Mapping Made Easy

Sensor Placement for GxP Temperature Mapping

Paul Daniel
Sr. GxP Regulatory Expert

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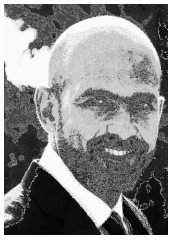
Vaisala Team



Speaker:

Paul Daniel
Sr. GxP Regulatory Expert

Chat operator:

Janice Bennett-Livingston
Marketing Manager

Vaisala in Brief

- We serve customers in weather and controlled environment markets.
- 80+ years of experience in providing a comprehensive range of innovative observation and measurement products and services.

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Vaisala - Life Science

Our Offering

Provides measurement instrumentation, continuous monitoring systems and validation systems for regulated or highly controlled life science environments.

Our Goal is to help customers

- Reduce risk of lost product
- Reduce their risk of failing to meet GxP regulations and guidelines

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VAISALA

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PIC/S

FDA

ICH
harmonisation for better health

Health Canada
www.hc-sc.gc.ca

History

2011

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

- ISPE
  - Good Practice Guide: Cold Chain Management

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History

2012

- PDA
  - Technical Report 58 – Risk Management for Temperature Controlled Distribution

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

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History

2013

- 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

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History

2014

- EMA (Europe)
  - Ref Ares(2014)968163 – 28/03/2014 Good Distribution Practice of Medicinal Products for Human Use – Questions and Answers – Version 1
- PIC/S
  - PIC/S Guide: Good Distribution Practice for Medicinal Products

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History

2015

- WHO
  - Temperature mapping of Storage Areas
    - Technical Supplement to Report Series, No. 961

History

2016

- ISPE
  - Good Practice Guide: Controlled Temperature Chamber Mapping and Monitoring

Goals

- Review Mapping Regulations
- "Make Mapping Easy"
  - 5 Rules for Sensor Placement
- Review Current Guidance on Sensor Placement

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Regulations and Mapping

- 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 helpful for sensor placement!

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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

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5 Rules for "Mapping Made Easy"

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

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Rule 1: Map the Extremes

- Extremes of Geometry
  - Place sensors at each end of the storage area.
- Extremes of Conditions
  - Apply validation principle of worst cases

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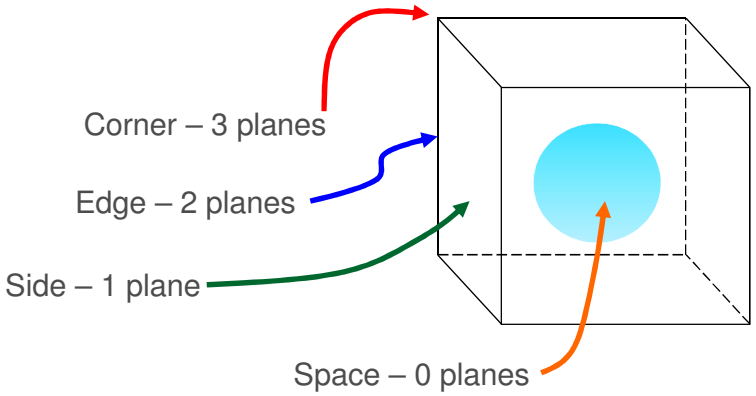
Parts of a Cube



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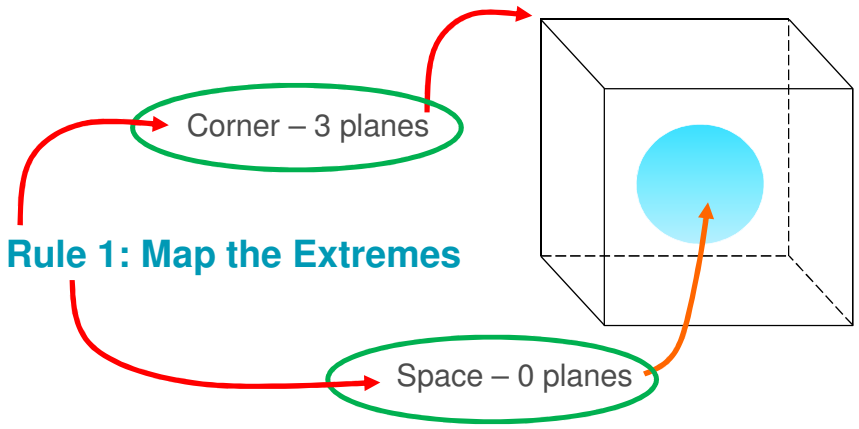
Parts of a Cube



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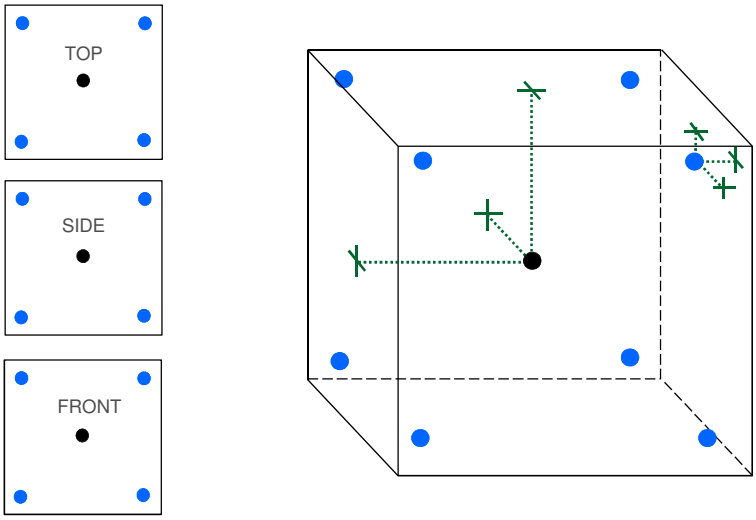
Corollary 1A: If ≤ 2m³, use 9 + 1.



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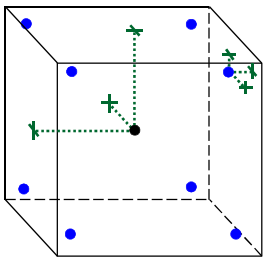
9 spots = worst case?

- 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)

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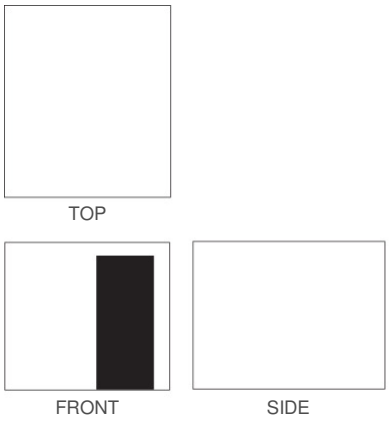
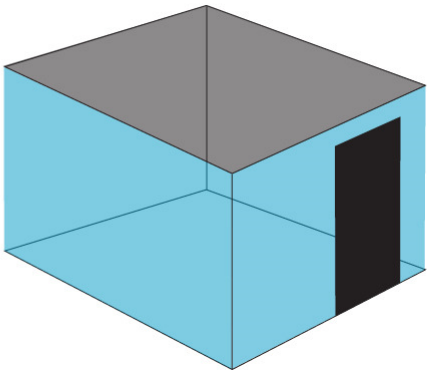
How many? Where? < 20m^3





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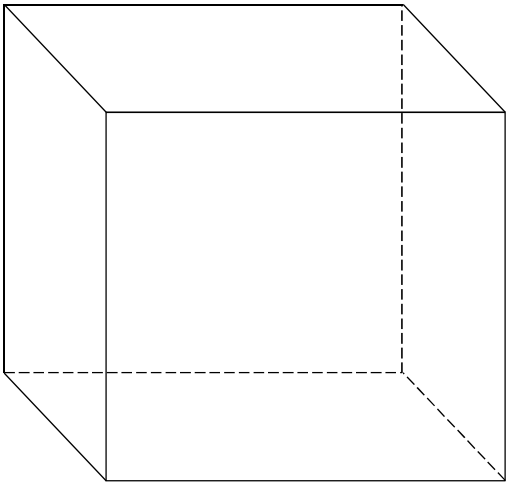
How many? Where? < 20m³

TOP

SIDE

FRONT

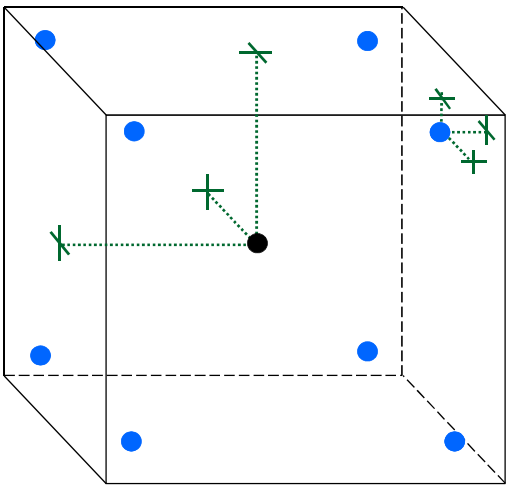


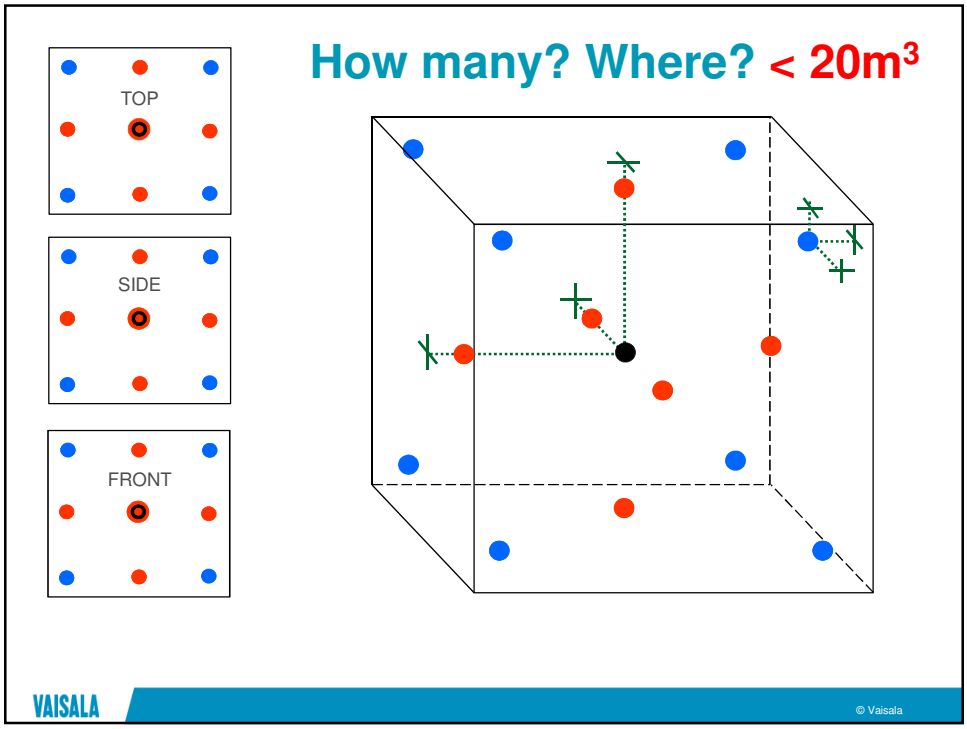
How many? Where? < 20m³

TOP

SIDE

FRONT




How many? Where? < 20m3
TOP
SIDE
FRONT
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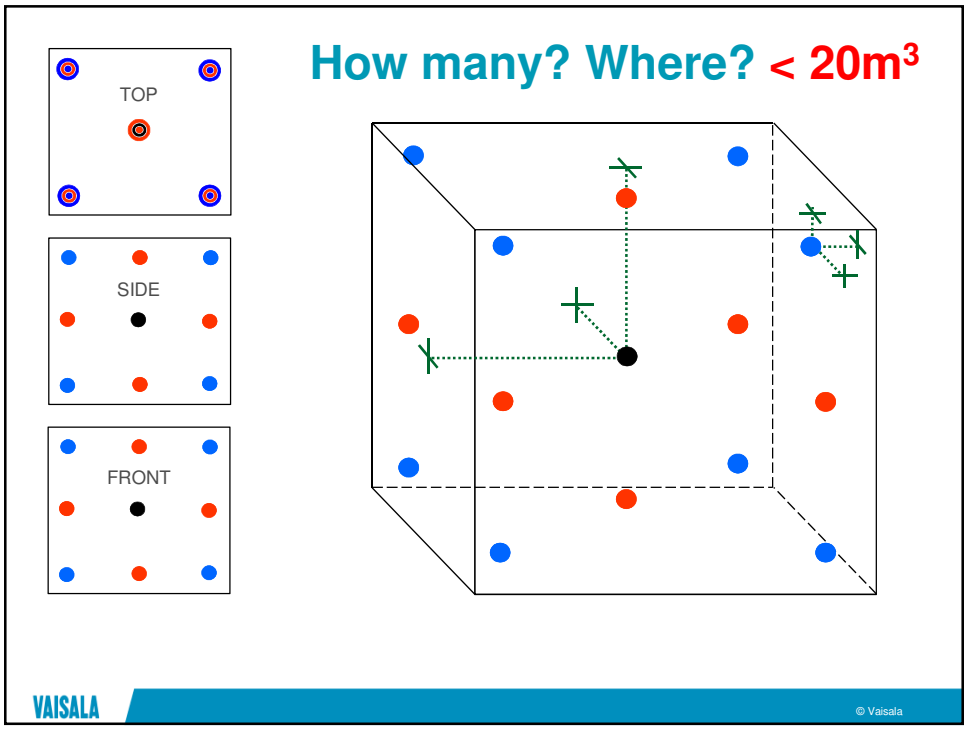
How many? Where? < 20m3
TOP
SIDE
FRONT
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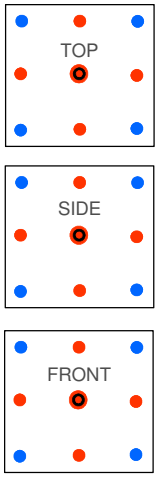
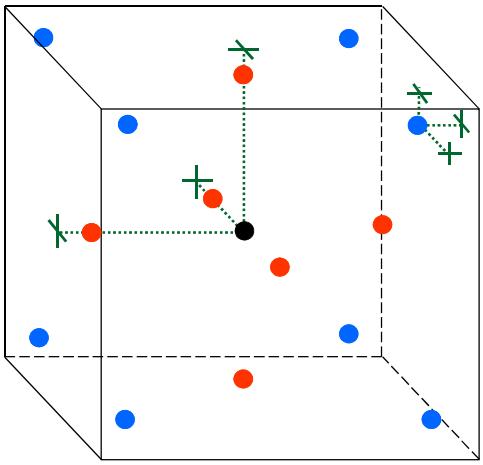
Corollary 1B: If ≤ 20m^3, use 15 +1.





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Guidance describes 9 +1 and 15 +1

- ISPE Good Practice Guide: Cold Chain Management
- ISPE Good Practice Guide: Controlled Temperature Chambers

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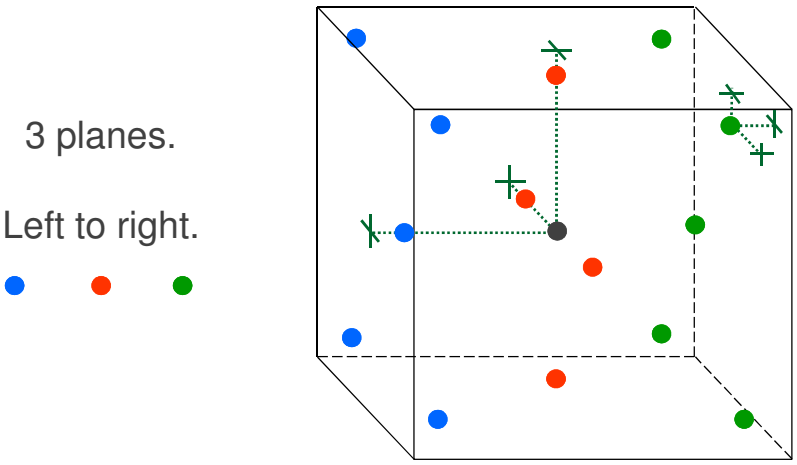
Rule 2: Map in 3 Dimensions.

3 planes.

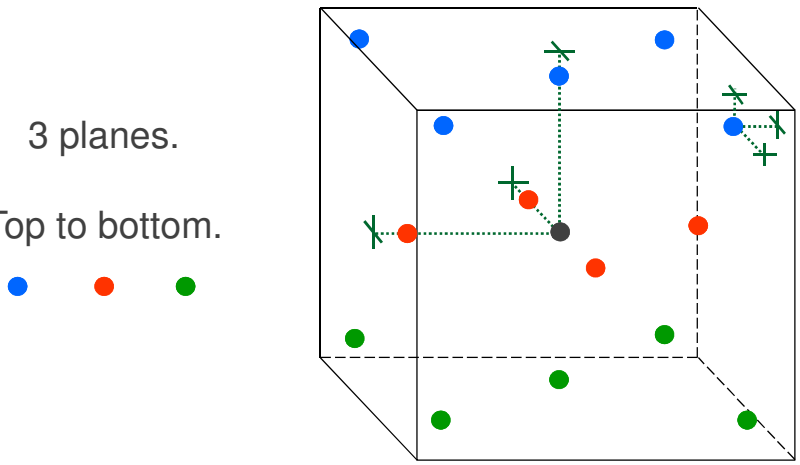
Left to right.



Rule 2: Map in 3 Dimensions.

3 planes.

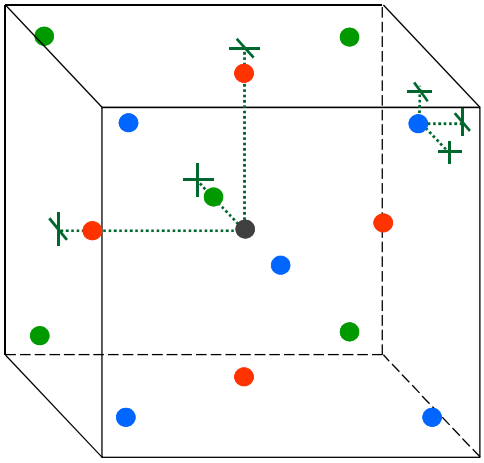
Top to bottom.



Rule 2: Map in 3 Dimensions.

3 planes.

Front to back.

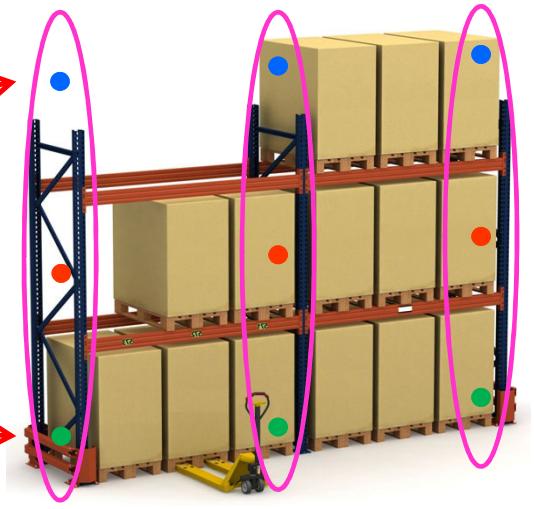


Corollary 2A: If ≥ 20m^3, use Stacks of 3.

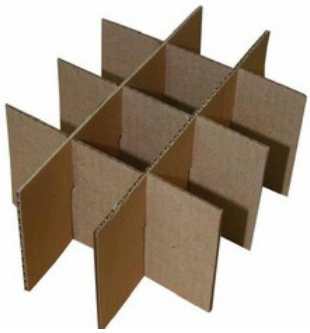
High

Middle

Low



Stacks of 3, in 3 dimensions.



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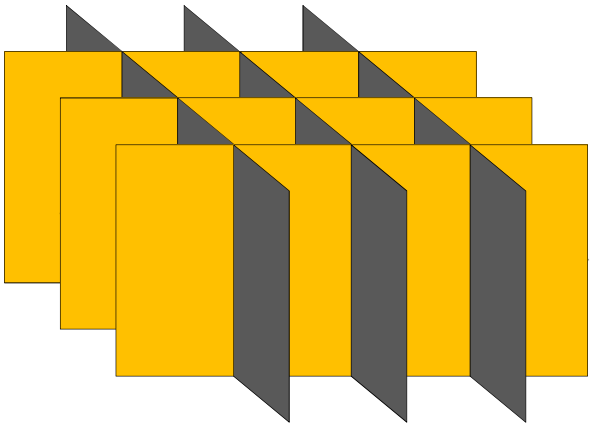

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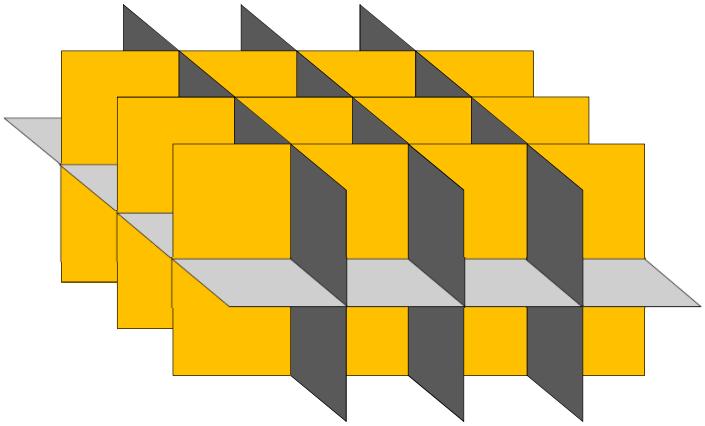

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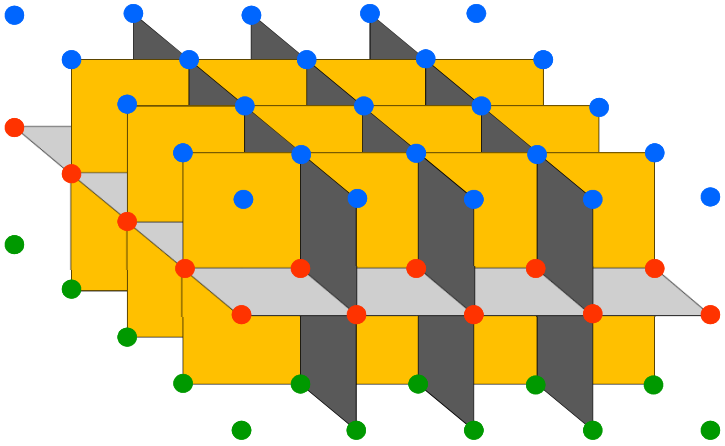
Stacks of 3, in 3 dimensions.



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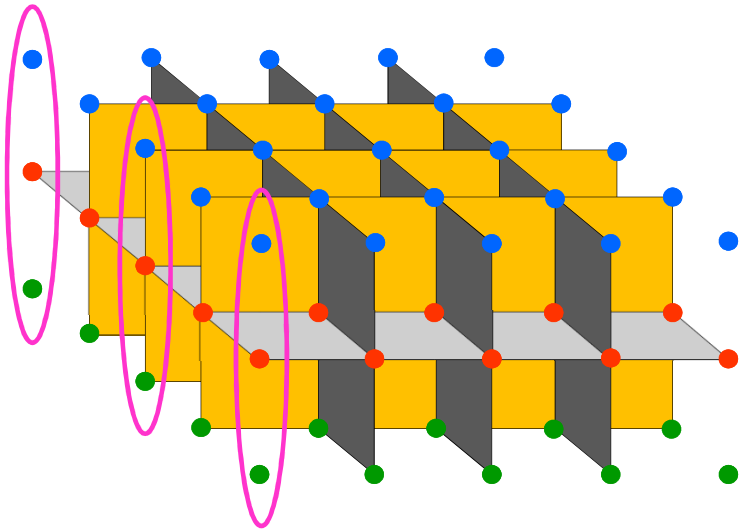

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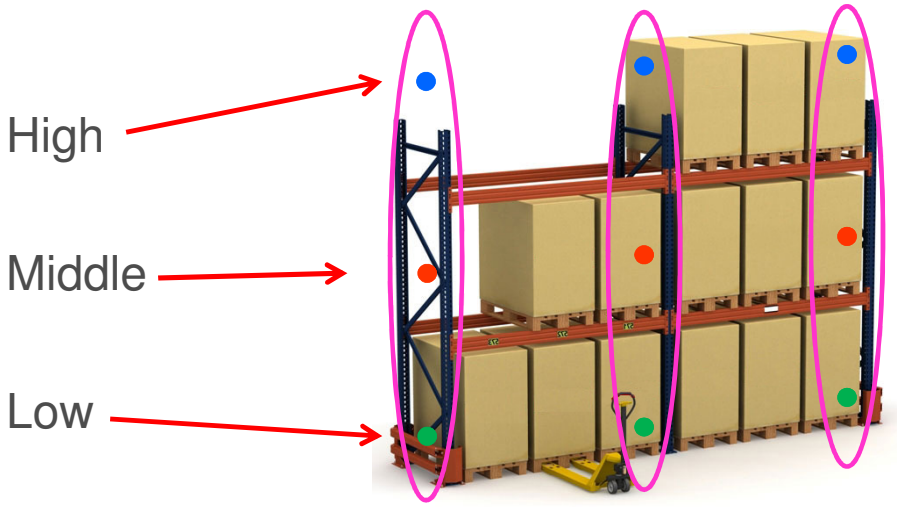
Corollary 2A: If ≥ 20m^3, use Stacks of 3.



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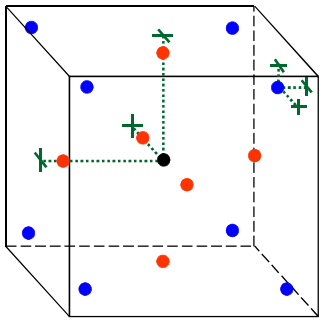
Corollary 2B: Remove sensors if possible.

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



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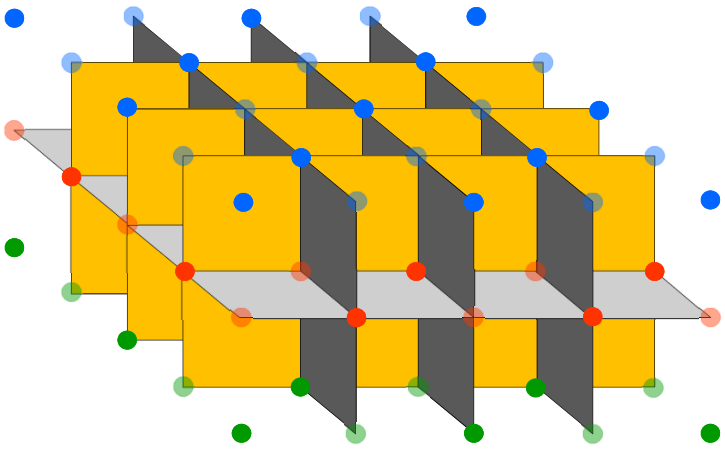
Stacks of 3, in 3 dimensions.



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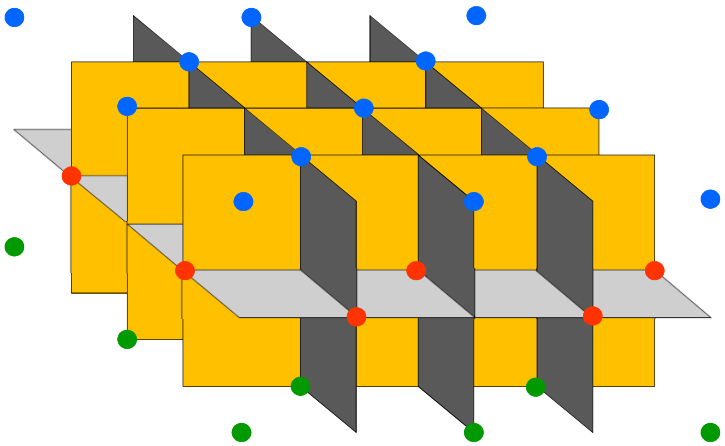
Stacks of 3, in 3 dimensions.



More published support...

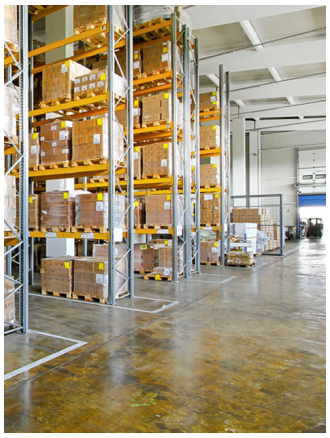
"Completing a three-dimensional temperature profile should be achieved by measuring points at not less than three dimensional planes in each direction/axis—top-to-bottom, left-to-right, front-to-back…"

USP 36 Chapter <1079> Good Storage and Distribution Practices for Drug Products (2013)

USP U.S. Pharmacopeial Convention™

Rule 3: If ≥ 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



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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."

USP 36 Chapter <1079> Good Storage and Distribution Practices for Drug Products (2013)

USP U.S. Pharmacopeial Convention™

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Rule Summary (so far…)

- Rule 1 – Map the Extremes
  - Corollary 1A – If ≤ 2m^3, use 9+1.
  - Corollary 1B – If ≤ 20m^3, use 15+1

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Rule Summary (so far…)

- Rule 1 – Map the Extremes
  - Corollary 1A – If ≤ 2m^3, use 9+1.
  - Corollary 1B – If ≤ 20m^3, use 15+1
- Rule 2 - Map in 3 Dimensions
  - Corollary 2A – If ≤ 20m^3, use Stacks of 3
  - Corollary 2B – Remove Sensors if Possibl

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Rule Summary (so far…)

- Rule 1 – Map the Extremes
  - Corollary 1A – If ≤ $2m^3$, use 9+1.
  - Corollary 1B – If ≤ $20m^3$, use 15+1
- Rule 2 - Map in 3 Dimensions
  - Corollary 2A – If ≤ $20m^3$, use Stacks of 3
  - Corollary 2B – Remove Sensors if Possible
- Rule 3 - If ≥ $20m^3$, map storage only.

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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)

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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.

USP U.S. Pharmacopeial Convention™

Rule 4: Identify Variables

- Volume
- Temperature Δ
- 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

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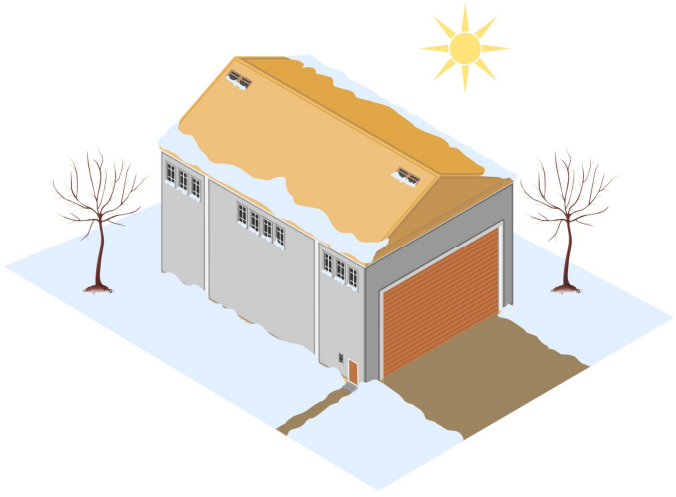
Temperature Δ



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Height

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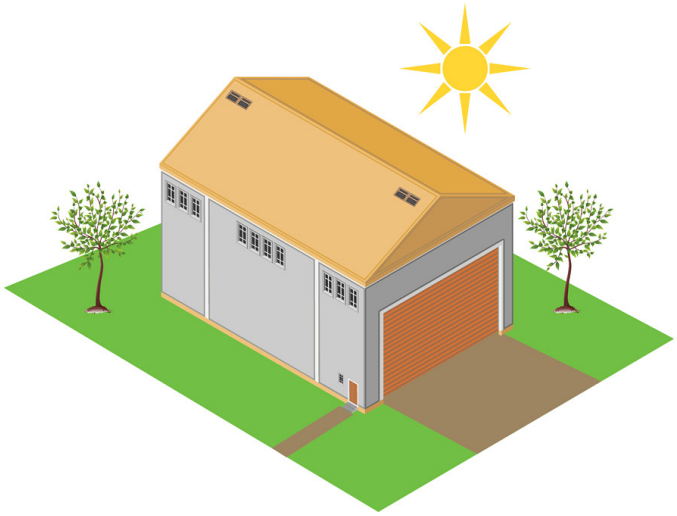
Exterior Walls



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Construction Materials

Doors and Windows

Lighting

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Gradients

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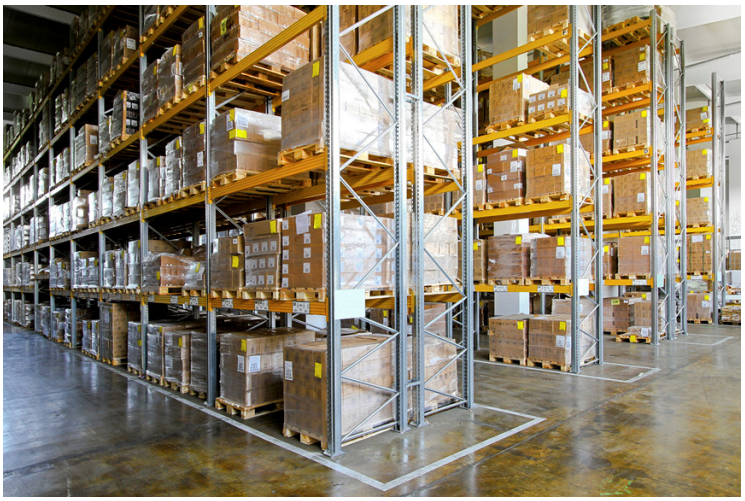
HVAC Vents and Returns

Air Circulation

Control Sensors

Energy Sources

Racks, Shelves, and Product



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Traffic Patterns

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Rule 4: Identify Variables

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

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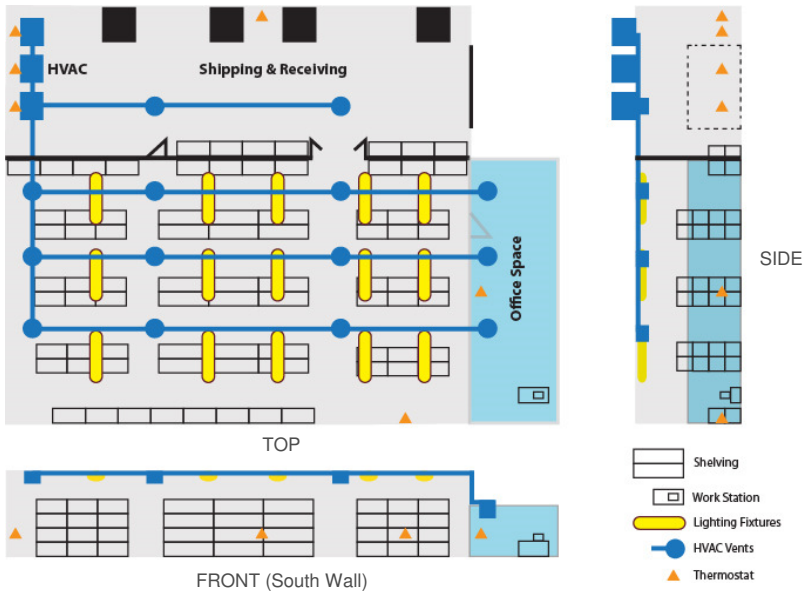

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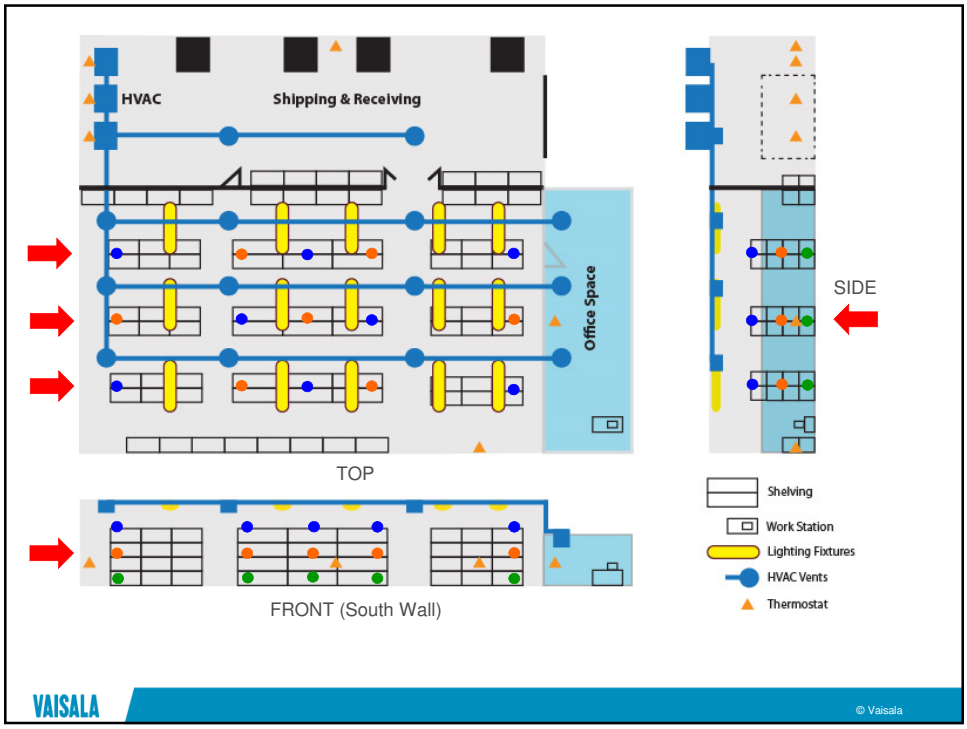
HVAC
Shipping & Receiving
Office Space
TOP
FRONT (South Wall)
SIDE
Shelving
Work Station
Lighting Fixtures
HVAC Vents
Thermostat
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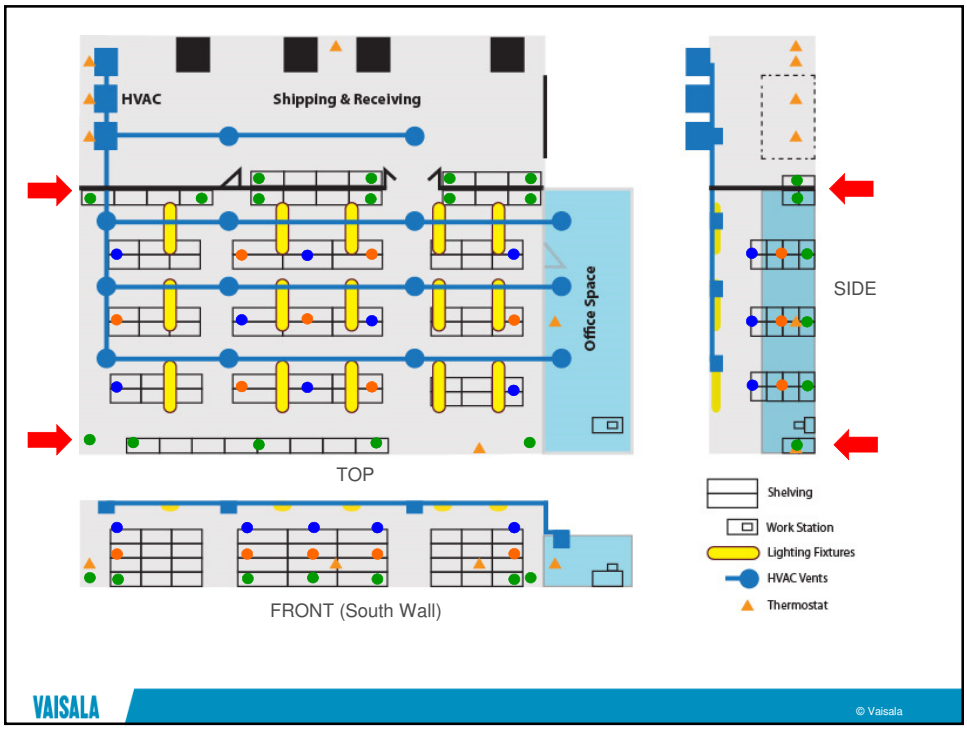
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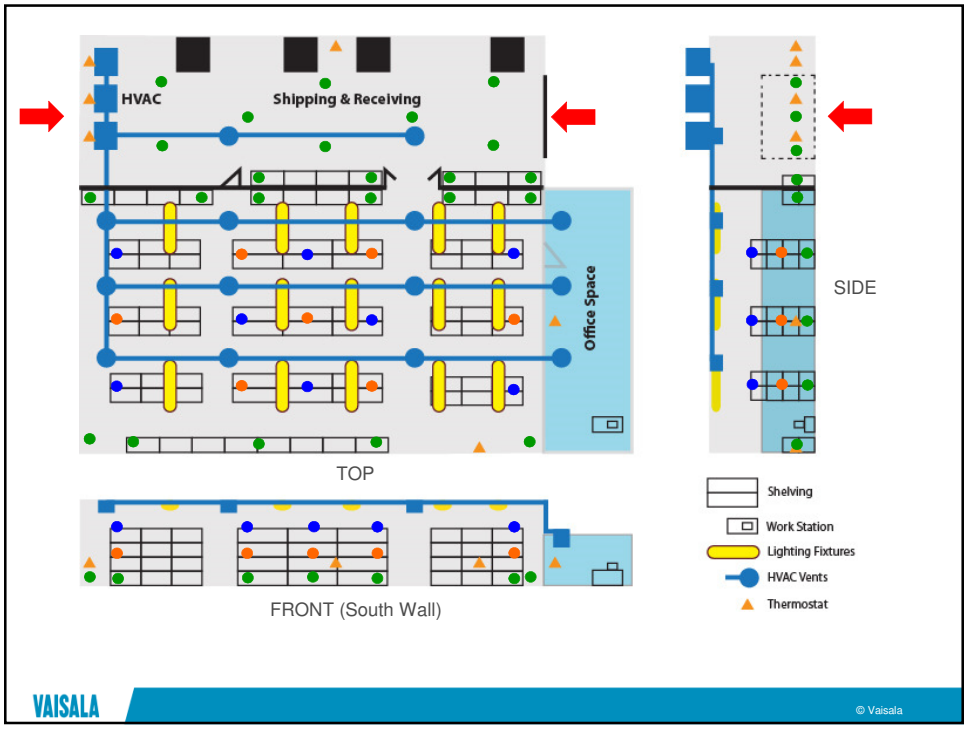
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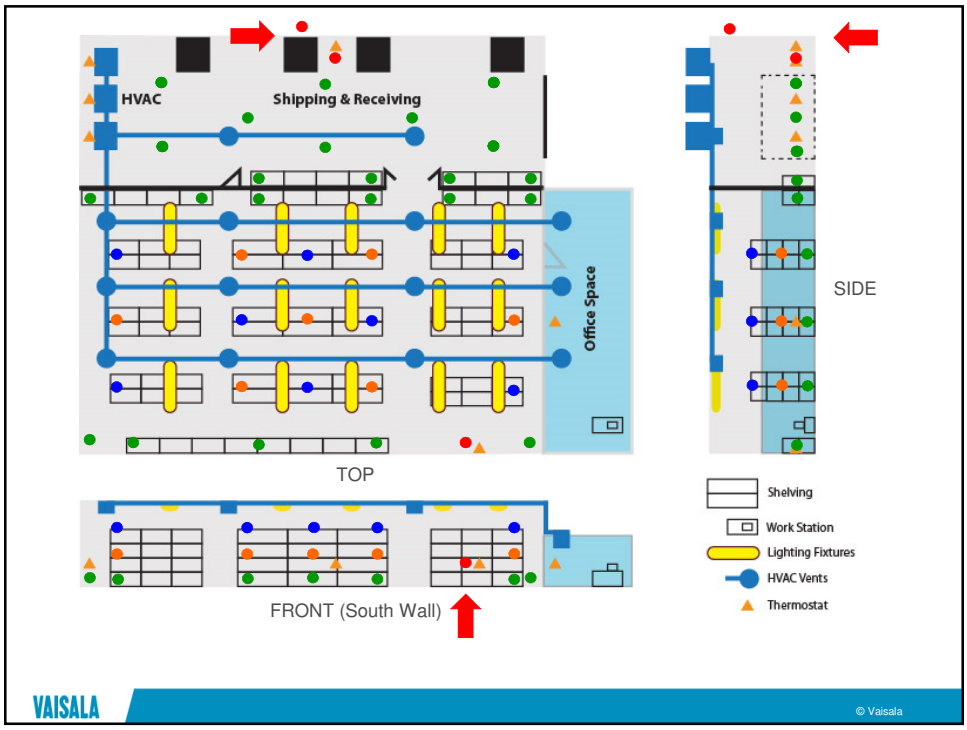
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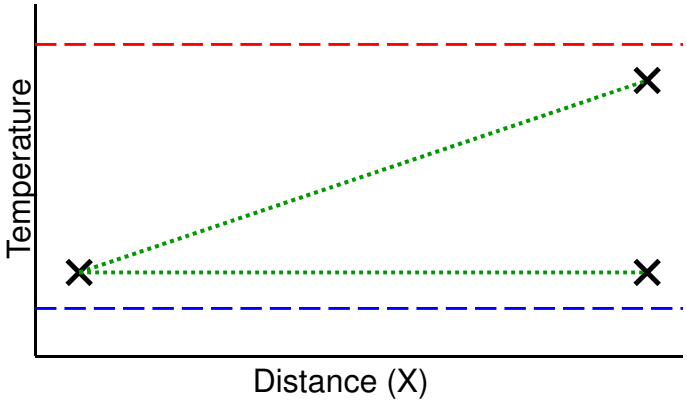
Distance Between Points



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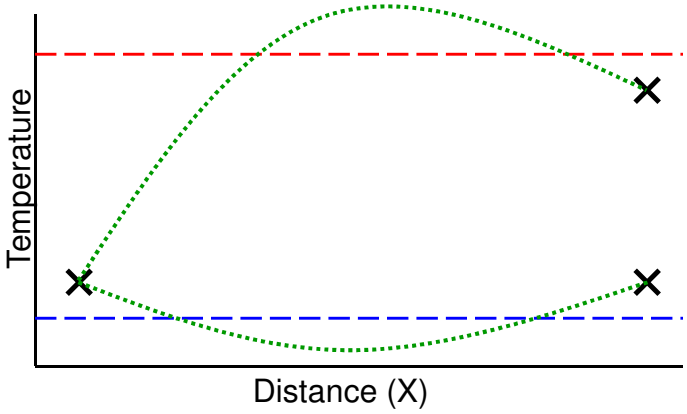

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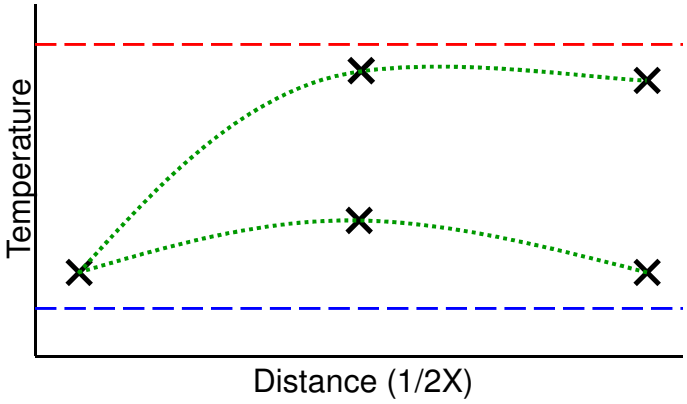

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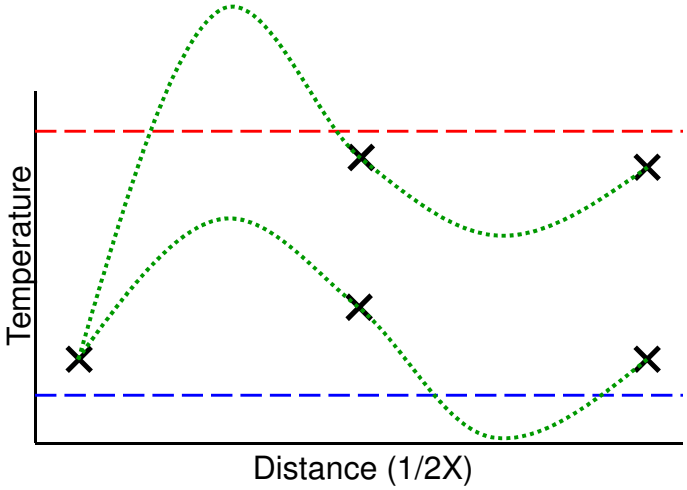

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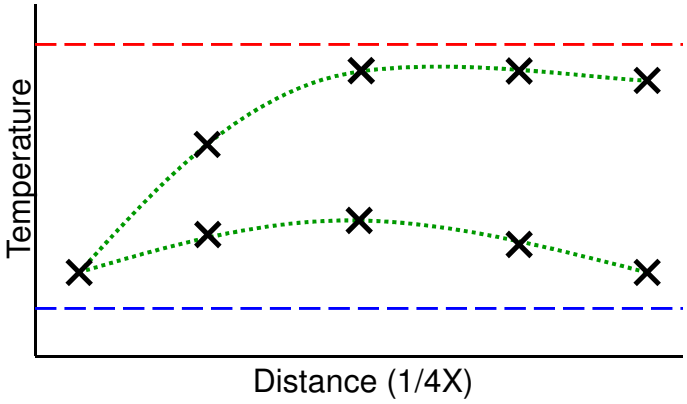
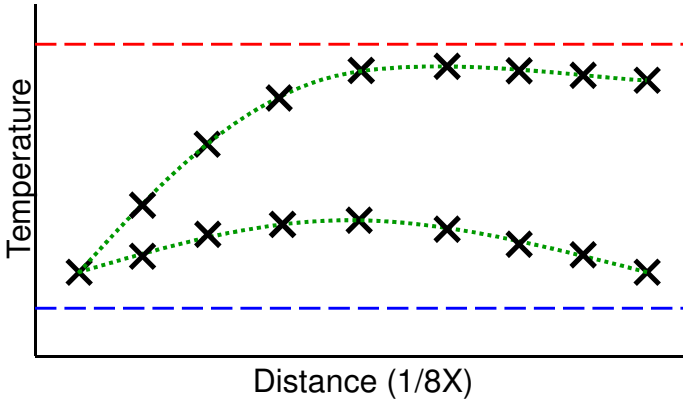
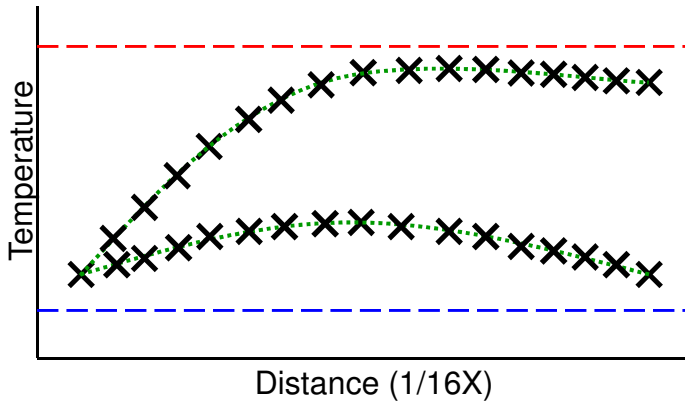
Distance Between Points



Distance Between Points



Distance Between Points



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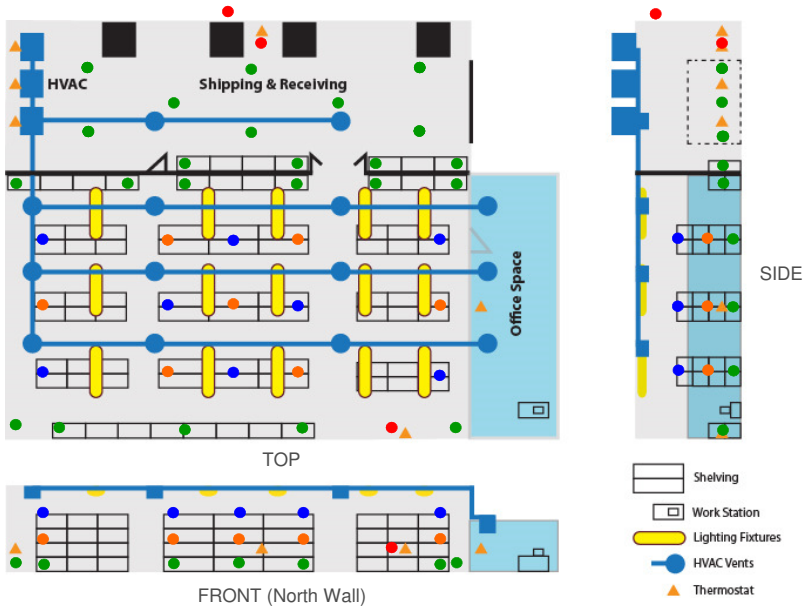

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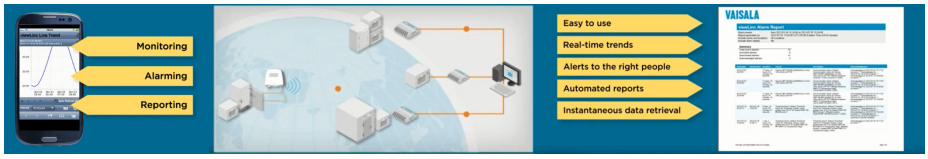
Rule 5: If it is worth mapping… It is worth monitoring.

- Find the hot and cold spots and place sensors.
- Select the right monitoring solution.
- Qualify the monitoring system.



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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."

PDA Technical Report No. 58: Risk Management for Temperature Controlled Distribution (2012)

PDA

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Rule Summary (so far…)

- **Rule 1 – Map the Extremes**
  - Corollary 1A – If ≤ $2m^3$, use 9+1
  - Corollary 1B – If ≤ $20m^3$, use 15+1
- **Rule 2 - Map in 3 Dimensions**
  - Corollary 2A – If ≤ $20m^3$, use Stacks of 3
  - Corollary 2B – Remove Sensors if Possible
- **Rule 3 - If ≥ 20m3, Map Storage Only**
- **Rule 4 – Identify Variables**
- **Rule 5 – If it is worth Mapping, it is worth Monitoring**

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What about product temperature?

- Its 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)

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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)

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Summary

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

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Thank you for your time!

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If you want more…

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