VVM FOR ALL

BCG, OPV, HepB, DTP, DTP-HepB, DT, T4, TT, Hib, YF, Measles, MR, MMR

**Technical Session on Vaccine Vial Monitors**

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# Getting started with vaccine vial monitors

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**"Without VVMs I could never be sure what happened to the vaccine before it came to the health center".**

*Health worker from Kenya*

Umit Kartoglu

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## Questions and answers on field operations

# 1. How the vaccine vial monitor (VVM) works

## 1.1 What is a vaccine vial monitor (VVM)?

A vaccine vial monitor (VVM) is a label containing a heat-sensitive material which is placed on a vaccine vial to register cumulative heat exposure over time.

The combined effects of time and temperature cause the inner square of the VVM to darken, gradually and irreversibly. A direct relationship exists between the rate of colour change and temperature:

- The lower the temperature, the slower the colour change.
- The higher the temperature, the faster the colour change.

## 1.2 Does the VVM measure vaccine potency?

No, the VVM does not directly measure vaccine potency but it does give information about the main factor that affects potency: heat exposure over a period of time.

The VVM does not register information about other factors that contribute to vaccine degradation, such as sunlight and age (time).

## 1.3 What does the VVM look like?

The VVM is a circle with a small square inside it. It can be printed on a product label, attached to the cap of a vaccine vial or tube, or attached to the neck of an ampoule.

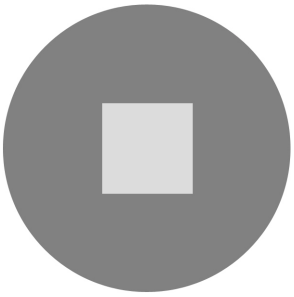

Figure 1: Vaccine Vial Monitor
(showing no heat exposure)

## 1.4 How does the VVM work?

The **inner square** of the VVM is made of heat sensitive material that is light at the starting point and **becomes darker** with exposure to heat.

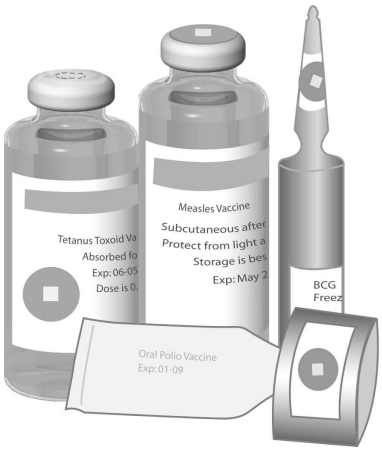


Figure 2: VVM Locations

At the starting point, the inner square is a lighter colour than the outer circle. From then on, until the temperature and/or duration of heat reaches a level known to degrade the vaccine beyond acceptable limits, the inner square remains lighter than the outer circle.

At the discard point, the inner square is the same colour as the outer circle. This reflects that the vial has been exposed to an unacceptable level of heat and the vaccine degraded beyond acceptable limits. The inner square will continue to darken with heat exposure until it is much darker than the outer circle. Whenever the inner square matches or is darker than the outer circle, the vial must be discarded.

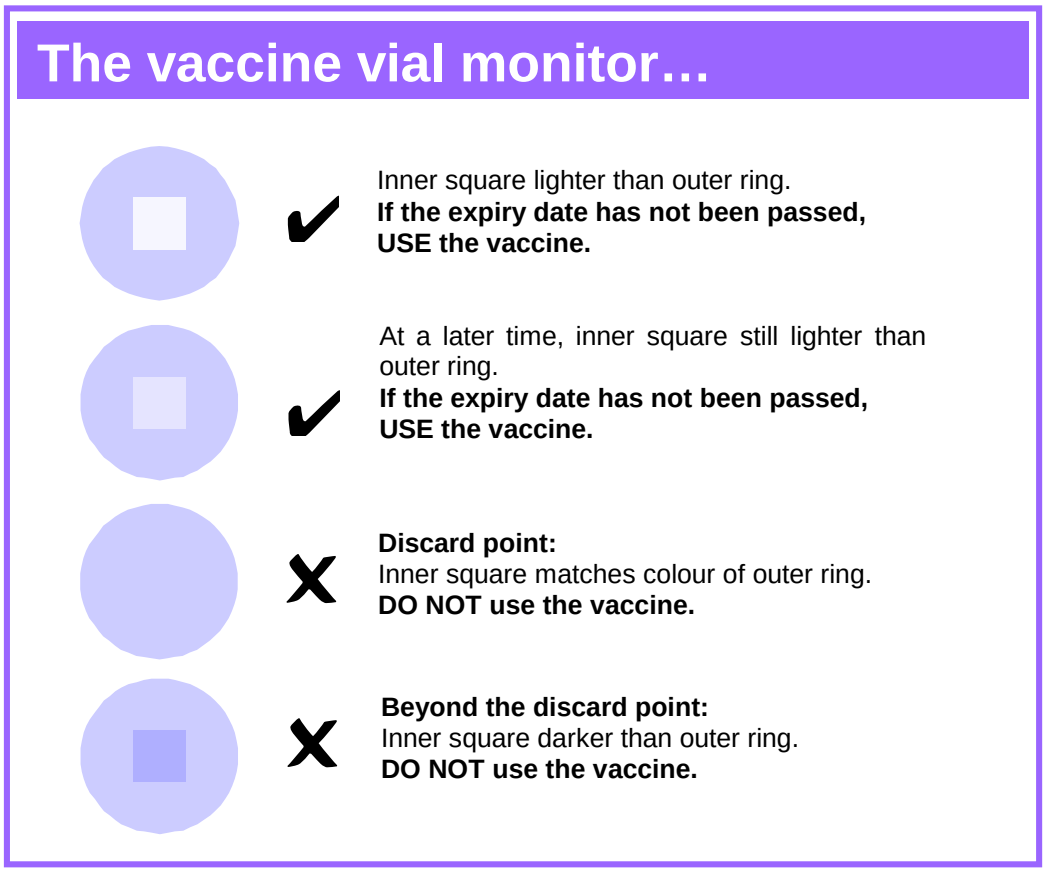


Figure 3: How to read a VVM

## 1.5 Are there different type VVMs for different vaccines?

Yes, there are four different types of VVMs designed for different types of vaccines depending on their heat stability. The below Table describes VVM reaction rates by category of heat stability.

**VVM reaction rates by category of heat stability**

| **Category: (Vaccines)** | **No. days to end point at +37°C** | **No. days to end point at +25°C** | **Time to end point at +5°C** |
|---|---|---|---|
| VVM30<br>HIGH STABILITY | 30 | 193 | > 4 years |
| VVM14<br>MEDIUM STABILITY | 14 | 90 | > 3 years |
| VVM7<br>MODERATE STABILITY | 7 | 45 | > 2 years |
| VVM2<br>LEAST STABLE | 2 | NA* | 225 days |

**VVM (Arrhenius) reaction rates determined at two temperature points*

## 1.6 What are the rules for reading the VVM?

The point to focus on is the colour of the inner square relative to the colour of the outer circle:

- Rule 1: If the inner square is lighter than the outer circle, the vaccine may be used.
- Rule 2: If the inner square is the same colour as, or darker than, the outer circle, the vaccine must not be used.

## 1.7 Does the VVM immediately change colour when it is exposed to temperatures above 8°C?

No. The VVM reflects the heat stability of the vaccine to which it is attached and doesn't, therefore, undergo an immediate colour change with a brief exposure to moderate heat.

Vaccines have a level of heat stability that enables them to withstand temperatures above 8°C, outside the cold chain, for a limited amount of time. The rate at which the VVM changes colour reflects the ability of that particular vaccine to withstand heat.

## 1.8 If vaccine is left at room temperature, how long will it take the VVM to change from "start point" to "discard point"?

This depends on the room temperature and can vary greatly, according to the place, season, time of the day, and type of vaccine. The table below shows sample times recorded for a VVM attached to a vial of OPV and for a VVM attached to a vial of hepatitis B vaccine. OPV is one of the most heat-sensitive vaccines and hepatitis B is one of the least heat-sensitive vaccines.

| Constant temperature, day and night | Time for VVM on a vial of OPV to reach "discard point" | Time for VVM on a vial of hepatitis B vaccine to reach "discard point" |
|---|---|---|
| In a refrigerator: 4°C | 240 days | 5670 days |
| Room temperature: 20°C | 20 days | 385 days |
| Room temperature: 25°C | 10 days | 176 days |

## 1.9 If vaccine is returned to a refrigerator after being outside the cold chain, will the colour change reverse?

No. The colour change is irreversible as, indeed, is the damage to the vaccine. The VVM indicates the total, accumulated heat exposure that the vaccine has been subjected to.

## 1.10 If the vaccine inside the refrigerator freezes, will the VVM register any change?

No. The VVM is not affected by freezing temperatures so it cannot give any information about freezing.

## 1.11 How does the VVM cope with variations in heat tolerance between different types of vaccine?

VVMs are manufactured in specific batches for each type of vaccine. Each VVM is designed to mimic the exact sensitivity of the vaccine to which it is attached.

## 1.12 What testing and quality control procedures are used to ensure that the VVM will perform correctly?

Each batch of VVMs is tested twice to ensure that they will change colour correctly in response to heat exposure. The first test is conducted at the factory before shipment and the second by the vaccine manufacturer before despatch. A special instrument, a colour reflectance densitometer, is used for the tests.

Before WHO approved the use of VVMs, this technology in all its aspects was subjected to extensive independent laboratory testing and field trials.

## 1.13 How does the VVM message relate to the 3M Cold Chain Monitor (yellow card)?

The Cold Chain Monitor (CCM), packaged with each consignment of vaccine from UNICEF, indicates when the temperature limits of the cold chain have been passed. The VVM takes the monitoring procedure one step further and shows the impact of any such temperature changes on each individual vial of vaccine. The CCM monitors the journey while the VVM shows how "each passenger" has fared.

The CCM is a useful managerial tool for checking the arrival of vaccine shipments at central and provincial stores and may also be used in conducting national cold chain surveys. The VVM provides guidance on the use of each vial of vaccine.

# 2. Advantages and costs involved

## 2.1 Why should a VVM be used?

A VVM enables the health worker to know whether vaccine has been damaged by heat.

Vaccine itself exhibits no visible change with heat exposure. Before the development of the VVM, health workers had no means of identifying whether vaccine had suffered damage from heat exposure at any point during transport and/or storage.

National recommendations for vaccine handling have consequently been very conservative in order to prevent the use of vaccines damaged by heat. Health workers have been trained to discard all vaccines after any break in the cold chain, even a *suspected* break. If a health centre refrigerator malfunctions overnight, the vaccine is thrown away as soon as the problem is discovered. In some places health workers are instructed to discard all vaccine that has been taken to the field twice without being used, even if no heat exposure has occurred. These precautions against *possible* heat damage result in large amounts of usable vaccine being discarded -- often unnecessarily.

The VVM can change this situation. Its gradual and irreversible colour change makes it possible to assess cumulative heat exposure and the remaining shelf life of vaccines, even with vials which have been out of the cold chain or stored in a malfunctioning refrigerator.

WHO recommends that VVMs be used in order to:

- ensure that vaccine administered has not been damaged by heat, and
- reduce vaccine wastage.

## 2.2 Will VVMs raise the cost of vaccines?

*Yes.* Vaccine buyers will have to pay a little more for vaccines with a VVM attached. It is, however, expected that any cost increase will be much less than the amount that will be saved by reducing the quantity of wasted vaccines.

# 3. Using a Vaccine Vial Monitor (VVM)

## 3.1 If the VVM has not reached "discard point", can the vaccine still be used if it has passed its expiry date?

No! Vaccine must never be used if it has passed its expiry date.

The expiry date is calculated on the assumption that vaccine will be stored within an appropriate range of temperatures (2-8°C) throughout the cold chain. Even under correct storage conditions, however, vaccine undergoes gradual degradation due to factors such as simple ageing and exposure to light. Once a vaccine has passed its expiry date, it cannot be expected to stimulate sufficient immunity.

## 3.2 If vials have a VVM, do they still need to be kept in the cold chain?

Yes, most of the time. All vaccines are sensitive to heat and will stay potent longer if they are kept refrigerated. The VVM doesn't change the vaccine's sensitivity to heat exposure. It simply gives a visible sign to show how much of the vaccine's "resistance" has been used up, i.e. when heat exposure has exceeded the limit for that vaccine. Each vaccine has a certain level of resistance to small amounts of heat which is variable for different types of vaccine -- OPV, for example, has the least resistance. Careful cold chain handling preserves the vaccine's ability to withstand any accidental or unavoidable heat exposure.

Under certain circumstances, vaccine can be taken outside of the cold chain. These circumstances should be carefully planned and monitored. Also, freeze-dried vaccines should not be transported for outreach without ice since the ice will be needed to keep the vaccine cool after it is reconstituted.

## 3.3 Should other monitors, such as the Freezewatch or 3M Cold Chain Monitor (CCM), still be used?

Yes. FreezeWatch indicators and CCMs track temperatures in refrigerators and during transport. They are not replaced by VVMs.

## 3.4 If the information provided by a CCM differs from the information of the VVM, which reading is the more accurate?

As described above (para. 1.12), CCMs monitor the cold chain, VVMs monitor the vaccine in an individual vial.

If the readings do not relate to freezing temperatures, the reading of the VVM will be the more accurate. It will give an exact indication of the level of heat exposure for the specific vial to which it is attached.

## 3.5 Is there a limit to the number of times an unopened vial can be taken for outreach (or used in NIDs)?

No, not as long as the VVM is still a safe colour.

## 3.6 Will vaccines with a VVM showing some heat exposure, but not yet at discard point, be handled differently?

Yes. These vaccines must be selected for distribution first. The VVM enables the storekeeper to pick out vaccines for use on the basis of most exposed batches rather than "first in, first out".

## 3.7 Can the VVM be used to help in storage and cold chain management?

Yes. The VVM gives a visual measure of the heat exposure of each vial and this enables the health worker to:

- Use vaccine selectively. For instance, vials with minimal heat exposure can be selected for use in outreach sessions or mobile services.
- Estimate remaining shelf life of vaccines and rotate inventories. Vials that register more heat exposure can be selected for use before those with less.
- Identify cold chain problems or confirm problems suggested by VVMs or refrigerator thermometers. Each significant exposure to heat registers some colour change on the VVM; in some cases it may be possible to check where this has happened.
- Reduce wastage by selecting vials of vaccine nearer to the endpoint of the VVM while they are still good.

If health workers are thoroughly trained in the use of the VVM the "first-in-first-out" policy for vaccine handling can be modified. In larger stores, however, where vaccines are kept in their cartons and the VVMs are not visible, the "first-in, first-out" policy may still be the most appropriate management option.

## 3.8 Under what circumstances, if any, can vaccine bearing a VVM be taken out of the cold chain?

Vaccine with VVMs can be taken out of the cold chain only in circumstances where training provided to health workers and others handling the vaccines has established a level of competence that can assure (a) the VVM is accurately interpreted, and (b) any vial bearing a VVM which has reached its end point is discarded.

Managerially, however, it is wise to maintain vaccine within the cold chain for as long as possible during distribution. This will ensure the maximum viable life in the field.

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 only under special circumstances, such as:

- National Immunization Days;
- Inaccessible geographic areas;
- Immunizations provided in the home;
- Cool seasons.
- Storage and transport of freeze-sensitive vaccines (DTP, TT, DT, Td, hepatitis B and Hib vaccines) where the risk of freezing has been determined to be greater than the risk of heat exposure.

Remember freeze-dried vaccines (measles, BCG, yellow fever, and freeze-dried formulations of Hib) should not be transported to their point of use without ice since the ice will be needed to keep the vaccine cool after it is reconstituted.

## 3.9 How can we evaluate the impact of VVMs on the EPI?

Conduct a Knowledge, Attitudes and Practices (KAP) survey, based on a standard protocol. WHO and other agencies may be willing to assist in this type of evaluation.

Alternatively, introduce a checklist for district supervisors to check such points as the following:

- Are health workers interpreting VVMs correctly?
- Are the vaccines bearing VVMs being correctly handled?
- What is the level of vaccine wastage due to heat exposure now that VVMs are being used?
- Are there any negative consequences of using VVMs?

- Are there any unexpected benefits of using VVMs?
- Do health staff have ideas for other ways in which VVMs could promote a more efficient use of EPI resources?

# *4.* Getting started with Vaccine Vial Monitors (VVMs)

## 4.1 Which vaccines will be labelled with the VVM?

All OPV supplied through UNICEF has been labeled with VVMs since 1997. VVM availability on other EPI vaccines began in 2001 and VVMs should be available on all UNICEF-supplied EPI vaccines by 2002.

## 4.2 Can VVMs be included on vaccines that are not purchased through UNICEF?

Yes, Countries or agencies purchasing their own vaccines should include WHO-approved VVMs in the specifications provided to the vaccine manufacturers.

## 4.3 How will the VVM be integrated into the current immunization programme?

Extensive training at several levels must precede the introduction of the VVM. Cold room personnel and all staff responsible for vaccine storage and handling, from the central store to peripheral health centres, must be trained to read and interpret the VVM.

Health workers in the periphery will be trained to check every VVM before administering a vaccine. They will report any damaged vaccine to their supervisors who will in turn pass such reports on to the next level supervisor in the system.

## 4.4 What are the guidelines for the initial period when there might be some vials with VVMs and some without in the health centre stocks?

Vaccines with VVMs should be sent to the areas with the poorest cold chains. Once this has been done, the guiding rule is to use the vials without VVMs first.

Vials with VVMs should not be used as proxy indicators of heat exposure for vials without VVMs. Vials without VVMs should be handled as they always were.

# 5. Training

## 5.1 Which categories of personnel will require special training?

All staff members who handle vaccines (including stock managers, workers who transport vaccines, health workers, and National Immunization Day volunteers) need training to interpret the VVMs and to learn the vaccine handling policy that applies to vials with VVMs.

In addition, district managers need to learn about the changes to the monitoring system with respect to vaccine discarded once the VVM reaches its end-point.

## 5.2 How can this training be provided?

Existing health workers can learn about VVMs during refresher or special training, such as that given before National Immunization Days.

New health staff should learn about VVMs during their basic training. VVM interpretation and related policies should be introduced into their curricula.

# 6. IMPACT ON PROGRAMME OPERATIONS

## 6.1 How does the availability of VVMs affect the WHO policy regarding use of opened multi-dose vials of liquid vaccine in subsequent immunization sessions?

VVMs will provide added information on the heat-exposure status of opened vials of liquid vaccines (DTP, TT, DT, Td, hepatitis B, liquid formulations of Hib, and oral polio) that can now be used for longer time periods in accordance with this policy. Introduction of the policy can be tied to availability of VVMs on these vaccines. This decision depends on the risk of heat exposure and the flexibility of health workers in dealing with changes.

## 6.2 How is vaccine consumption affected by the use of VVMs and the implementation of the multi-dose-vial policy?

Vaccine wastage is expected to fall, especially in areas where the number of immunizations with the affected liquid vaccines is, on average, less than ten per session.

Vaccine wastage correction factors should be checked and adjusted by measuring vaccine wastage changes, particularly:

- in areas where wastage is already high;
- in areas where the cold chain is known to be weak;
- in areas where vaccine is beginning to be taken out of the cold chain.

In areas where the cold chain is poor or vaccine is taken out of the cold chain for long periods in hot weather, it is possible that wastage rates might increase.

## 6.3 How are EPI strategies affected by these changes?

Lower rates of vaccine wastage associated with the multi-dose vial policy should encourage re-establishment of the policy of immunization at every opportunity and more frequent immunization sessions.

In the past, high vaccine wastage rates discouraged EPI managers from advocating immunization at every opportunity, even though missed opportunity surveys

[1] See document: *WHO Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions.* (reference: WHO/V&B/00.09).

consistently show that significant improvements in immunization coverage can be achieved *and* sustained by immunizing at every opportunity.

If sessions are smaller and more frequent, wastage of freeze-dried vaccines (BCG, measles, yellow fever, and freeze-dried formulations of Hib vaccine) will tend to rise. One way of preventing this is to order freeze-dried vaccine in vials containing fewer doses per vial.

VVMs may extend the reach of mobile, NID and outreach operations and thus raise immunization coverage. In the past, immunization was curtailed once the icepacks melted and there was a fear that the vaccine might be impotent. VVMs, however, will show if there has been any heat damage to the vaccine and, if not, immunization can continue.

## 6.4 How should we monitor the wastage of vaccine once the VVMs are in use?

Quantities of vaccine discarded due to a VVM indication of excessive heat exposure should be specifically noted on inventory forms and reported to supervisors. Supervisors should review vaccine wastage statistics and strengthen the cold chain, supervise vaccine administration, or change vaccine orders as appropriate.

## 6.5 How can VVMs be introduced into the EPI?

At central level:

- Convene a national policy meeting to review the WHO literature on VVMs to decide on the changes to be made in local vaccine handling policies and develop a national strategy to introduce them. This meeting should produce a written official statement:

    outlining the changes in national vaccine handling policy;

    make necessary changes to vaccine inventory forms;

    scheduling the necessary briefings, training and distribution of materials;

    quantifying the training materials needed and the source of funds.

- Train district level managers in preparation for the arrival of VVMs on all vaccines.

At district level:

- Assign district managers the task of instructing heath centre personnel in the interpretation of the VVMs and the new vaccine handling policies as soon as possible after the first batches of vaccine with VVMs reach the field.

NOTE: Failure to inform managers and health workers is not likely to cause damage or disruption to the EPI. However, the benefits of using the VVMs will be delayed until training has been completed.

## 6.6 Can opened vials of measles, yellow fever, freeze-dried Hib, and BCG vaccine be used again the following day if the the VVM has not reached "discard point"?

No! Opened vials of measles, yellow fever, freeze-dried Hib, and BCG vaccines cannot be used beyond one immunization session. They **must** be discarded within 6 hours of reconstitution or at the end of the session, whichever comes first. The VVMs for these vaccines will be attached to the vial caps and should be discarded when the vaccine is being reconstituted.

[Before reconstitution, measles, yellow fever, freeze-dried Hib, and BCG are more heat stable than OPV. However, once they are opened and the diluent is added, they become less stable.]