GDP Focus Session: Deep Dive into Good Distribution Practices

Qualification for the Storage of Finished Drugs and Drug Products

- Storage Qualification (Temperature Mapping)
- Package Qualification (Thermal Protection)
- Transportation Qualification (Lane Mapping)

March 11, 2021

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Previously

<1079> Risk and Mitigation Strategies for the Storage and Transportation of Finished Products

- Risk Identification:
  - Product knowledge
  - Process knowledge
- Mitigation Strategies:
  - Documentation and Procedures
  - Training
  - Resources for Storage, Transportation, and Personnel
  - Qualification and Validation

<1079.2> Mean Kinetic Temperature in the Evaluation of Temperature Excursions During Storage and Transportation of Drug Products

- How MKT should be used in the evaluation of a temperature excursion
  - Controlled Room Temperature
    - 20º and 25ºC
  - Controlled Cold Temperature
    - 2º and 8ºC

[1] Seevers RH, Hofer J, Harber P, Ulrich DA, Bishara R. The use of mean kinetic temperature (MKT) in the handling, storage and distribution of temperature sensitive pharmaceuticals. Pharmaceutical Outsourcing. May/June 2009;12–17.

[2] Anderson C, Seevers R, Hunt D. The use of mean kinetic temperature to aid evaluation of temperature excursions: proper and improper application. Pharm Forum. 2018;44(4)

[3] Anderson C, Seevers R, Hunt D. The Use of Mean Kinetic Temperature to Aid Evaluation of Temperature Excursions for Controlled Cold Temperature Drugs: Proper and Improper Application PF 45(5), September 3, 2019

Deeper Dive

- Storage Qualification
  - Temperature Mapping
- Package Qualification
  - Thermal Protection
- Transportation Qualification
  - Lane Mapping

Presenters

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Temperature Qualification for the Storage of Finished Drugs and Drug Products

Purpose

- Storage and handling areas need to maintain labelled temperature ranges to ensure product efficacy and expiry.
- Even small excursions outside of labelled product storage can an impact over time that may even be greater that large excursions over a short period of time.
- All excursions must be evaluated:
  - For USP storage ranges and allowable excursions and limitations please see USP <659> Package and Storage Requirements.
  - For the use of Mean Kinetic Temperature (MKT) please see USP <1079.2> Mean Kinetic Temperature in the Evaluation of Temperature Excursions During Storage and Transportation of Drug Products

Qualification/Mapping Steps

1. Evaluate area to be qualified / mapped
2. Obtain calibrated monitoring equipment and calibration documentation
3. Develop probe placement map based on the evaluation
4. Schedule and execute mapping
5. Retrieve and evaluate data
6. Determine mitigation strategies (if needed)
7. Complete report for approval

Evaluate Area

Step 1: Evaluate Area to be Qualified/Mapped

A. Size of the space (obtain layout to include dimensions, height, ceiling height changes, walls and wall openings)

B. Location of HVAC equipment, space heaters, and air conditioners

C. Sun-facing walls

D. Geographic location of the area being mapped

E. Airflow inside the storage location

F. Temperature variability outside the storage location

G. Workflow variation and movement of equipment (weekday vs. weekend)

H. Loading or storage patterns of product

I. Equipment capabilities (e.g., defrost mode, cycle mode);

J. SOPs (workflow)

Evaluate Area

Step 1: Evaluate Area to be Qualified/Mapped (Probe Guideline)

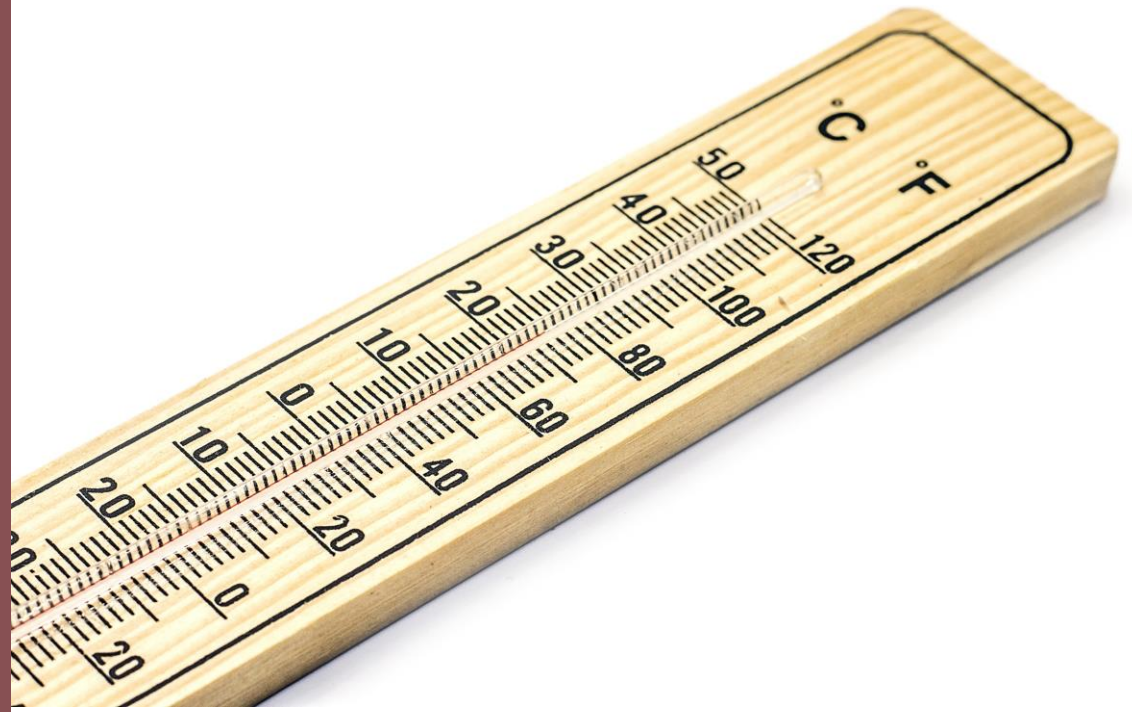
- Establish the number of temperature probes to be used following your organizations policy, government requirements, or a rationale to meet such standards. This is a suggested guidance by the USP Packaging and Distribution Expert Committee and should be interpreted as guidance and not a requirement or standard that supersedes any other requirement.
- EXAMPLES:
  - < $2m^3$ ($70.5ft^3$) = 10
  - $2m^3$ to 20 m^3 (70 to $706ft^3$) = 16
  - > $20m^3$ ($706ft^3$) = 28
- Area separated by a demising wall, doors, different ceiling height, or floor layout should be considered separate areas.

Evaluate Area

Step 1: Evaluate Area to be Qualified/Mapped

(Temperature Storage Areas)

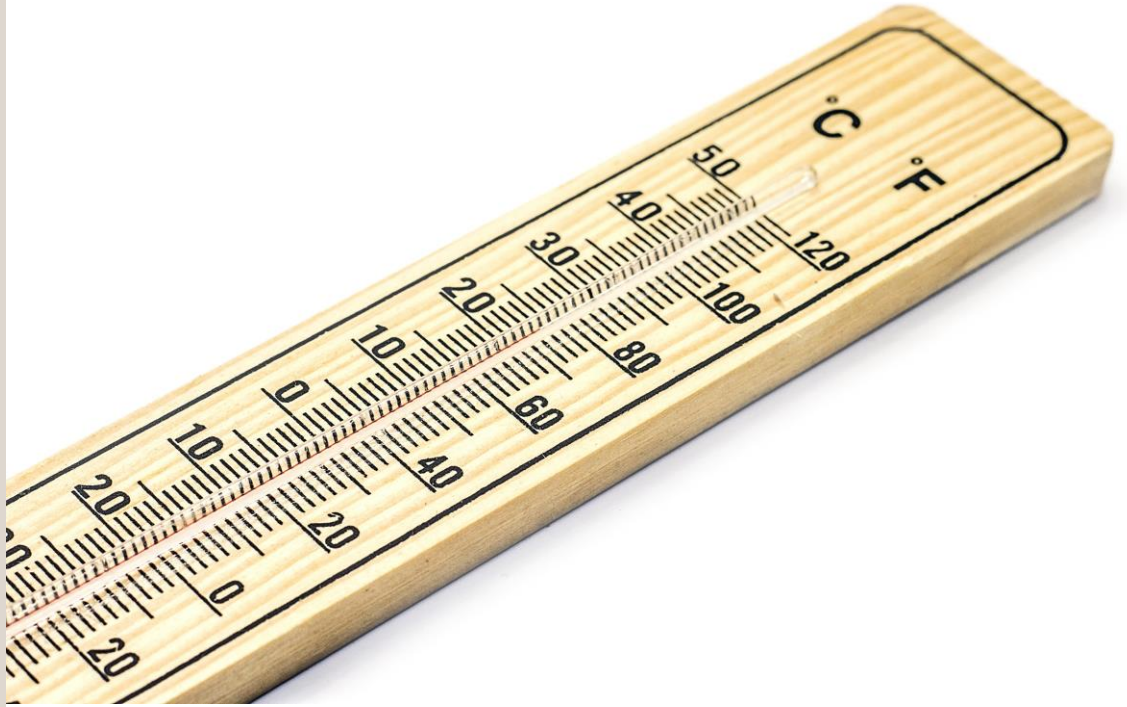
- Controlled Room Temperature (CRT) – Temperature maintained thermostatically that maintains 20º to 25ºC. Allowable Excursions:
  - 15º to 30ºC
  - Transient spikes not more than 40ºC
  - Excursion time not more than 24 hours
  - MKT not more than 25ºC (measured back 30 days or time product in possession)
  - Product labelled CRT can be stored Cool (8º to 15ºC) or CCT (2-8ºC) unless otherwise specified on the individual monograph or label
    - Storage time in Cool or CCT cannot be used to calculate excursion temperatures outside of CRT range!



Evaluate Area

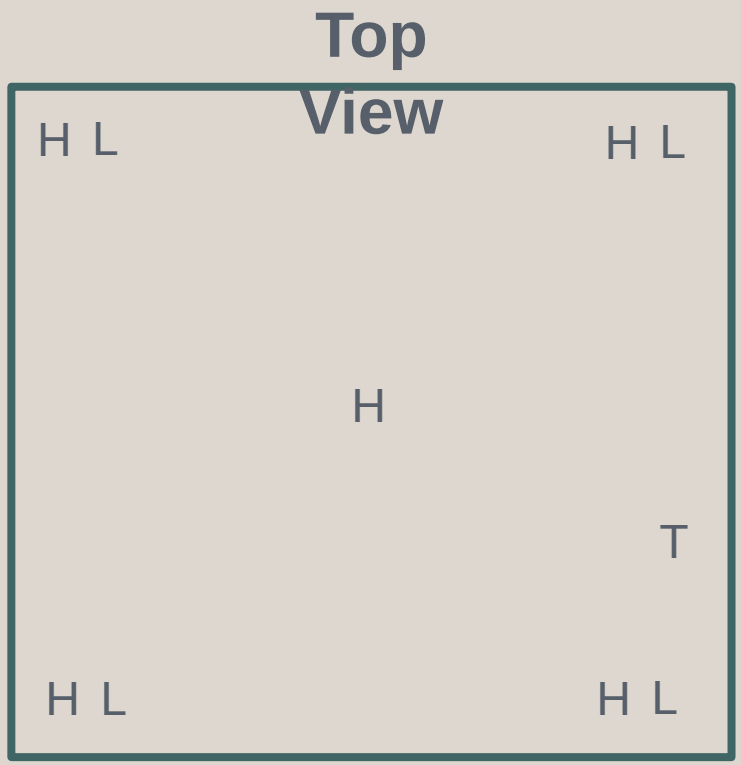
Step 1: Evaluate Area to be Qualified/Mapped (Temperature Storage Areas)

- Controlled Cold Temperature (CCT) – Temperature is controlled to maintained 2º to 8ºC. Allowable Excursions:
  - 2º to 15ºC
  - Excursion time not more than 24 hours
  - MKT not more than 8ºC (measured back 24 hours)
  - Each excursion must be evaluated as a separate event
- Frozen – Temperature is controlled between -20º and -10ºC.
  - Some products require storage below -20ºC (+/- 10ºC)
  - Some products (such as some COVID-19 Vaccines) require -20ºC (+/- 5ºC)
- Ultra-Low – Typically -80ºC (+/- 10ºC)



Monitoring Probe Placement

Example: Areas < 2m³ (70.5ft³) = 10 Probes



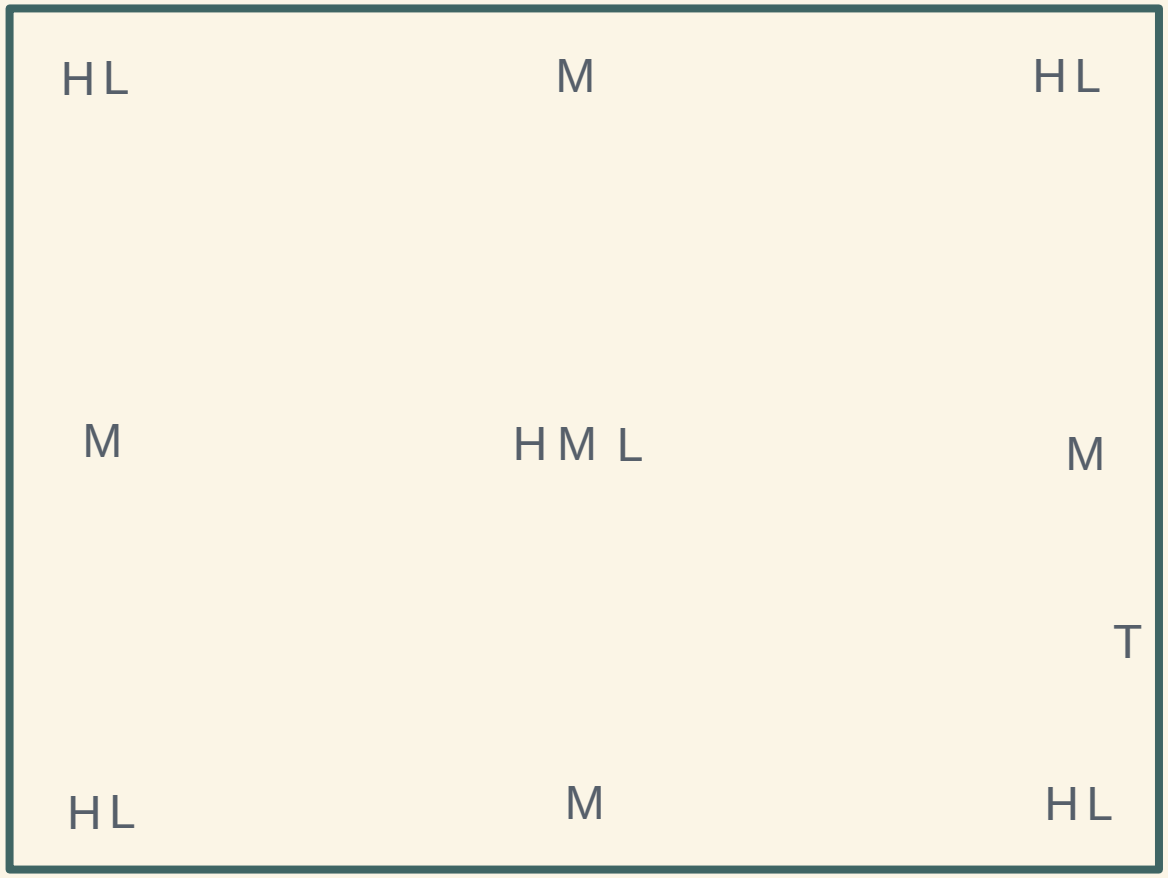
- H = High Probe
  - Highest level product is stocked
- L = Low Probe
  - Lowest level product is stocked
- T = Probe placed directly next to the Thermostat that controls the temperature in this area

Reach in freezers may have two or more separate storage area with doors to access, all these areas must be evaluated

Monitoring Probe Placement

Example: Areas between 2m³ to 20m³ (70 to 706ft³) = 16 Probes

Top View

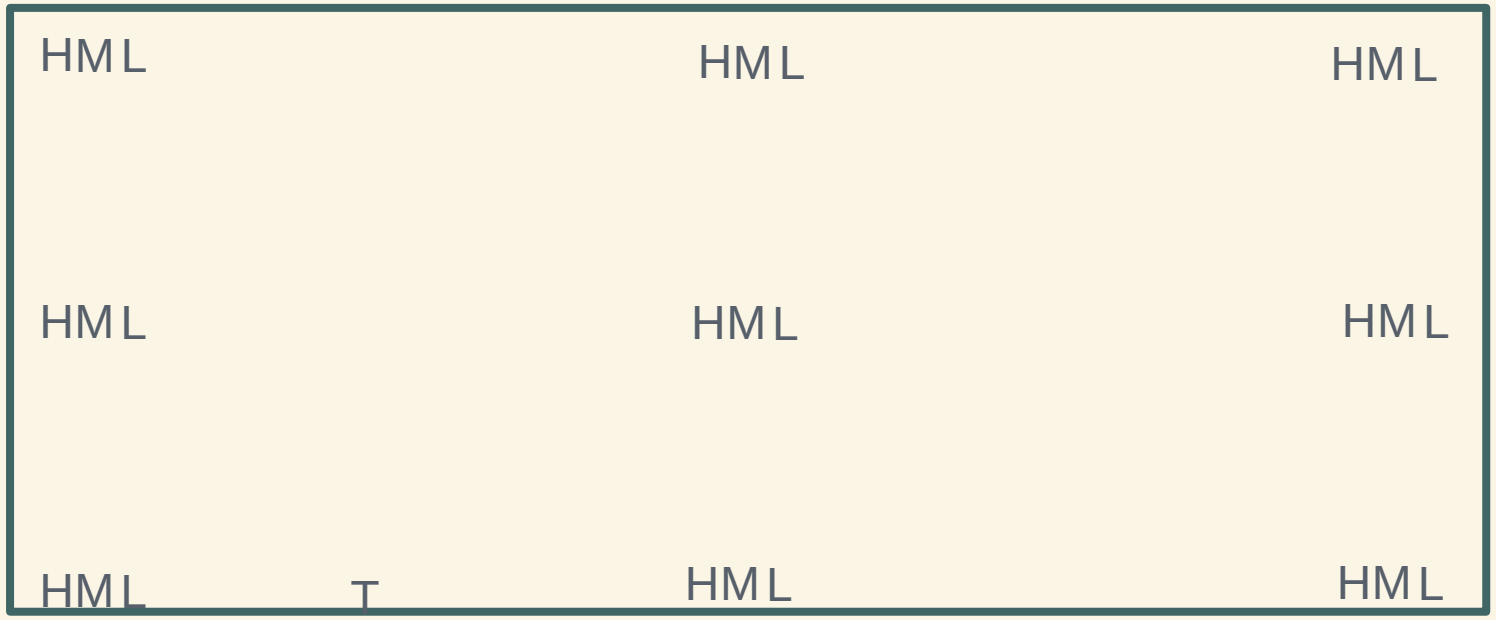


- H = High Probe
  - Highest level product is stocked
- M = Mid Probe
  - Middle level product is stocked
- L = Low Probe
  - Lowest level product is stocked
- T = Probe placed directly next to the Thermostat that controls the temperature in this area

Monitoring Probe Placement

Example: Areas >20m^3 (706ft^3) = 28 Probes

Top View

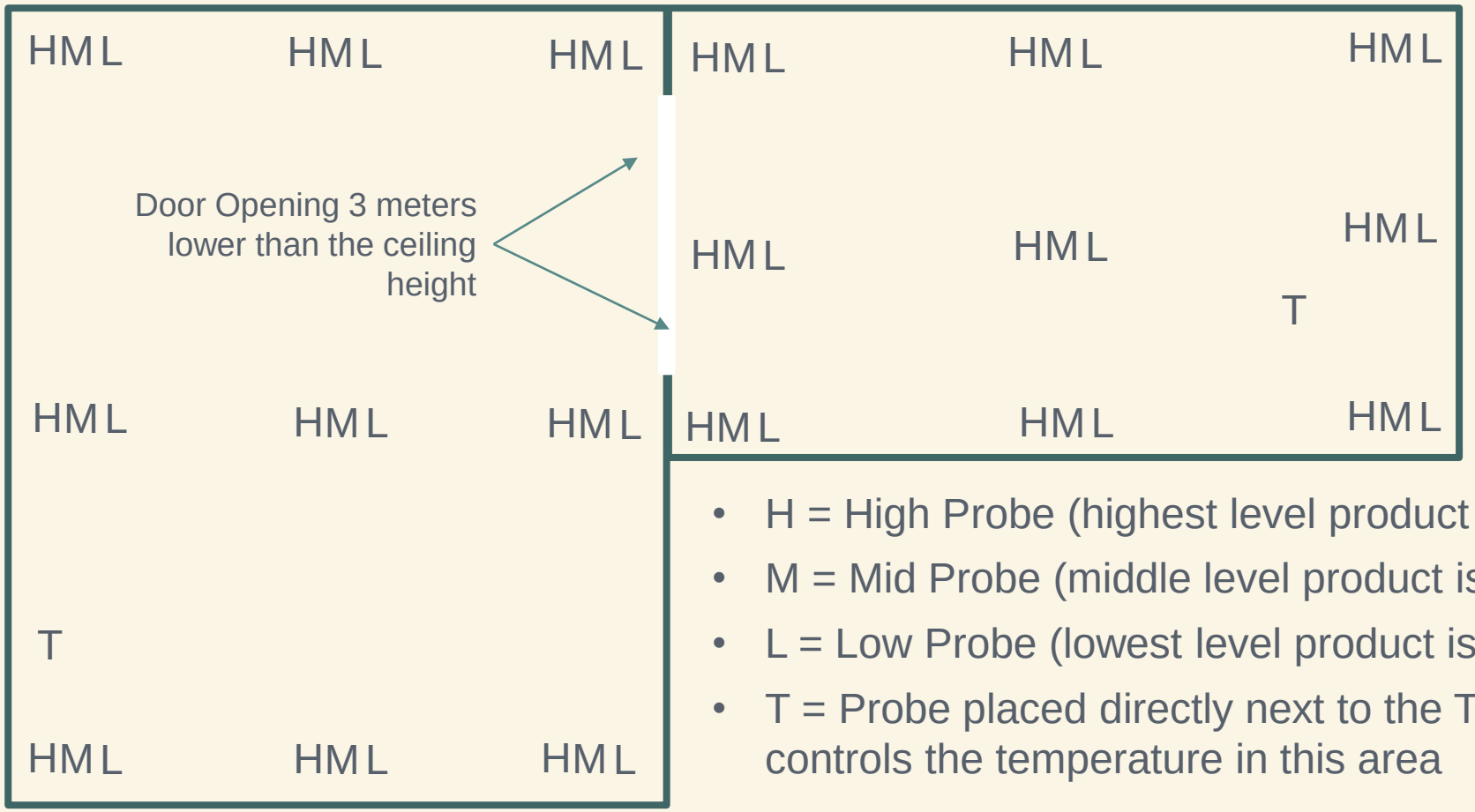


- H = High Probe (highest level product is stocked)
- M = Mid Probe (middle level product is stocked)
- L = Low Probe (lowest level product is stocked)
- T = Probe placed directly next to the Thermostat that controls the temperature in this area

Monitoring Probe Placement

Example: Multiple Connected Areas (both over 20m$^{3)}$

Top View



- H = High Probe (highest level product is stocked)
- M = Mid Probe (middle level product is stocked)
- L = Low Probe (lowest level product is stocked)
- T = Probe placed directly next to the Thermostat that controls the temperature in this area

Monitoring Equipment

Step 2: Obtaining Monitoring Equipment

A. Obtain the number of calibrated monitors for the storage range(s) that you are evaluating. It is suggested that you obtain extra monitors (10%) in the event of a failure.

B. If you are mapping a refrigerator, freezer, or an ultra-low freezer, ensure that you have a monitor with a probe wire long enough to have at least one probe inside of the area being mapped, placed next to the thermostat, that can be read outside.

- This helps early detection of a thermostat controller reading the correct temperature.
- This can also be used during open-closes door (or power off-on) test to see when the temperature has recovered to the normal operating range without opening the door.

C. Ensure that you have or can download current (not expired) calibration certificates.

D. Ensure devices are programmed with the correct date, time zone and temperature ranges.

Probe Placement Map

Step 3: Develop probe placement map based on the evaluation

A. Probes should be placed with location that product may be stored or staged.

B. All areas dived by walls, accessed with doors, or with different ceiling heights should be mapped as separate areas.

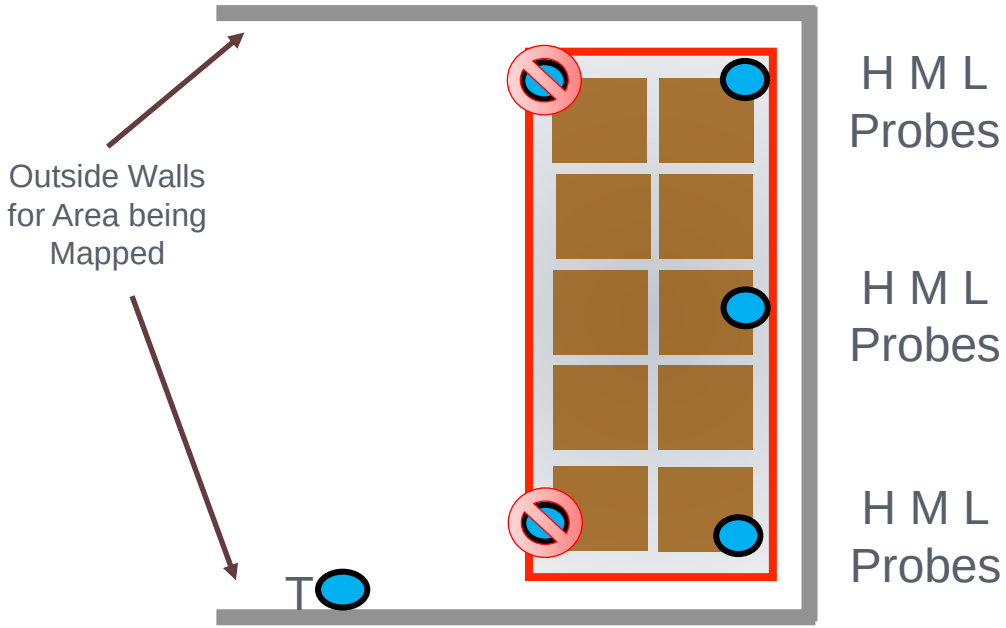
C. Probes should be securely fastened to remain in place during the study period.

D. The probe placed next to the thermostat controller should have a wire lead to the outside of the storage area so that you can observe how the thermostat reading reacts when compared to the monitoring device (this is especially true for reach in refrigerators, freezers, and ultra-low freezers and the wire lead for remote reading may not be necessary or feasible for large walk-in refrigerators or freezers).

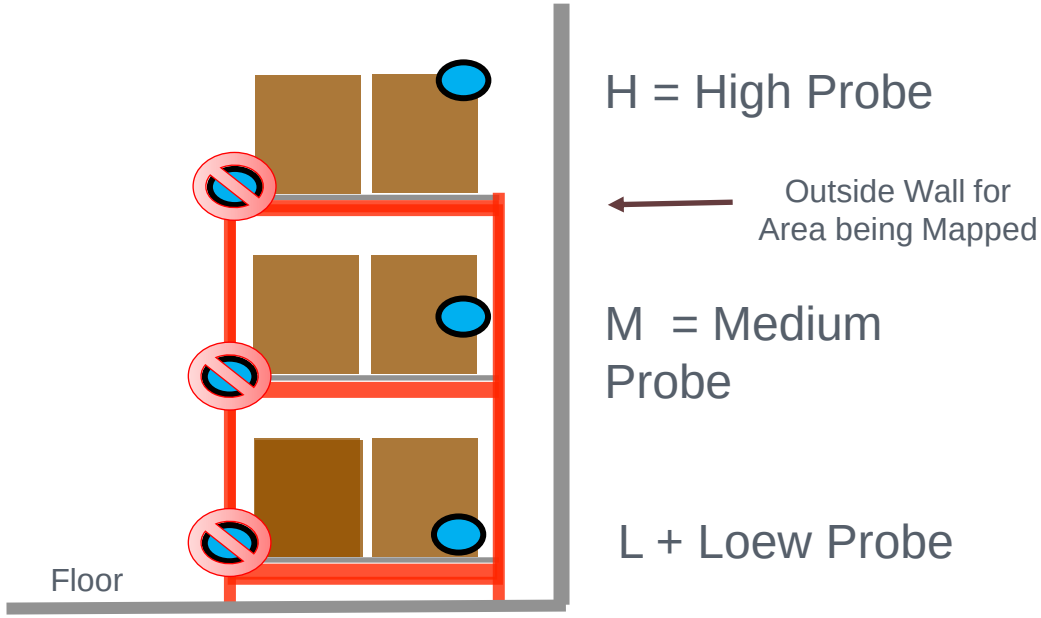
Monitoring Probe Placement

Example: Detail Probe Placements

Top View – Product Shelf Racking



Front View – Product Shelf Racking



Correct Probe Placement = outer limits of where product will be stored or staged

Incorrect Probe Placement

Mapping Execution

Step 4: Schedule and Execute Mapping

A. The duration of temperature recordings during the thermal mapping of a warehouse or cold room should capture workflow variation that may impact arrow and the resulting temperature fluctuation; for example, this process could last from 1 day to 1 week, depending on the workflow cycle.

B. If a no-load (no product) is conducted prior to storage of the product or if the mapping is done over a weekend or holiday without the normal personnel workflow traffic, open-door/close-door tests should be done to determine to impact and recovery time is necessary (this is especially critical, but not limited to, freezers and refrigerators).

C. If an area is mapped during a time period when the area is not accessed (no less than 24 hours), open-closed door test and power on-off tests should be executed at the end] of this initial test period.

Mapping Execution

Step 4: Schedule and Execute Mapping (cont'd)

D. Open-Closed Door Tests:
   - Open for 15 seconds, 30 seconds, 1 minute, and 10 minutes.
   - After each opening, wait until the temperature recovers before opening again.

E. Power On-Off Test:
   - Power failure – until unit goes out of range (limit) .
   - Turn back on until the temperature gets back to set point.
   - Do not do this with product.

Data Evaluation

Step 5: Retrieve and evaluate data

1. Download electronic data and review start and stop times as well as dates to ensure devices were programed appropriately.
2. Evaluate data from each probe looking for any out-of-range temperatures.
3. Organize data by storage area, device/probe and calibration documentation per your protocol / SOP instructions.
4. If there are any out-of-range readings, investigate time and placement, and the evaluation completed in Step 1. This includes heating and air equipment and location, operations workflow like opening and closing of doors, and time of day/location.

Mitigation Strategies

Step 6: Determine Mitigation Strategies (if needed)

A. Probes that indicate temperature close to a storage temperature limit (ort beyond) may be mitigated in a variety of ways. These gaps (performance qualification criteria gaps) can be mitigated in a variety of ways, including but not limited to:

- Ensure storage area is thermostatically controlled to prevent excursions outside of the storage area limits (see USP <659> Packaging and Storage Requirements).
- Adjustment and securing of thermostats.
- Evaluation of airflow turns and installing (or adjusting) air moving fans to increase airflow turns.
- Addition of insulation on walls nearest the excursions.
- Upgrade temperature management system.

B. If unforeseen excursion do occur, please reference the use and limitation of using Mean Kinetic Temperature (MTK) to evaluate excursions (see USP <1079.2> Mean Kinetic Temperature in the Evaluation of Temperature Excursions during Storage and Transportation of Drug Products)

Approval

Step 7: Complete Report for Approval

A. Components of the protocol :

- Detailed map (s) with dimensions, ceiling heights, doors, product racking or storage areas, heating and cooling units, fans, thermostat locations and probe placements
- List on temperature monitoring devices, serial numbers, and placement
- Calibration certificates
- Temperature readouts highlighting readings within the temperature storage ranges
- List of deviations, if applicable, and resolutions
- Executive summary to include the need for remediation, if applicable

B. Approval of the study report guidelines (follow your organization's procedures):

- Study leader completing the report
- Quality and/or regulatory
- Operation or business leader responsible for the operations

Presenters

Chris J Anderson

Quality Director, Cardinal Health
USP Expert Committee Member
Co-Chair USP GDP Chapters

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Temperature Qualification for the Storage of Finished Drugs and Drug Products

Purpose

- Packaging at the tertiary level (e.g., outer, external, or shipping package) or thereafter for the distribution should be selected and tested to ensure that product quality is maintained and to protect the contents from the rigors of distribution, including environmental or physical damage.
- Finished Drug products that are shipped between locations and shipped to the healthcare provider (hospital, pharmacy, clink, or long-term care facility) need to maintain labelled temperature ranges to ensure product efficacy and expiry.
- Most thermal shipping containers (or systems) are for Controlled Cold Temperature (CCT)
  - More Frozen (-20C +/- 5C) and Ultra-Frozen (-80C) products being developed, such as the Covid-19 Vaccines
  - Controlled Room Temperature Product (CRT) may require qualified thermal shipping containers (or systems) if the USP allowable excursion ranges cannot be maintained
- All excursions must be evaluated:
  - For USP storage ranges and allowable excursions and limitations please see USP <659> Package and Storage Requirements
  - For the use of Mean Kinetic Temperature (MKT) please see USP <1079.2> Mean Kinetic Temperature in the Evaluation of Temper

Scope

Determine Scope

1. System
   - Qualified Cooler (that can be moved or shipped)
   - Vehicle
2. Passive or Active
3. Delivery routes, environment, season, and times
   - Lane and route mapping
4. Payloads
5. Standards for Design Qualification (DQ), Operational Qualification (OQ), and Performance Qualification (PQ) or Performance Verification (PV)
6. Competent thermal labs (DQ, OP, and PQ or may be limited to OQ)
7. SOPs
8. Ongoing evaluation

System

- Qualified cooler for desired temperature range
  - These can be custom designed for your needs (payload, qualification time, etc.)
    - Start with a Design Qualification (DQ) to determine the specifications
    - Operation Qualification (simulate actual conditions in environmental chambers)
    - Performance Qualification (PQ) or Performance Verification (PV) on actual lane / routes
  - Off-the-shelf qualified shipper (service vendor already has the DQ and OQ
    - Obtain a copy to evaluate and to support decision to use
    - Perform a PQ or PV in the field (with actual or simulated product) to confirm that the system works as demonstrated in the OQ
- Vehicle
  - May require mapping
    - Model/type and not each truck
  - Perform a PQ or PV in the field (with actual or simulated product) to confirm that the system works as demonstrated in the OQ (may be provided by vendor) or as advertised/contracted

System (cont.)

Typical Storage and Shipping Temperatures

- Controlled Room Temperature (CRT) – Temperature maintained thermostatically that maintains 20º to 25ºC. Allowable Excursions:
  - 15º to 30ºC
  - Transient spikes not more than 40ºC
  - Excursion time not more than 24 hours
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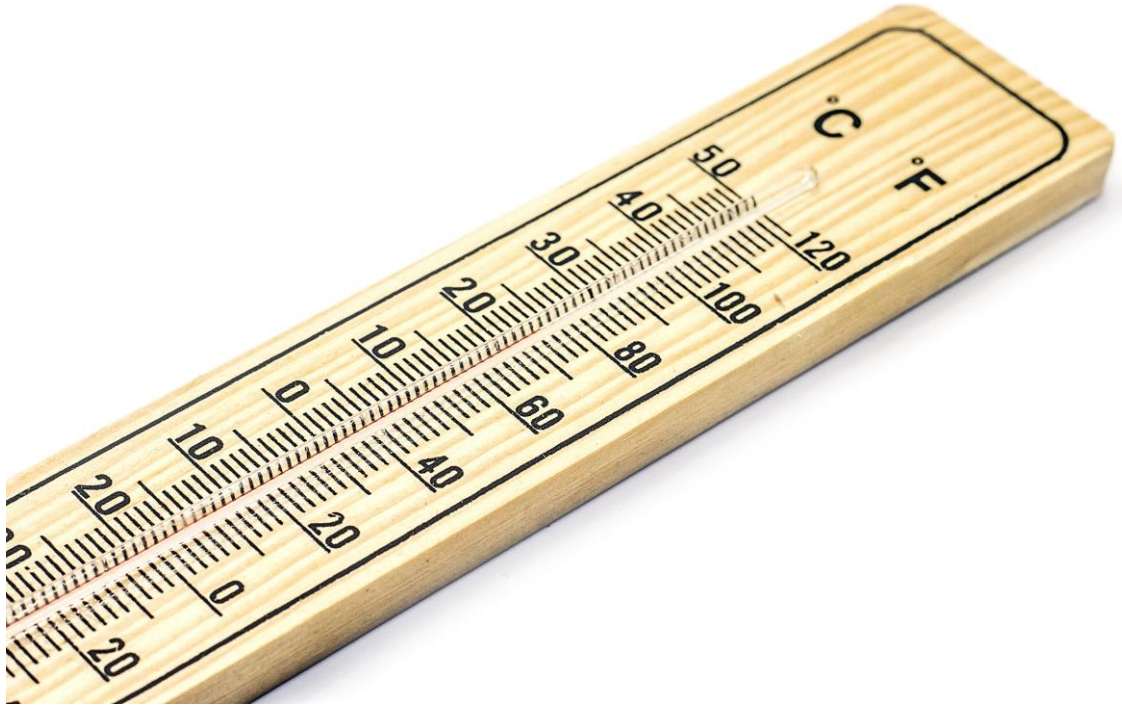

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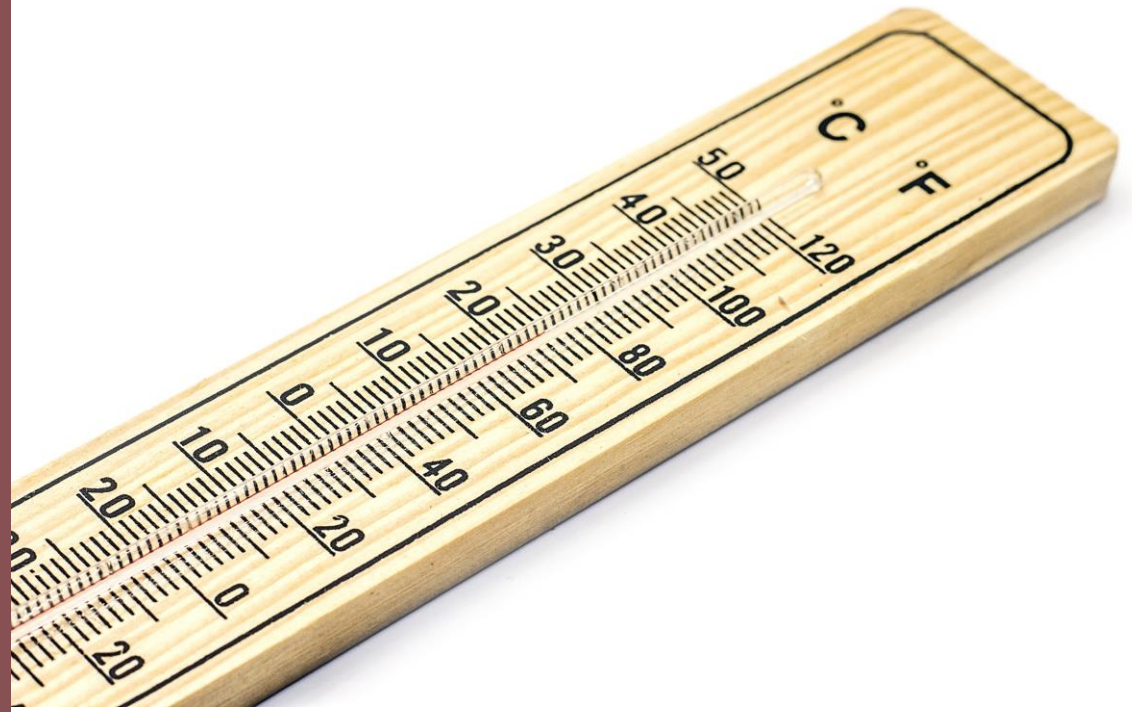


Active or Passive

- Passive uses a combination of insulation and coolant to maintain temperature
  - Does not rely on electrical power (battery or otherwise)
  - Single use or multiple use
  - Cheaper
  - Traditional design was Expanded Polystyrene (EPS) and water-based frozen and refrigerated or ambient gel-packs
  - Designs have become much more sophisticated (and expensive) utilizing phase change materials that can hold a narrow temperature range for longer with less weight and better insulating materials
    - Such as Polyurethane (PUR) and Vacuum Insulated Panels (VIP)
- Active uses an external device to enhance heat transfer, such as electric fans and compressors
  - Some may hold a narrower temperature
  - Requires electrical power (battery or otherwise)
  - More Expensive
  - Mechanical components that can fail

Delivery Routes, Environment, Season, and Times

- Before you can select a shipper, you need to know where it is going
  - Typical delivery time from packing, shipment, to final delivery
  - What is the route (air with multiple stops, direct ground delivery, or hub and spoke delivery)
  - What is along the route (mountains, deserts, etc.)?
  - What is the chance of delays (historical data) due to weather, traffics, customs, etc.
  - What are the conditions of the roads (smooth freeways or rough rural roads)?
  - Ensure documentation for temperature extremes and delays
- This information should be considered in the Design Qualification Phase and must be used in the Operational Qualification to ensure that the simulated environment for testing has taken these considerations into the qualification criteria

Payloads

- The right shipper should not only accommodate all possible payloads (minimum ands maximum loads) but will need to be tested for load variants in the Operational Qualification phase
  - Testing will take place in an environmental chambers during testing laboratory
- If you are shipping a fixed product and payload this is all that needs to be tested
- If you are a distributor that ships cases of product down to small glass vials, you must qualify both the minimum and maximum payload that you may ship
  - Testing for the worse-case scenario

Qualification Phases

- Design Qualification (DQ) to determine the specification
  - Needed for custom shipper
  - Establish requirements and design
  - Not needed if purchasing a pre-qualified cooler (
    - Vendor did qualification as part of their product development
- Operation Qualification
  - Simulate actual conditions in environmental chambers)
  - If purchasing a pre-qualified shipper, the purchaser should review the vendor's Operational Qualification to ensure it meets the intendent use requirements
- Performance Qualification (PQ) or Performance Verification (PV) on actual lane / routes
  - Simple verification of the qualified solution and the operational process (SOPs) for handling and shipping
  - Must be completed on the actual transportation lanes / routes
  - May be done with actual product or a simulated product
  - Minimum recommended n=3
  - Should be repeated if there is a change of lanes / routes
  - Consideration should be made about completing a Performance Verification (PV) for each initial seasonal change, our lane / route change
  - Ongoing temperature monitoring such as continuous monitoring/recording, electronic or chemical indicators may be used in place of PQ or PV

Qualification Phases

Operational Qualification

1. Probe placement should be inside or directly attached to the product (e.g., thermocouples) or representative samples. The number if product probes should cover the worst-case placement of product (e.g., outer walls and top corner).
2. Perform a minimum of three tests on each package size containing a representative payload for each season (e.g., summer and winter with minimum and maximum payloads).
    - Tests may be performed at the same time in an environmental chamber by season.
3. Allow the product payload as well as coolant to condition before beginning testing per protocol (standard is 24 hours).
4. Utilize a recognized standard to conduct thermal qualification (see Additional Sources of Information) or develop a written rationale for a qualification.

Qualification Phases

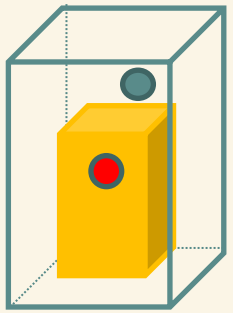
Operational Qualification (Cont'd)

6. All probes must be calibrated such as ISTA (certificates required) and accurate with +/- 0.5°C.
7. Temperature probes should record a minimum of every 15 minutes and should provide readouts in Celsius to include a single decima point data (e.g., 5.6°C) .
8. Probes must be Type T Thermocouples for product and product payload space. Temperature monitoring devices (e.g., TempTale®) may be used for payload space air and ambient temperatures.
9. Environmental chambers must maintain +/-3°C tolerance from the set point.
10. Ambient probes: a single ambient probe must be used to independently monitor the ambient conditions that the cooler is be qualified to. In the event of probe failure, the test would fail unless a second ambient probe was used.
11. Air probes: a single air probe must be placed next to product (outside of manufacturers secondary packaging).

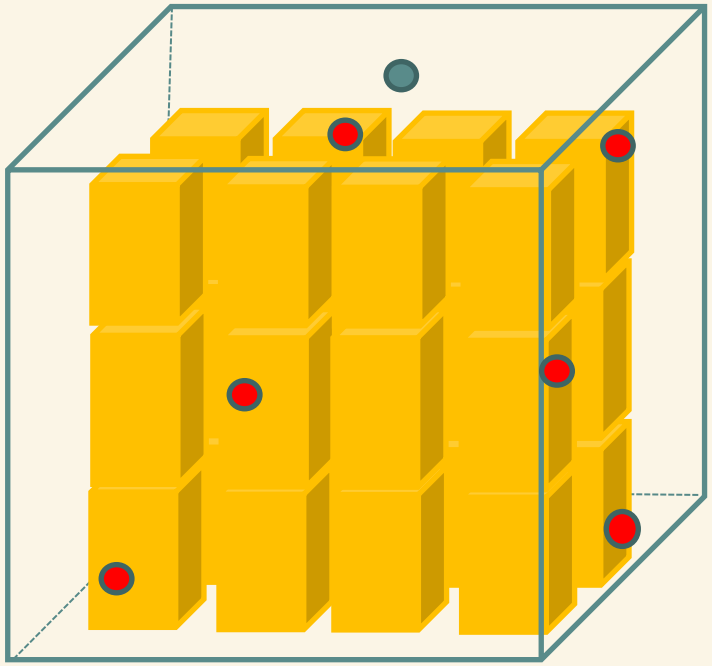
Qualification Phases

Operational Qualification (cont.)

Probe Placement Examples



Small – 8 vials and 2 probes



Large – 24 vials, 6 of which have probes

Air Probe

Product Probe

Competent Thermal Laboratory

- Can be used for DQ, OP, and PQ or may be limited to OQ.
- ISTA (International Safe Transit Association) Certified Thermal Testing Laboratory.
- Follows accepted standards such as (see others listed in References):
  - American Society for Testing and Materials International. ASTM D3103-14. Standard Test Method for Thermal Insulation Performance of Distribution Packages.
  - American Society for Testing and Materials International. ASTM D4169-16. Standard Practice for Performance Testing of Shipping Containers and Systems.
  - American Society for Testing and Materials International. ASTM D4332-14. Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing.
- May be a laboratory owned and run by the thermal packaging service supplier.
- If a 3rd party Thermal Testing Laboratory is used, your organization may want to enter into a Non-Disclosure Agreement (confidentiality agreement).
- Consider a suppler quality qualification and agreement.

SOPs and Ongoing evaluation

SOPs

- Standard Operating Procedures (SOPs) should cover handling to ensure qualified packaging is handled as it was tested in the Operational Qualification phase

Ongoing Evaluation

- Training and effectiveness checks of training should be conducted to ensure compliance to SOPs Effectiveness checks could be formal audits or informal observation of operational activities
- Effectiveness of packaging and processes to an intended delivery lane or route could be performed by a Performance Qualification (PQ) or Performance Verification (PV)

Establishing a Temperature Profile or Lane and Route Mapping for Temperature Shipment of Finished Drugs and Drug Products

Purpose

- Before drug products can be transported, we must understand the environment they will be exposed to, which includes:
  - Mode
    - Post, courier vans, trucks, rail, ocean containers, or aircraft
  - Route(s) environment and topography
    - Mountains or altitude, desert, juggle, ocean
  - Season and weather patterns
  - History of delays
    - Customs, weather, traffic, as well as departure and arrival performance
- Only after we understand the environment that drugs will be transported can we determine what thermal protection may be required, from packaging to transportation mode

Lane Mapping

1. Lanes - Routes
2. Frequency
3. Plan
4. Execution
5. Evaluation
6. Uses of data

Lanes

- **Determine how many lanes you have (e.g., 6 versus 600)**
  - A smaller number may justify mapping each lane
  - A larger number may require sampling
    - Risk based
    - Mode
    - Length (distance and travel times)
    - Environment (e.g., mountains, tropics, desert, and seasonal)
    - History of delays
      - Boarders / customs
      - Traffic (cities, rush hours, holidays
      - Transportation provider service history

Canada Example

Delivery Points (9,563)

- 0–250 km (7,469) x1 (Courier) per Distribution Center = 8
- 251-500 km (1,379) x1 (Courier) per Distribution Center = 8
- 501-750 km (556) x1 per (LTL-Courier) Distribution Center = 8
- 751-1000 km (159) x1 per (LTL-Courier) Distribution Center = 8
- 1000+ km (35) x1 per (Air or Courier-Boat) Distribution Center = 8

Shipping Points

- Distribution Centers (8) to Delivery Points
  6 Rail Routes (Replenishment Distribution Center to other DCs)
  1 Ship Route

48 Lanes (16 courier, 16 LTL-courier, 6 Air, 2 LTL-Boat, 6 rail, 1 boat

Frequency

- Ideal study would cover an entire year (all seasons, if applicable)
- One shipment per week (if possible) – per lane chosen
- Shorter time period if results are needed quickly
  - May need additional mapping for seasonal changes or to get a larger sample size (increased statistical significance)

Plan

- Obtain temperature recoding devices:
  - Temperature monitors/indicators may include calibrated monitoring or recording devices, and real-time monitors such as GPS. Monitoring devices may include an alert mechanism if the preset ranges are breached
  - Specifications (temperature ranges, how often the data is recorded (at least every 15 minutes), battery life, how to start and stop, and how to obtain the data
  - Calibration – devices must be calibrated to a recognized standard (e.g., NIST).
- Determine how to ship:
  - Non-insulated box – if your objective is to capture the environment that your product will be exposed to
  - If you the device inside of simulated product boxes, this is really performance qualification (PQ) or performance verification (PV)
  - Include instructions to receiver (e.g., how to stop recording and return)
  - Send enough to the shipping site(s) – consider a month or a quarter at a time
- Determine how to return:
  - Pre-paid return envelop (ship back via post or shipping service)
  - If mapping several lanes from several different shipping locations, consider all units being returned to one location (internal or contracted service)
- Training for shipping and receiving locations as well as whoever is responsible for receiving devices after use

Execution

- Ship devices:
  - Log device into a control sheet (serial number) for route, date, and time shipped
  - Press start
  - Close box and ship
- Received returned units:
  - Log into control log (keep on a shared folder for logging at start and return)
  - Download data
  - Quick review of data to demine if unit was not turned of or not turned off immediately – verify possible discrepancies with sipper and destination
  - Research missing devices listed on control log (or determine if any were not logged)

Evaluation

- Per shipment:
  - Minimum, Maximum, and Mean Temperature
  - Standard Deviation
  - Mean Kinetic Temperature (MKT)
  - Minimum, Maximum, and Mean Time by Week and Month
- Summarize by week, month, and season:
  - Minimum, Maximum, and Average Temperature
  - Standard Deviation
  - Mean Kinetic Temperature (MKT)
  - Minimum, Maximum, and Average Time by Week and Month

Evaluation (Cont'd)

- Evaluate temperatures
  - Controlled Room Temperature (CRT) – Temperature maintained thermostatically that maintains 20º to 25ºC. Allowable Excursions:
    - 15º to 30ºC
    - Transient spikes not more than 40ºC
    - Excursion time not more than 24 hours
    - MKT not more than 25ºC (measured back 30 days or time product in possession)
    - Product labelled CRT can be stored Cool (8º to 15ºC) or CCT (2-8ºC) unless otherwise specified on the individual monograph or label
    - Storage time in Cool or CCT cannot be used to calculate excursion temperatures outside of CRT range!

Evaluation (Cont'd)

- Evaluate temperatures
  - Controlled Cold Temperature (CCT) – Temperature is controlled to maintained 2º to 8ºC. Allowable Excursions:
    - 2º to 15ºC
    - Excursion time not more than 24 hours
    - MKT not more than 8ºC (measured back 24 hours)
    - Each excursion must be evaluated as a separate event

Use data

- Confirm that data matches temperature profile chosen for CCT package qualification criteria
- Confirm that data matches USP <659> CRT storage and excursion ranges
- Developed mitigation plans, if data does not meet USP <659>:
  - Adjust temperature profile for CCT package qualification
  - If CRT range is not within storage and excursion ranges, change transportation mode or service provider (e.g., temperature-controlled transpiration system), utilize thermal blankets, or use protective packaging
  - Implemented mitigation strategies should be confirmed to address excursion within USP excursion limits. This can be accomplished adding 100% temperature monitoring or performance verification (e.g., three runs monitored to ensure mitigation strategy implemented mitigated the risk

Future GDP Chapters

- **<1079> Risk and Mitigation Strategies for the Storage and Transportation of Finished Drug Products**
- **<1079.1> Storage and Transportation of Investigational Drug Products**
- **<1079.2> Mean Kinetic Temperature in the Evaluation of Temperature Excursions During Storage and Transportation of Drug Products**
- <1079.3> Monitoring Devices – Time, Temperature, and Humidity (<1118>)
- <1079.4> Qualification of Storage Areas
- <1079.5> Qualification of Shipping Systems
- <1079.6> Transportation and Route Profiling Qualification
- <1079.7> Informational Systems for Distribution/Verification Studies

Thank You

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Questions

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Thank You

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