Adapting VVM for the Next Generation Supply Chain

28 October 2018
Temptime Continues to Adapt VVM for Evolving Program Needs

- Improved VVM7
- New VVM types (VVM11 and VVM250)
- VVM+®: combined VVM and peak threshold indicator
- Hybrid 2D Bar Codes with embedded VVM active area or threshold indicator
- EDGE Electronic Devices
Landscape of vaccine product attribute innovations in scope of VIPS

Scope of innovations: antigen-agnostic or antigen-specific

Primary containers
- i.e. Compact pre-filled autodisable device (cPAD);
- Blow-fill-seal (BFS) container
- Dual-chamber technology;
- Microarray patch (MAP);
- Optimised doses per container;
- Multi-mono-dose;
- Pre-filled syringe;
- Cartridge based injection

Formulation
- i.e. Heat-stable formulations;
- Freeze-stable formulations

Packaging
- i.e. Bundling accessories;
- Packed volume

Labelling
- i.e. barcode including global trade item number (GTIN);
- temperature indicators

Delivery technologies
- i.e. Autodisable syringe;
- Reuse prevention (RUP) syringe;
- Safety syringe;
- Sharps injury protection (SIP) syringe;
- Biodegradable implant injector (w/ biodegradable implant formulation);
- Disposable syringe jet injector;
- Dry powder inhaler;
- Nebuliser;
- Liquid intranasal spray or drop device;
- Needle-based intradermal delivery device;
- Electroporation device;
- Fast-dissolving tablets;
- Sublingual films;
- Thermo-responsive gels;
- Intradermal adapter
Evolution of VVM Types

- 1996 - VVM2 for OPV
- 2002 - VVM7, VVM14 and VVM30 added
- 2018 - VVM11 and VVM250 added
- 2018 – Combined VVM and peak threshold indicator in development
VVM7 - Improved

5 years of research at cost of $2 million to adjust formulation

- VVM7 - improved
  - VVM7 naturally develops color at 5°C over the course of two years
  - Current specification is ≥ 2 years to end point at 5°C
  - Improved formulation for full label is ≥ 2 years 4 months to end point at 5°C and typical time of 2 years and 6 months
  - Improved formulation for dot construction is ≥ 2 years 8 months to end point at 5°C and typical time of 2 years and 10 months
  - Now approved for use by WHO
  - No premium charge for improved VVM7
VVM Line Extensions to Address Programmatic Needs: VVM11

- Why VVM11
  - Some vaccines have stability > VVM7 but < VVM14
  - Some vaccines have moved to 3 year expiry date but with < 14 days at 37°C
  - Change to statistical modeling of vaccine stability can possibility lead to a lower VVM type
    - e.g., VVM14 now would revert to VVM7
- VVM11 fills the gap between VVM7 and VVM14
  - Provides ≥ 2.5 years at 5°C
  - Project initiated based initially on potential IPV stability
- Status
  - Prequalified and now included in new VVM specification
- No premium charge for VVM11

<table>
<thead>
<tr>
<th>Type (Vaccines)</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>

*VVM (Artemis) reaction rates determined at two temperature points
VVM Challenge – Highly Stable Rotavirus Vaccine
540 days at 37°C

Stability of heat stable, live attenuated Rotavirus vaccine (ROTASIIIL®)

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The thermo-stability of ROTASIIIL®, ironically, has thrown up a new challenge in terms of vaccine vial monitors (VVM). The presently available VVM portfolio (Max VVM30: 30 days at 37 °C) does not begin to cover the extreme thermo stability of ROTASIIIL which is 18 months- (540 days) at 37 °C. Efforts to develop a more appropriate VVM are on-going.

It has been already noted that there is remarkable reduction in mortality from diarrheal disease after vaccine introduction in
VVM 250 Specifications

Table 1b: VVM reaction rates by type

<table>
<thead>
<tr>
<th>Type (Vaccines)</th>
<th>Maximum time to end point at +55°C</th>
<th>Maximum time to end point at +45°C</th>
<th>Approximate Maximum time to endpoint at +37°C</th>
<th>Time to end point at +25°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>VVM250: Very High Stability</td>
<td>17 days</td>
<td>73 days</td>
<td>250 days*</td>
<td>≥900 days</td>
</tr>
</tbody>
</table>

*VVM (Arrhenius) reaction rates determined at 55°C and 45°C, the 37°C values are approximate.

Samples submitted to independent lab for testing
Now Six VVM Types

VVM11 and VVM250 added on 18 May 2018 for six VVM types
HEATmarker VVM+
VVM Plus Peak Indicator in Same Device

- VVM+ reacts like a VVM up to 37°C
- At 40°C, VVM+ reaches the end point rapidly to show exposure to critical peak temperature
Concern with Exposures Above 40°C for Vaccines Stored at Room Temperature

Vaccines stored at room temperature (Rotasiil) may likely be exposed to inadvertent excursions to very high temperatures.

VVM+250
WHO and Serum Institute of India agree on VVM+250 for Rotasiil

Prequalification activities underway
Add another dimension to 2D barcodes with embedded temperature monitoring

2D Barcode with Embedded Temperature Sensor
• **VVM** – gradual, irreversible color change from light to dark develops with cumulative time and temperature exposure

Before heat exposure

After excessive heat

Time and temperature exposure
Transformational Innovation: 2D Barcode with Temperature Sensor
Digitize Chemical Indicators with Unit of Sale Level Data Connection

Enhance the value of 2D barcodes (for stock management, patient safety and anti-counterfeiting) by incorporating temperature integrity:

- Specific area has cumulative (VVM) and/or threshold ink printed as part of barcode
- Rapid reading with phone or scanner
- Connect with cloud based data set of other sensors
Status of OneScan App Development

• Finalizing algorithm for threshold indicator
• Optimizing algorithm for VVM color shade reading
• GS1 and AIM approval of Application Identifier (AI) for threshold indicator imminent, TTI/VVM in process
15th TechNet Conference – Cascais Portugal

Building the next generation immunization supply chain

2D Barcode with embedded VVM wins Pitch Fest
Proof of Concept Pilot in India – Phase 1

- Apply 2D barcode label with VVM on secondary cartons at manufacturer
- Scan cartons on shipment out and receipt at each transfer to district level using smartphone with OneScan™ app
- Automated data collection and digitized VVM readings
- Push data to the cloud
- Understand interoperability with eVIN

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1 Dr. Pradeep Haldar Ministry of Health and Family Welfare, India
15th TechNet Conference Portugal, 16-20th October, 2017
Continuous End-to-End Temperature Monitoring with Dynamic 2D Barcode Indicator

Serialized barcodes on individual saleable units are a key enabling technology of global identification and tracking regulations.

The OneScan™ System
- Merges unit serialization and temperature monitoring in a single scan
- Improves stock management
- Enhances product integrity, patient safety, supply security and temperature compliance without inference

End-to-end unique identifier and unique temperature monitor
EDGE™ Portfolio

Transport/Facility Data Loggers

Wireless Facility Data Loggers
## EDGE Transport Solution vs USB dataloggers

<table>
<thead>
<tr>
<th>Feature</th>
<th>Bluetooth</th>
<th>USB Port</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication Technology</td>
<td>✓</td>
<td>✗ (pre-defined)</td>
</tr>
<tr>
<td>Versatile configurations</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>Multiple Start-Up Modes</td>
<td>✓ (4)</td>
<td>✗</td>
</tr>
<tr>
<td>Handling time to access data</td>
<td>10 sec</td>
<td>10+ minutes</td>
</tr>
<tr>
<td>Ability to read data mid-shipment</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>Datalogger reset available</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>Read data through packaging</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>Automatic data transfer to Cloud</td>
<td>✓</td>
<td>✗</td>
</tr>
</tbody>
</table>
Dynamic Barcodes Allow Unit Level Data Connection from Manufacture to End Use
THANK YOU!!!