

Transformative Innovations Beyond Vaccine Vial Monitor (VVM)



Prior to freezing After freezing



Temptime Corporation

- Working Globally to Improve Public Health
 - More than 600 Million HEATmarker devices used per year.
 - Vaccine manufacturers worldwide apply HEATmarker at the time of manufacture to monitor the vaccine until use.
 - HEATmarkers are used worldwide on vaccine and other heat sensitive medical products (5 billion used since 1996).
- Only company able to develop a time-temperature indicator to meet strict requirements of the World Health Organization.
- Experts in technologies that monitor temperature sensitive medical products.
- Our expertise and customer satisfaction has made Temptime the world leader in time-temperature indicators.
- Privately held company, headquartered in Morris Plains, NJ.
 - Spin-off from Allied-Signal in 1987
- Successful business expansion
 - Globally: Customers in more than 15 countries Customer base: manufacturers, distributors, governments, NGOs

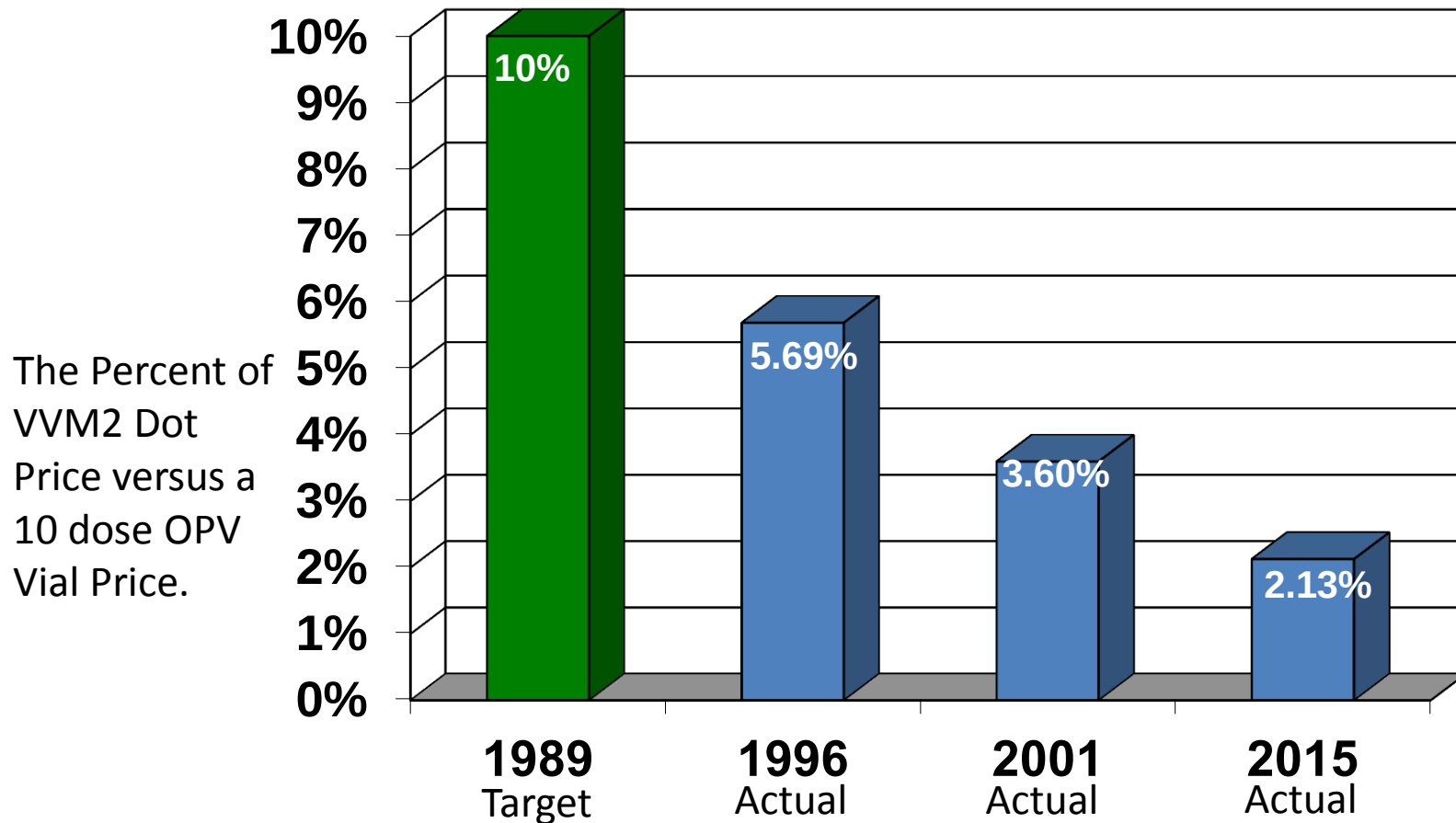
Commitment to Highest Quality, Lowest Cost, Uninterrupted Supply

Enhanced Business Continuity Plan

- Prevention and mitigation
- 2nd Manufacturing Site
- 2 year safety stock of critical active ingredient for VVM
- 6 months safety stock of each category of VV
- Main Site expansion completed
- \$ 8 Million in capital expenditures during last 2 years including new state of the art printing machine

VVM as a Percentage of OPV Price

VVM2 Dot Price as a % of 10 Dose Vial of OPV Price



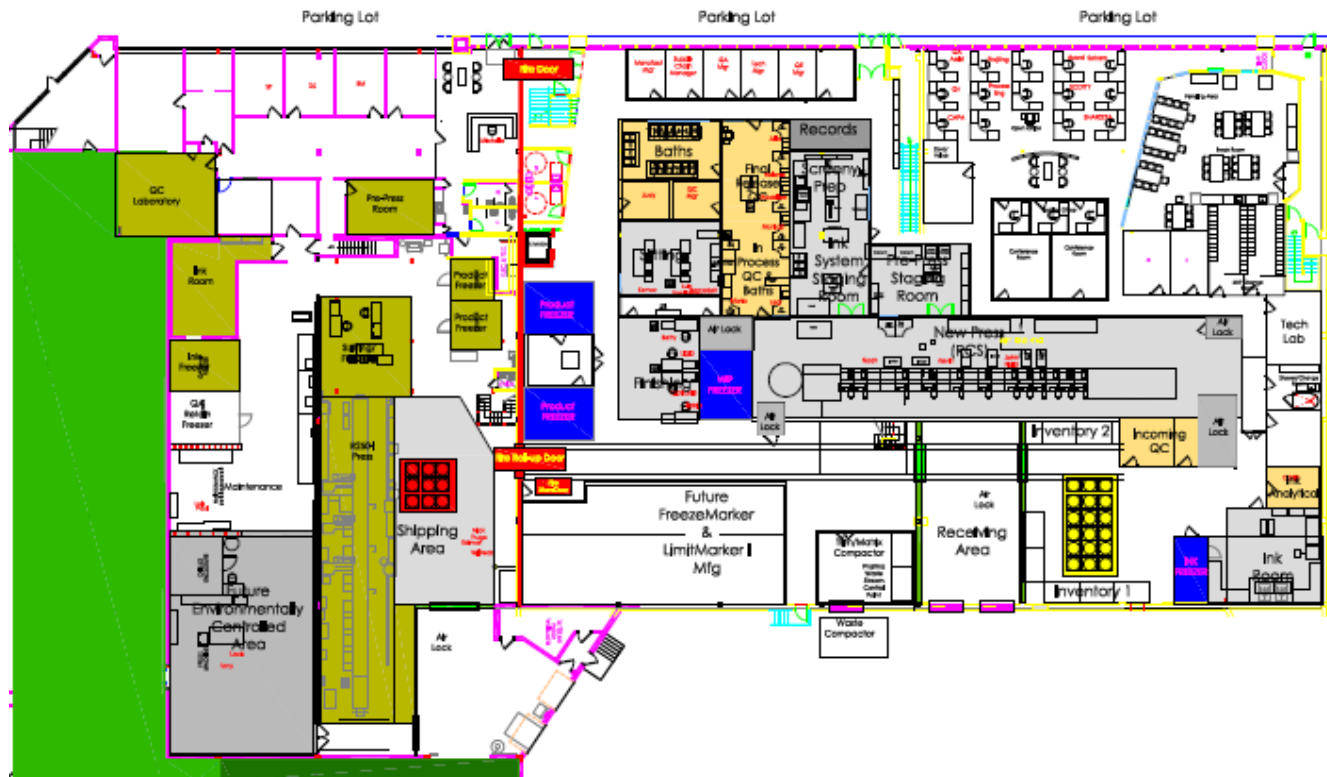
Source: UNICEF Supply Division

Main Site Expansion Completed

Building The Temptime of Tomorrow

Before

Now Added and Operational





**TEMPTIME
COMMITMENT
TO QUALITY**

New State of the Art Manufacturing Equipment



New State of the Art Manufacturing Equipment



VVM Continued Expansion in China

Beijing CDC Launches HEATmarker® VVM for Flu Vaccine Program in 2014
and Now on All Type II Vaccines



VVM Continued Expansion in China

Beijing CDC Launches HEATmarker® VVM for Flu Vaccine Program in 2014
and Now on All Type II Vaccines



- NCDC launched a study covering 5 vaccines in three provinces
- Beijing CDC requiring VVM on all private vaccines

The HEATmarker TTI Is Easy To Read



The Active Square is lighter than the Reference Circle.

If the expiry date is not passed, USE the vaccine.



USE



USE



**DO NOT
USE**



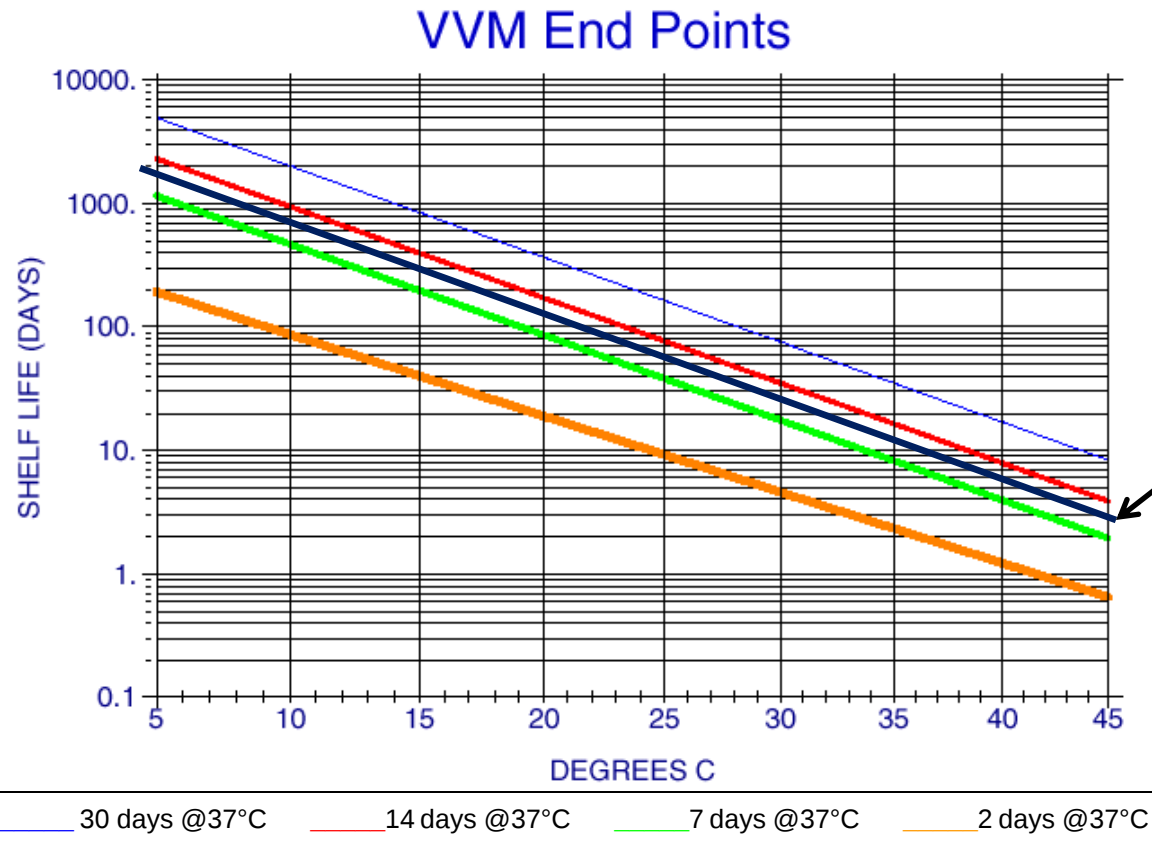
**DO NOT
USE**

The Active Square matches or is darker than the Reference Circle.

DO NOT USE the vaccine.

Current HEATmarker VVM Categories

VVM2, 7, 14, 30



VVM11 has been developed to fill a gap, and recently submitted to PQS

VVM11

Background

- There are 4 VVM categories: VVM2, 7, 14 and 30
- VVM7 has about 2 years to end point at 5°C
- VVM14 has more than 3 years to end point at 5°C
- Vaccines with VVM7 and 3 year expiry are at risk of wastage

Rationale for VVM11

- If vaccine stability data supports 11 days at 37°C, VVM11 would help close the gap of 3 years at 5°C and reduce risk of wastage (Target > 30 months at 5°C)
- Recent application of statistical approach to vaccine stability in CTC suggests that the lower VVM category would be chosen versus the current practice using the compliance model
 - Vaccines currently using VVM14 might be required to use VVM7
 - VVM11 would be more programmatically suitable

Status

- Temptime has completed three qualification runs of VVM11 and internal testing is near completion based on draft specification
- Temptime wishes to submit dossier and initiate external lab evaluation once accredited lab situation is clarified
- Submission date to accredited lab – November 2015
- Product launch – June 2016
- Field evaluation not required for line extension of VVM category

FREEZEmarker® - Monitoring Freeze Events

- The FREEZEmarker® is a single use freeze indicator that signals whether or not there has been a freeze event during a shipment.



**Before
Freezing**



**After
Freezing**

*“Magnified view of the
FREEZEmarker® indicator”*

Response Temperatures

- $-1^{\circ}\text{C} \pm 1^{\circ}\text{C}$
- $0^{\circ}\text{C} \pm 1^{\circ}\text{C}$
- $-6^{\circ}\text{C} \pm 2^{\circ}\text{C}$



FREEZEmarker on Individual Units or MultiPacks

- Self-adhesive indicator attached to the product, product packaging or blister pack.



- Small card inserted into secondary box or package.





Before Freezing



After Freezing

FREEZEmarker® Progress

Peer Reviewed Article Published in Infectious Diseases for Clinical Practices

Study In US Peditricians' Practices Shows Vaccines Exposed to Freezing Temperatures

http://journals.lww.com/infectdis/Abstract/publishahead/Visual_Indicators_on_Vaccine_Boxes_as_Early_99324.aspx

ORIGINAL ARTICLE

OPEN

Visual Indicators on Vaccine Boxes as Early Warning Tools to Identify Potential Freeze Damage

Ronald Angoff, MD, FAAP,*† Jillian Wood,† Maria C. Chernock,‡ and Diane Tipping§

Background: The aim of this study was to determine whether the use of visual freeze indicators on vaccine boxes would assist health care providers in identifying vaccines that may have been exposed to potentially damaging temperatures.

Methods: Twenty-seven sites in Connecticut involved in the Vaccine for Children Program participated. In addition to standard procedures, visual freeze indicators (FREEZEmarker®; Temptime Corporation, Morris Plains, NJ) were affixed to each box of vaccine that required refrigeration but must not be frozen. Temperatures were monitored before daily deliveries.

Results: During the 24 weeks, all 27 sites experienced triggered visual freeze indicator events in 40 of the 45 refrigerators. A total of 66 triggered freeze indicator events occurred in all 4 types of refrigerators used. Only 1 of the freeze events was identified by a temperature-monitoring device. Temperatures recorded on vaccine data logs before freeze indicator events were within the 35°F to 46°F (2°C to 8°C) range in all but 1 instance. A total of 46,954 doses of freeze-sensitive vaccine were stored at the time of a visual freeze indicator event. Triggered visual freeze indicators were found on boxes containing 6566 doses (14.0% of total doses). Of all doses stored, 14,323 doses (30.3%) were of highly freeze-sensitive vaccine. 1789 of these doses (12.5%) had triggered indicators on the boxes.

Conclusions: Visual freeze indicators are useful in the early identification of freeze events involving vaccines. Consideration should be given

cost of \$3.6 billion.² The VCP program is administered by the US Centers for Disease Control and Prevention (CDC).

For vaccines to be effective, they must be properly stored and handled from the time of manufacture through delivery to and storage in the provider's office.³ Whereas exposure to any inappropriate conditions, including excessive heat or cold exposure, can affect potency of refrigerated vaccines, a single exposure to freezing temperatures will destroy some vaccines, such as liquid vaccines that contain an aluminum adjuvant.⁴ Should loss of potency occur, patients who receive the vaccine will not be protected against vaccine-preventable diseases.

In recent years, there have been indications that storage and handling of vaccines within required temperature ranges, including shipment of vaccine from the distributor to a hospital,⁴ were an ongoing problem in the United States. A survey conducted in 2008 by the Association of Immunization Managers (AIM) demonstrated considerable variability among city and state immunization projects in the United States.⁵ A field survey conducted by the California Department of Public Health found that a hospital in Santa Ana, Calif, had stored various vaccines at lower than freezing temperatures for 7 months in 2009. As a result, 1641 newborns were given potentially defective hepatitis B vaccine.⁶ In 2010, another investigation found a significant 76% correlation

Used in US CDC Distribution of Vaccines to 46,000 providers



Field Verification of FREEZEmarker Performance versus Electronic Freeze Indicators²

Research

Frequent exposure to suboptimal temperatures in vaccine cold-chain system in India: results of temperature monitoring in 10 states

Manoj V Murhekar,^a Srihari Dutta,^b Ambujam Nair Kapoor,^c Sailaja Bitragunta,^d Raja Dodum,^e Pramit Ghosh,^f Karumanagounder Kolanda Swamy,^g Kalyanranjan Mukhopadhyay,^h Somorjit Ningombam,ⁱ Kamlesh Parmar,^j Devegowda Ravishankar,^k Balraj Singh,^l Varsha Singh,^m Rajesh Sisodiya,ⁿ Ramaratnam Subramanian^o & Tana Takum^e

²Bulletin of the World Health Organization 2013;91:906-913. doi: <http://dx.doi.org/10.2471/BLT.13.119974>



Before Freezing



After Freezing

FREEZEmarker® Progress

Revision of WHO PQS Specification for Irreversible Freeze Indicator Submitted

Vial Level Freeze Risk Indicator



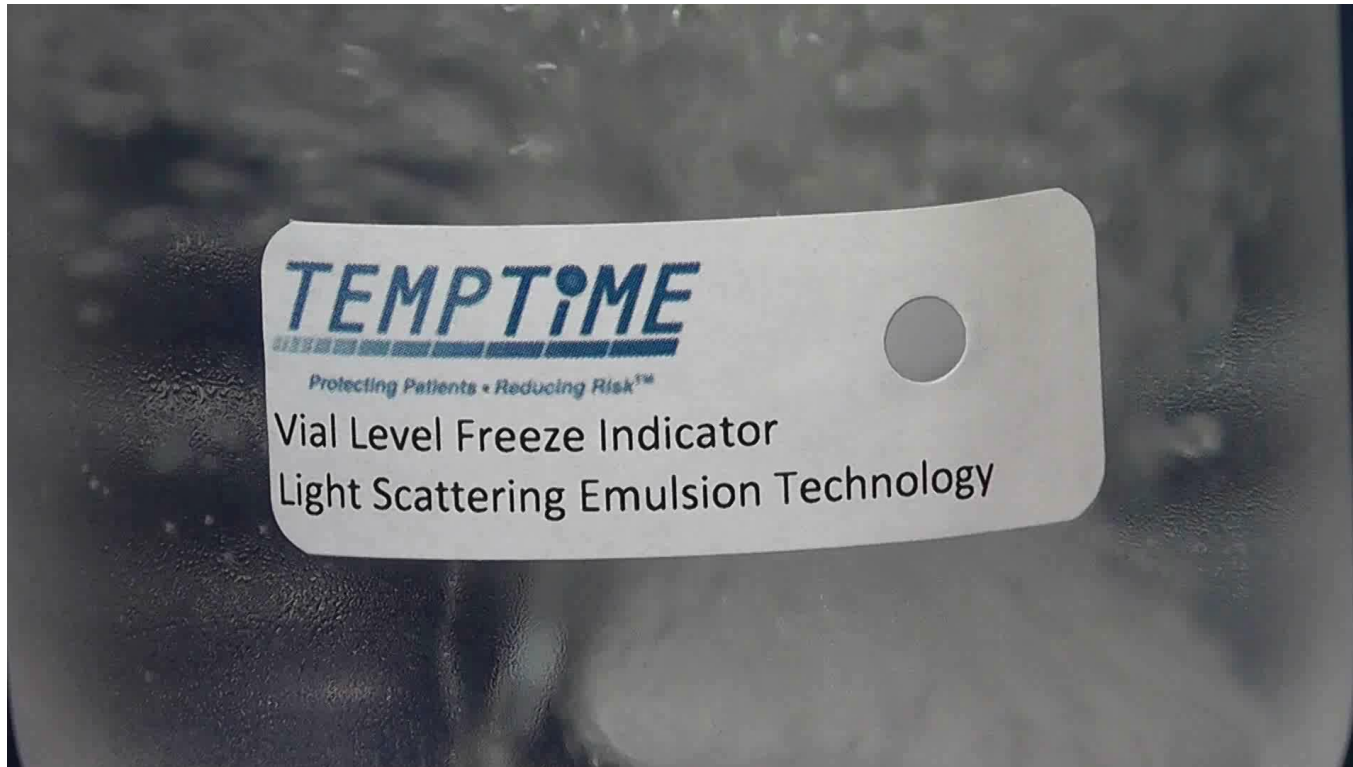
Prior to freezing



After freezing

Does the world need vial level freeze risk indicator?

Vial Level Freeze Risk Indicator



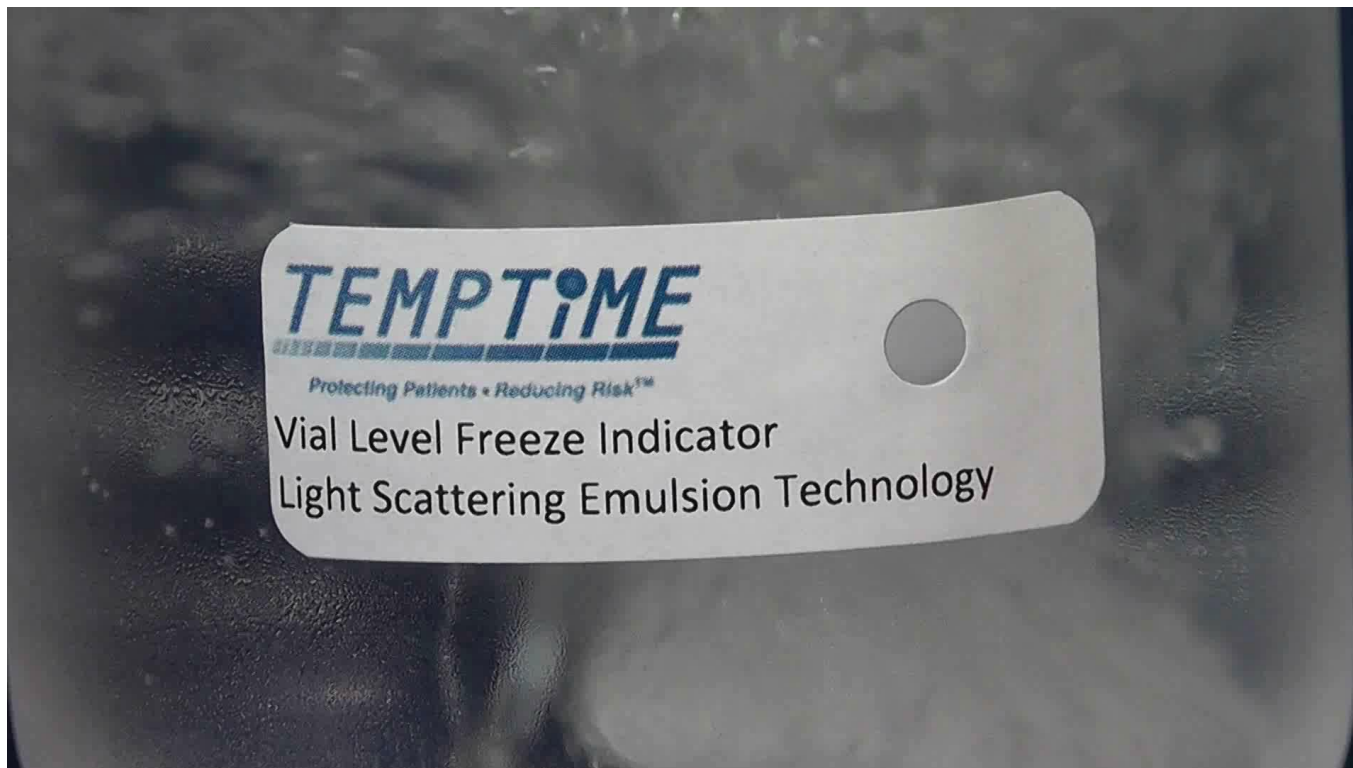
Prior to freezing



After freezing

Does the world need vial level freeze risk indicator?

Vial Level Freeze Risk Indicator



Prior to freezing



After freezing

Does the world need vial level freeze risk indicator?

The innovation of the Controlled Temperature Chain (CTC) – where do we go from here?



**World Health
Organization**

Anna-Lea Kahn - WHO-HQ/ EPI
14th TechNet Conference - Bangkok, Thailand
13 May 2015

CTC licensure to date

- December 2012 – **Meningitis A Vaccine** (MenAfriVac) licensed, prequalified and pilot tested for CTC
 - 4 days / 40°C
- May 2015 – **Pneumococcal Conjugate Vaccine** 13-valent (Pneumovax13) licensed and prequalified for CTC, guidance to be developed
 - 3 days / 40°C
- End of 2015 – **Oral Cholera vaccine** (Shanchol) expected to be licensed and prequalified for CTC
- 8 manufacturers working on generating data in support of CTC for at least 10 different vaccines.

New Product Concept – VVM+™

VVM plus Peak Indicator

Temptime is BMGF GCE Grant Awardee



+



VVM

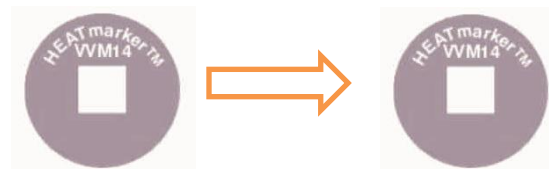
- VVM active square is translucent and the substrate color is seen through the monomer

Reactive Substrate

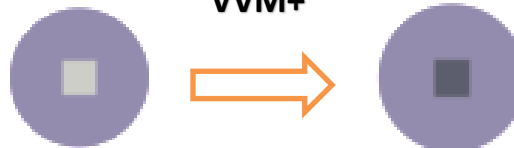
- Substrate develops color quickly at high temperature

Response after short exposure to 40°C

VVM



VVM+™



Comparison of VVM+ and VVM Above Threshold Temperature



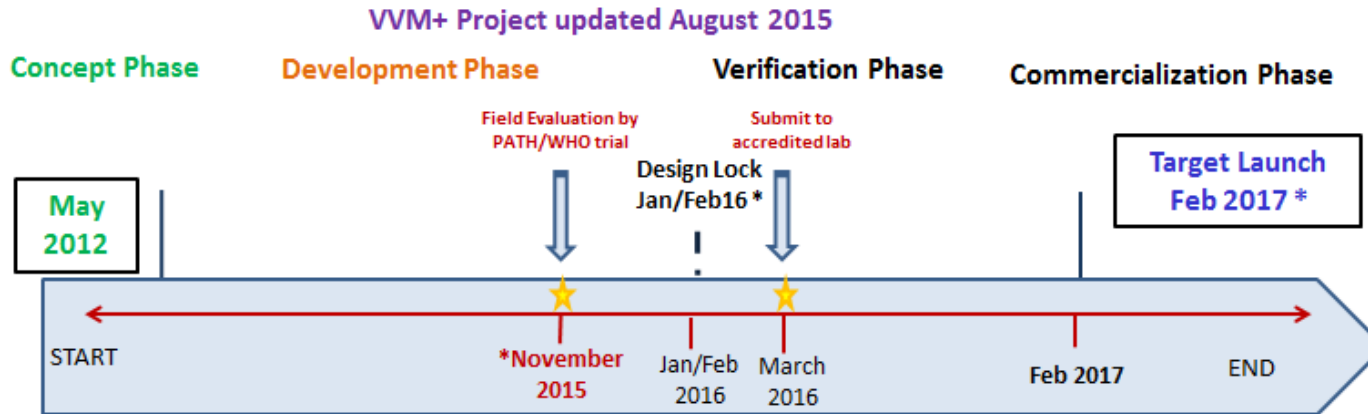
Comparison of VVM+ and VVM Above Threshold Temperature



- Field study being planned for November
- Possibility for VVM+ to be the new standard

VVM+

Development Update and Field Evaluation



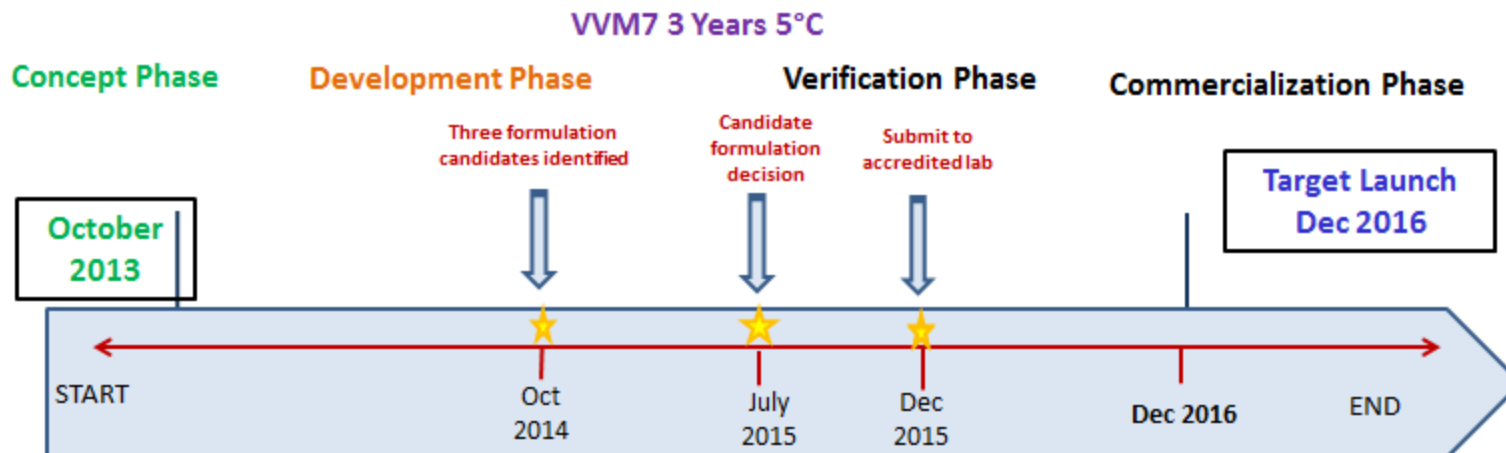
Development Status:

- Submission date to accredited lab – March 2016
- Product launch – February 2017

Field Evaluation:

- Protocol for field evaluation under development (WHO/PATH/Temptime)
- Mid-October prototype samples will be available for lab assessment of “+”
- November field evaluation

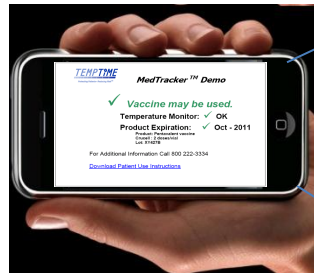
Update: VVM7 with 3 years at 5°C



Development Update:

- October 2013 – identified need for extended time to end point at 5°C based on 3 year expiry date given to IPV and other antigens
- February 2014 – research project launched based on current VVM monomer technology
- October 2014 – 3 formulation candidates identified
- January 2015: Qualification activities (IQ/OQ/PQ) begin for the new manufacturing process.
- July 2015: Final selection of formulation candidate. PPQ activities underway.
- Submission date to accredited lab – December 2015
- Assume field evaluation not required
- Product launch – December 2016

✓ MedTracker®



TEMPTIME
Protecting Patients • Reducing Risk™

MedTracker™ Demo

✓ **Vaccine may be used.**

Temperature Monitor: ✓ OK

Product Expiration: ✓ Oct - 2011

Product: Pentavalent vaccine
Crucell : 2 doses/vial
Lot: XY427B

For Additional Information Call 800 222-3334

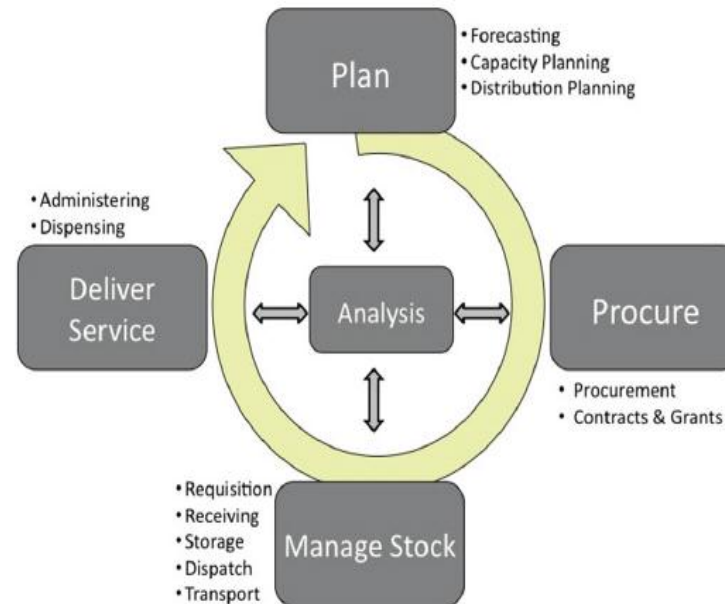
[Download Patient Use Instructions](#)

What is the MedTracker System?

- MedTracker is a smart phone app that reads a 2D barcode and color shade of VVM
- MedTracker
 - provides immediate feedback to the user which can include
 - Product identification
 - VVM status
 - Lot number
 - Expired or not
 - Authenticity (if serialized)
 - sends information to the server where aggregation or inventory management software is running
 - Includes all of the above plus
 - GPS location
 - Time/date stamp

The Global Framework is Being Developed

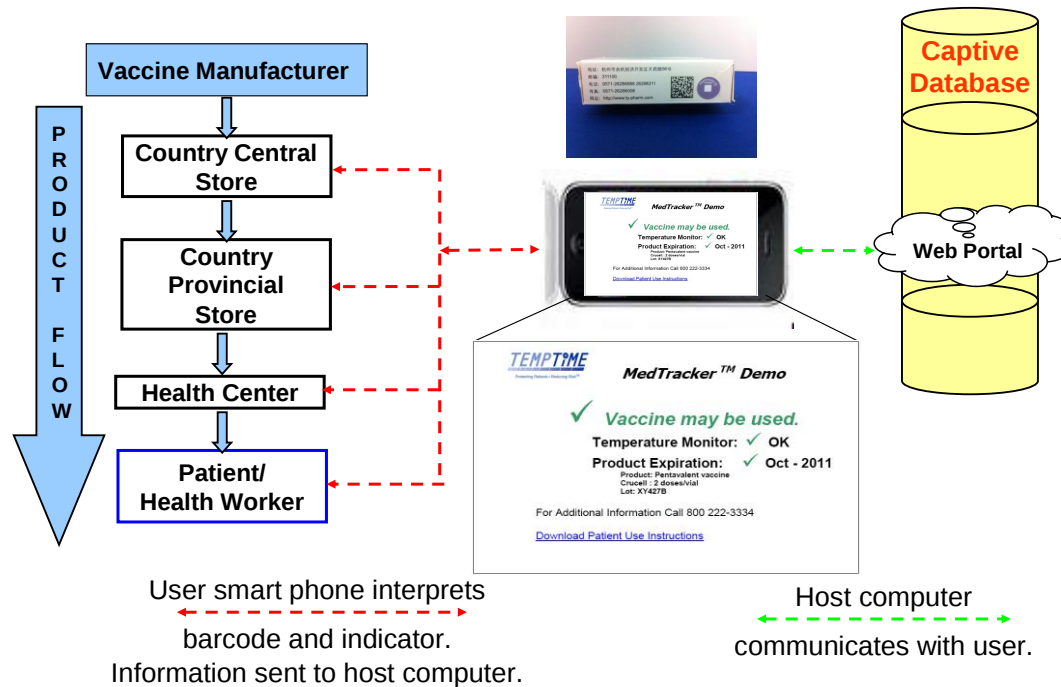
Logistics Management Information System (LMIS)¹



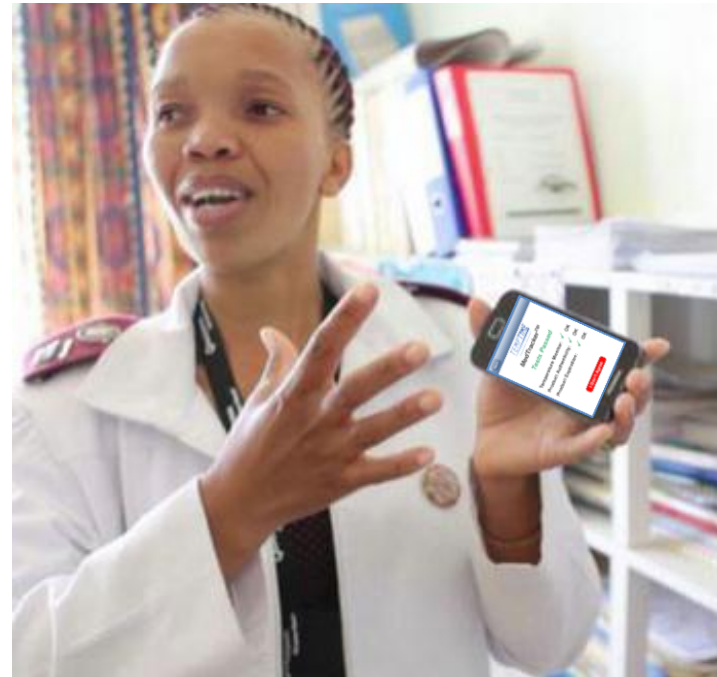
- Capturing accurate routine administration, dispensing, and consumption data.
- Real-time end-to-end logistics management from the point of origin to service-delivery point.
- Demand forecasting, capacity planning and modeling based on consumption
- MedTracker used as a data capture device

Typical Product and Information Flow

MedTracker 1: Vaccine Public Market Pilot



MedTracker Demo



The Wall Street Journal news department was not involved in the creation of this content.

PRESS RELEASE | March 31, 2014, 6:05 a.m. ET

Thinfilm and Temptime Collaborate to Deliver Printed Electronic Temperature Indicators for Use in Distribution, Storage and Management of Sensitive Medical Products



- Printed Electronics Technology
- Credit Card Sized Device
- Indicates High or Low Excursion
- Irreversible & Disposable
- Lower Cost than Standard Electronics

TransTracker Digital™

Printed Electronics to Detect Temperature Excursions During Transport



NFC Data Logger

Technology Under Review



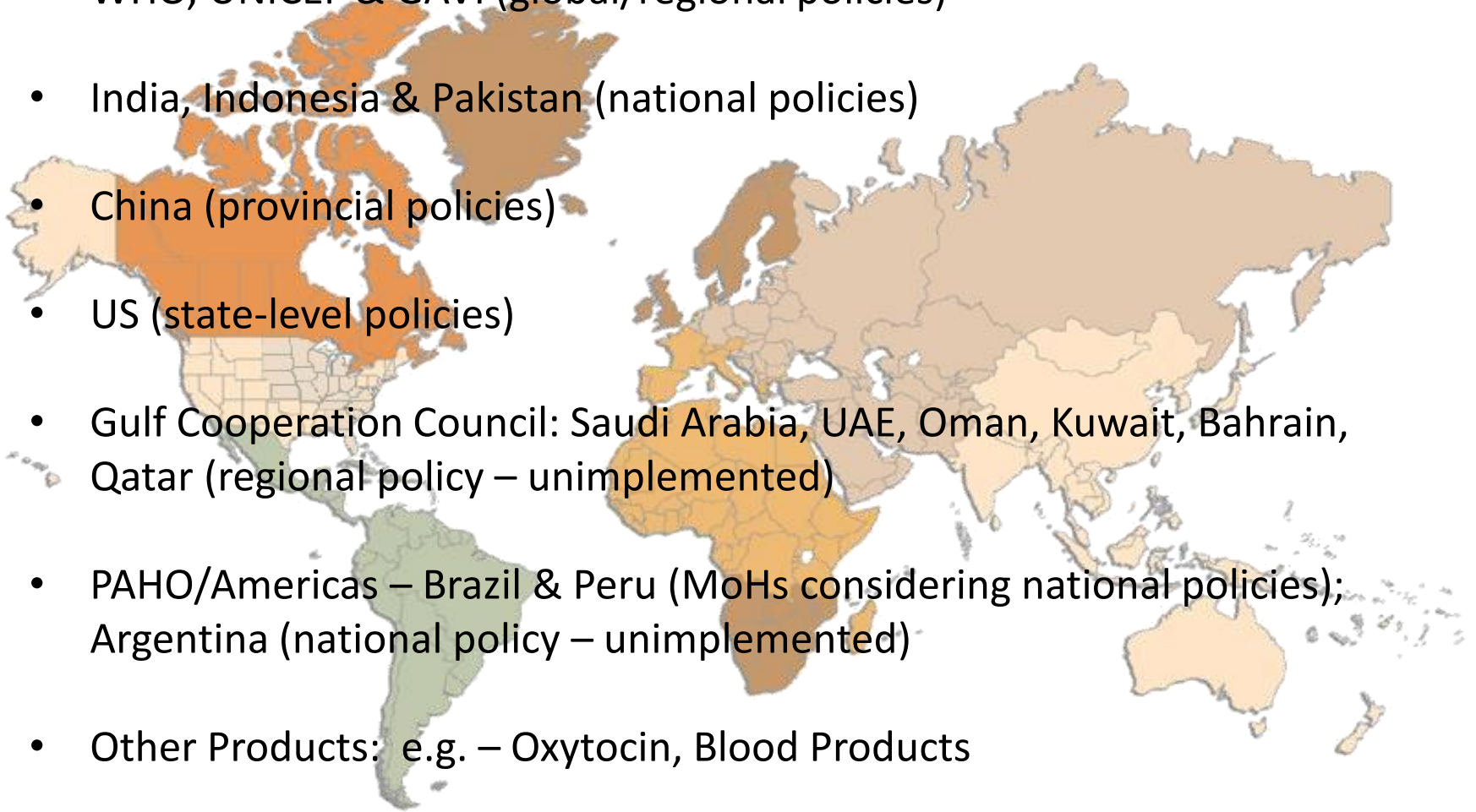
Cost effective, single use, disposable

Recent References



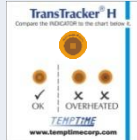
Global Health Policies related to Temperature-Monitoring

- WHO, UNICEF & GAVI (global/regional policies)
- India, Indonesia & Pakistan (national policies)
- China (provincial policies)
- US (state-level policies)
- Gulf Cooperation Council: Saudi Arabia, UAE, Oman, Kuwait, Bahrain, Qatar (regional policy – unimplemented)
- PAHO/Americas – Brazil & Peru (MoHs considering national policies); Argentina (national policy – unimplemented)
- Other Products: e.g. – Oxytocin, Blood Products



Thank you!!!!

HEATmarker for Other Uses

<u>Pharmaceutical Product</u>	<u>Indication</u>	<u>Customer</u>	<u>Temptime Product</u>	<u>Value Delivered</u>
	Oxytocin, Post-partum hemorrhaging	BIOL Gland		Help avoid morbidity/mortality rates of new mother by preventing administration of heat damaged medicine
	Diagnostic test for HIV, AIDS, Hepatitis	Standard Diagnostics Span Diagnostics		Ensures test effectiveness and accurate results
	Decontamination of skin exposed to chemical weapons	EZ-EM Canada (Bracco)		Helps protect troops from health consequences of chemical warfare

Temptime Core Technologies Applied to Address Unmet Market Needs

Core Products

Freeze



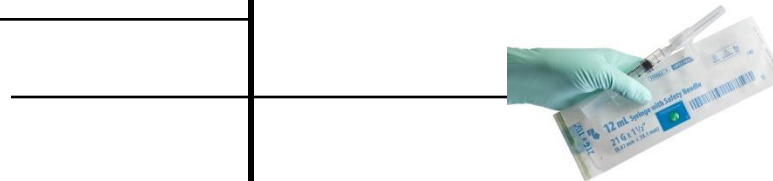
Cumulative Heat



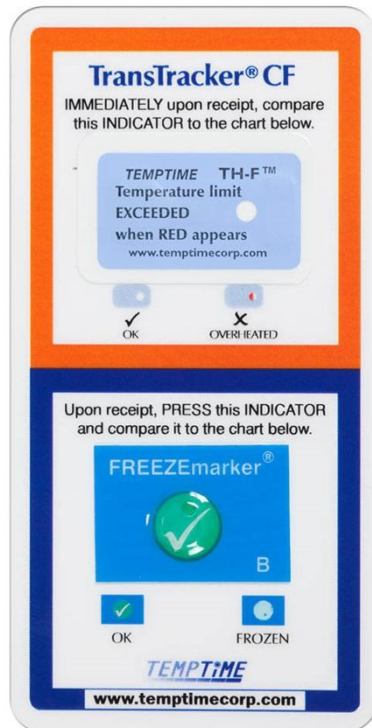
Delayed Heat Threshold



Instant Heat Threshold



TransTracker Dual Indicators for Multiple Unit Secondary Packages and Shipping Cases



**Monitors short
Heat Threshold
And/or Freeze Events**



**Monitors
Cumulative Heat
and/or Freeze Events**



**Monitors
Instantaneous Heat
and/or Freeze Events**

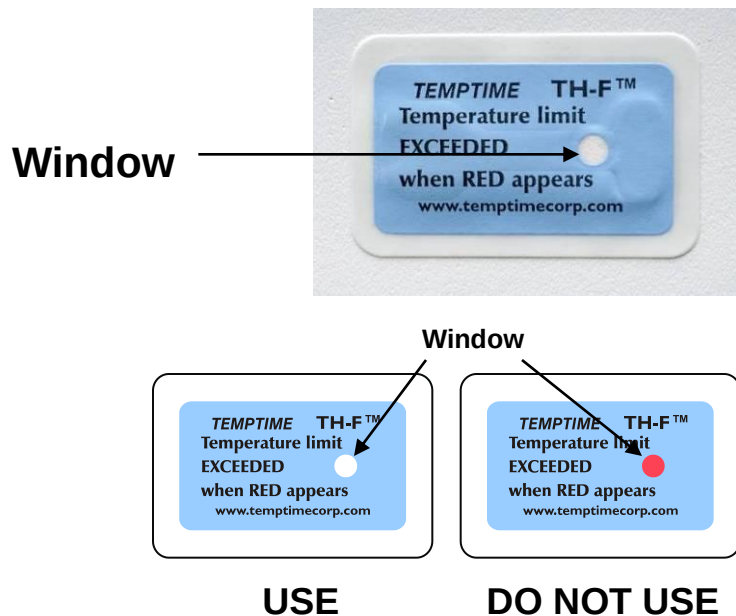
Other combinations are possible

Threshold Indicators

- Single use threshold indicators.
- Multiple unit secondary packages or shipping boxes.
- Ability to customize temperature thresholds.

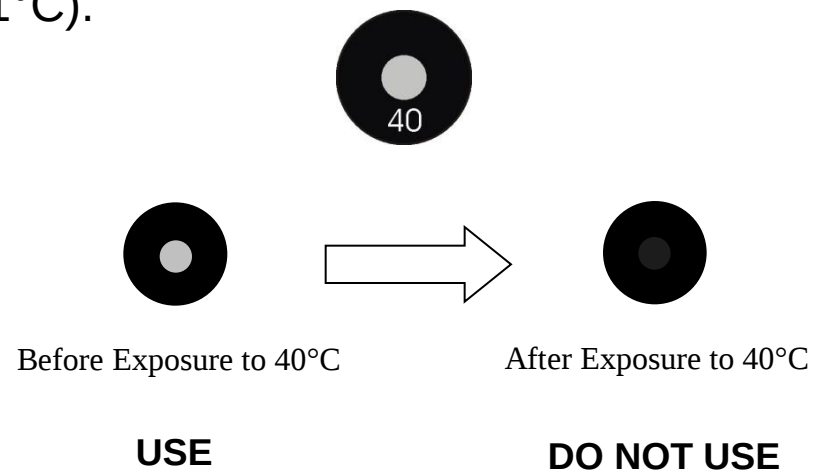
LIMITmarker® Indicators

Formulated to signal short excursions above the set response temperatures: 9°C, 25°C and 31°C (all +/- 1°C).



LIMITmarker® I Indicators

Formulated to immediately signal upon excursions above the set response temperatures: 40°C, 44°C and 50°C (+/- 1°C).



TransTracker for Monitoring Shipments

Pharmaceutical Product	Indication	Customer	Temptime Product	Value Delivered
	Medical Imaging Contrast Media	Lantheus		Ensures enhanced imaging quality for more precise diagnosis
	Childhood vaccines for VFC Program	Novartis Sanofi Pasteur		Prevent vaccination with freeze damaged vaccines
	Rheumatoid Arthritis	AbbVie		Protect patients from self-administering heat damaged medicines
	Migraine headaches	Zogenix		Improved drug delivery for chronic migraines
	M.S. Psoriasis Crohn's Anemia	Value Drug and London Drug for: - Biogen - Janssen - Amgen - Teva	 For shipments in specialty pharmacy	- Protect patients from administering temperature damaged medicines - Reduces risk of adverse affects, ineffective treatment