Vaccines and Biologicals Update*

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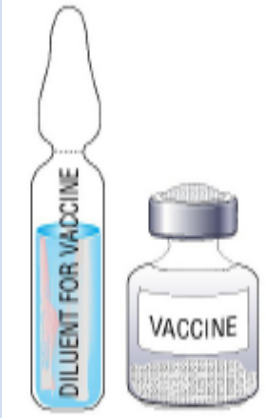
Proper handling and reconstitution of vaccines avoids programme errors

Highlights

- Only diluent supplied by the manufacturer, specific for the vaccine, should be used. No other diluent may be used.
- Diluent must be shipped and distributed together with the vaccine vials that it will be used to reconstitute. This ensures that the correct diluent will be used for the vaccine. Before reconstitution, diluent must be cooled to below +8°C to avoid thermal shock to the vaccine.
- Reconstituted vaccines may become contaminated with staphylococcus and other organisms from improper handling. Once this happens, a chemical called a toxin is produced that may be deadly if injected. To avoid this, reconstituted BCG, measles and yellow fever vaccines must be kept cooled, and must be discarded after 6 hours after reconstitution.
- Some newly introduced vaccines also require diluents, and all reconstituted vaccines should be discarded before the time limit indicated in the manufacturer's leaflet, or not longer than 6 hours after reconstitution, whichever is the shorter.
- 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.



Correct storage of diluent with vaccine ready for reconstitution

DEPARTMENT OF VACCINES AND BIOLOGICALS

World Health Organization
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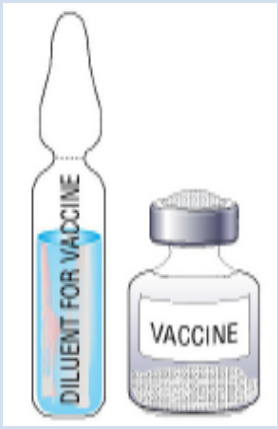
* This was previously published as EPI Update

"Only diluent supplied by the manufacturer for that vaccine should be used. No other diluent may be used"



Correct storage of diluent with vaccine ready for reconstitution

Incorrect storage of diluent
- Do not use these for reconstitution

Background

Some vaccines arrive at the point of use from the manufacturer as liquids and ready to administer. Others come as frozen powders (freeze-dried) and need to have liquid (diluent) added before they can be injected. As for all injections, a single sterile syringe and sterile needle must be used to give the injection. But there are special problems posed by adding the diluent to the powdered vaccine (a process called reconstitution). First, for each vial the process requires a sterile syringe and sterile needle to mix the powder with the diluent. Second, vaccinators needs training in the process of reconstitution so that human error is kept to a minimum. This UPDATE particularly focuses on the proper handling of freeze-dried vaccines.

Incorrect use of diluent may occur either because stock control or shipment errors have resulted in the wrong diluent being available. Or the vaccinator may select the wrong vial through poor training, or carelessness, compounded by incorrect storage procedures.

Shipment and storage of freeze-dried vaccine

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.

Ship vaccines and diluent together

The diluent must be shipped and distributed at the same time and in the same quantity as the vaccine vials. It does not need to be at the same temperature, but freezing must be avoided so the vial does not crack. This ensures that the correct diluent will be available for the vaccine.

Diluent must be at the correct temperature (below 8°C) at the moment of reconstitution to avoid thermal shock to the vaccine.

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.

Diluents

The diluent supplied with a vaccine is part of the licensed product and is specific for each vaccine. The vaccine "package" is not complete without the diluent. Diluents are specifically designed for the needs of each vaccine with respect to volume, pH (acid-alkali balance) and chemical properties of the final solution containing the immunizing agent. Using the wrong diluent may also mean a different volume of diluent is used for each vial of vaccine, so resulting in incorrect doses. It is essential that diluents for vaccines are stored, distributed and used in the proper way so that they are not the cause of damaged vaccines, adverse events or incorrect doses.

- Diluents vary in their composition.
- Not all diluents are sterile water for injection. This is a common misconception. Diluents may contain:
  - stabilizers that affect heat lability;
  - bactericides to maintain the sterility of the reconstituted vaccine;
  - chemicals to assist in dissolving the vaccine into a liquid;
  - buffers to ensure the correct pH.

In the past, the practice of supplying, transporting and storing diluents separately from the vaccine has caused confusion, and resulted in shortage of the correct diluents in the field. Poorly labelled and identified vaccines and diluents have compounded this, as has the lack of adequate training for health workers. WHO now recommends that vaccines and diluents be distributed together to avoid this confusion.

Vaccinators and store keepers should always ensure that no other medication or substance which might be confused with the vaccine or its diluent is stored in the refrigerator of the immunization centre.

Newly-introduced vaccines

It is likely that many vaccines of the future will continue to require reconstitution with diluents. 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. Products such as freeze-dried Hib vaccine are being introduced in many countries and, as for all freeze-dried vaccines, require the use of their own specific diluent for reconstitution.

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.

Reconstitution process

Only the diluent supplied by the manufacturer should be used to reconstitute a freeze-dried vaccine. A sterile needle and sterile syringe must be used for each vial for adding the diluent to the powder in a single vial or ampoule of freeze-dried vaccine.

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 ultra-violet rays.

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.

■

Use only the diluent that is indicated for each type of vaccine and manufacturer.

■

Ensure the volume of diluent used is correct so that the proper number of doses per vial is obtained.

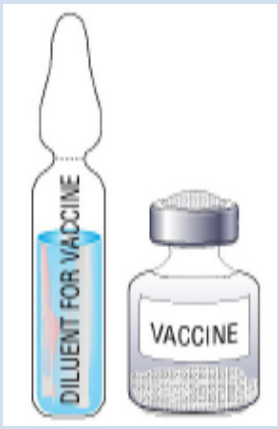
■

Ensure that no other medication or substance which might be confused with the vaccine or its diluent is stored in the refigerator of the immunization centre.

■

Reconstituted vaccine should be kept on ice to preserve its potency (by maintaining the maximum possible number of live organisms in each dose). A sterile needle and sterile syringe must be used for each separate dose of reconstituted vaccine drawn from the vial. The reconstituted vaccine must be kept cool and any remaining liquid must be discarded after 6 hours.

* "Thermal shock" is the process of damage to the vaccine resulting from the use of diluent that is at too high a temperature (above +8°C). It results in the death of some or all of the essential live organisms in the vaccine.



Avoiding programme errors

Toxic shock. Reconstituted vaccine is an ideal environment for growing a number of organisms. Live vaccines do not contain a preservative (as many of the other types of vaccines in multi-dose containers do). Once the vial is contaminated with staphylococcus or other organism from improper handling, the organism grows extremely fast. As it grows, it produces a deadly chemical called a toxin. If a contaminated vial is kept (even in the refrigerator), by morning there is enough toxin in the vial to kill an infant. A number of instances are recorded when several infants have been given the remains of the reconstituted measles vaccine from the previous day. They have died in shock several hours later. This is called "toxic shock syndrome". If toxic shock syndrome happens, at least two programme errors have occurred together: non-sterile reconstitution/ injection technique, and failing to discard the vaccine after 6 hours. *BCG, measles and yellow fever vaccines must never be kept longer than 6 hours after reconstitution*.

Wrong diluents. The practice of separate distribution of diluents and vaccines can lead to severe problems. Peripheral immunization clinics may receive consignments of vaccine followed by consignments of diluent from other manufacturers or other types of vaccine from the same manufacturer. This leaves staff little choice except to reconstitute the vaccine incorrectly. Major adverse reactions, including a number of deaths, have resulted from the practice of mixing diluents.

Wrong storage. Potentially dangerous medications such as muscle relaxant anaesthetic agents are sometimes kept inappropriately in the same refrigerator where vaccines are stored. These medications may be packed in vials or ampoules similar to vaccines or their diluents. They may be used by mistake for reconstitution of freeze-dried vaccines. Many examples of adverse events have been documented, some of them ending in the death of infants minutes to a few hours after vaccination.

Something went wrong – what do I do?

- *Wrong diluent used*. Check for adverse reaction. Give properly reconstituted vaccine.
- *Adverse event*. Treat anaphylaxis or other reaction. Refer to base hospital if serious. Inform supervisor.
- *Abscess*. Treat, if necessary, by referral to base hospital. Inform supervisor.
- *Diluent for live vaccine was too warm, thermal shock suspected*. Repeat vaccination with correct reconstitution procedures.

Identify what the error was and correct it so it cannot happen again. Discuss with supervisor and parents.

Department of Vaccines and Biologicals

Access to Techologies

Expanded Programme on Immunization

Quality and Safety of Biologicals

Vaccine Assessment and Monitoring

Vaccine Development

This document is available on the Internet at:
www.who.int/vaccines-documents/

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