VVM Innovation

Thermostability monitoring of vaccines for global supply

Why bother about temperature monitoring ?

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Objectives of the immunization supply chain	Impacts of temperature excursions…	
	If undetected	If detected
Availability of vaccines at the right place in the right time		Potential stockouts
Vaccines are potent and have not been impacted by temperature excursions	Potential damaged	
Resources are used efficiently	May not achieve sero-conversion	Wastage

Temperature monitoring: detects excursions and can help avoid future excursions

Challenges in vaccine Cold Chain management

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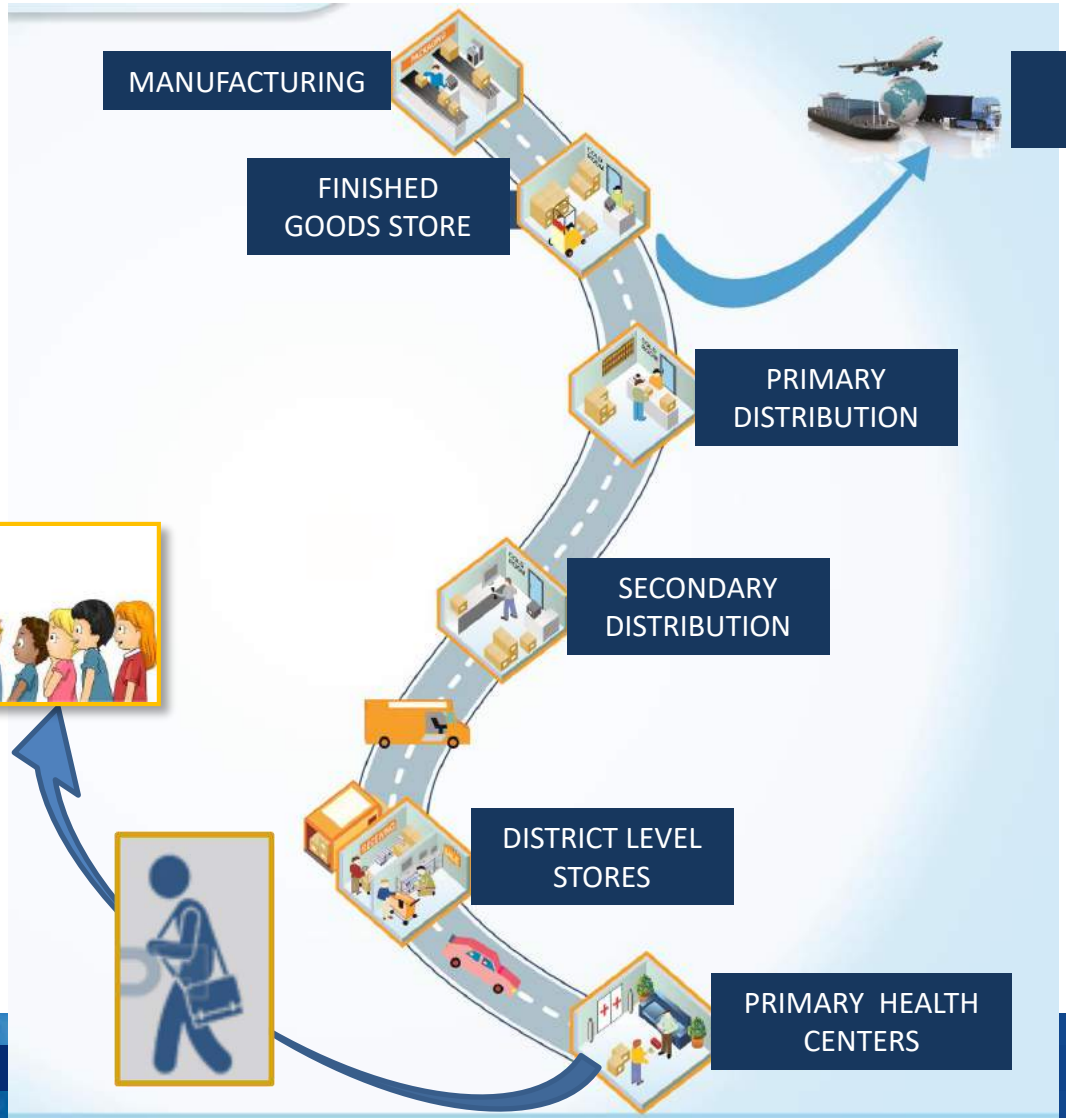

Challenges in vaccine Cold Chain management

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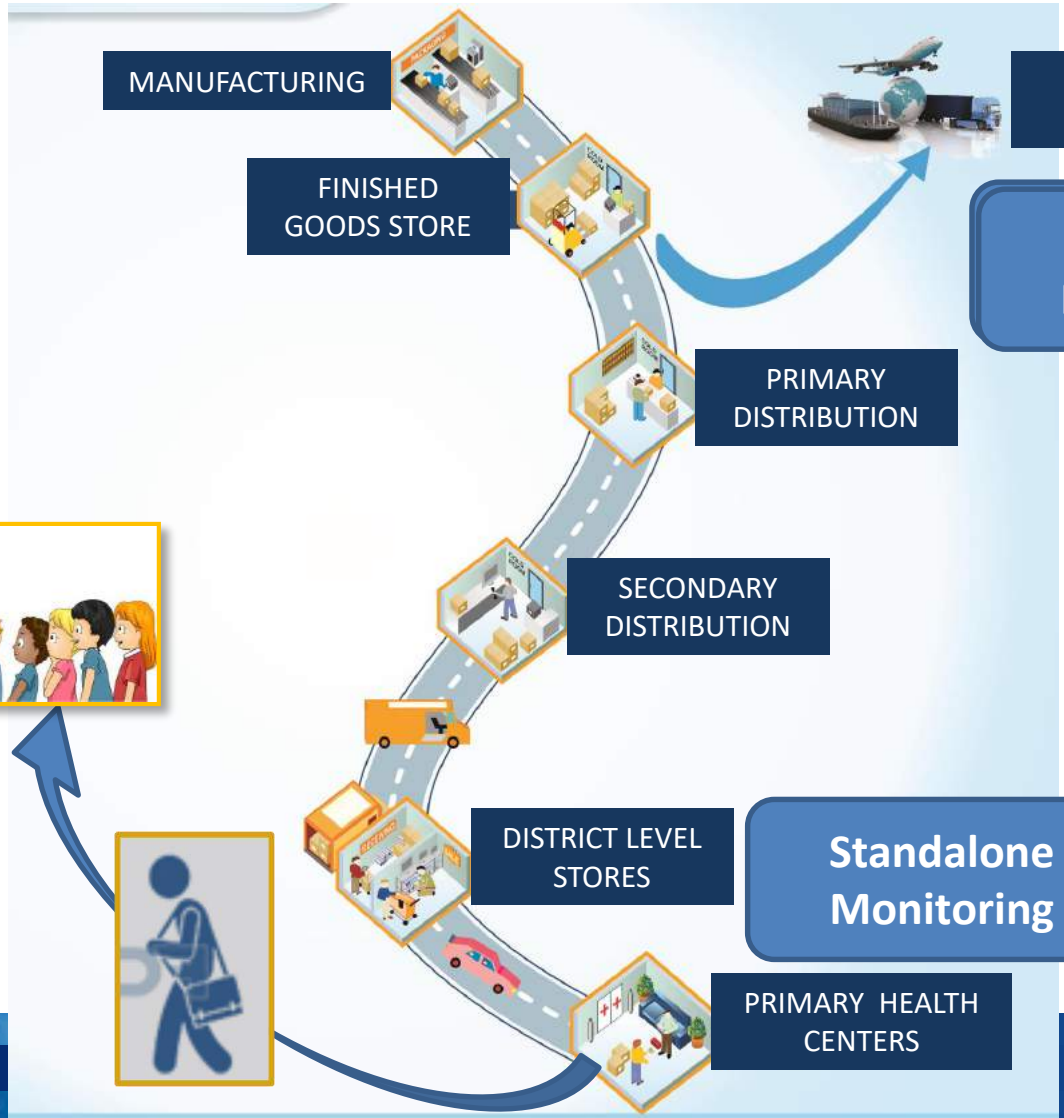

Facility Monitoring

Shipment Monitoring

OUT REACH SESSION

Product Monitoring

Standalone Monitoring

Vaccine exposure to Heating & freezing - Current reality

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Too hot

"Easier to detect"

Health worker in Niger shows bottles with vaccine vial monitors. Source: WHO

What do we know from the EVM Data Analysis

Over 90% of storekeepers and health workers know how to read VVMs.

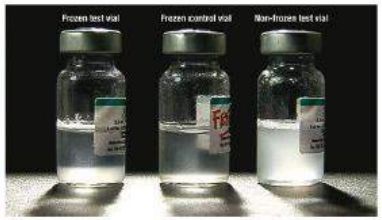
Continuous temperature monitoring

"What about excursions during weekends?"

Too cold

"Harder to detect"

Example Freeze indicators



Shake test. Source WHO

Only 11 % of facilities pack freeze indicators with deliveries of freeze-sensitive vaccines

Vaccine Temperature Sensitivity

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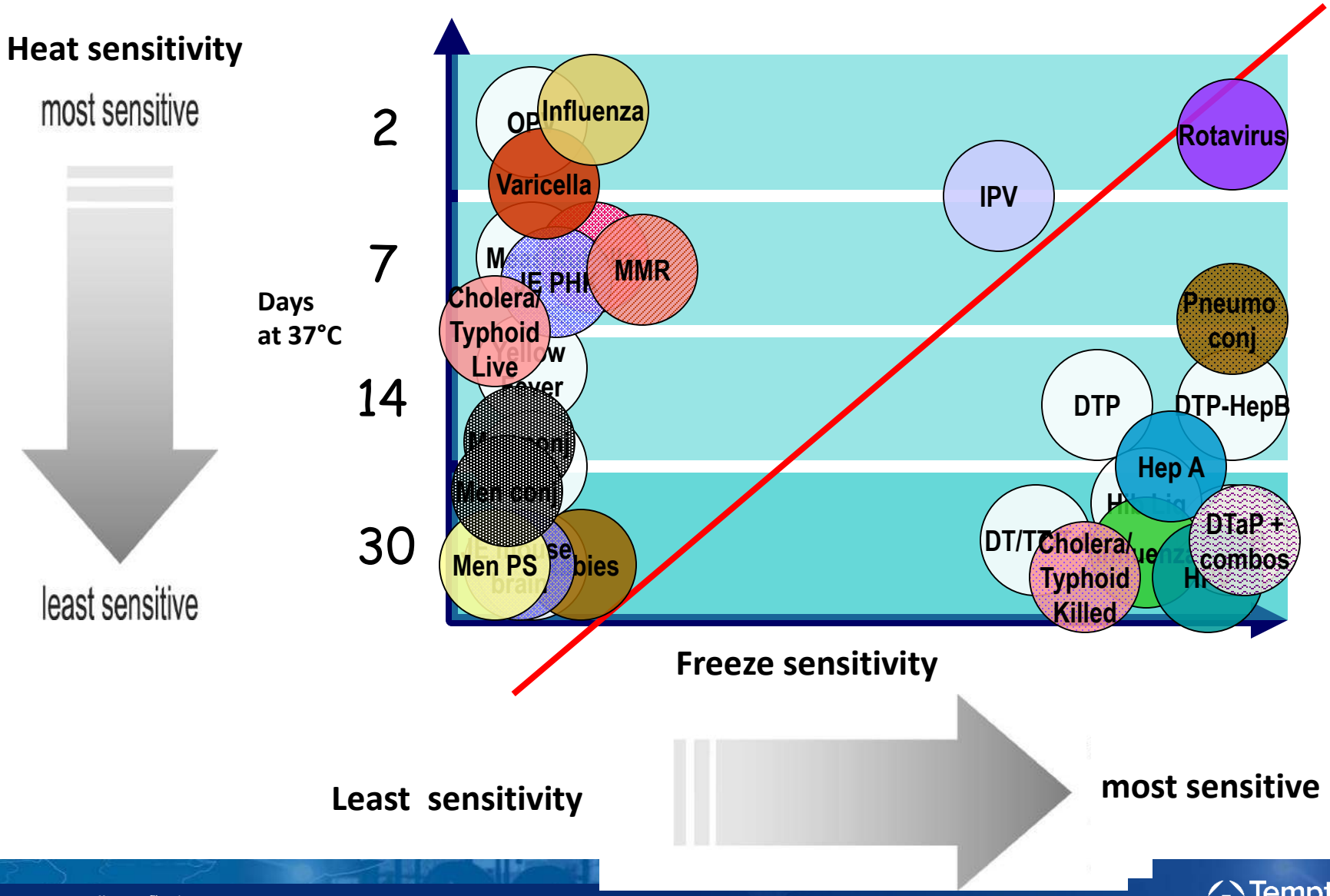

Four WHO VVM Categories to Monitor Vaccines with Different Heat Sensitivities

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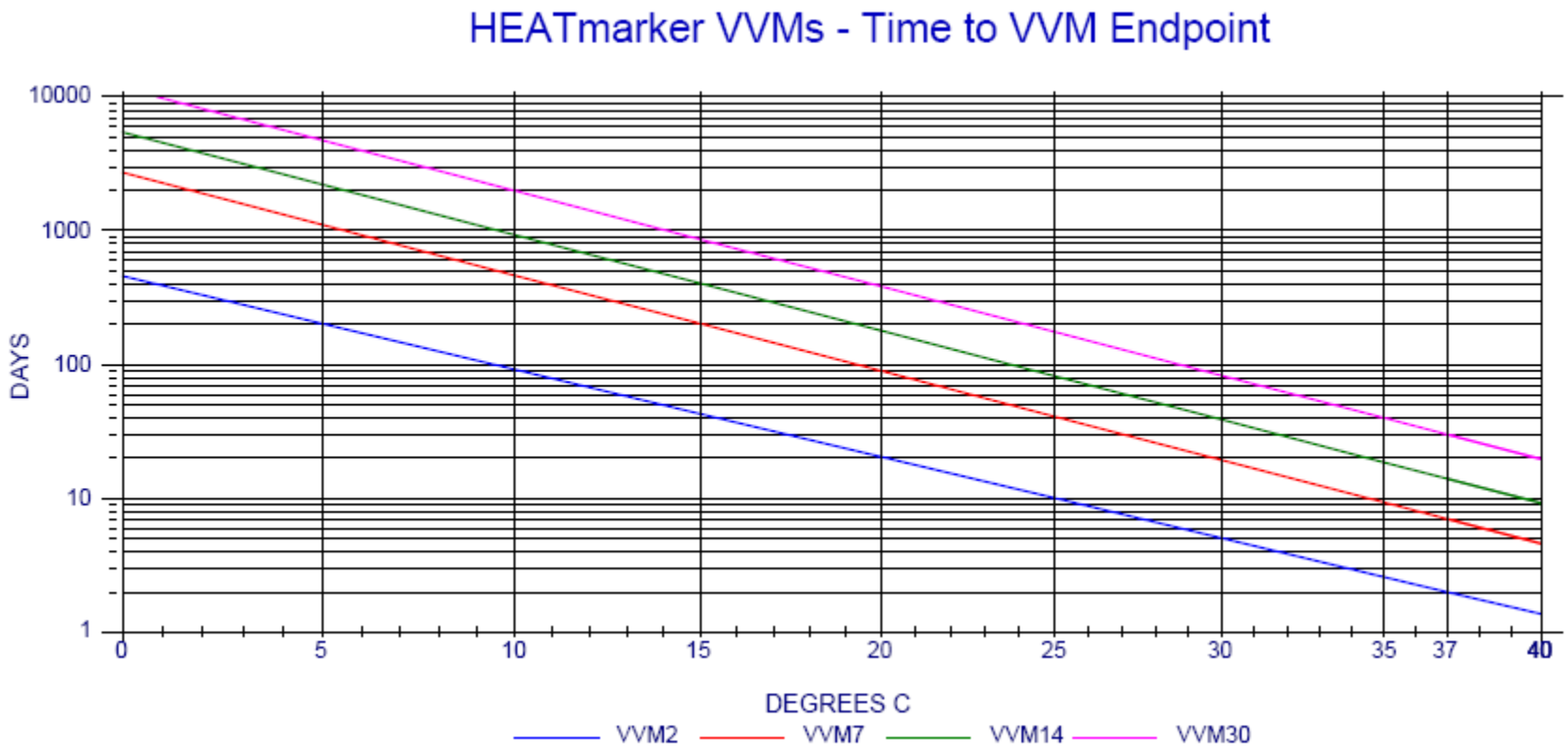

Temptime Continues to Invest in Product Innovations

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- VVM: new categories
- CTC & VVM+™: combined VVM and peak threshold indicator
- Hybrid 2D Bar Codes with embedded VVM active area: improve patient safety and address evolving international anti-counterfeiting/track & trace and serialization requirements

VVM7 - Improved

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- 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
  - Independent lab tests have been completed and dossier submitted to PQS

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
  - Included in VVM spec revision to be published soon

VVM New categories

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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*

~~Four~~ Five WHO VVM Categories – VVM11 is Imminent

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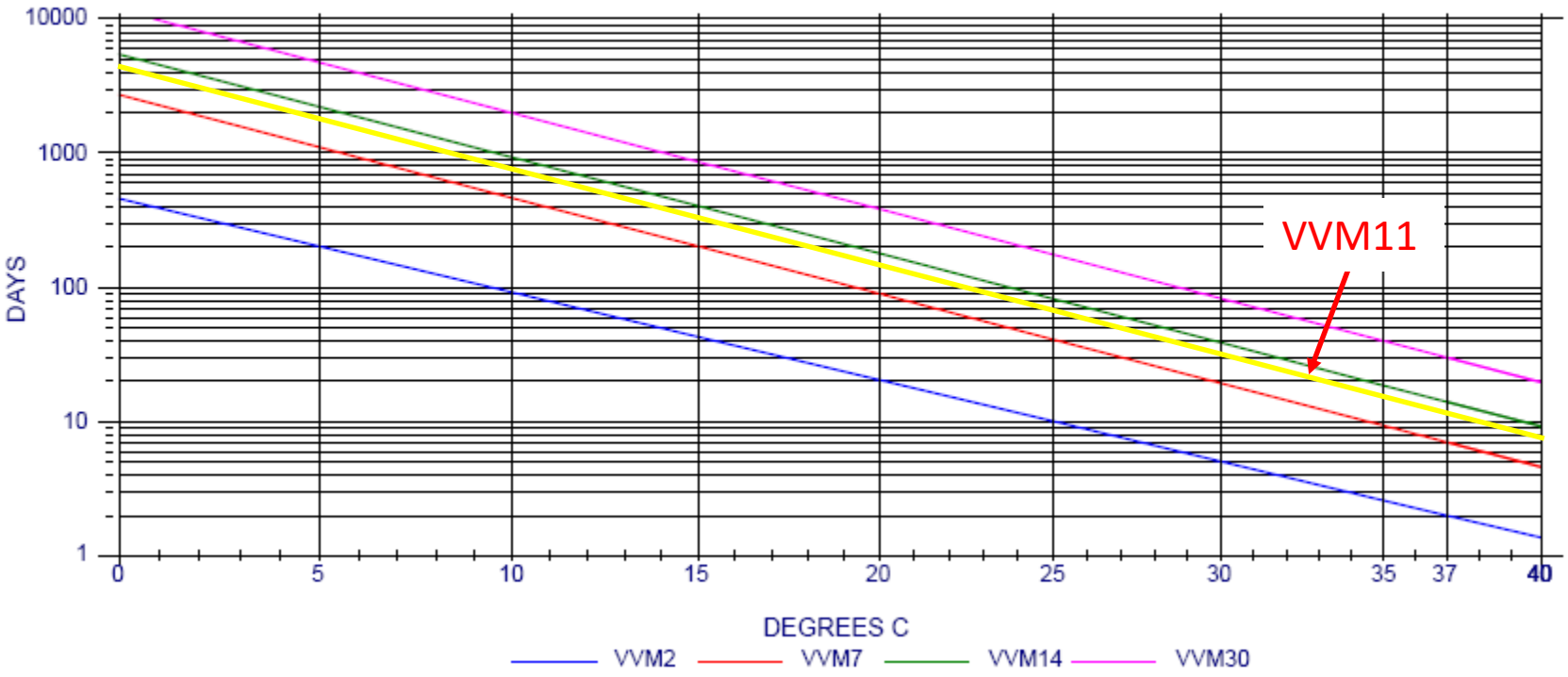
VVM11



VVM11

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The Next Challenge – Controlled Temperature Chain (CTC)

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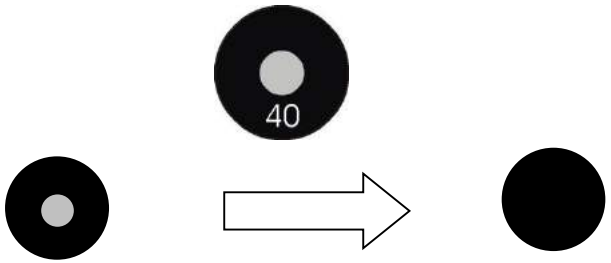
Objective: on-label use of vaccines in a CTC allowing specific vaccines to be kept and administered at ambient temperatures, up to 40C for one, limited period of time

- All CTC pilot studies with

- VVM on each vial

- And Temptime's LIMITmarker®
  threshold indicator in each vaccine carrier



Before Exposure to 40°C After Exposure to 40°C

New Product Innovations Address High Temperature Excursions

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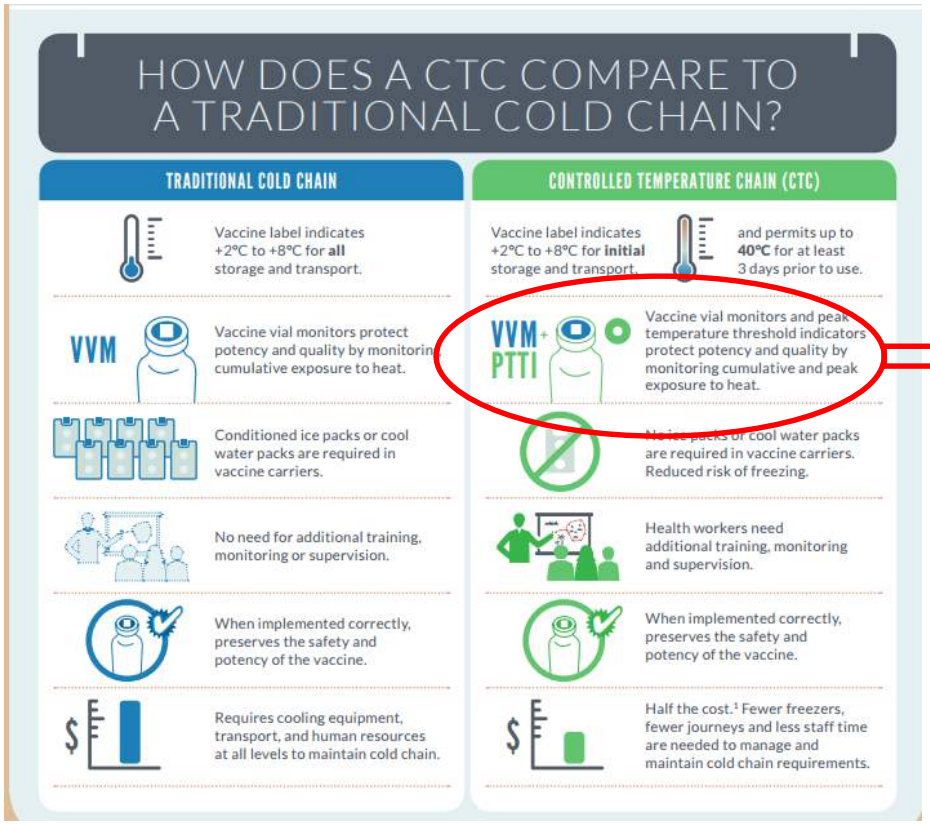
VVM+™

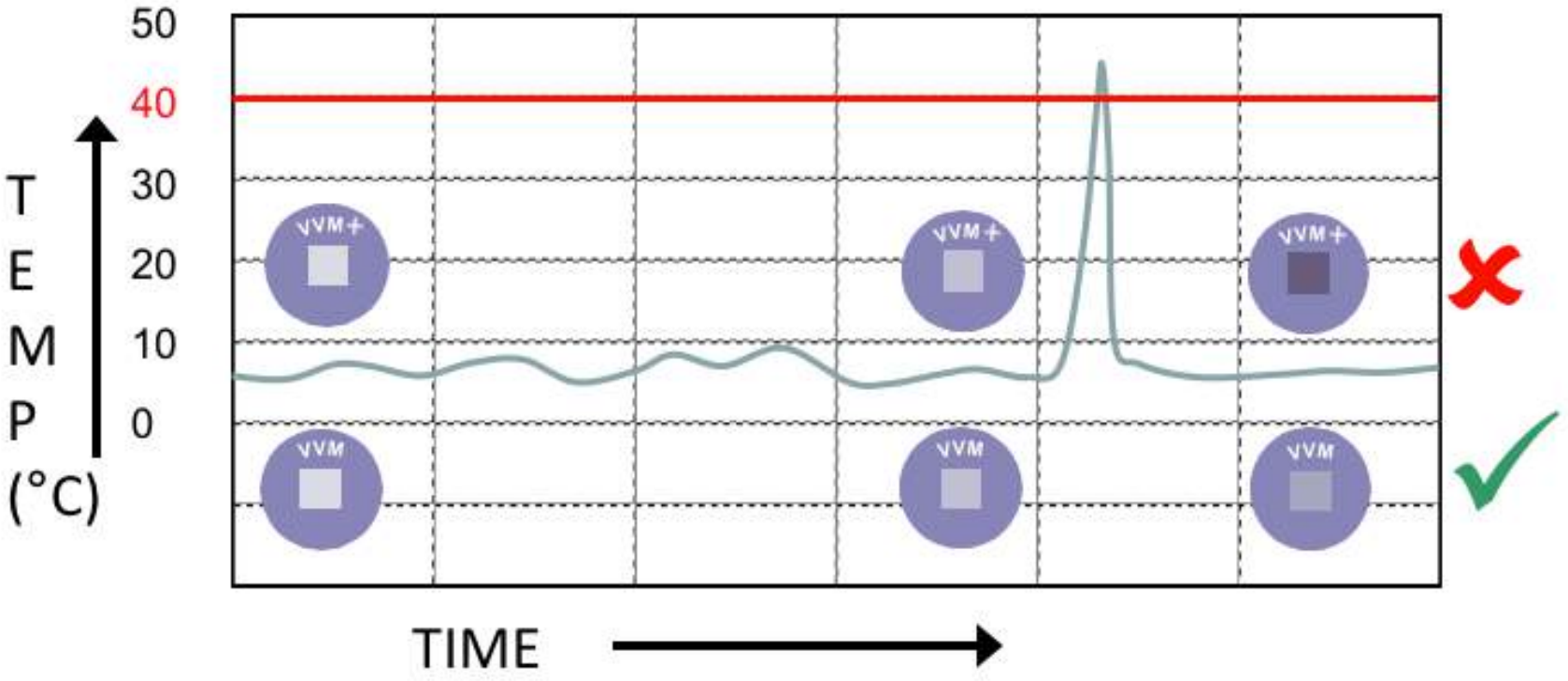
- Combined VVM response and high temperature threshold in a single indicator



VVM+

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



Comparison of VVM+ and VVM at Threshold Temperature

~~Four~~ Five WHO VVM Categories and VVM+

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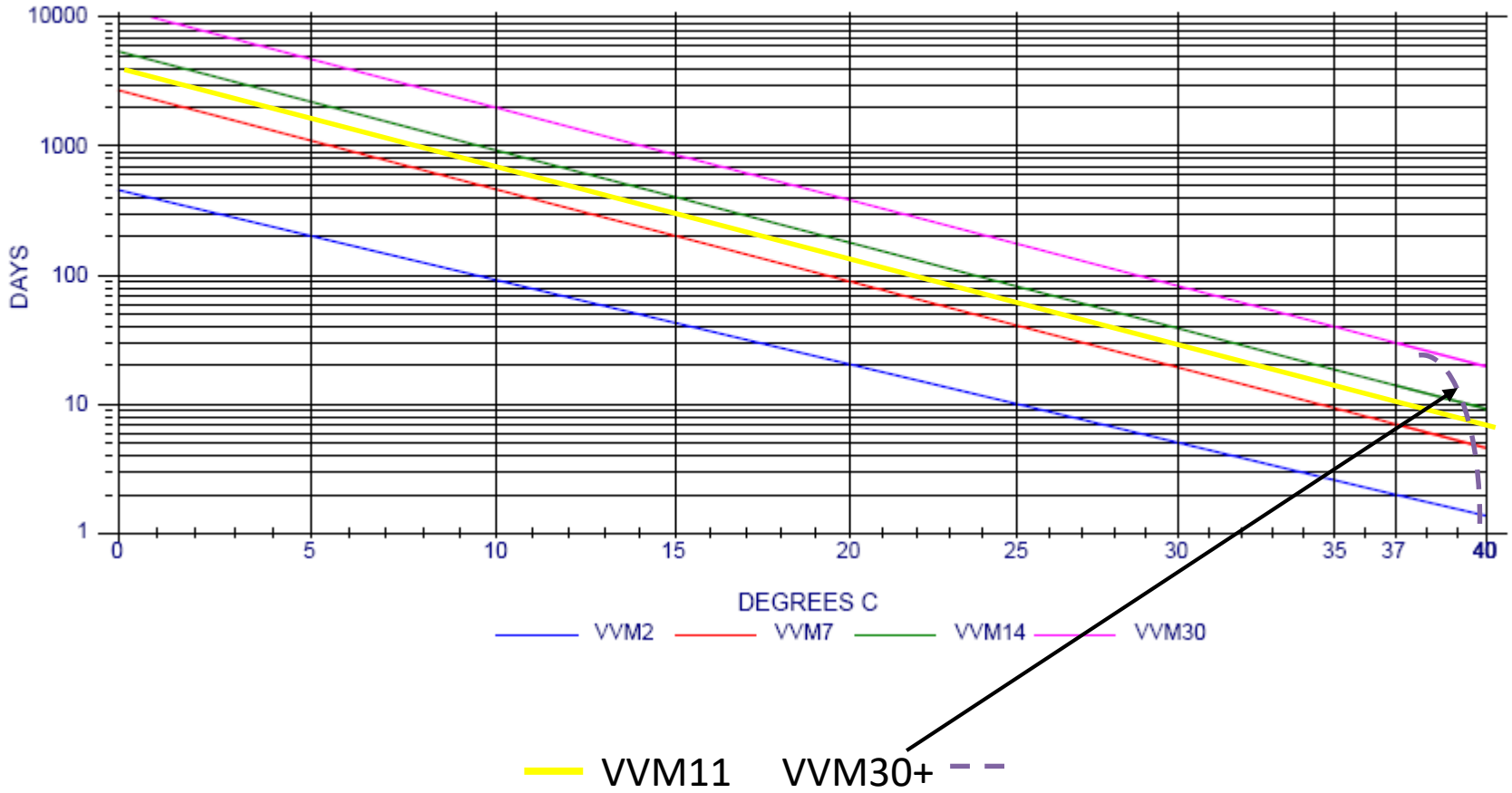
VVM+ In Progress



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

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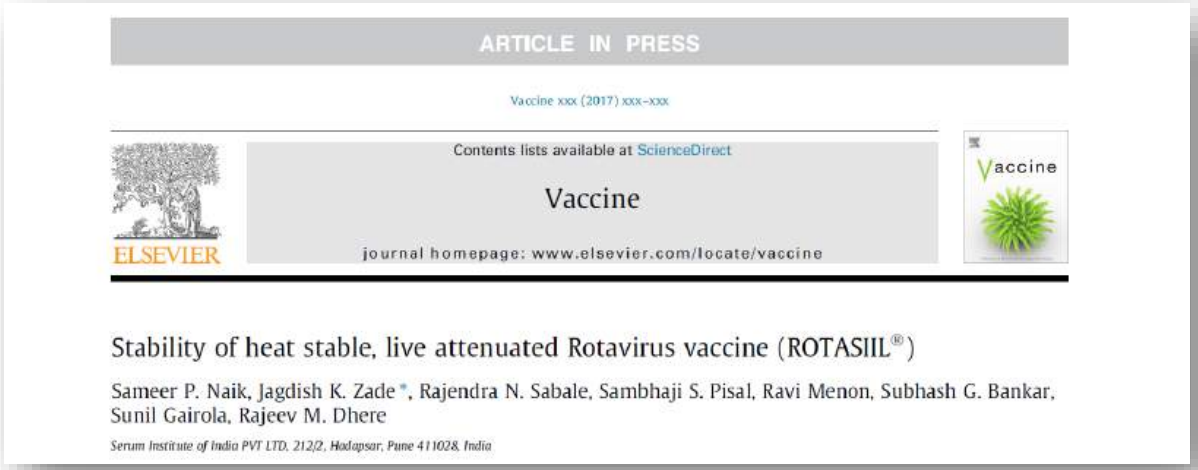

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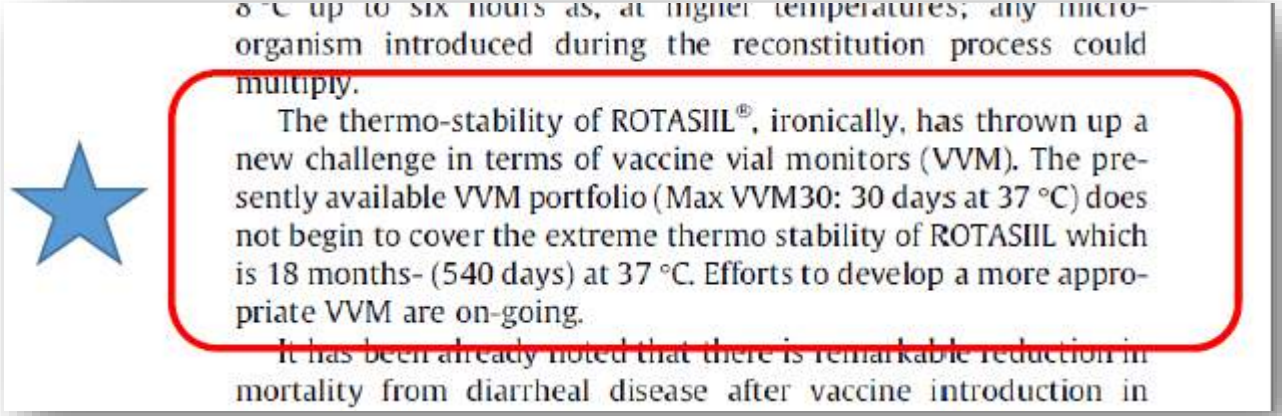
Vaccine

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 Line Extensions to Address Programmatic Needs VVM250 – Technology Capability

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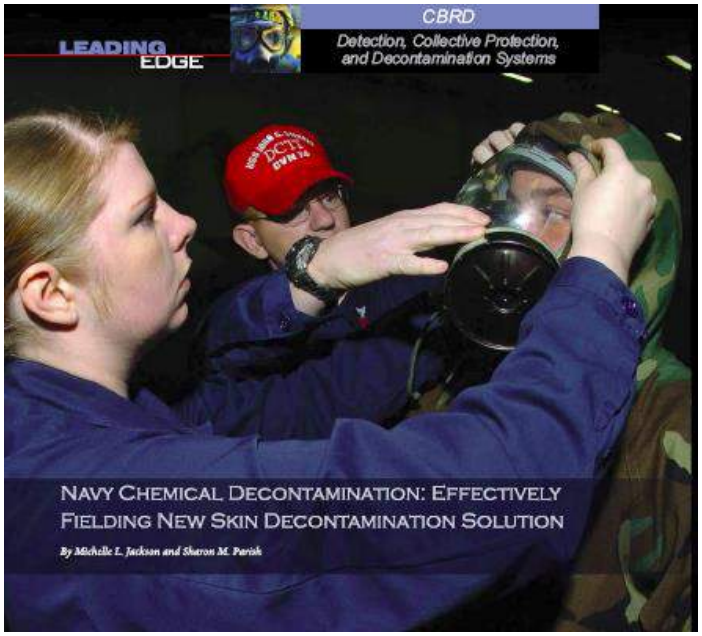

Temptime has supplied TTIs for use by US Military with 3 year life at 26°C for more than 20 years and a more stable category for use on Rapid Skin Decontamination Lotion

Additionally, the Joint Program Executive Office for Chemical and Biological Defense has developed a time temperature indicator (TTI) to include on RSDL packets when manufactured. TTIs incorporate MKT to accurately determine the service life limits of RSDL exposed to various temperatures. TTIs, therefore, assist with RSDL management by providing visible information reflecting product quality. An example TTI is shown in Figure 3.

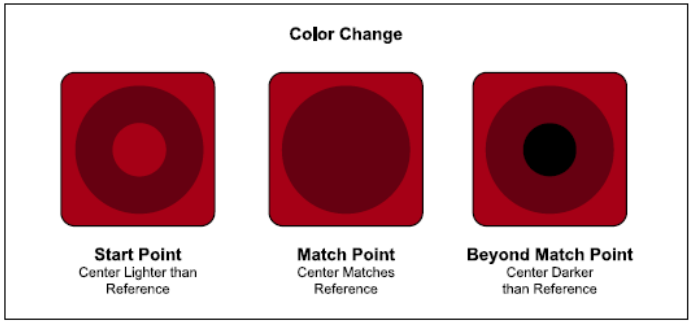

Figure 3. Time Temperature Indicator

VVM 250 – Upper limit of 250 days at 37°C

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Draft WHO PQS specification would be:

Maximum time to end point at +55°C	Maximum tim e to end point at +45°C	Time to end point at +25°C
17.0 days	73 days	≥ 900 days

New VVM category developed for thermostable vaccines!!

~~Four~~ ~~Five~~ Six WHO VVM Categories and VVM+

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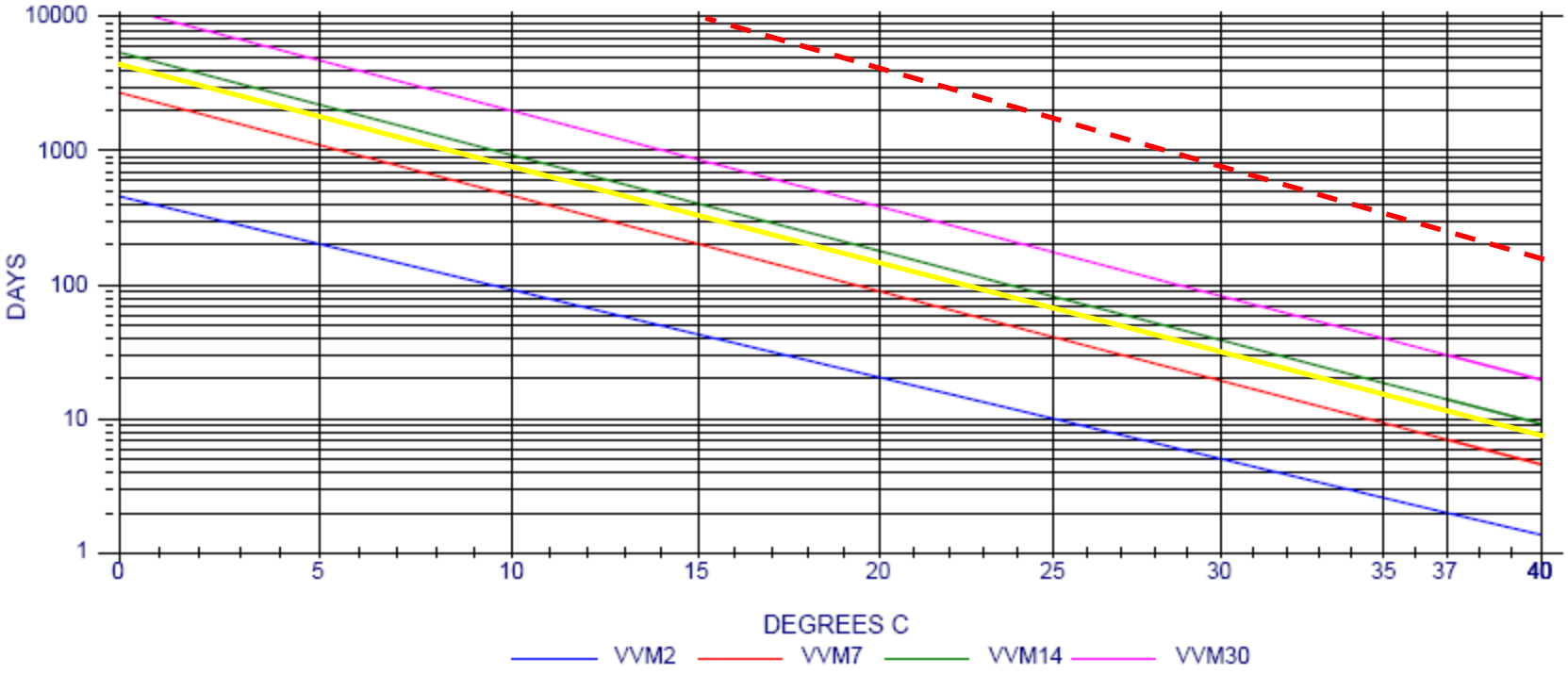
VVM250



VVM11 VVM250

Strengthening the Immunization Supply Chain

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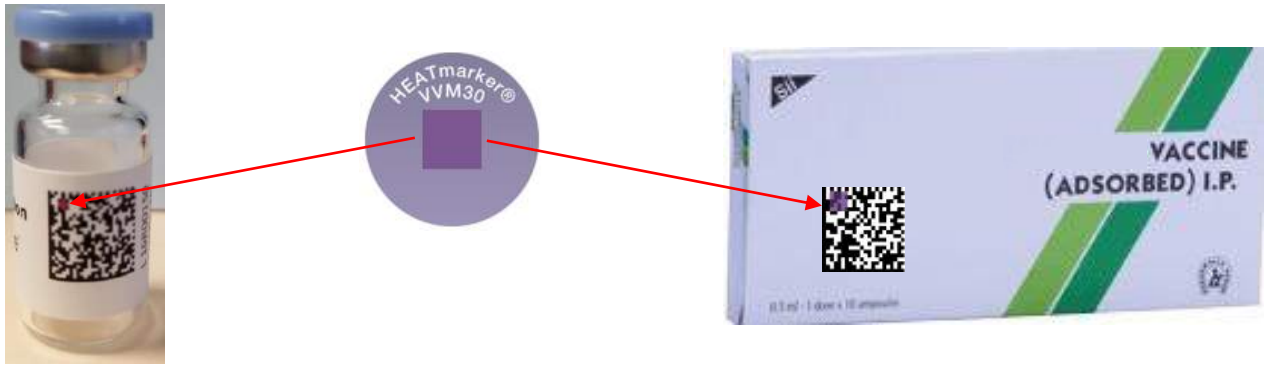
2D Barcode with Embedded VVM



Transformational Innovation: 2D Barcode with Embedded VVM

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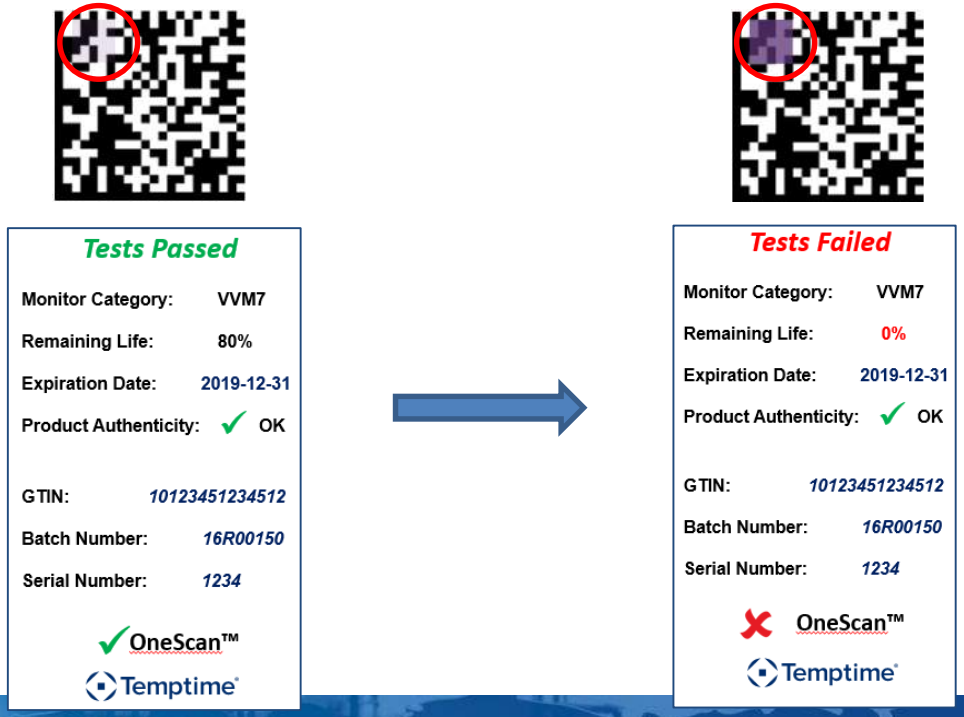
Digitization of Chemical Indicators & Unit of Sale Level Data Connection

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

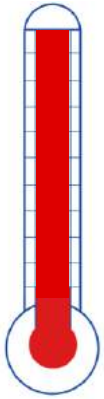
- Specific area has cumulative (VVM) and/or threshold ink printed as part of barcode
- Rapid reading with phone or scanner
- Connect with cloud based data set of other sensors



GS1 2D Data Matrix with Threshold Sensor

- **Threshold Indicator** – rapid, irreversible color change when peak temperature threshold is exceeded

Below threshold temperature



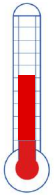
Exceed threshold temperature

Exceed Threshold Temperature

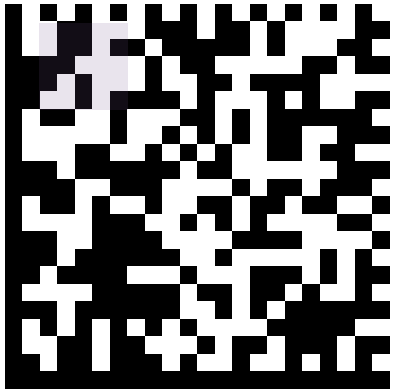
GS1 2D Data Matrix with VVM

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

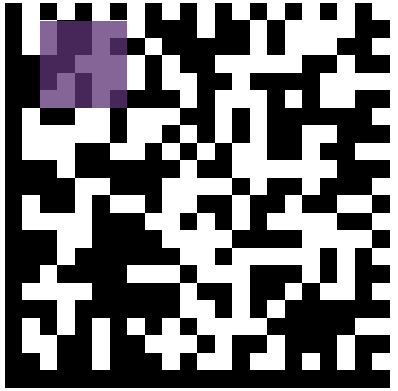
Before heat exposure



After excessive heat



Time and temperature exposure



Demo of Data Matrix Processing - Status

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- Developed and demonstrated algorithm on computer to decode binary change or measure color shades
- Developing app for phone or scanner
- GS1 organized a Working Group to create the Application Identifiers

Continuous End-to-End Temperature Monitoring with Dynamic 2D Barcode Indicator

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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

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

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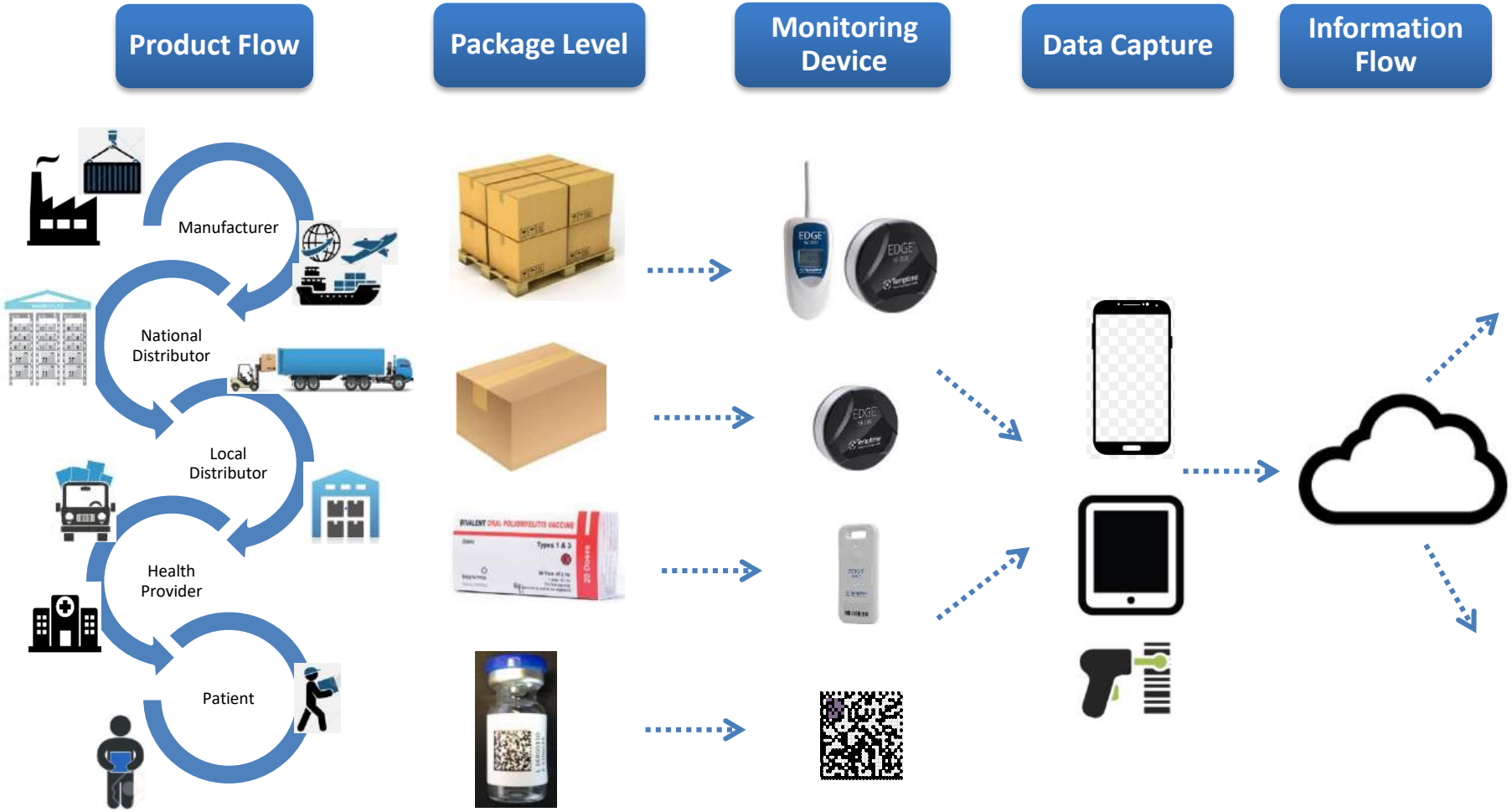

The OneScan™ Value Proposition

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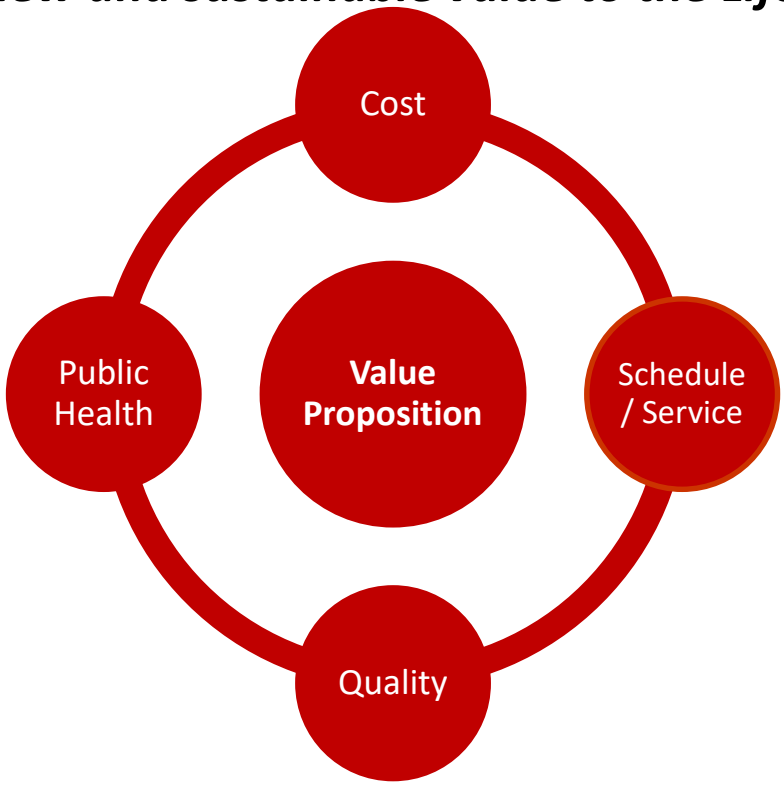
Serving the needs of

- *serialized supply chain tracking*
- *product authentication*
- *temperature assurance*
- *additional layer of anti-counterfeiting*

Delivering new and sustainable value to the Life Sciences industry



Close collaboration with GS1 and AIM[1] to Develop Standards for Temperature Sensors

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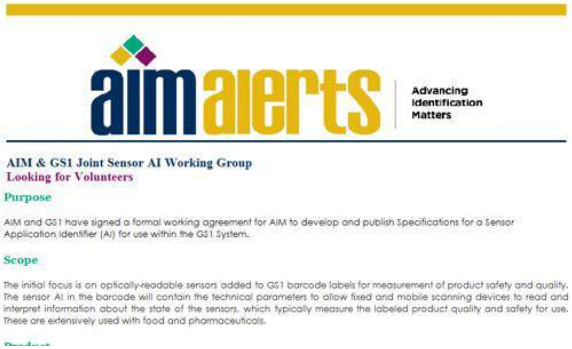

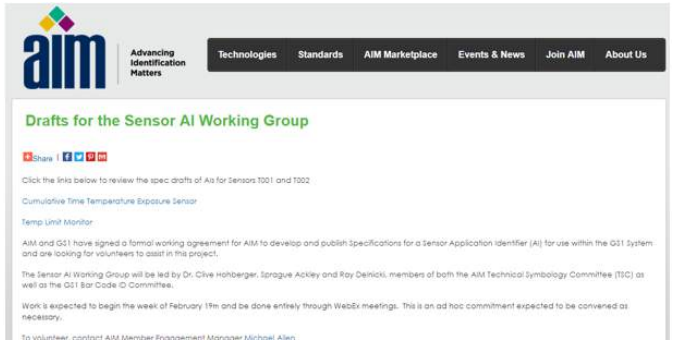

[1]Association for Automatic Data Capture, Identification and Mobility

India EVM Assessment

- 2013 (latest assessment) shows good understanding of VVM but low scores on effective use of VVM for stock management

- Scores have likely improved in recent years but 2D barcode with VVM would automate stock management processes and set the new standard for best practices

Some of the aspect of the vaccine management which is very critical for safe immunization programme and performance scores are at very low level, like:

- All parameters of vaccines (type of vaccine, vial size, quantity received, vaccine manufacturer, batch number, expiry date of each vaccine batch, VVM status and location in the store) are not recorded and performance score ranges between 52-60% at PHC and District VS.

Indicator wise Score

Indicator	Aspects	4 GMSD	18 State / RVS	14 Divisions	28 Districts	52 HF
	No. of sites	4	16	14	28	52
E7_11a	Do received vouchers have VVM and FI information	0%	12%	8%	4%	

V. Chhatisgarh

State / Region	Division	District	HF-1	HF-2
Raipur SVS		Surguja District VS	Narmadapur CHC	Lakhanpur CHC

Criteria	SVS level	DVS level	Block level
Stock management	58%	33%	36%
Standard stock book format used (including all necessary columns for recording)	VVM status not available	Vaccine presentation, Manufacturer name and VVM status missing	Vaccine presentation, Manufacturer name and VVM status missing

	c. Stock keeping Diluent and VVM record keeping was not seen in majority of the vaccine stores Verify stock records for sufficiency of working and buffer stocks, and in and out transactions and ensure that immediate action is taken when buffer stock is breached.	All salient parameter of vaccine & diluents must be noted, particularly the • VVM stage (for vaccines), • Manufacturer, • Batch number and • Expiry date.

Proof of Concept Pilot – Phase 1 under discussion

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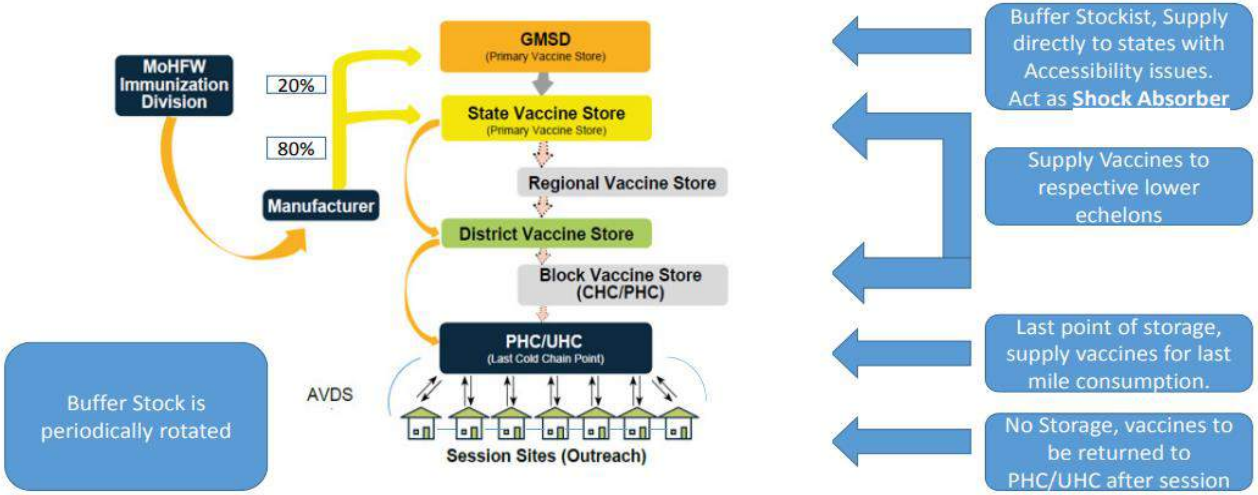
- Apply 2D barcode label with VVM on secondary cartons at manufacturer
- Scan cartons on shipment out and receipt at each transfer to district level using smartphone with OneScan™ app
- Automated data collection and digitized VVM readings
- Push data to the cloud

Immunization Supply Chain in India[1]



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

Standards, Serialization and Smartphones for Interoperability

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- PoC design based on global standards for scalability and interoperability

> Bar codes can help track and trace health products in the supply chain. But to do so efficiently, they should be based on global standards rather than a proprietary system, and the captured data should be integrated into national health information systems to achieve end-to-end data visibility.


GLOBAL HEALTH: SCIENCE AND PRACTICE
Dedicated to what works in global health programs

FIELD ACTION REPORT

More Than Bar Codes: Integrating Global Standards-Based Bar Code Technology Into National Health Information Systems in Ethiopia and Pakistan to Increase End-to-End Supply Chain Visibility

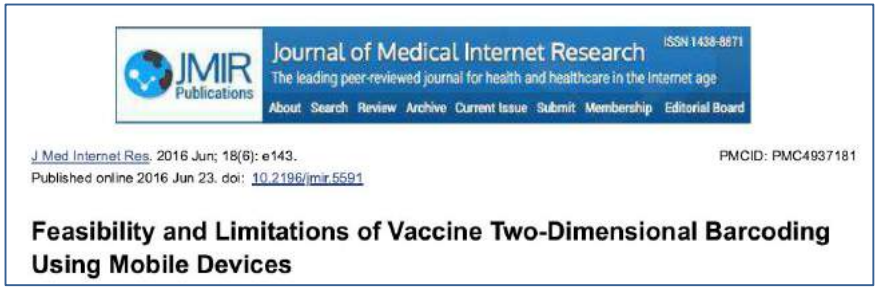
Luichi Hara,[a] Romy Guirguis,[b] Keith Hummel,[c] Monica Villanueva[d]

Bar codes can help track and trace health products in the supply chain. But to do so efficiently, they should be based on global standards rather than a proprietary system, and the captured data should be integrated into national health information systems to achieve end-to-end data visibility.


USAID | DELIVER PROJECT
FROM THE AMERICAN PEOPLE

Brief

Traceability in Ethiopia's Health Sector: Piloting GS1 Barcodes with Global Trade Item Number Serialization to Track Health Commodities from Supplier to Health Facility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J Med Internet Res. 2016 Jun; 18(6): e143.
Published online 2016 Jun 23. doi: 10.2196/jmir.5591
PMCID: PMC4937181

Feasibility and Limitations of Vaccine Two-Dimensional Barcoding Using Mobile Devices

Goal: Integrate Stock Management and VVM Data into National Programs with Global Interoperability

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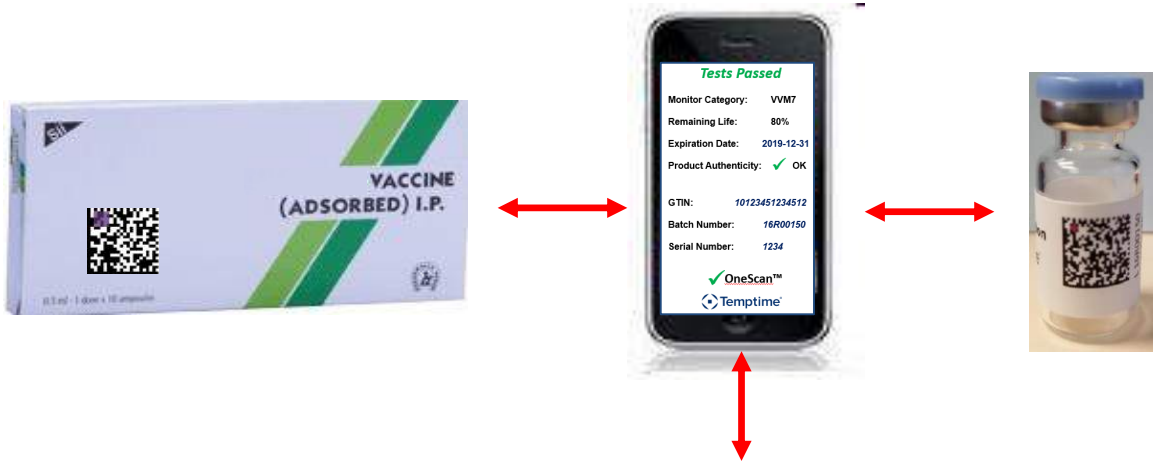
- After successful Phase 1 PoC on secondary carton, consider new phase on vial level with serialization



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THANK YOU!!!