Vaccine vial monitor (VVM) assignments for different WHO-prequalified vaccines and their proper handling

INFORMATION BULLETIN – July 2014

This information bulletin addresses the varied implications of different types of vaccine vial monitors (VVMs), notably VVM category type 7 (VVM7) and VVM category type 14 (VVM14), on vaccines such as the Inactivated Polio Vaccine (IPV) and the fully-liquid Diphtheria-Tetanus- whole cell Pertussis-Hepatitis B-Haemophilus influenzae type b (DTP-HepB-Hib, commonly referred to as pentavalent). The note is directed to countries that are currently supplied by UNICEF Supply Division with these specific presentations of vaccine. The information is intended for WHO/UNICEF staff, as well as EPI managers or other partner agencies which support immunization programmes.

I. Summary

Different VVM types present important implications for the handling of a given vaccine, as the VVM category assigned by WHO reflects the respective heat stability of the vaccine. **As discussed in this information note, vaccine products with a lower VVM assignment will naturally reach their discard point more quickly than those with a higher VVM assignment, even when stored within the +2˚C to +8˚C temperature range. Countries should be alert to the type of vaccine product they receive and are handling so that effective vaccine management measures are in place to preserve the life of the VVM for as long as possible.**

II. VVM assignments for IPV and DTP-HepB-Hib

At the time of this Information Note, *Table 1* lists the IPV and DTP-HepB-Hib vaccine products prequalified by WHO. Most pentavalent vaccine presentations come with a VVM of the thermostability category type 14 (VVM14). However, there is one vaccine product which is currently pre-qualified with a thermostability category type 7 (VVM7).

Similarly, for IPV, two manufacturers supply IPV with a VVM7 and a third supplies two different presentations of IPV with a VVM14, while yet another offers IPV in a ten dose vial with no VVM at all.

Specifications per WHO pre-qualified vaccine can be found on the individual vaccine product page, available online through the following link:

http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/

Table 1 *– Varied VVM types per manufacturer of fully liquid vaccines*

Manufacturer	Presentations (fully liquid)	Vaccine trade name	VVM type
Pentavalent Vaccine for Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenzae type b			
Biological E Limited, India	1 and 10 dose vials	N/A	7**
Crucell (Berna Biotech Korea)	1 dose vial	Quinvaxem	14
Panacea Biotec, India	1 and 10 dose vials	Easyfive-TT	14
Serum Institute of India Ltd, India	1, 2 and 10 dose vials	N/A	14
Shanta Biothech, India	1 and 10 dose vials	Shan5	14
Inactivated Poliomyelitis Vaccine			
Bilthoven Biologicals, Netherlands	1 dose vial *(5 dose available end 2014)*	Poliomyelitis vaccine	7
GlaxoSmithKline, Belgium	1 and 2 dose vials	Poliorix	14
Sanofi Pasteur, France	10 dose vial *(5 dose available end 2014)*	Imovax	7
Statens Serum Institute, Denmark	1 dose	IPV Vaccine SSI	7
** At the time of this information bulletin, this product is supplied with a VVM7. By the end of 2014, this pentavalent DTwP-HepB-Hib product will be supplied with a VVM14.			

III. Vaccine Vial Monitors and reaction rates

There are four types of VVM, which are assigned based on the different stability characteristics of the products. VVM product specifications can be found on the following site:

http://www.who.int/immunization_standards/vaccine_quality/who_pqs_e06_in05_rev_july2011.pdf

Table 2 below summarizes different levels of vaccine stability and VVM categories as well as the number of days that it would take a VVM to reach its end-point if it were exposed continuously to 37°C, 25°C and 5°C temperatures.

Table 2 *– VVM reaction rates by category of heat stability*

Category (Vaccines)	No. of days to end point at +37°C	No. of days to end point at +25°C	Time to end point at +5°C
VVM 30: High Stability	30	193	> 4 years
VVM 14: Medium Stability	14	90	> 3 years
VVM 7: Moderate Stability	7	45	> 2 years
VVM 2: Least Stable	2	N/A*	225 days
**VVM (Arrhenius) reaction rates determined at two temperature points*			

Vaccine produced by different manufacturers may have different heat stability characteristics and may therefore be assigned a different VVM category by WHO, based on the thermostability data available. As VVM reaction rates differ by VVM category, vaccine products with different VVM assignments will behave differently under the same cold chain conditions. For example, as illustrated in *Table 3*, VVM7 can react twice as fast to heat than the VVM14 under the same temperature conditions. Consequently, one must never compare a VVM on one product with the VVM on another product.

Table 3 *– VVM7 and VVM14 reaction to various temperatures for 365 days*

Temperature	VVM7 days lost (in percent)	VVM14 days lost (in percent)	VVM7	VVM14
Start point	0	0		
5°C	38%	19%		
6°C	45%	23%		
7°C	54%	27%		
8°C	64%	32%		

Additional guidance on how to interpret VVMs is offered in the instructional video available at the following link: https://vimeo.com/58747176. ("*How does a VVM work*", by Denis Maire, WHO)

IV. Temperature Monitoring and Stock Control

Effective vaccine management dictates that temperatures to which vaccines are exposed must be monitored, recorded and reported throughout the vaccine supply chain, from the manufacturer's point of origin to the point of vaccination. This provides documented evidence of the temperatures to which products have been exposed during storage and transport; it also provides a means to detect cold chain equipment failures and other operational problems so that they can be rectified. To achieve these outcomes, countries should develop suitable policies and standard operating procedures (SOPs) and provide adequate training, tools, and resources to ensure that these policies and procedures are properly implemented.

Responsible personnel need to know the correct storage conditions for all vaccines in their country's schedule, and pay particular attention to keeping vaccines within manufacturer's or WHO's recommended temperature intervals of +2˚C and +8 ˚C, or between -15 ˚C and -25 ˚C, as relevant. They should know how to use the appropriate temperature monitoring devices, how to recognize and respond to temperature excursions, how to record temperatures and how to take corrective action when problems occur.

It is also important to note that the handling of products with VVM7 assignment requires more vigilance than products with VVM14, given the increased susceptibility to heat of these vaccines. Cold rooms should be temperature mapped to identify hot and cold zones, such that products with VVM7 should be stored in the appropriate part of the room to prolong the product's VVM life.

Country resources to support proper temperature monitoring and stock control are available at the WHO-UNICEF Effective Vaccine Management link:

http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index2.html

Furthermore, the importance of evaluating VVM status with respect to vaccine expiry must be kept in mind when managing stocks. While the "*earliest expiry, first out*" principal usually applies in vaccine stock management, the status of a VVM overrules this, whereby any batch showing a darker VVM should be used sooner, regardless of a later expiry date. This highlights the necessity to review the status of the VVM of each vaccine batch in order to maintain the integrity of the stocks throughout the time a vaccine is stored or transported in the cold chain. The color change of the inner square of the VVM reflects the cumulative effect of time and temperature exposure on the vaccine. Even if a vaccine vial is kept within recommended temperature ranges, the inner square of the VVM will naturally darken over time. Furthermore, even within the recommended temperature range of +2˚C to +8 ˚C, the VVM will darken at a faster rate if the average temperature is closer to +8°C. This color change becomes more evident when comparing VVM7 to VVM14. For more detail on using VVM as a stock management tool, please consult the following instructional video: https://vimeo.com/58161022. ("*Using VVM as a stock management tool*", by Umit Kartoglu, WHO)

V. Future communications

For any inquiries or concerns on this issue, please contact the following UNICEF or WHO personnel:

***Bertrand Jacquet**, Supply Chain Specialist*
UNICEF Supply Division
Tel: +45 45 33 55 97
E-mail: bjacquet@unicef.org

***Anna-Lea Kahn,** Technical Officer, EPI*
World Health Organisation
Tel: +41 22 791 31 35
Email: kahna@who.int