INFORMATION BULLETIN – March 2017

Change in vaccine vial monitor (VVM) assignment for GlaxoSmithKline Rotarix® product

This information bulletin addresses the implications and required guidance associated with the upcoming scheduled shift in vaccine vial monitor (VVM) of the GlaxoSmithKline Biologicals SA (GSK) Rotavirus vaccine, Rotarix®, from VVM type 14 (VVM14) to VVM type 7 (VVM7). The information below is intended for WHO/UNICEF staff, as well as Expanded Program for Immunization (EPI) managers or other partner agencies which support immunization programmes.

Summary

A WHO statement on Rotarix® and VVM compliance was released in February 2017, indicating that in Quarter 3 2017, **the VVM attached to the current Rotarix® product is expected to change from a VVM 14 to a VVM7**.[i] This change was deemed necessary by GSK and WHO in light of new information that the stability of the product under accelerated temperature studies is better reflected by a different VVM type, with a shorter discard point, given that some batches fall below specification following storage for more than 45 days at 25°C or higher. While such circumstances could theoretically affect vaccine potency, the safety profile of the vaccine remains the same. Furthermore, GSK has provided WHO with clinical trial data that support the conclusion that this VVM compliance concern carries no risk if the vaccine is stored in a 2–8°C cold chain as per the product's label. Storage above these temperatures carries a very low public health risk. Even if a child received the two recommended doses from an affected batch of Rotarix, vaccine efficacy can still be expected.

Since discovering this VVM compliance issue, GSK has taken precautionary measures to modify the internal release limit for potency until the product can be supplied with the VVM7. This will ensure that current batches with VVM14 will continue to meet full potency specifications. The implication is that global vaccine availability of Rotarix® will be impacted in 2017. This has therefore led to some delays in shipment, which UNICEF is communicating about separately with affected countries.

It is recognized that there will be a period of transition from use of Rotarix® with a VVM14 to use of Rotarix® with a VVM7, during which specific vaccine management practices are advisable. These are highlighted below, organized under six critical questions of which UNICEF and WHO consider that stakeholders should be aware. Should additional questions or uncertainties as to appropriate practices arise, contact points are provided for further guidance.

I. What should be done with current stock of Rotarix® with VVM14 in my programme? Can we still use it or will it be recalled?

If you currently have stock of Rotarix® with a VVM14 or receive a shipment of this version of the vaccine, you can and should still use it. The evidence indicates that there are no concerns as to the quality of the product and therefore no product recall is required for Rotarix® with a VVM14. The vaccine is safe and can continue to be used safely as before, provided that appropriate cold chain adherence has occurred. Health workers and vaccinators should be advised to continue to administer this vaccine.

II. Why and when is it still suitable to use the Rotarix® with a VVM14?

As indicated in the WHO statement, only temperature excursions at 25˚C or higher for over 45 days could lead to sub-potent vaccine without the VVM 14 indicating a need to discard. Consequently, while handling Rotarix® with a VVM14, extra attention should be placed on correct cold chain practices, including the use of continuous temperature monitoring devices, where appropriate and as recommended by WHO and UNICEF.[ii] In the unlikely event that Rotarix® with a VVM14 undergoes an accidental temperature excursion above 25°C, for a duration exceeding 45 days, please consult WHO or UNICEF through the contact information provided below for further guidance. Apart from such a scenario, there should be continued reliance on the VVM as per established practices.

[i] http://www.who.int/immunization_standards/vaccine_quality/Rotarix_VVM_Statement-Feb2017.pdf

[ii] WHO Vaccine Management Handbook. Module VMH-E2-01.1. *How to monitor temperatures in the vaccine supply chain*. July 2015. Available at: http://apps.who.int/iris/bitstream/10665/183583/1/WHO_IVB_15.04_eng.pdf. UNICEF Agora E-Course. *Temperature monitoring in the vaccine cold chain*. Accessible at: https://agora.unicef.org/course/info.php?id=6645.

III. When will my programme receive a vaccine batch with the new VVM assignment?

Rotarix® with a VVM7 will not be available before Q3 of 2017. Countries will therefore continue to receive Rotarix® with a VVM14 during this transition period and some may still do so for a certain amount of time past the launch of Rotarix® with a VVM7. In order to avoid interruption to ongoing programs, UNICEF will work closely with the manufacturer to plan shipments with countries. As noted above, Rotarix® with a VVM14 can continue to be used provided that appropriate cold chain practices are maintained throughout the supply chain.

UNICEF Supply Division will issue a new shipment plan to countries in mid-March 2017.

IV. What is the difference between a VVM14 and a VVM7?

Different VVM types have important implications for the handling of a given vaccine, as the VVM category assigned by WHO reflects the respective heat stability of the vaccine. **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.

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.

Table 1 – 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 ("*How does a VVM work*", by Denis Maire, WHO) available at the following link.

https://vimeo.com/58747176

V. How can I make sure the vaccines stay potent?

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 of detecting 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 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 Rotavirus vaccines, as with all vaccines in their country's schedule, and pay particular attention to keeping vaccines within the manufacturer's and WHO's recommended temperature intervals of +2˚C and +8˚C. In the case of Rotarix®, **irrespective of the VVM, the product must not be frozen**. Appropriate temperature monitoring devices must be used and fully understood, including 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. Cold rooms should be temperature mapped to identify hot and cold zones, and products with VVM7 should be stored in the appropriate part of the room to prolong the product's VVM life. and ensure the product's potency.

In addition to the resources provided in this document's endnotes, 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

VI. What do I do if I have both the Rotarix® with VVM14 and the Rotarix® with VVM7 in the cold chain system?

Countries are encouraged to use up Rotarix® stocks with the VVM14 first, as these are likely to have the earliest expiry date. However, apart from a scenario of an extended accidental excursion as described above, the VVM should be the guiding determinant in prioritizing use.

Evaluating VVM status with respect to vaccine expiry remains critical when managing stocks, regardless of which type of Rotarix you have. While the "earliest expiry, first out" principle 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 of reviewing 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 colour 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 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 colour 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 ("Using VVM as a stock management tool", by Umit Kartoglu, WHO).

https://vimeo.com/58161022.https://vimeo.com/58161022

Future communications

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

Gideon Chelule
Contracts Manager, Rotavirus Vaccine
UNICEF Supply Division
Tel: +45 45 33 5781
Email: gchelule@unicef.org

Anna-Lea Kahn
Technical Officer, Supply, Technologies, and Financing
World Health Organization – Expanded Program for Immunization (EPI)
Tel: +41 22 791 31 35
Email: kahna@who.int

World Health Organization
Expanded Programme on Immunization
20 Avenue Appia, 1121 Geneva 27
Switzerland
vaccines@who.int
www.who.int

United Nations Children's Fund
3 United Nations Plaza
New York, NY 10017
USA
immunization@unicef.org
www.unicef.org