Transformative Innovations Beyond Vaccine Vial Monitor (VVM)
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
- 2\textsuperscript{nd} 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
The Percent of VVM2 Dot Price versus a 10 dose OPV Vial 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

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

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

**Response Temperatures**

- **Before Freezing**
  - -1°C ± 1°C
  - 0°C ± 1°C
  - -6°C ± 2°C

- **After Freezing**

“Magnified view of the FREEZEmarker® indicator”
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.
FREEZEmarker® Progress

Peer Reviewed Article Published in Infectious Diseases for Clinical Practices

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

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

http://journals.lww.com/infectdis/Abstract/publishahead/Visual_Indicators_on_Vaccine_Boxes_as_Early.99324.aspx

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 Murheka,¹ Srihari Dutta,² Ambujam Nair Kapoor,² Sailaja Bitragunta,² Raja Dhul,² Pramit Ghosh,¹ Karuniangounder Kolanda Swamy,³ Kalyanranjan Mukhopadhyay,⁴ Somorjit Ningombam,⁴ Kamlesh Parmar,⁴ Deveshwar Ravishankar,⁴ Rakesh Singh,⁴ Varsha Singh,⁴ Rajesh Sisodiya,³ Ramanatham Subramanian⁴ & Tana Takum⁴

Revision of WHO PQS Specification for Irreversible Freeze Indicator Submitted
Vial Level Freeze Risk Indicator

Does the world need vial level freeze risk indicator?
Vial Level Freeze Risk Indicator

Does the world need vial level freeze risk indicator?
Vial Level Freeze Risk Indicator

Does the world need vial level freeze risk indicator?

Prior to freezing

After freezing
The innovation of the Controlled Temperature Chain (CTC) – where do we go from here?
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 (Prevnar13) 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
Not presently available for sale.
Not cleared for sale as a medical device in the U.S.
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

*Toward a global framework for e-health information systems, David Lubinski and Jan Grevendonk, PATH, Optimize Newsletter June 2010*
Typical Product and Information Flow

MedTracker 1: Vaccine Public Market Pilot

- Vaccine Manufacturer
  - Country Central Store
  - Country Provincial Store
  - Health Center
  - Patient/Health Worker

User smart phone interprets barcode and indicator. Information sent to host computer.

Host computer communicates with user.

Captive Database
Web Portal

MedTracker™ Demo

Vaccine may be used.
Temperature Monitor: ✓ OK
Product Expiration: ✓ Oct - 2011
For Additional Information Call 500-222-3934
Download Patient Use Instructions
MedTracker Demo
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

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

Will there be PQS process for uses beyond vaccines?
## Temptime Core Technologies
Applied to Address Unmet Market Needs

### Core Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freeze</td>
<td><img src="image" alt="Freeze" /></td>
</tr>
<tr>
<td>Cumulative Heat</td>
<td><img src="image" alt="Cumulative Heat" /></td>
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<tr>
<td>Delayed Heat Threshold</td>
<td><img src="image" alt="Delayed Heat" /></td>
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<tr>
<td>Instant Heat Threshold</td>
<td><img src="image" alt="Instant Heat" /></td>
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*Temptime Core Technologies*  
*Protecting Patients - Reducing Risk™*
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).

Before Exposure to 40°C

After Exposure to 40°C
<table>
<thead>
<tr>
<th>Pharmaceutical Product</th>
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<th>Customer</th>
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<th>Value Delivered</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Medical Imaging</td>
<td>Lantheus</td>
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<td>• Ensures enhanced imaging quality for more precise diagnosis</td>
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<td>Contrast Media</td>
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<td></td>
<td>Childhood vaccines</td>
<td>Novartis</td>
<td></td>
<td>• Prevent vaccination with freeze damaged vaccines</td>
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<td></td>
<td>for VFC Program</td>
<td>Sanofi Pasteur</td>
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<td></td>
<td>Rheumatoid Arthritis</td>
<td>AbbVie</td>
<td></td>
<td>• Protect patients from self-administering heat damaged medicines</td>
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<td></td>
<td>Migraine headaches</td>
<td>Zogenix</td>
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<td>• Improved drug delivery for chronic migraines</td>
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<tr>
<td>M.S. Psoriasis</td>
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<td>Value Drug and London Drug for:</td>
<td></td>
<td>• Protect patients from administering temperature damaged medicines</td>
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<tr>
<td>Crohn's Anemia</td>
<td></td>
<td>• Biogen</td>
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<td>• Reduces risk of adverse affects, ineffective treatment</td>
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<td>• Janssen</td>
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<td>• Amgen</td>
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<td>• Teva</td>
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