To remain safe and effective, vaccines must be kept at the right temperature, but if they become damaged by heat or cold, they do not show any visible signs. The vaccine vial monitor (VVM) informs the healthcare worker if the vaccine vial has been exposed to high temperatures or not. The VVM is a heat indicator that is triggered by a temperature rise above a specified threshold. Therefore, any change in the color of the VVM indicates that the vaccine vial has been exposed to high temperatures for an undetermined amount of time.

This guideline has been prepared to provide healthcare workers with information on the different types of VVM that are attached to vaccine vials and on how to interpret the rate of the color change. The Pan American Health Organization (PAHO) has not issued a statement on the use of VVMs. Therefore, all immunization programs and healthcare workers should continue to follow the national guidelines/norms on the use of continuous temperature monitoring devices for the proper handling, storage, and distribution of vaccines. VVMs may provide information on whether vaccine vials have suffered heat exposure where there is no temperature monitoring device (TMD).

There are five different types of VVM designed for different types of vaccine, depending on the heat stability of the vaccine. The heat stability of a vaccine is dependent on how fast (the rate) a vaccine will lose its potency when exposed to ambient temperature. For classifying the heat stability of a vaccine, three temperature classes are used – 37 °C, 25 °C, or 5 °C – for assigning the length of time it will take for each VVM to reach its end point, when the square matches the dark color of the reference circle. Consequently, given the specific heat stability for a vaccine, as measured by the reaction rate in the change in the color of the VVM over time, each vaccine is assigned a specific VVM type.

Guidelines for healthcare workers on the proper interpretation of vaccine vial monitors and their use
Guidelines for healthcare workers on the proper interpretation of vaccine vial monitors and their use

Washington, D.C., 2023
Acknowledgments

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Introduction

To remain safe and effective, vaccines must be kept at the right temperature, but if they become damaged by heat or cold, they do not show any visible signs. The vaccine vial monitor (VVM) informs the healthcare worker if the vaccine vial has been exposed to high temperatures or not. The VVM is a heat indicator that is triggered by a temperature rise above a specified threshold. Therefore, any change in the color of the VVM indicates that the vaccine vial has been exposed to high temperatures for an undetermined amount of time.

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Description of the vaccine vial monitor

A VVM is a thermal label that is placed on a vaccine vial, prefilled syringe, ampoule, and other vaccine presentations. VVMs are small indicators that adhere to vaccine vials and change color as the vaccine is exposed to cumulative heat, letting health workers know whether the vaccine has exceeded a preset heat-exposure limit beyond which the vaccine should not be used (Figure 1). The VVM gives the user a visual indication of whether the vaccine has been kept at the temperature recommended by the manufacturer in order to preserve its potency. The square in the middle of each type of VVM label contains different chemical substrates that change color when the VVM label is exposed to high temperatures over time. Healthcare workers must be trained to interpret the color change(s) in the VVMs. If the color change is minimal, the vaccine can be used. But if the square displays a dark color that matches the reference circle which surrounds the square, the vaccine must not be used but be discarded following the safe disposal procedures and norms in place in each country (Figure 2). Independent of the color in the square, the vaccine must not be administered if it has reached its expiry date.

FIGURE 1  Vaccine vial monitors on vaccine vials

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The VVM label registers the cumulative heat exposure over time. The combination of the passage of time and exposure to higher temperatures causes the inner square of the VVM to gradually darken, and the color change is irreversible. The rate of color change and temperature change is referred to as heat exposure. Higher changes in temperature, especially abrupt changes, will cause a more rapid color change of the inner square. If a vial or vials show changes in the color in the square, it could be an indication of cold chain equipment malfunction or mishandling of the vaccine by the healthcare worker(s), which could include:

- Not using the proper cold chain container/cold box/vaccine carrier.
- Not using sufficient ice packs to keep the vaccine under 8 °C until it is used or arrives at its destination/delivery point.
- Not properly planning the amount of time for transporting the vaccine, given the route and conditions and type of transportation (fluvial; vehicle; rural, mountainous roads; or air travel).

**FIGURE 2** Infographic on interpreting vaccine vial monitor color change and decision-making

**Vaccine Vial Monitor (VVM)**

- **USE**
  - Square is lighter than outer circle
  - The colour of the inner square of the VVM starts with a shade that is lighter than the outer circle and continues to darken with time and/or exposure to heat.

- **DO NOT USE**
  - Square matches outer circle
  - Once a vaccine has reached or exceeded the discard point, the colour of the inner square will be the same colour or darker than the outer circle.
  - Square is darker than outer circle
  - Inform your supervisor

**Inform your supervisor**

**Discard point**

**Cumulative heat exposure over time**

There are five different types of VVM designed for different types of vaccine, depending on the heat stability of the vaccine. The heat stability of a vaccine is dependent on how fast (the rate) a vaccine will lose its potency when exposed to ambient temperature. For classifying the heat stability of a vaccine, three temperature classes are used – 37 °C, 25 °C, or 5 °C – for assigning the length of time it will take for each VVM to reach its end point, when the square matches the dark color of the reference circle. Consequently, given the specific heat stability for a vaccine, as measured by the reaction rate in the change in the color of the VVM over time, each vaccine is assigned a specific VVM type. Table 1 shows VVM reaction rates (number of days to change color) by heat stability category.

**Note:** Each VVM does not immediately change color when it is exposed to temperatures above 8 °C. The VVM reflects the heat stability of the vaccine to which it is attached and does not, therefore, undergo an immediate color 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. Remember, the rate at which the VVM changes color reflects the ability of that particular vaccine to withstand heat exposure.

### Table 1  Vaccine vial monitor (VVM) reaction rates by heat stability category and temperature exposure

<table>
<thead>
<tr>
<th>VVM TYPE (VACCINE HEAT STABILITY)</th>
<th>MAXIMUM TIME TO END POINT AT 37 °C</th>
<th>MAXIMUM TIME TO END POINT AT 25 °C</th>
<th>MAXIMUM TIME TO END POINT AT 5 °C</th>
<th>TIME TO END POINT AT 5°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>VVM30 High stability</td>
<td>30 days</td>
<td>193 days</td>
<td>NA*</td>
<td>≥4 years</td>
</tr>
<tr>
<td>VVM14 Medium stability</td>
<td>14 days</td>
<td>90 days</td>
<td>NA*</td>
<td>≥3 years</td>
</tr>
<tr>
<td>VVM11 Intermediate stability</td>
<td>11 days</td>
<td>71 days</td>
<td>NA*</td>
<td>≥2.5 years</td>
</tr>
<tr>
<td>VVM7 Moderate stability</td>
<td>7 days</td>
<td>45 days</td>
<td>NA*</td>
<td>≥2 years</td>
</tr>
<tr>
<td>VVM2 Least stable</td>
<td>2 days</td>
<td>NA*</td>
<td>225 days</td>
<td>NA*</td>
</tr>
</tbody>
</table>

*Note:* * VVM (Arrhenius) reaction rates determined at two temperature points. NA, not applicable.
Table 2 shows the estimated length of time it will take for the VVM to change from “start point” to “discard point” – i.e., to dark color – for a vaccine that is left at room temperature. The change in color depends on the room temperature and can vary greatly, according to the place, season, time of the day, and type of vaccine. Table 2 shows sample times recorded for a VVM attached to a vial of oral polio vaccine (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 most heat-stable vaccines.

**TABLE 2** Comparison of the estimated time for a vaccine vial monitor (VVM) to reach “discard point” for oral polio vaccine (OPV) and hepatitis B vaccine

<table>
<thead>
<tr>
<th>CONSTANT TEMPERATURE, DAY AND NIGHT</th>
<th>TIME FOR VVM ON A VIAL OF OPV TO REACH DISCARD POINT</th>
<th>TIME FOR VVM ON A VIAL OF HEPATITIS B VACCINE TO REACH DISCARD POINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refrigerator: 4 °C</td>
<td>240 days</td>
<td>5 670 days</td>
</tr>
<tr>
<td>Room temperature: 20 °C</td>
<td>20 days</td>
<td>385 days</td>
</tr>
<tr>
<td>Room temperature: 25 °C</td>
<td>10 days</td>
<td>176 days</td>
</tr>
</tbody>
</table>
The color change of the VVM due to heat exposure is irreversible, and change in the color of the VVM indicates possible loss of potency of the vaccine.

The VVM indicates the total accumulated heat exposure that a vaccine vial has been subjected to. Although the exact temperature reached and the duration are unknown, the darker the color (dark purple) of the square indicates that the VVM has reached the threshold of discard point.

If the vaccine inside the refrigerator freezes, will the VVM register any change? NO. The VVM is not affected by freezing temperatures and so it cannot give any information about freezing. The VVM is not designed to indicate exposure to freezing temperatures.

VVMs are manufactured in specific batches for each type of vaccine. Each VVM is designed to simulate the exact sensitivity of the vaccine to which it is attached. Therefore, each type of VVM is designed to cope with variations in heat tolerance given the heat stability for different types of vaccine. (See Table 1.)

The VVM does not change the vaccine’s sensitivity to heat exposure. It simply gives a visual 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 varies depending on the type of vaccine. (See Table 2 as an example.)

As long as the VVM shows a lighter color than the outer circle it still can be used. Is there a limit to the number of times an unopened vial can be taken for outreach (or used in National Immunization Days – NIDs)? NO, as long as the VVM square is not dark.

If the VVM shows some heat exposure but is not yet at discard point, these vaccines must be distributed for administration first. The VVM enables the storekeeper to pick out vaccine vials with VVMs that show color changes that do not match the color of the reference circle, instead of applying the practice of “first in, first out.”

All vaccines are sensitive to heat and will stay potent longer if they are kept refrigerated according to the manufacturer’s recommendations on storage temperature.
Vaccine vial monitor rules for decision-making

- Vaccine vials (and other vaccine presentation containers) with minimal heat exposure can be selected for use in outreach sessions or mobile services.

- Vials that register more heat exposure but are not showing colors that match the outer circle can be selected for use before those vaccine vials with VVMs which display less color change.

- Vials with VVMs whose squares match the dark colors with the reference color or outer circle cannot be distributed for administration.

- If a health worker has doubts about using a vaccine with a VVM that has changed color, or may not have changed color despite a known heat exposure, he or she should immediately contact the supervisor for guidance. The health worker should note:
  - the lot number and manufacturer;
  - date of expiry of the vaccine;
  - date that the vaccine arrived at the point of use; and
  - any information that the health worker has on estimated duration of the heat exposure and estimated ambient temperature.

- If many vials of the vaccine in question have VVMs with dark squares, the health worker should keep the vaccine in a refrigerator until the supervisor provides guidance on what actions to take with the vaccine.

**Note:** When various vials of vaccines with VVMs have reached their discard point, where the squares match the dark colors of the reference color or outer circle, health staff should investigate and identify the cause of this change by investigating cold chain problems or confirm poor vaccine handling practices. Problems could be:

- Refrigerator thermometers or loggers not working properly.

- Malfunctioning of refrigeration equipment, including refrigerated vehicles and cold boxes/vaccine carriers.

- Delays in the delivery of the vaccine due to vehicle mechanical problems.

- Not using the correct number of icepacks and/or not planning the distance and time required for a vaccine shipment to reach its delivery point while keeping the vaccine under 8 °C.

Health workers should document their findings and provide their supervisors with the results of their investigation for corrective actions to be taken.
Training

Integrating VVMs into the current immunization program will demand extensive training at all levels and must precede the introduction of the VVMs. Personnel responsible for the cold chain, supply chain, and logistics, and all staff responsible for vaccine storage and handling, from the central store to peripheral health centers, must be trained to read and interpret the VVM. Health workers in the periphery should be trained to check every VVM before administering a vaccine. They will report any vaccine with VVMs that have changed color or have reach their discard point to their supervisors, who will in turn pass such reports on to the next level supervisor in the system. Health staff who are colorblind or have visual impairments should not be responsible for making decisions on the use of a vaccine if the VVMs change color. They can take photographs and ask someone else to provide the color change of the VVM to a supervisor.
Establishing a vaccine vial monitor management information system

Good management practices regarding the introduction and use of VVMs requires an information system to be established to collect the number of VVMs showing a color change or dark squares, which is an indication of excessive heat exposure of the vaccines in question. This information should be collected by the health service point, along with the reason for the heat exposure and actions. More importantly, the health staff should report outbreaks of vaccine-preventable diseases among vaccinated individuals, especially if VVMs have been used.


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