 hours. Protect from light.	Inactivation within 1 hour.
Meningococcal C conjugate vaccine (MenCCV) NeisVac-C Meningitec (freeze-dried or lyophilised vaccine)	DO NOT FREEZE. Discard if exposed to temperatures of 0°C or below.	Store in refrigerator between 2 and 8°C. Shelf life 18 months at this temperature.	Not available.	Not available.	Not available.
Meningococcal C conjugate vaccine (MenCCV) Menjugate	DO NOT FREEZE. Discard if exposed to temperatures of 0°C or below.	Store between 2 and 8°C. Shelf life is 24 months at this temperature. Reconstituted vaccine must be used immediately. Diluent – do not freeze (5) Store between 2 to 8°C.	Not available.	Not available.	Not available.
Oral poliomyelitis vaccine (OPV) opened vials (3) (4)	May be stored for up to 2 years at around –20°C. The freeze-thaw-refreeze cycle can occur until the vial is empty.	Can be stored at 2°C to 8°C between use as long as the expiry date has not passed, and the vaccine has not been taken out of the health centre (eg outreach immunisation setting).	Stable for at least 1 week at 20°C to 25°C.	Not available.	Remains potent for 24 hours.
Pneumococcal conjugate vaccine (7vPCV)	DO NOT FREEZE. Discard if exposed to temperature of 0°C or below.	Store between 2°C and 8°C.	Not available.	Not available.	Not available.
Pneumococcal polysaccharide vaccine, 23-valent (23vPPV)	DO NOT FREEZE. Discard if exposed to temperature of 0°C or below.	Store between 2°C and 8°C.	Not available.	Not available.	Not available.

Varicella-zoster vaccine: Varivax Refrigerated, Varilrix (freeze-dried or lyophilised vaccine) (3) (4)	May be stored in frost-free freezer at an average temperature of -15°C or colder. Maintains potency for 24 months (Varilrix) or 18 months (Varivax Refrigerated). Protect from light.	Prior to reconstitution, varicella-zoster vaccine retains potency when stored between 2°C to 8°C for up to 2 years (Varilrix) <i>or</i> 18 months (Varivax Refrigerated). Diluent – do not freeze (5) Store between 2°C and 8°C.	Not available.	Not available.	Not available.
Reconstituted varicella-zoster vaccine: Varilrix and Varivax Refrigerated (3) (4)	DO NOT FREEZE. Protect from light.	Administer immediately after reconstitution to minimise loss of potency. Discard if reconstituted vaccine is not used within 90 minutes (Varilrix) <i>or</i> within 30 minutes (Varivax Refrigerated). Diluent – do not freeze (5) Store between 2°C and 8°C.	Not available.	Not available.	Not available.
<p>(1) For thermostability information on other vaccines not listed in this Table, refer to the specific chapter in this <i>Handbook</i>.</p> <p>(2) The information in this Table is in many cases not consistent with the Australian product information documents. However, this Table provides guidelines based on the WHO (1998) Thermostability of Vaccines, WHO/GPV/98.07.</p> <p>(3) The vaccines that are most unstable at room temperature are OPV and reconstituted MMR, varicella-zoster and BCG vaccines.</p> <p>(4) OPV and reconstituted MMR, varicella-zoster and BCG vaccines must be protected from exposure to light.</p> <p>(5) DO NOT FREEZE DILUENT AS THIS MAY CAUSE UNDETECTABLE CRACKS IN THE AMPOULE LEADING TO CONTAMINATION.</p>					

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