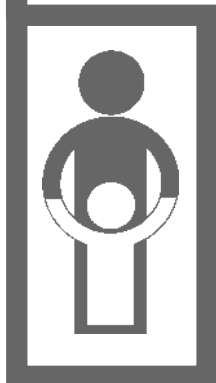


WHO Policy Statement

The use of opened multi-dose vials of vaccine in subsequent immunization sessions



**DEPARTMENT OF VACCINES
AND BIOLOGICALS**



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Glossary

BCG	Bacillus Calmette-Guérin (vaccine against tuberculosis)
DT	diphtheria and tetanus toxoid vaccine
DTP	Diphtheria, tetanus, pertussis vaccine
Hib	Haemophilus influenzae vaccine
OPV	Oral polio vaccine
TT	tetanus toxoid vaccine
VVM	vaccine vial monitor

Preface

Sufficient data have been collected on the safety and potency of vaccines recommended for use in immunization services to warrant a change in the World Health Organization's (WHO) policy on the use of multi-dose vials of vaccine*. The intent of this policy statement is to emphasize safe use of opened multi-dose vials of vaccine: liquid vaccines as described below at 2.1 and 2.2, and reconstituted vaccines, as described at 2.3. The revised policy has the potential to reduce vaccine wastage rates by up to 30%, resulting in annual savings worldwide of US\$ 40 million in vaccine costs.

This document summarizes the previous policy on the use of opened multi-dose vials of vaccine, describes the revised policy, outlines the scientific rationale for the policy change, and discusses operational implications for immunization programme managers.

This document revises and replaces *WHO policy statement: The use of opened vials of vaccine in subsequent immunization sessions*, WHO/EPI/LHIS/95.01, issued in 1995 when the policy was first launched.

* See attached list of references.

1. WHO policy

1.1 Previous policy

The previous EPI policy stated that all vaccine vials that had been opened¹ for an immunization session had to be discarded at the end of that session, regardless of the type of vaccine or the number of doses remaining in the vial.

1.2 Revised WHO policy

1.2.1 The revised policy applies only to OPV, DTP, TT, DT, hepatitis B, and liquid formulations of Hib vaccines that:

- meet WHO requirements for potency and temperature stability;
- are packaged according to ISO standards²; and
- contain an appropriate concentration of preservative, such as thiomersal (injectable vaccines only).

Note: Vaccines supplied via UNICEF meet these requirements.

1.2.2 For these vaccines, the revised policy states:

Multi-dose vials of OPV, DTP, TT, DT, hepatitis B, and liquid formulations of Hib vaccines from which one or more doses of vaccine have been removed during an immunization session *may be used in subsequent immunization sessions for up to a maximum of 4 weeks³, provided that all of the following conditions are met:*

- The expiry date has not passed;
- The vaccines are stored under appropriate cold chain conditions;
- The vaccine vial septum has not been submerged in water⁴
- Aseptic technique has been used to withdraw all doses;
- The vaccine vial monitor (VVM), if attached, has not reached the discard point.

¹ In this document, “opened vials” refer to multi-dose vials from which one or more doses of vaccines have been used, in line with standard sterile procedures.

² ISO Standard 8362-2.

³ See guideline in paragraph 3.2.

⁴ See guideline in paragraph 3.2.

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- 1.2.3 The revised policy does not change recommended procedures for handling vaccines that must be reconstituted, that is, BCG, measles, yellow fever, and some formulations of Hib vaccines. Once they are reconstituted, vials of these vaccines *must be discarded* at the end of each immunization session or at the end of six hours, whichever comes first.

2. Rationale for changing the policy

Two concerns must be addressed in setting policy on the use of vaccine in opened multi-dose vials in subsequent sessions:

- The potency of vaccine; and
- The safety of its administration.

Since the original policy statement was issued, research has provided more information about the impact of time and other factors on potency and safety.

2.1 Potency

The potency of vaccine in an opened vial over time is determined primarily by:

- the heat stability of the particular vaccine; and
- whether or not the vaccine has been reconstituted.

The vaccine in opened vials of OPV, TT, DTP, DT, hepatitis B, and liquid formulations of Hib remains potent as long as vials are stored under appropriate cold chain conditions (as recommended by the manufacturer) and the expiry date has not passed. A good indicator of excessive exposure to heat is the VVM, which is now in use for OPV and will become available for other vaccines within the next year.

The heat stability of freeze-dried (lyophilized) vaccines drops substantially when these vaccines are reconstituted with their diluent.

2.2 Safety

The safety of vaccine in a multi-dose vial is primarily dependent on:

- risk of contamination with a pathogenic organism; and
- bacteriostatic or virucidal effect of preservatives in the vial.

The risk of contamination is higher in a multi-dose vial than in a single-dose vial because the vaccine is repeatedly exposed - every time a dose is withdrawn.

Most freeze-dried (lyophilized vaccines) do not contain preservatives and consequently must not be kept more than the manufacturer's recommended limit and never longer than *six hours* after they are reconstituted. *Death due to toxic shock syndrome has resulted when reconstituted live virus vaccines kept longer than the recommended period have been injected.*

Liquid injectable vaccines such as DTP, TT, DT and hepatitis B contain preservatives that prevent growth of bacterial contamination. Should contamination take place within the vial, the action of these preservatives prevents any increase in bacterial growth over time and actually decreases the level of contamination. A time limit has been set in this policy for managerial reasons only. Time limits less than 4 weeks may be imposed nationally, or sub-nationally, according to the interval between immunization sessions and the average number of children immunized at a session.

Multi-dose vials from which at least one dose has been removed may be at risk of contamination of the vial septum. These vials should never, therefore, be allowed to be submerged in water (from melted ice for example) and the septum should remain clean and dry. NOTE: Well-sealed icepacks should be used in vaccine carriers and water should not be allowed to accumulate where the vials are stored.

3. Introducing the new policy

The new policy may have the following operational implications:

3.1 Training

Health workers must be able to distinguish between vials that can be used in subsequent sessions and vials that must be discarded. Training and supervision materials should be revised to reflect the policy change.

3.2 Vaccine vial monitors

The new policy may be introduced either for all vaccines, or only for vaccines with VVMs, or delayed until all vials are supplied with vaccine vial monitors. This decision depends on the risk of heat exposure and the flexibility of health workers in dealing with changes.

3.3 Vaccine forecasting

Programme managers will need to re-evaluate vaccine wastage rates for vaccines affected by the new policy. The new rate of wastage is estimated to be approximately 15% to 20%, but this figure should be confirmed locally before radically changing vaccine forecasts or orders.

3.4 Using opened multi-dose vaccine vials during campaigns or outreach

The new policy applies to all vaccine vials, including those that have been transported in the cold chain for outreach immunization sessions, provided that standard handling procedures are followed. This means that opened vials can be used in subsequent immunization sessions, in different sites, over several days, provided that they have been stored in vaccine carriers or cold boxes with a suitable number of frozen icepacks and all the conditions outlined in 2.2 are met.

3.5 *Haemophilus influenzae* type b vaccine

Haemophilus influenzae type b vaccine (Hib), now in use in the immunization services of several countries, is available in different formulations and combinations, including liquid single antigen, liquid combined with other antigens, and freeze-dried for reconstitution with a diluent or with another liquid vaccine (DTP).

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- All liquid formulations of Hib vaccine contain a preservative and can be used in subsequent immunization sessions.
 - The freeze-dried formulation contains no preservative, and after being reconstituted with a diluent, must be discarded at the end of the session or within 6 hours, whichever comes first (the same as for BCG, measles, and yellow fever).
 - Certain formulations of lyophilized Hib vaccine are supplied with DTP liquid vaccine. However, although these can be used safely over an extended period, implementing a decision to use them requires additional management and supervision activities, and is not therefore recommended in the absence of specific training of personnel.

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