Modern Rules for an Old Practice:
Sensor Placement for GMP Temperature Mapping

Paul Daniel
Senior Regulatory Compliance Expert
Vaisala, Inc

Goals

- Review Mapping Regulations.
- Discuss 5 Rules for Sensor Placement.
Recent History

- Health Canada
  - GUI-0069 – Guidelines for Temperature Control of Drug Products during Storage and Transportation

- ISPE
  - Good Practice Guide: Cold Chain Management
Recent History

- **PDA**

- **CDSCO (India)**
  - Draft Guidelines on Good Distribution Practice for Biological Products

Recent History

- **CFDA (China)**
  - Good Supply Practices for Pharmaceutical Products

- **EMA (Europe)**
  - (2013/C 68/01) Good Distribution Practice of Medicinal Products for Human Use

- **USP 36**
  - Chapter <1079> Good Storage and Distribution Practices for Drug Products
The regulations don’t tell us how to map, or even to map.

Regulatory Summary
1. Determine if environmental parameters affect product quality.
2. Do stability testing to determine appropriate storage specifications.
3. Ensure that storage spaces are controlled to meet specifications.

Mapping and monitoring is industry GMP response to #3.

Therefore, regulations aren’t very helpful for sensor placement!

Resources for Sensor Placement

- Tradition and Precedence
  - What has been done at your facility before?

- Equipment
  - What equipment do you already have?

- Science
  - What makes sense based on scientific principles?
  - Guidance
5 Rules

- Map the Extremes.
- Map in 3 Dimensions.
- For Large Spaces, Map Storage Only.
- Identify and Address Variables
- If it’s worth mapping, it’s worth monitoring.
Rule 1: Map the Extremes.

- Geometric
  - Place sensors at each end of the storage area.

- Conditions
  - Apply validation principle of worst cases.

Parts of a Cube

- Corner – 3 planes
- Edge – 2 planes
- Side – 1 plane
- Space – 0 planes
Parts of a Cube

Rule 1: Map the Extremes

Corollary 1A: If $\leq 2m^3$, use $9 + 1$. 
9 spots = worst case?

- Air Flow:
  - Corners have least air circulation.
  - Center has most air circulation.

- Heat Exchange:
  - Corners have the most exposure (3 planes)
  - Center has the least exposure (0 planes)

How many? Where? < 20m³
How many? Where? < 20m³

- TOP
- SIDE
- FRONT
How many? Where? $< 20m^3$

- TOP
- FRONT
- SIDE
Corollary 1B: If $\leq 20m^3$, use 15 +1.

Guidance describes 9 +1 and 15 +1

- ISPE Good Practice Guide: Cold Chain Management (2011)
Rule 2: Map in 3 Dimensions.

3 planes.
Left to right.

3 planes.
Top to bottom.
Rule 2: Map in 3 Dimensions.

3 planes.
Front to back.

Corollary 2A: If $\geq 20m^3$, use Stacks of 3.

High
Middle
Low
Stacks of 3, in 3 dimensions.
Stacks of 3, in 3 dimensions.
Corollary 2A: If $\geq 20m^3$, use Stacks of 3.
Corollary 2B: Remove sensors if possible.

- Remove “extra” sensors.
  - 15 +1 diagram.
  - With “Stacks of 3, in 3-D”, it would have 27 sensors.

Stacks of 3, in 3 dimensions.
Stacks of 3, in 3 dimensions.

More published support....

“Completing a three-dimensional temperature profile should be achieved by measuring points at not less than three dimensional planes in each direction/axis—top-to-bottom, left-to-right, front-to-back…”

Rule 3: If $\geq 20m^3$, map storage only.

- As the space gets larger, it is not necessary to map hallways and access areas.
- Map only the shelves and areas where product is actually stored.
- Requires controls to prevent storage in wrong areas.
  - SOPs
  - Training
  - Signs

More published support....

“Completing a three-dimensional temperature profile should be achieved by measuring points at not less than three dimensional planes in each direction/axis—top-to-bottom, left-to-right, front-to-back, where product will be present.”

Rule Summary (so far…)

- Rule 1 – Map the Extremes
  - Corollary 1A – If ≤ 2m³, use 9+1.
  - Corollary 1B – If ≤ 20m³, use 15+1

- Rule 2 - Map in 3 Dimensions
  - Corollary 2A – If ≤ 20m³, use Stacks of 3
  - Corollary 2B – Remove Sensors if Possible
Rule Summary (so far…)

- Rule 1 – Map the Extremes
  - Corollary 1A – If ≤ 2m³, use 9+1.
  - Corollary 1B – If ≤ 20m³, use 15+1

- Rule 2 - Map in 3 Dimensions
  - Corollary 2A – If ≤ 20m³, use Stacks of 3
  - Corollary 2B – Remove Sensors if Possible

- Rule 3 - If ≥ 20m³, map storage only.

It’s just guidance. It’s a place to start.

“...additional points may be needed depending on airflow sources/characteristics, shelving (storage locations), external temperature sources, and previous experience with similar units and their thermal behavior.”

– ISPE Good Practice Guide: Cold Chain Management (2011)
More from USP 36 Chapter <1079>...

The following factors should be considered during temperature mapping of storage locations:

- Size of the space
- HVAC Locations
- Sun-facing walls
- Low ceilings or roofs
- Geography
- Airflow
- Outside temperature variability
- Weekly workflow variation
- Equipment movement
- Storage patterns of product
- Equipment capabilities
- SOPs.

Rule 4: Identify Variables

- Volume
- Temperature $\Delta$
- Height
- Exterior Walls
- Construction Materials
- Doors and Windows
- Lighting
- Gradients
- HVAC Vents and Returns
- Air Circulation
- Control Sensors
- Energy Sources
- Racks and Shelving
- Traffic Patterns
- Human Factors
Volume

Temperature \(\Delta\)
Height

Exterior Walls
Construction Materials

Doors and Windows
Lighting

Gradients
HVAC Vents and Returns

Air Circulation
Control Sensors

Energy Sources
Racks, Shelves, and Product

Traffic Patterns
Rule 4: Identify Variables

- Place sensors near representative variables!
- Adjust ideal “grid” to intersect variables.
Distance Between Points

Temperature

Distance (X)
**Distance Between Points**

![Graph showing temperature variation with distance](image)

**Distance Between Points**

![Graph showing temperature variation with half the distance](image)

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*Source: Sensor Placement for Validation Mapping – GxP Webinar ©Vaisala*
Distance Between Points

Distance Between Points

Distance (1/8X)

Distance (1/16X)
Rule 5: If it is worth mapping…
It is worth monitoring.

- Find the hot and cold spots and monitor them.
- Select the right monitoring solution.
- Validate the monitoring system.
Monitoring....

“Temperature monitoring... documents the temperatures during the qualification and operation. It allows conclusions on whether the product is stored and shipped within the approved temperature range. Therefore, an appropriate temperature monitoring strategy should be selected and qualified.”


Rule Summary

- Rule 1 – Map the Extremes
  - Corollary 1A – If \( \leq 2\text{m}^3 \), use 9+1.
  - Corollary 1B – If \( \leq 20\text{m}^3 \), use 15+1

- Rule 2 - Map in 3 Dimensions
  - Corollary 2A – If \( \leq 20\text{m}^3 \), use Stacks of 3
  - Corollary 2B – Remove Sensors if Possible

- Rule 3 - If \( \geq 20\text{m}^3 \), map storage only.

- Rule 4 – Identify Variables

- Rule 5 – If it is worth Mapping, it is worth Monitoring
What about product temperature?

- It's always best to measure air temperature.
  - Worst case scenario provides best challenge.

“It is normal practice to use air temperature as the reference source for the stored [product]…” and is “the worst case representation of the stored product temperatures.”

- ISPE Good Practice Guide: Cold Chain Management (2011)

What about mapping humidity?

- The same concepts apply, but concerned with sources of moisture.

- Use the same number of sensors unless you have an expert who understands humidity theory.

“Where relative humidity is a critical factor, then humidity sensors could be located in the same locations – or fewer locations used with the impact of the temperature considered for other locations – as absolute humidity will be very similar throughout the space.”

- ISPE Good Practice Guide: Cold Chain Management (2011)
Summary

- Reviewed Mapping Regulations.
- Explored 5 Rules for Sensor Placement for Mapping Storage Areas.
- Reviewed Mapping Guidance.

Thanks for Attending!

Paul Daniel
Senior Regulatory Compliance Instructor
Vaisala, Inc.

Email: paul.daniel@vaisala.com