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

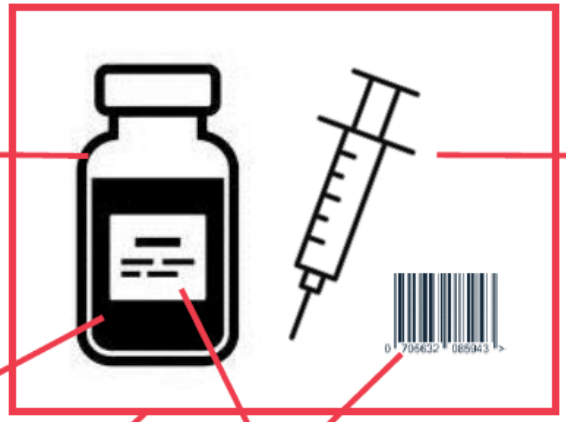
Landscape of vaccine product attribute innovations in scope of VIPS

VIPS VACCINE INNOVATION PRIORITISATION STRATEGY

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



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

Formulation

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

Labelling

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

Packaging

i.e. Bundling accessories; Packed volume

Gavi The Vaccine Alliance · World Health Organization · Bill & Melinda Gates foundation · PATH · unicef

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

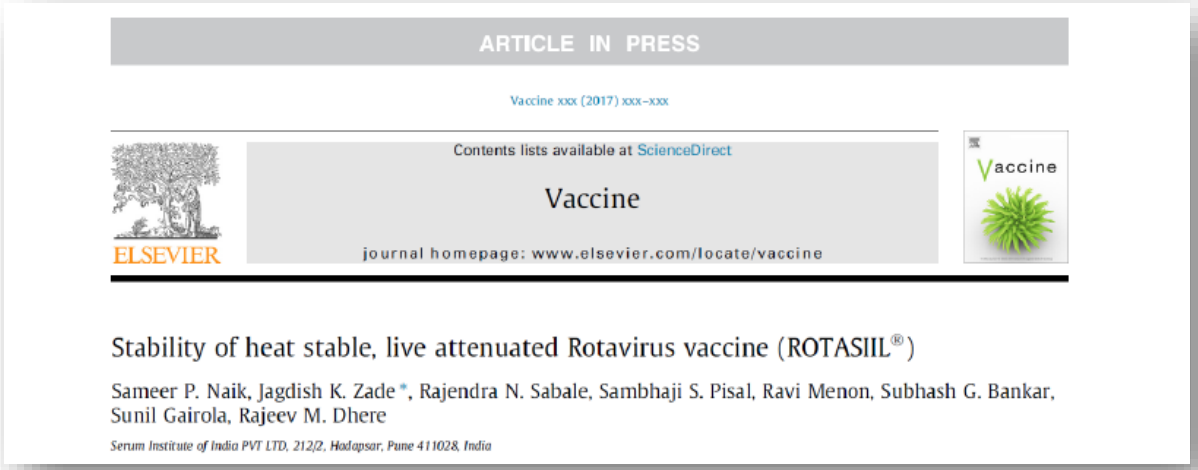
- Why VVM11
  - Some vaccines have stability > VVM7 but < VVM14
  - Some vaccines have moved to 3 year expiry date but with < 14 days at 37°C
  - Change to statistical modeling of vaccine stability can possibility lead to a lower VVM type
    - e.g., VVM14 now would revert to VVM7
- VVM11 fills the gap 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 1: VVM reaction rates by type

Type (Vaccines)	Maximum time to end point at +37°C	Maximum time to end point at +25°C	Maximum time to end point at +5°C	Time to end point at +5°C
VVM30: High Stability	30 days	193 days	NA*	≥4 years
VVM14: Medium Stability	14 days	90 days	NA*	≥ 3 years
VVM11: Intermediate stability	11 days	71 days	NA*	≥2.5 years
VVM7: Moderate Stability	7 days	45 days	NA*	≥2 years
VVM2: Least Stable	2 days	NA*	225 days	NA*

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

VVM Challenge – Highly Stable Rotavirus Vaccine
540 days at 37°C



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Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

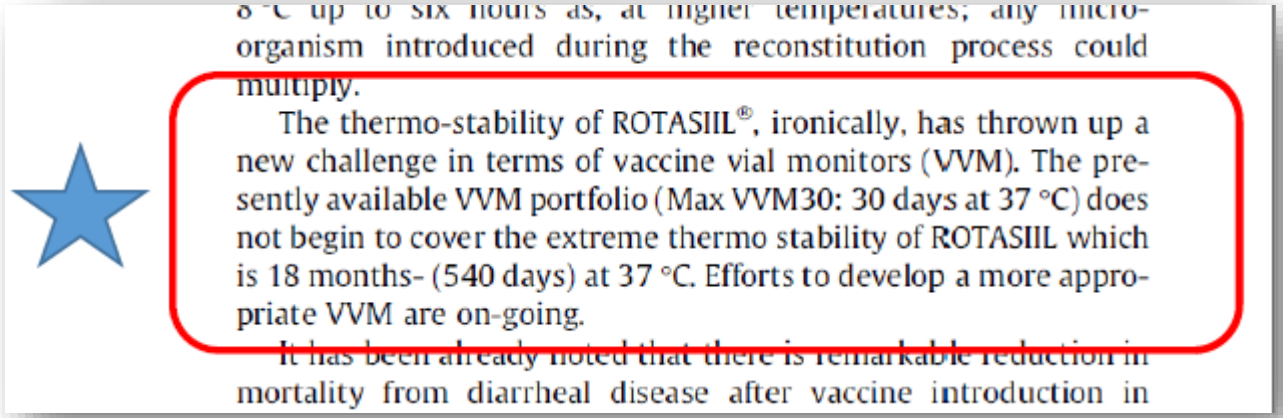
Vaccine

journal homepage: www.elsevier.com/locate/vaccine

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

Sameer P. Naik, Jagdish K. Zade *, Rajendra N. Sabale, Sambhaji S. Pisal, Ravi Menon, Subhash G. Bankar, Sunil Gairola, Rajeev M. Dhere

Serum Institute of India PVT LTD, 212/2, Hadapsar, Pune 411028, India



8 °C up to six hours as, at higher temperatures, any micro-organism introduced during the reconstitution process could multiply.

The thermo-stability of ROTASIIL®, 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 ROTASIIL 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

PQS performance specification

WHO/PQS/E006/IN05.3
Original: English
Distribution: General

TITLE: Vaccine Vial Monitor	
Specification reference:	E006/IN05.3
Product verification:	E006/IN05.VP.3
Issue date:	15 May 2018
Date of last revision:	19 January 2012

Table 1b: VVM reaction rates by type

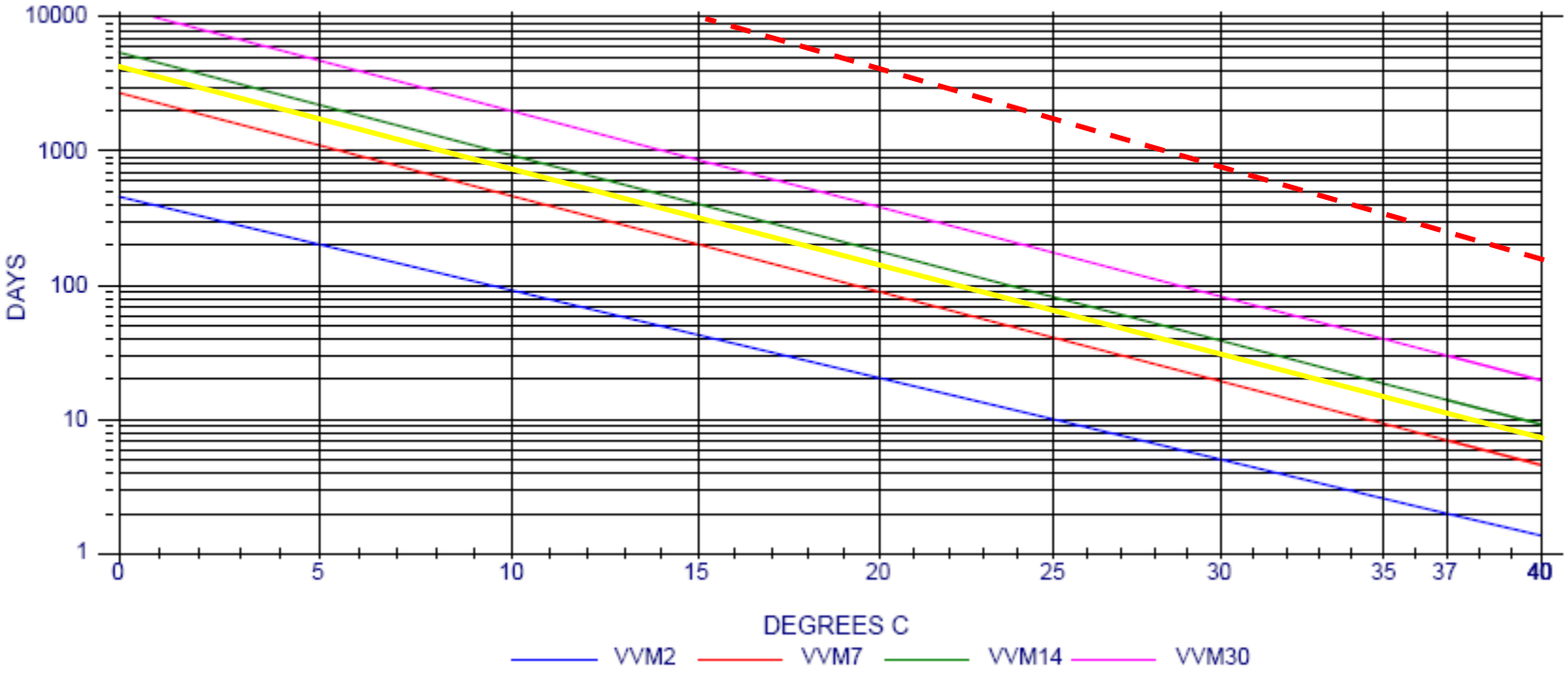
Type (Vaccines)	Maximum time to end point at +55°C	Maximum time to end point at +45°C	Approx-imate Maximum time to endpoint at +37°C	Time to end point at +25°C
VVM250: Very High Stability	17 days	73 days	250 days*	≥900 days

**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

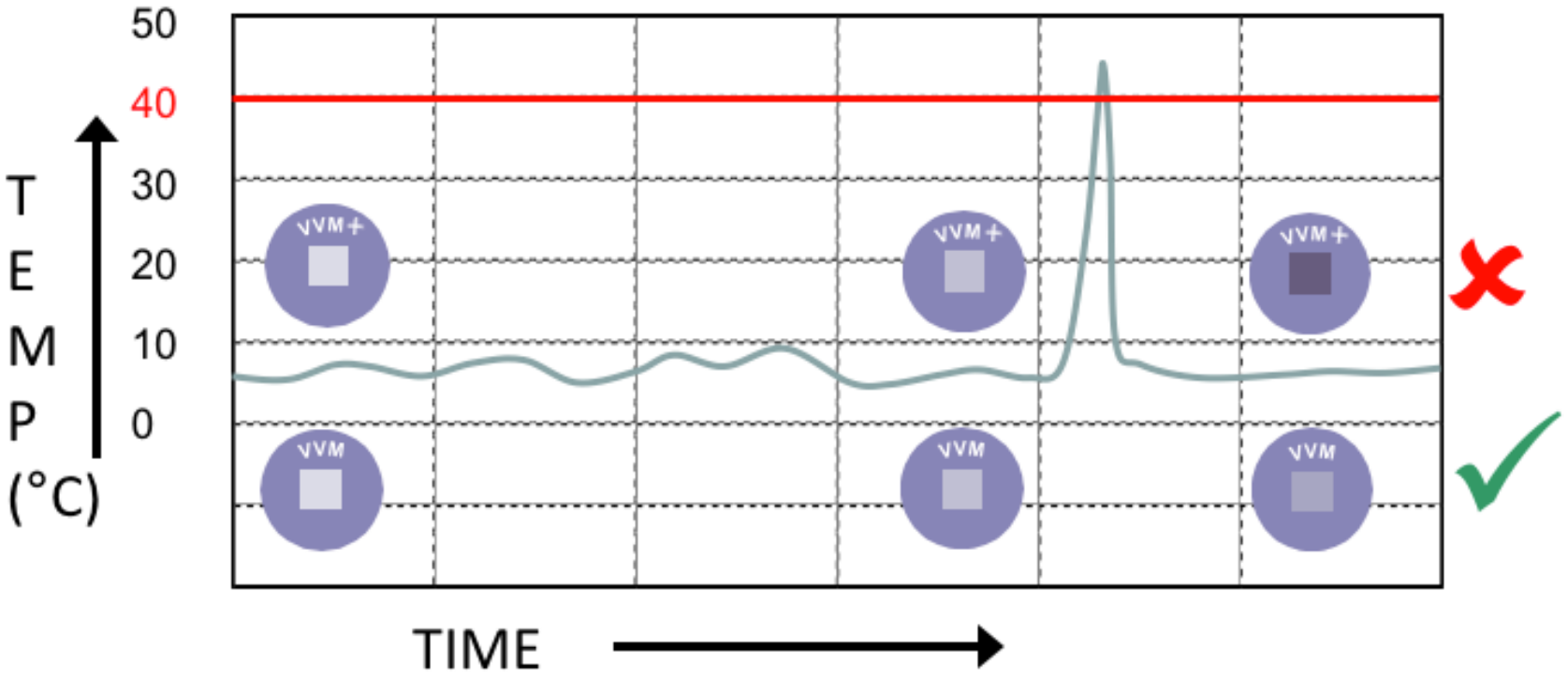
VVM11 and VVM250 added on 18 May 2018 for six VVM types



VVM11 VVM250

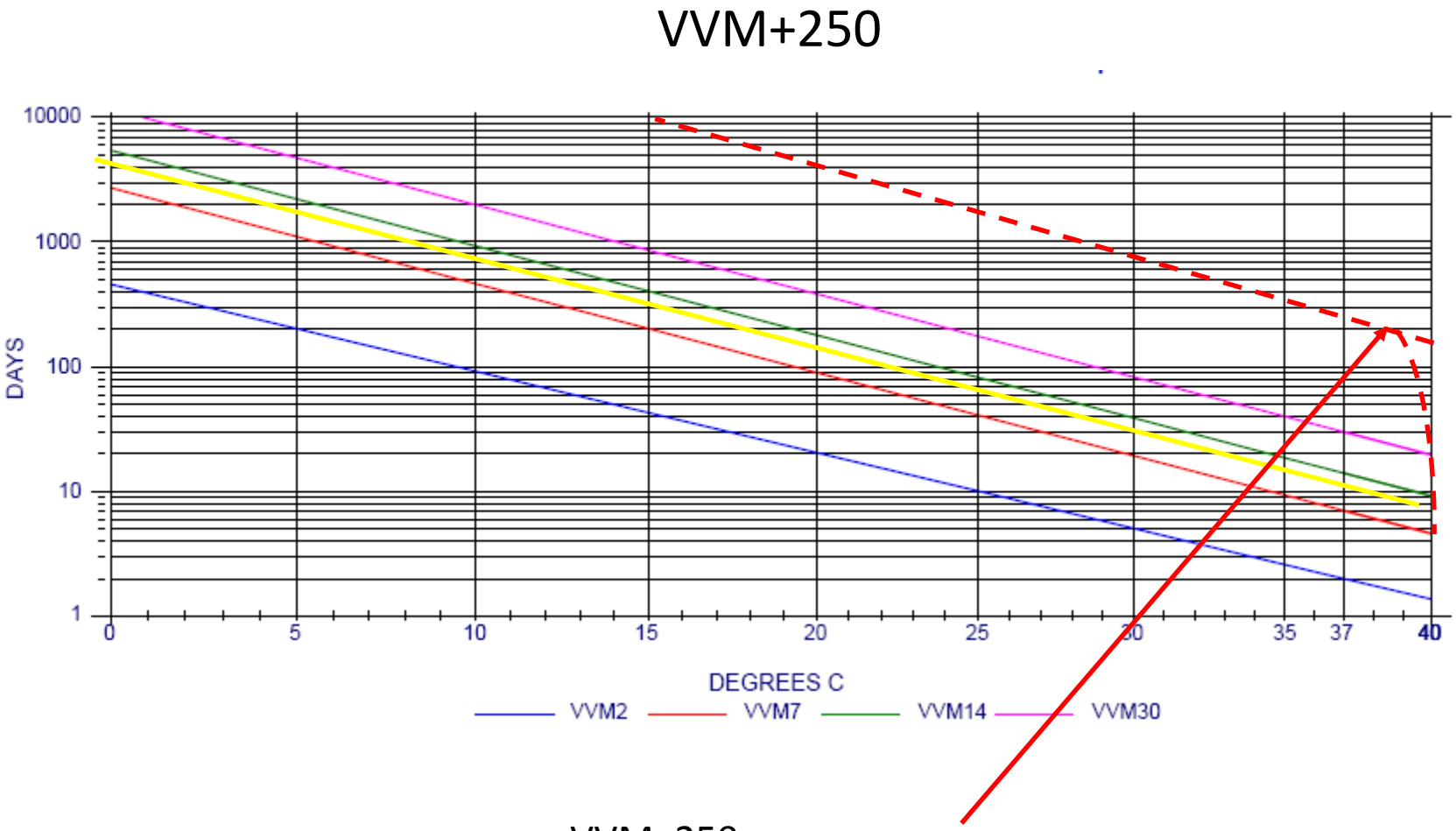
HEATmarker VVM+
VVM Plus Peak Indicator in Same Device

- 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



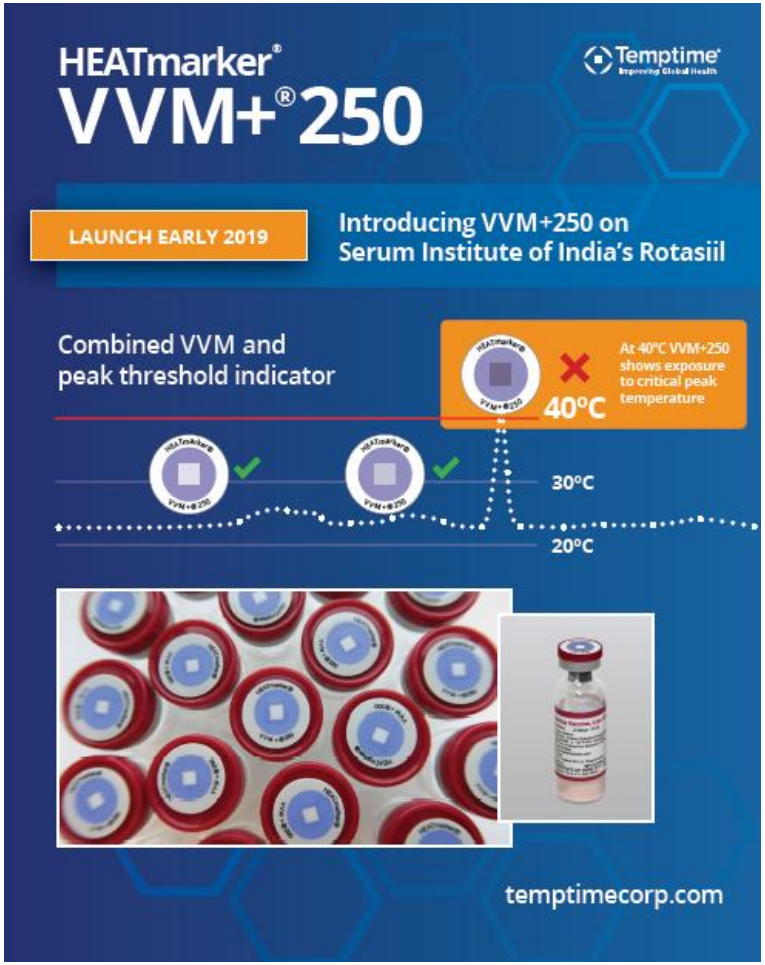
Concern with Exposures Above 40°C for Vaccines Stored at Room Temperature

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



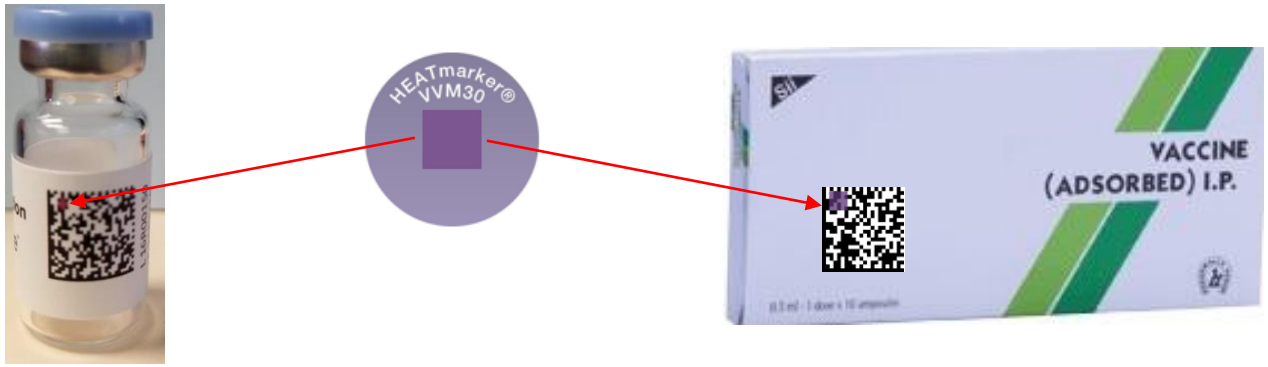
WHO and Serum Institute of India agree on VVM+250 for Rotasiil

Prequalification activities underway



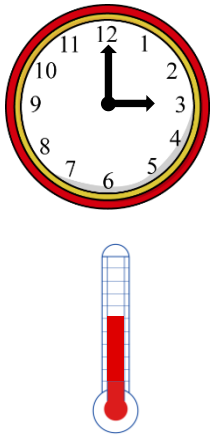
Add another dimension to 2D barcodes with embedded temperature monitoring

2D Barcode with Embedded Temperature Sensor

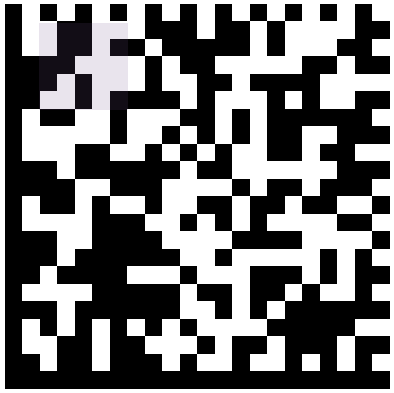


GS1 2D Data Matrix with Vaccine Vial Monitor (VVM)

- **VVM** – gradual, irreversible color change from light to dark develops with cumulative time and temperature exposure



Before heat exposure



Time and temperature exposure

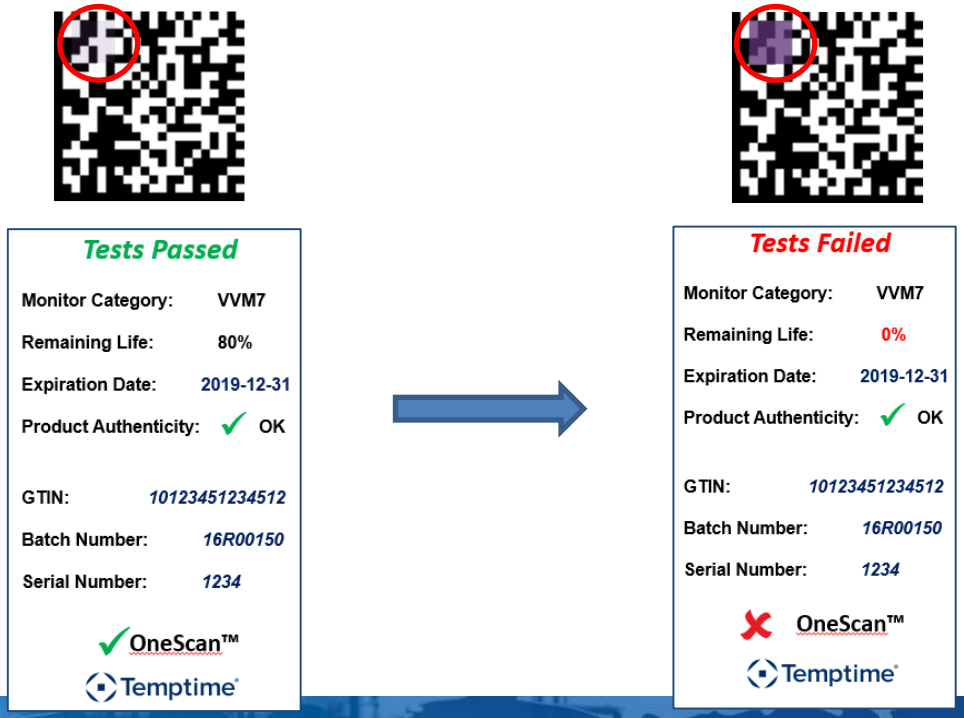
After excessive heat

Transformational Innovation: 2D Barcode with Temperature Sensor

Digitize Chemical Indicators with Unit of Sale Level Data Connection

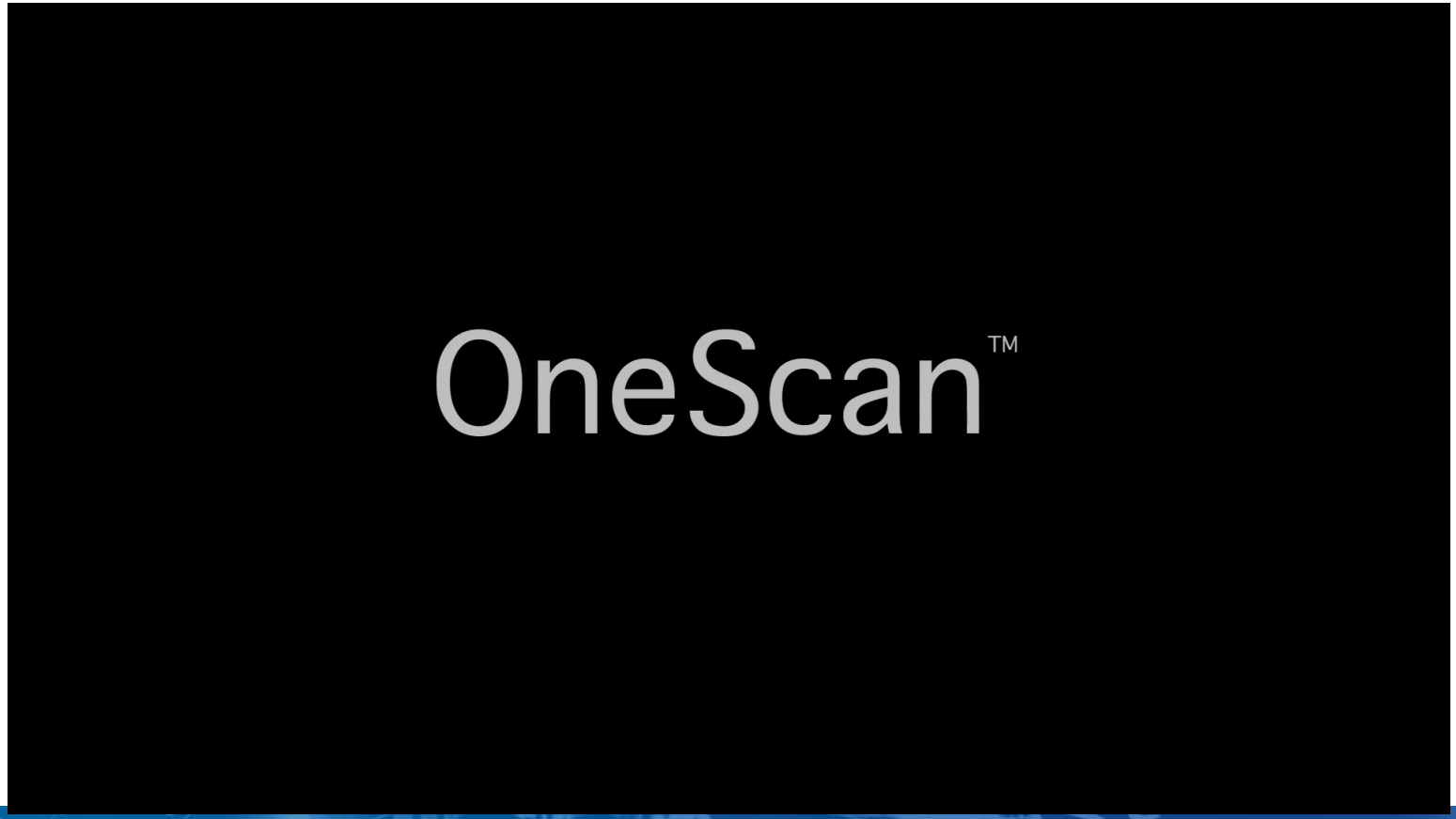
Enhance the value of 2D barcodes (for stock management, patient safety and anti-counterfeiting) by incorporating temperature integrity

- 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



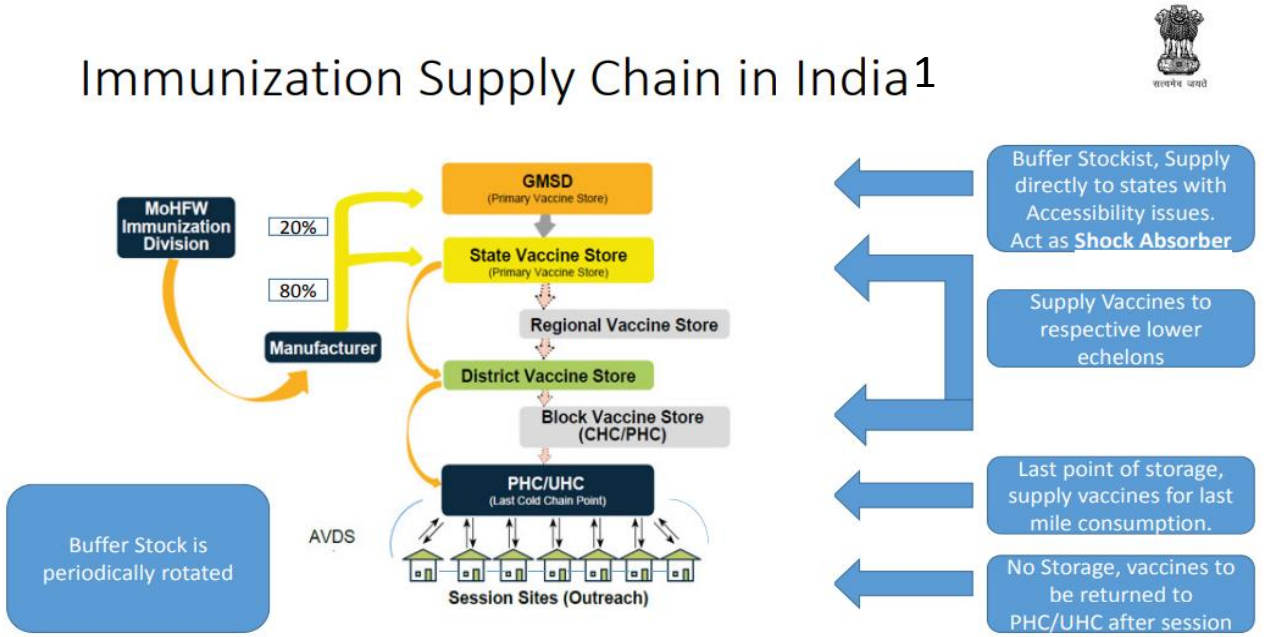
15th TechNet Conference – Cascais Portugal

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



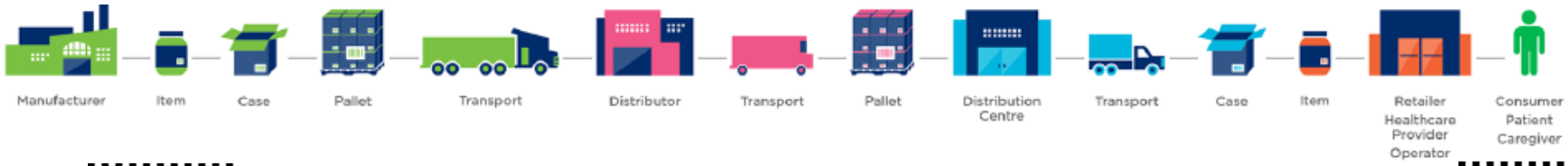
[1] Dr. Pradeep Haldar Ministry of Health and Family Welfare, India
15th TechNet Conference Portugal, 16-20th October, 2017

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

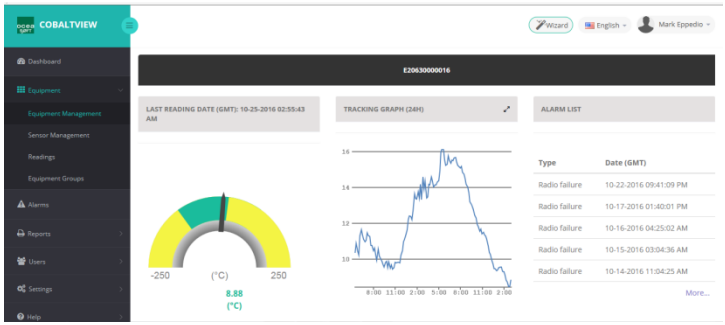


End-to-end unique identifier and unique temperature monitor

EDGE™ Portfolio

Transport/Facility Data Loggers

Wireless Facility Data Loggers



EDGE Transport Solution vs USB dataloggers

Communication Technology	Bluetooth	USB Port
Versatile configurations	✓	✗(pre-defined)
Multiple Start-Up Modes	✓(4)	✗
Handling time to access data	10 sec	10+ minutes
Ability to read data mid-shipment	✓	✗
Datalogger reset available	✓	✗
Read data through packaging	✓	✗
Automatic data transfer to Cloud	✓	✗

Dynamic Barcodes Allow Unit Level Data Connection from Manufacture to End Use

THANK YOU!!!