Introduction to Temperature Mapping of Controlled Temperature Storage Areas – Temperature Mapping 101

Presented by Grant South
7 February, 2018
Temperature Mapping 101: Welcome

- Introduction to temperature mapping
  - What and why
  - GMP requirements
  - Regulations and guidance

- Temperature mapping requirements and considerations
  - Performing a mapping study
  - Number of sensors and their locations
  - Identifying and addressing variables
  - OQ vs. PQ monitoring, loaded vs. unloaded studies
  - Duration, lagging and MKT
Temperature Mapping 101: What is temperature mapping?

• What?
  • Temperature mapping establishes the temperature distribution within the zone being mapped and it locates hot and cold spots.

• Why?
  • A temperature mapping exercise is required for any space allocated for the storage and handling of products with a specified labelled storage temperature. This includes freezer rooms, cold rooms, temperature-controlled storage areas, quarantine areas and receiving and loading bays. It may also include laboratories.
Temperature Mapping 101: What does PIC/S say?

• PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Part I PE 009-12, Oct 2015

Chapter 3 – Premise and Equipment
3.19

"Storage areas should be designed or adapted to ensure good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Where special storage conditions are required (e.g. temperature, humidity) these should be provided, checked and monitored.”
Temperature Mapping 101: What does PIC/S say?

Chapter 3 – Premise and Equipment
3.3 Temperature and Environment Control

"An initial temperature mapping exercise should be carried out on the storage area before use, under representative conditions. Temperature monitoring equipment should be located according to the results of the mapping exercise, ensuring that monitoring devices are positioned in the areas that experience the extremes of fluctuations. The mapping exercise should be repeated for significant changes according to the results of a risk assessment exercise. For small premises of a few square meters which are at room temperature, an assessment of potential risks (e.g. heater / air-conditioner) should be conducted and temperature monitors placed accordingly."
Temperature Mapping 101: Other agencies/groups

- CDSCO (India) – Guidelines on Good Distribution Practice for Biological Products (2012)
- EMA – (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
Temperature Mapping 101: Useful guidance

- Technical supplement to WHO Technical Report Series, No. 961, 2011 – Temperature mapping of storage areas


- AS 2853: 1986 Enclosures – Temperature-controlled – Performance testing and grading
Temperature Mapping 101: Useful guidance

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

- ISPE Concept Paper: Controlled Temperature Chamber Mapping (2012)

- ISPE Good Practice Guide: Controlled Temperature Chambers – Draft 1
  - Provides guidance on good practices for the mapping of controlled temperature chambers, warehouses, and refrigerated storage areas used to store raw material, work in progress, or finished product and which operate under current GMP.
Temperature Mapping 101: 5 considerations

1. Map the extremes
2. Map in 3 dimensions
3. Identify and address variables
4. For large spaces, map storage only
5. If it’s worth mapping, it’s worth monitoring
Temperature Mapping 101: Performing a study

1. Prepare a mapping protocol
   • Select the type of loggers to use
   • Designate the mapping team
   • Survey the site
   • Establish the acceptance criteria
   • Determine the logger locations

2. Carry out the mapping exercise
   • Record the logger locations
   • Label and program the loggers
   • Position the loggers
   • Run the study
   • Download the data

3. Prepare a mapping report

4. Implement recommendations
   • Remedial actions
   • Follow-up mapping exercise
Temperature Mapping 101: Number of sensors

- Chambers ≤ 2m³
  - ISPE recommendation
    - Adheres to AS2853 and WHO
  - Represents the minimum number of loggers
  - Additional loggers:
    - Airflow characteristics
    - Shelving
    - External temperature sources/conditions
    - Previous experience

- 9 + 1 rule
Temperature Mapping 101: Number of sensors

- Chambers >2m³ and ≤ 20m³
  - ISPE recommendation
    - Adheres to AS2853 and WHO
  - Represents the minimum number of loggers
  - Additional loggers:
    - Airflow characteristics
    - Shelving
    - External temperature sources/conditions
    - Previous experience

- 15 + 1 rule
Temperature Mapping 101: Number of sensors

- WHO recommendation

\[ h \approx 3.6 \text{m} \]

5-10m

Outside

Top

Middle

Bottom
Temperature Mapping 101: Number of sensors

- AS2853 recommendation
Temperature Mapping 101: Number of sensors
Temperature Mapping 101: Identifying variables

- Volume / load mass
- Temperature
- Height
- Exterior walls
- Construction materials
- Doors and windows
- Lighting
- Gradients
- HVAC supply/return vents
- Air circulation
- Control sensors

- Energy sources
- Racks and shelving
- Traffic patterns
- Human factors
- Loading / unloading patterns
Temperature Mapping 101: Number of sensors
Temperature Mapping 101: Recommendations

- Monitoring sensor placement
  - Best case
  - Worst case

- HVAC
  - Rebalance
  - Reconfigure
  - Move control sensor

- Windows
  - Cover
  - Blackout
  - Remove

- Change roller door to Rapid-roller door
Temperature Mapping 101: Loaded and unloaded

Why?
- The load mass/temperature will impact system performance
- The load volume will impact the air flow patterns

Note:
- Loads should be representative

- Unloaded/empty
  - Low thermal mass
  - High air flow
  - Temperature changes quickly

- Loaded
  - High thermal mass
  - Low air flow
  - Temperature changes slowly

- Partial load
  - Loading patterns
  - Air flow effects
Temperature Mapping 101: Duration

The duration of a study should be based on:
- the frequency of product movement
- equipment cycles (defrost cycles)
- operational schedules / business activities
- potential ambient conditions (and their potential to impact storage conditions)

<table>
<thead>
<tr>
<th>Type</th>
<th>Considerations</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warehouse</td>
<td>Walls/roof exposed to exterior conditions</td>
<td>7 to 14 days</td>
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<tr>
<td></td>
<td>High loading/unloading frequency</td>
<td></td>
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<tr>
<td></td>
<td>High volume and high door openings</td>
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</tr>
<tr>
<td>Walk-in cool room</td>
<td>Walls/roof exposed to interior conditions</td>
<td>3 to 7 days</td>
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<tr>
<td>or freezer</td>
<td>Low to medium loading/unloading frequency</td>
<td></td>
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<tr>
<td></td>
<td>Medium volume and medium door openings</td>
<td></td>
</tr>
<tr>
<td>Equipment</td>
<td>Walls exposed to temp-controlled conditions</td>
<td>1 to 4 days</td>
</tr>
<tr>
<td></td>
<td>Low to medium loading/unloading frequency</td>
<td></td>
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<tr>
<td></td>
<td>Low volume and high door openings</td>
<td></td>
</tr>
</tbody>
</table>
Temperature Mapping 101: OQ vs. PQ

Operational Qualification

- Full mapping exercise
  - Unloaded (empty)
  - Loaded (normal)
- Power failure
- Identify hot/cold spots
- Report/recommendations

Performance Qualification

- Full mapping exercise
  - 12 months
  - Seasonal variation
  - Normal operation
- Identify hot/cold spots
- Report/recommendations
Temperature Mapping 101: Thermal lagging

Lagging or filtering

- Appropriate justification required
- Lagging should be representative of product
- Suitable materials include:
  - Aluminium
  - Stainless Steel
  - Water
  - Glycol
  - Alcohol

AS3864: Medical refrigeration equipment – For the storage of blood and blood products

“The temperature and alarm sensors shall be thermally lagged in a manner that will reflect the temperature of the blood pack being stored.”
Temperature Mapping 101: Mean kinetic temperature (MKT)

- Simplified way of expressing the overall effect of temperature fluctuations during storage or transit of product.
- Used to determine if improper storage/handling has affected the product.

MKT is expressed as:

\[
\frac{\Delta H/R}{-\ln \left( \frac{e^{-\Delta H/RT_1} + e^{-\Delta H/RT_2} + \ldots + e^{-\Delta H/RT_n}}{n} \right)}
\]

Where:
- $\Delta H$ = activation energy (typically from 60 to 100 kJ/mol for solids and liquids)
- $R = 8.314472$ J/mol-K (universal gas constant)
- $T =$ temperature in degrees K
- $n =$ the number of sample periods over which data is collected

Note: $\ln$ is the natural log and $e$ is the natural log base.
Temperature Mapping 101: Summary

• Everyone tells us to do it, not many tell us how
• Useful guidance is available
• Prepare protocol, perform the study, prepare report, implement recommendations
• How many sensors
• Loaded, unloaded, OQ, PQ, duration, lagging, MKT
• 5 Considerations
  1. Map the extremes
  2. Map in 3 dimensions
  3. Identify and address variables
  4. For large spaces, map storage only
  5. If it’s worth mapping, it’s worth monitoring
Thank you for your time. Questions?

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