

# Modern Rules for an Old Practice:

Sensor Placement for GMP Temperature Mapping

**VAISALA**

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## Goals

- Review Mapping Regulations.
- Discuss 5 Rules for Sensor Placement.
- Review Current Guidance on 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
  - Technical Report 58 – Risk Management for Temperature Controlled Distribution



- 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

## Regulations and Mapping

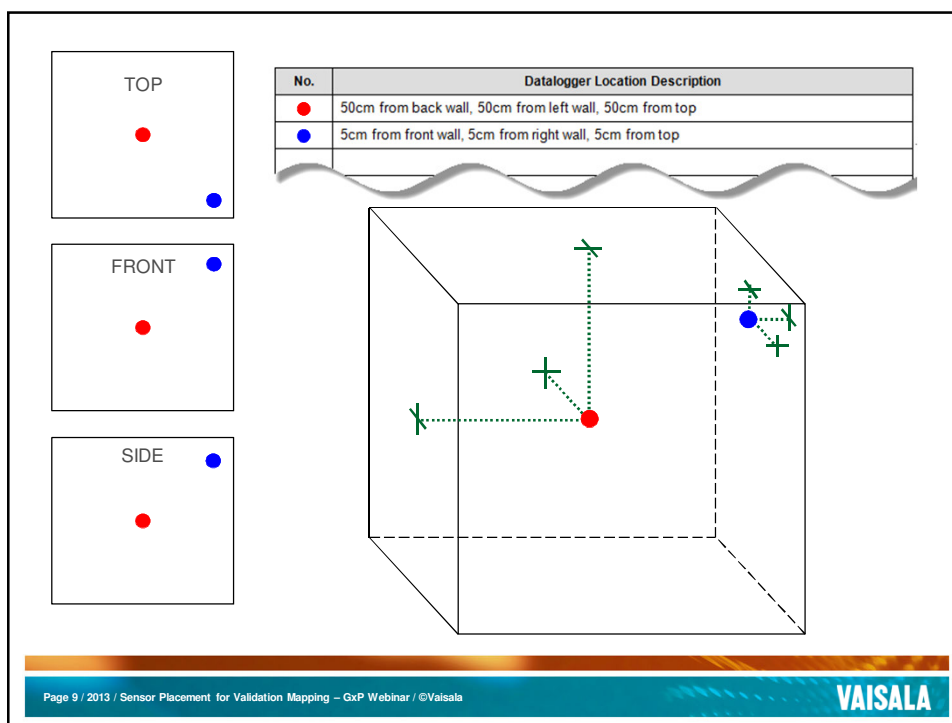


- The regulations don't tell us how to map, or even to map.
- Regulatory Summary
  1. Determine if environmental parameters affect product quality.
  2. Do stability testing to determine appropriate storage specifications.
  3. Ensure that storage spaces are controlled to meet specifications.
- Mapping and monitoring is industry GMP response to #3.
- Therefore, regulations aren't 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, its worth monitoring.

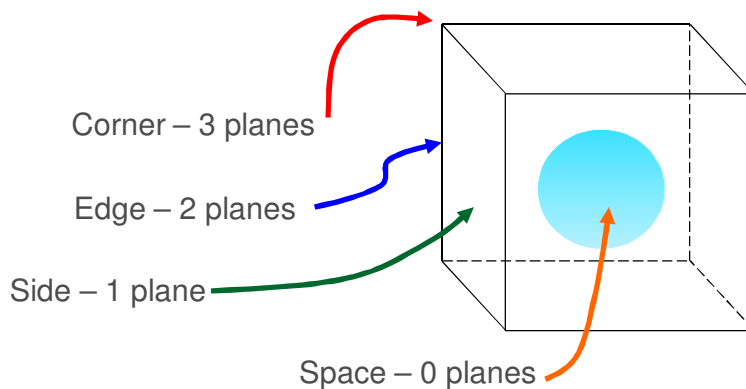


## Rule 1: Map the Extremes.

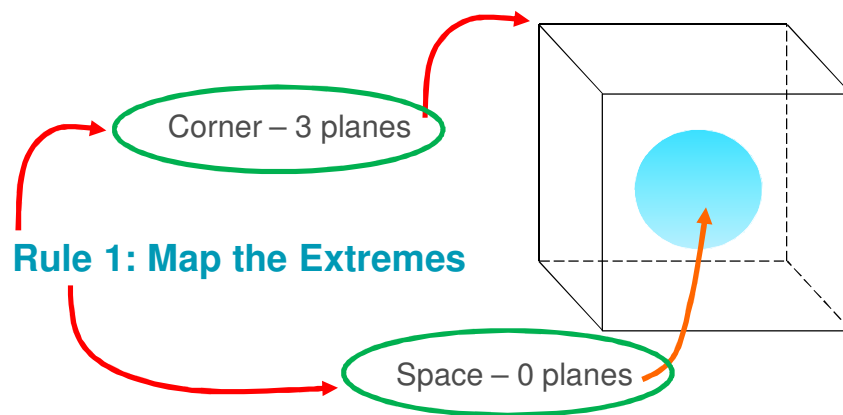
- Geometric
  - Place sensors at each end of the storage area.
- Conditions
  - Apply validation principle of worst cases.



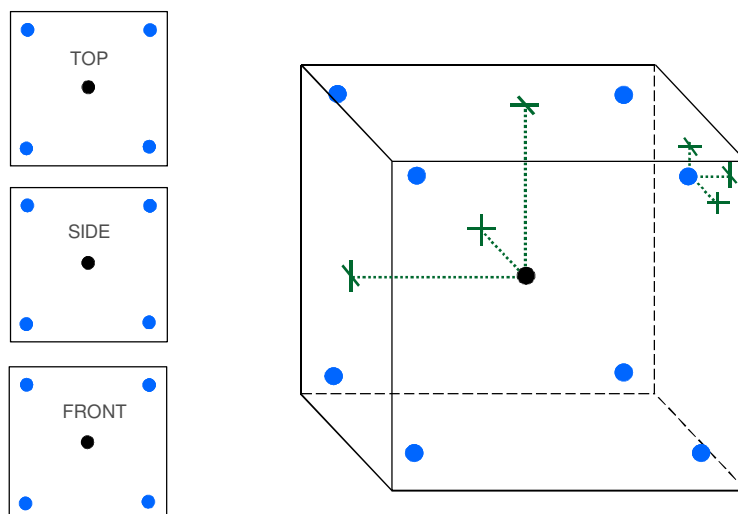
## Parts of a Cube



## Parts of a Cube



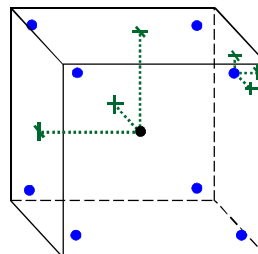
## Corollary 1A: If $\leq 2\text{m}^3$ , use 9 + 1.



## 9 spots = worst case?

### Air Flow:

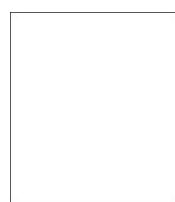
- Corners have least air circulation.
- Center has most air circulation.



### Heat Exchange:

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

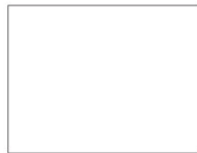
## How many? Where? < 20m<sup>3</sup>



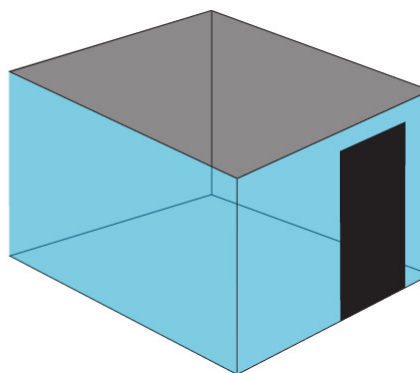
TOP



FRONT



SIDE





How many? Where? < 20m<sup>3</sup>

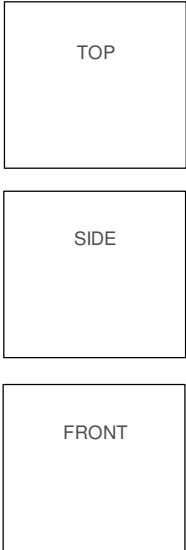


Diagram illustrating a 3D space (a cube) with three empty viewports labeled TOP, SIDE, and FRONT, intended for sensor placement.

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How many? Where? < 20m<sup>3</sup>

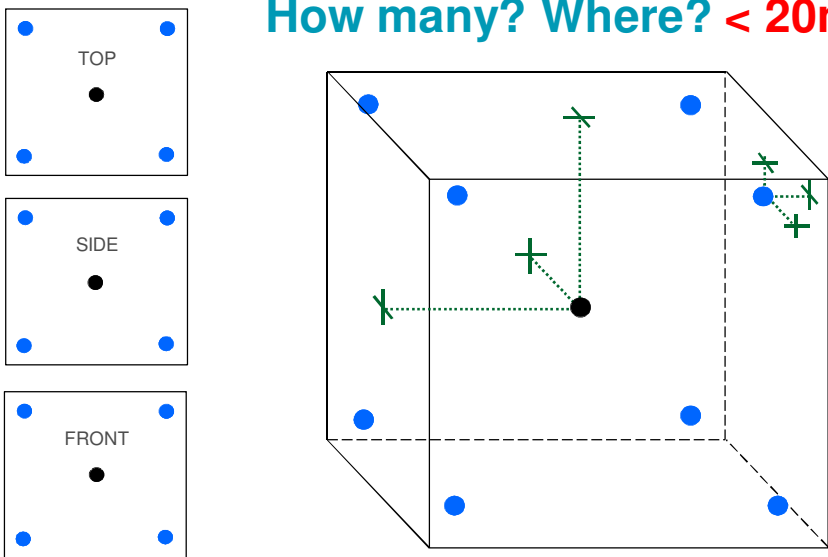
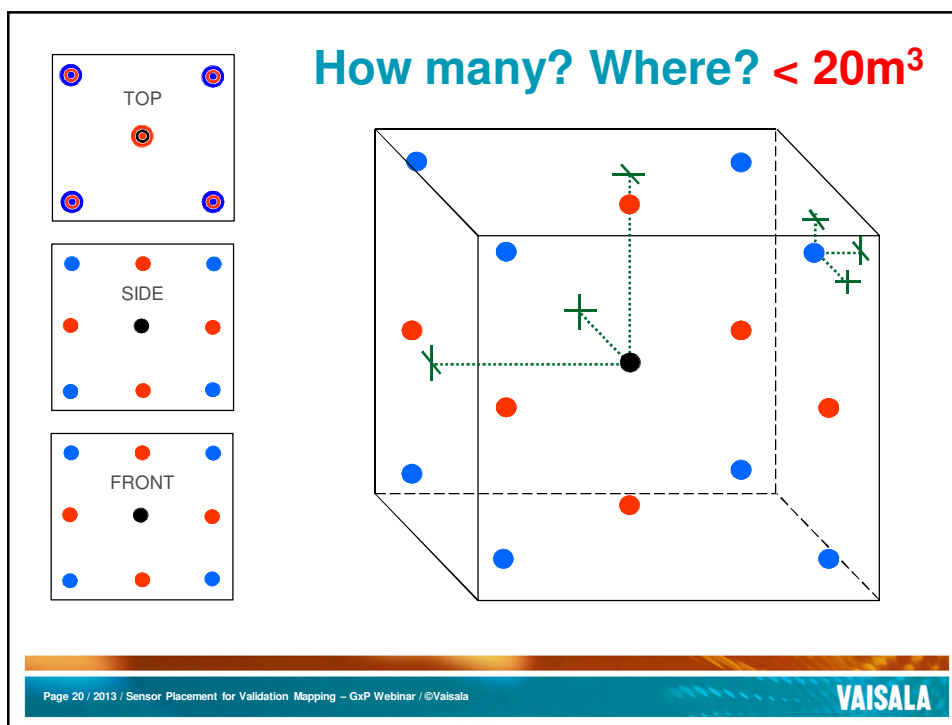
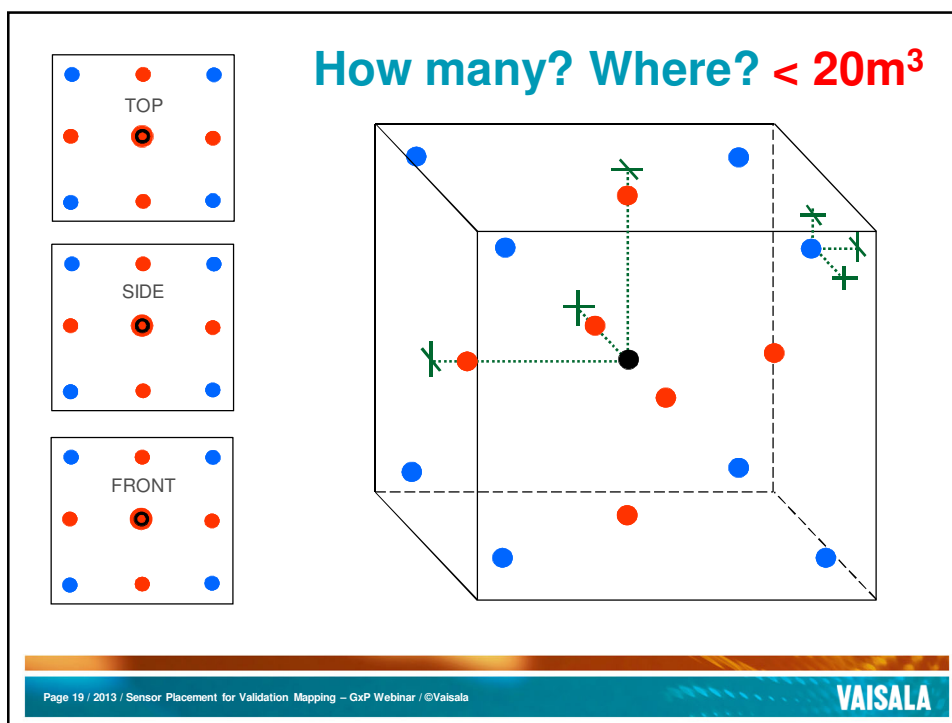


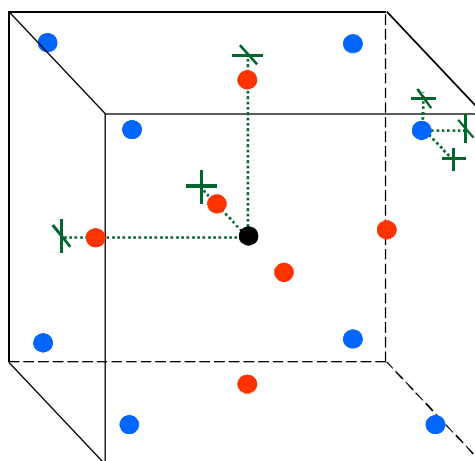
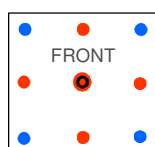
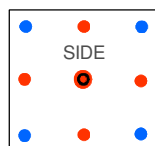
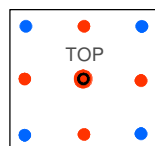
Diagram illustrating a 3D space (a cube) with three empty viewports labeled TOP, SIDE, and FRONT. The cube contains several blue dots representing sensor locations and green crosses representing measurement points. The viewports show the corresponding 2D projections of these points.

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## Corollary 1B: If $\leq 20\text{m}^3$ , use 15 +1.



## Guidance describes 9 +1 and 15 +1

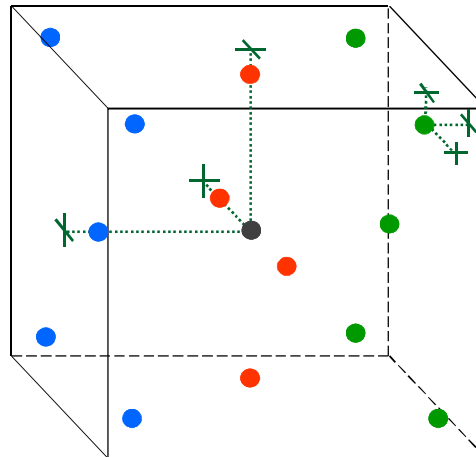
- ISPE Good Practice Guide: Cold Chain Management (2011)



## Rule 2: Map in 3 Dimensions.

3 planes.

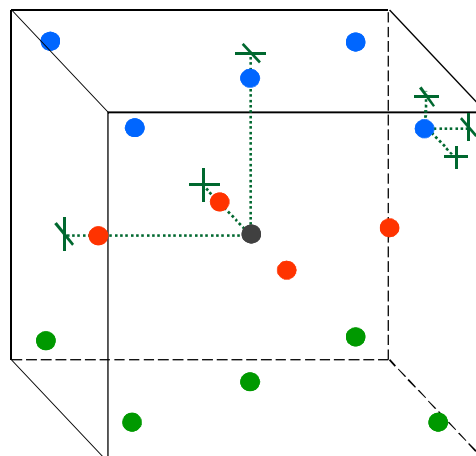
Left to right.



## Rule 2: Map in 3 Dimensions.

3 planes.

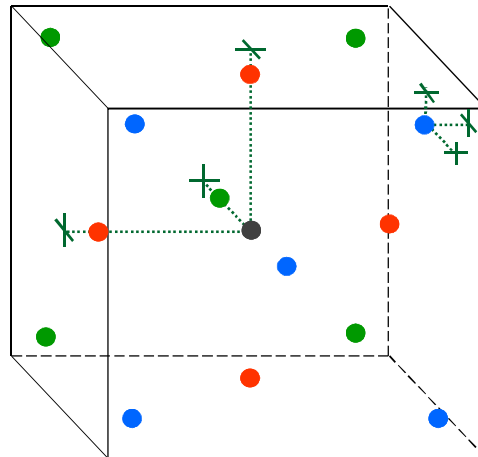
Top to bottom.



## Rule 2: Map in 3 Dimensions.

3 planes.

Front to back.

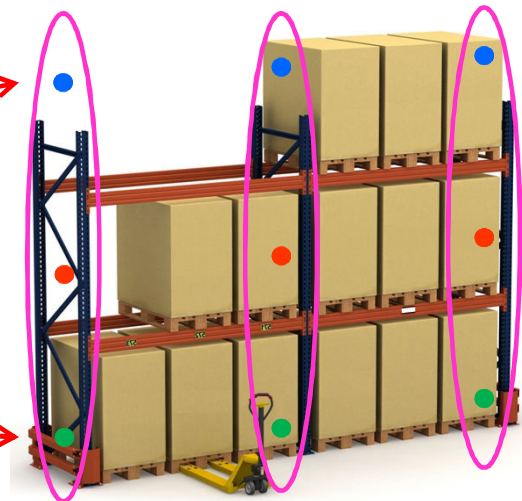


## Corollary 2A: If $\geq 20\text{m}^3$ , use Stacks of 3.

High

Middle

Low



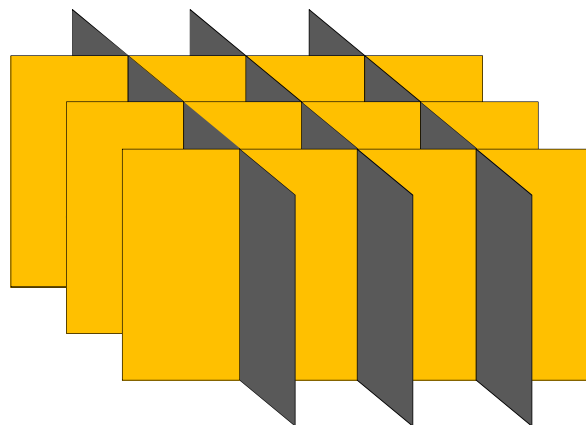
## Stacks of 3, in 3 dimensions.



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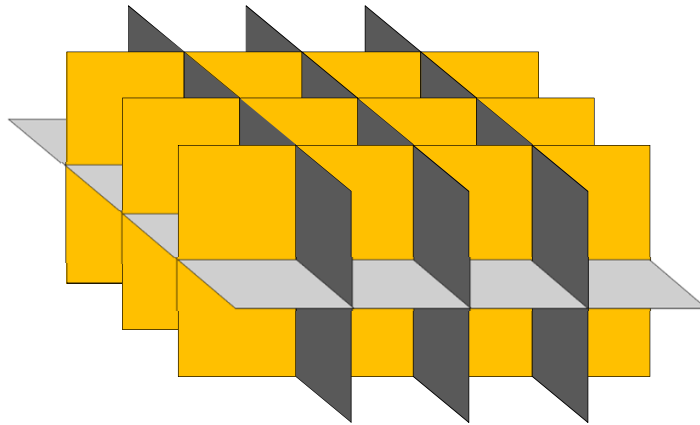
## Stacks of 3, in 3 dimensions.



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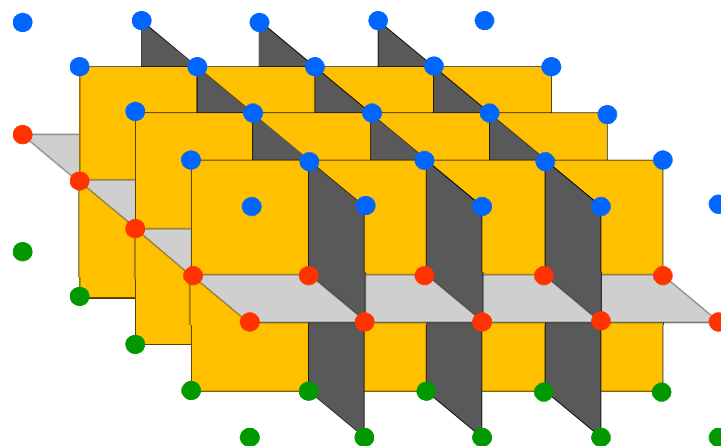
## Stacks of 3, in 3 dimensions.



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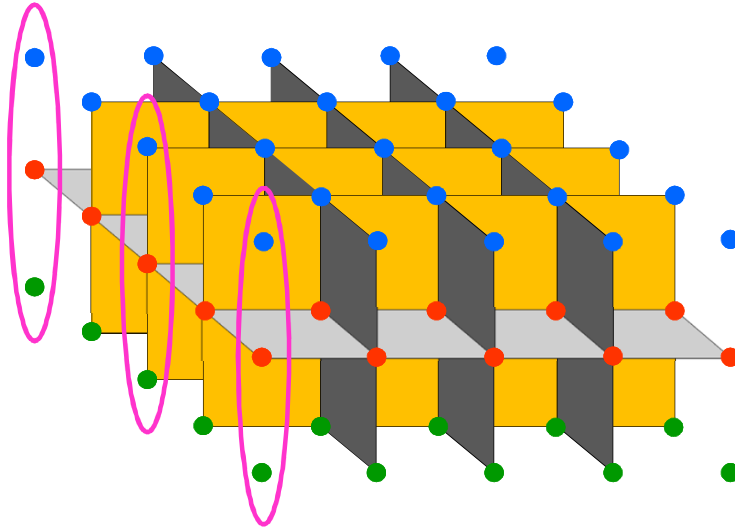
## Stacks of 3, in 3 dimensions.



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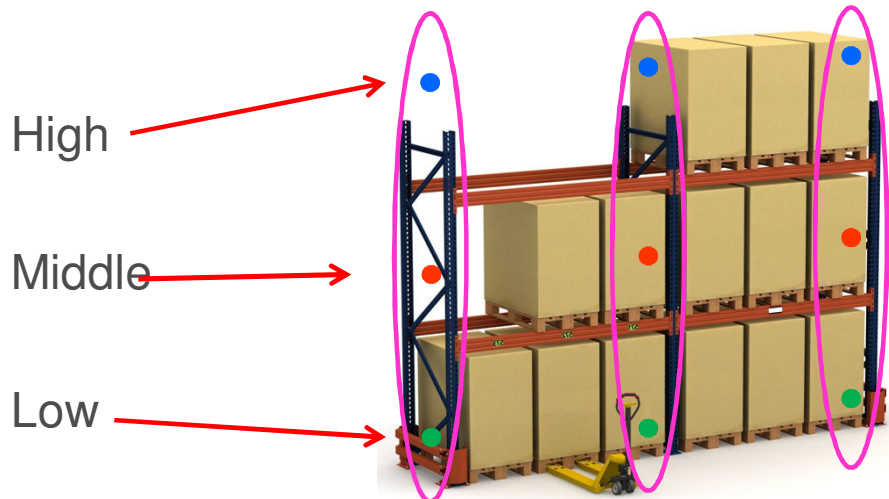
## Stacks of 3, in 3 dimensions.



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



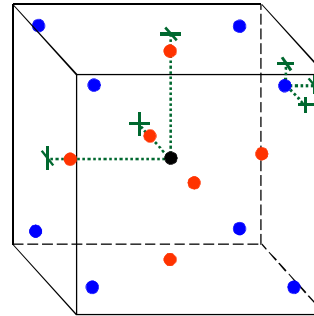
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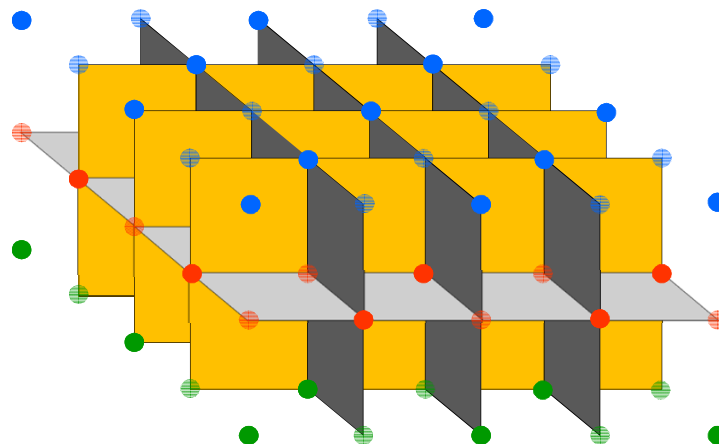


## Corollary 2B: Remove sensors if possible.

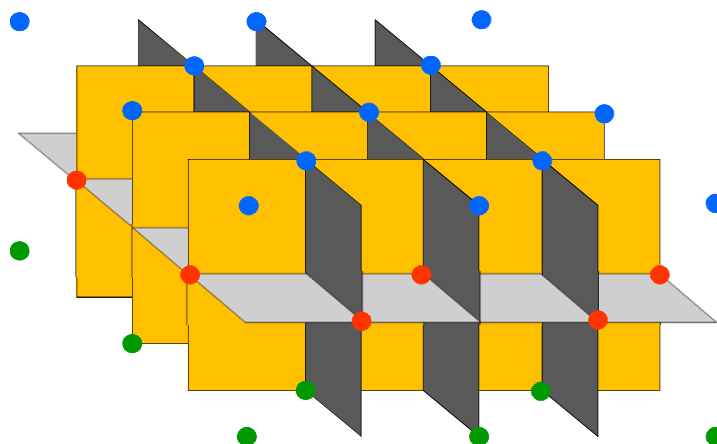
- Remove “extra” sensors.
  - 15 + 1 diagram.
  - With “Stacks of 3, in 3-D”, it would have 27 sensors.



## Stacks of 3, in 3 dimensions.



## Stacks of 3, in 3 dimensions.



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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...”*

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



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### Rule 3: If $\geq 20\text{m}^3$ , 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)**



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## Rule Summary (so far...)

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



## Rule Summary (so far...)

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- Rule 2 - Map in 3 Dimensions
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  - Corollary 2B – Remove Sensors if Possible



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- 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.



## 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

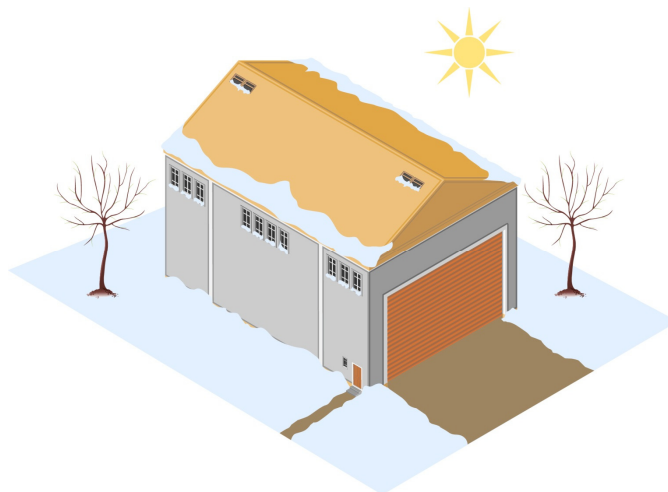
## Volume



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## Temperature $\Delta$



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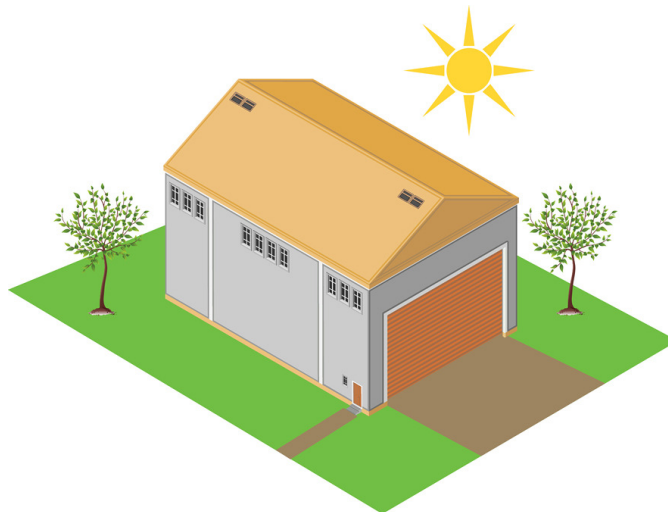
## Height



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## Exterior Walls



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## Construction Materials



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## Doors and Windows



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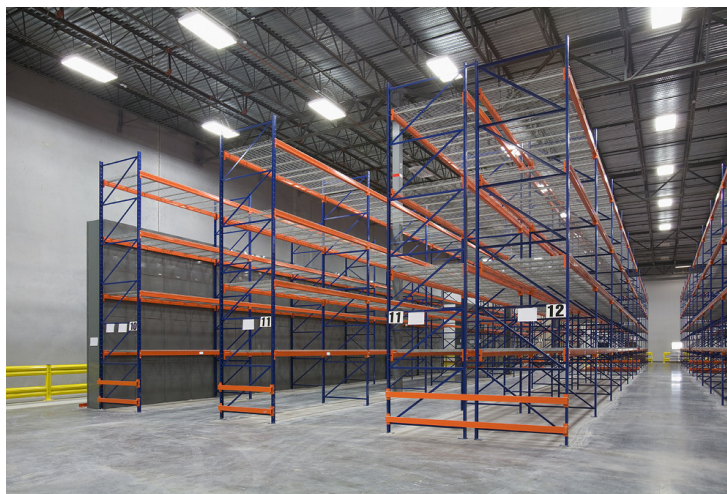
## Lighting



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## Gradients



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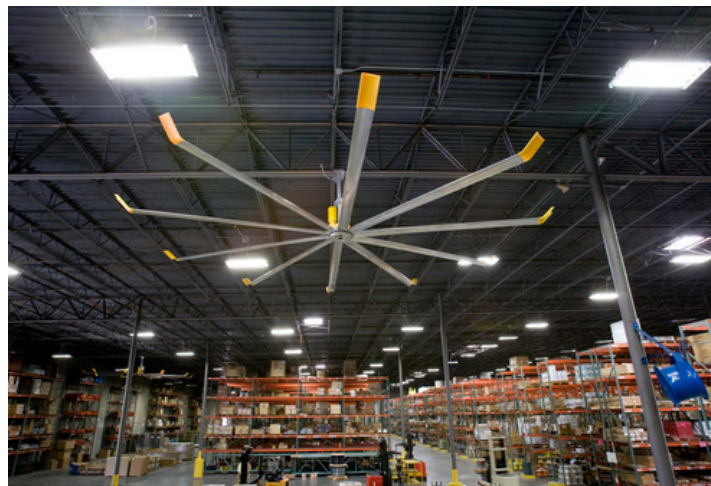
## HVAC Vents and Returns



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## Air Circulation



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## Control Sensors



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## Energy Sources



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## Racks, Shelves, and Product



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## Traffic Patterns



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## Human Factors

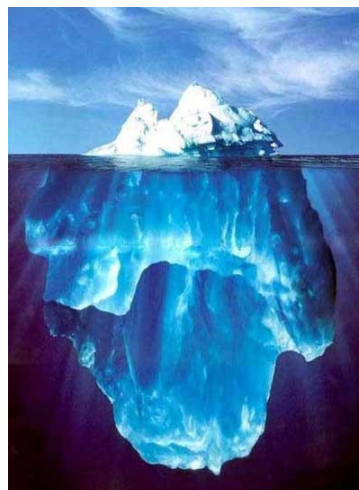


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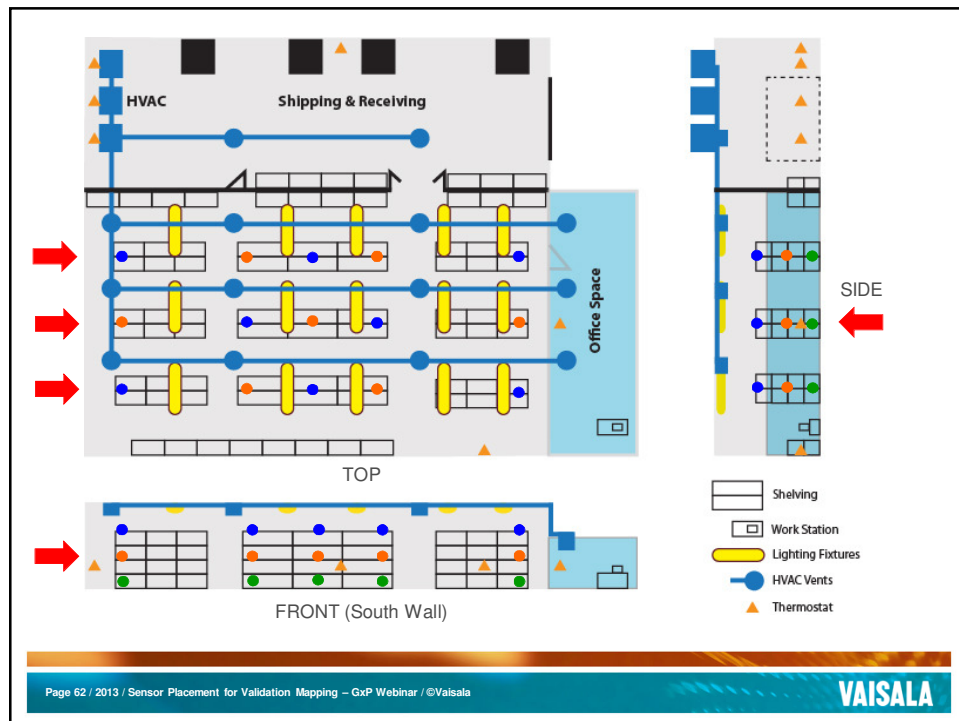
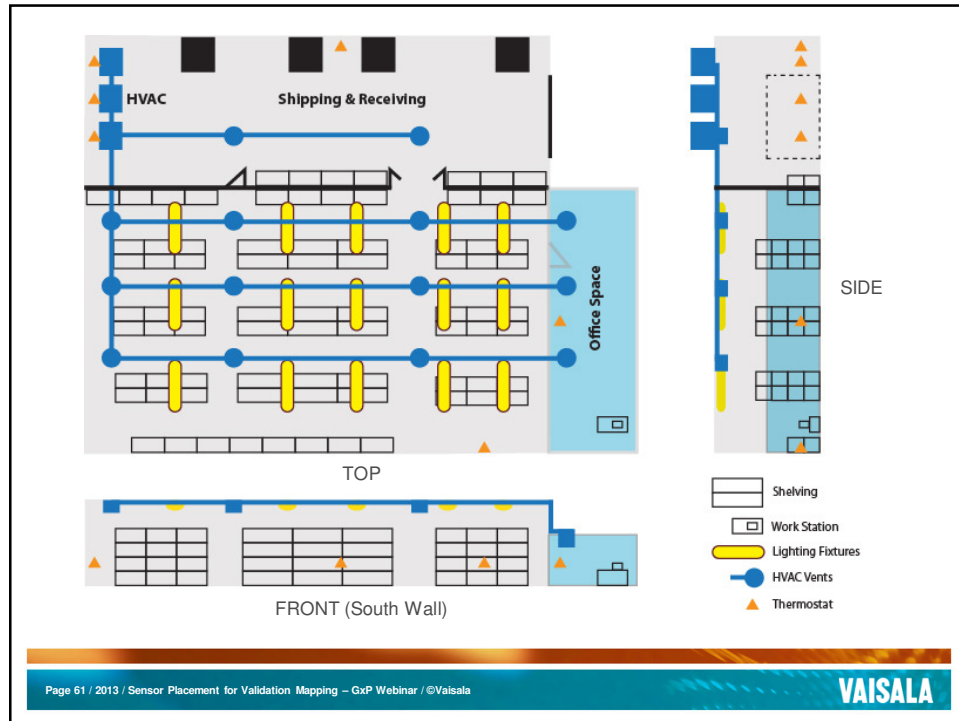
## Rule 4: Identify Variables

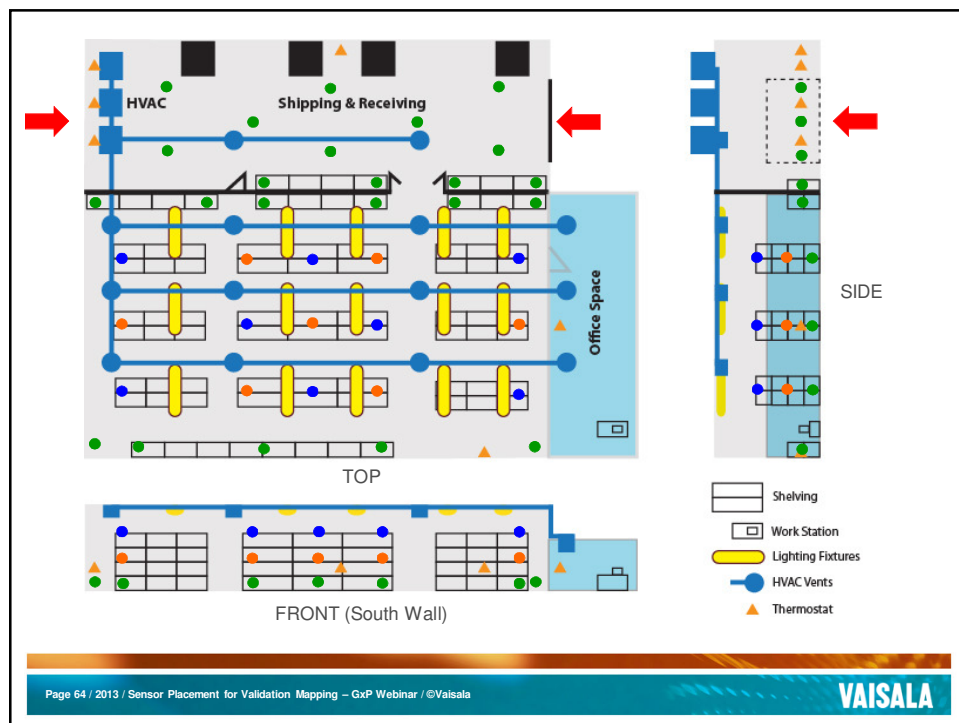
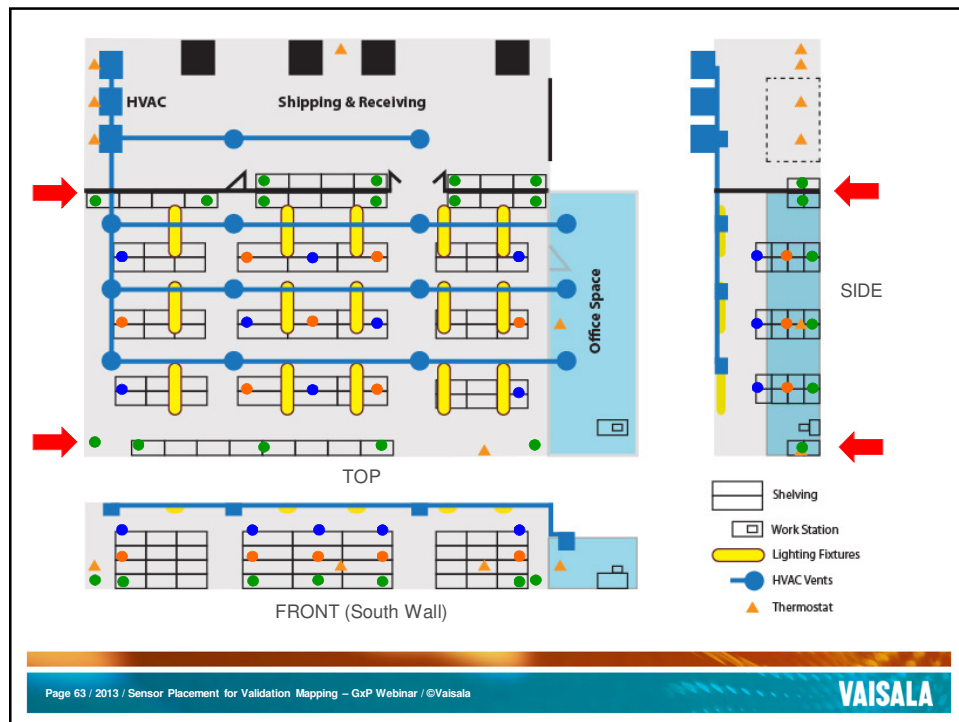
- Place sensors near representative variables!
- Adjust ideal “grid” to intersect variables.



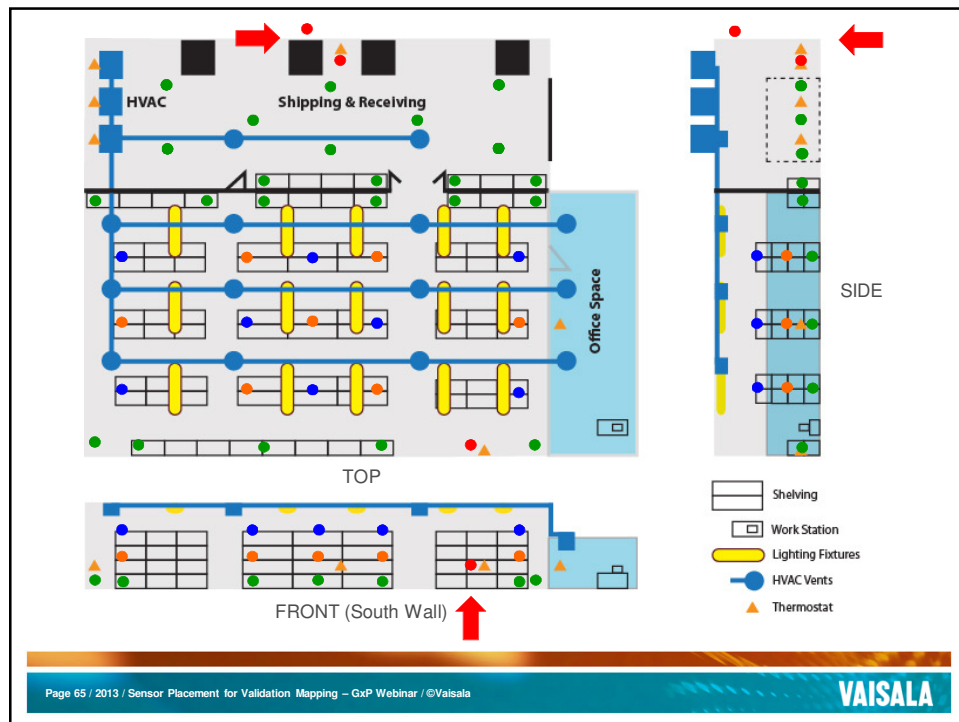
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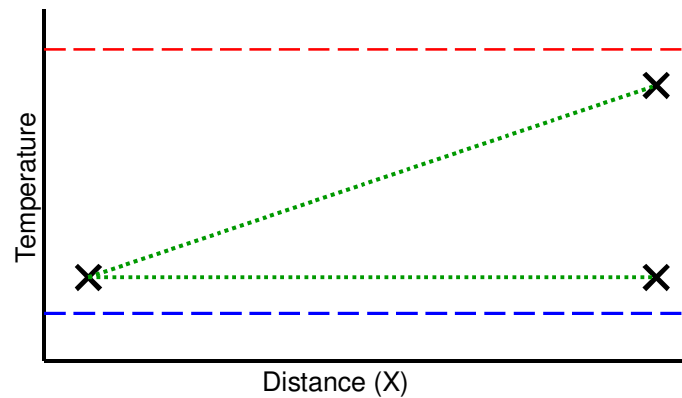




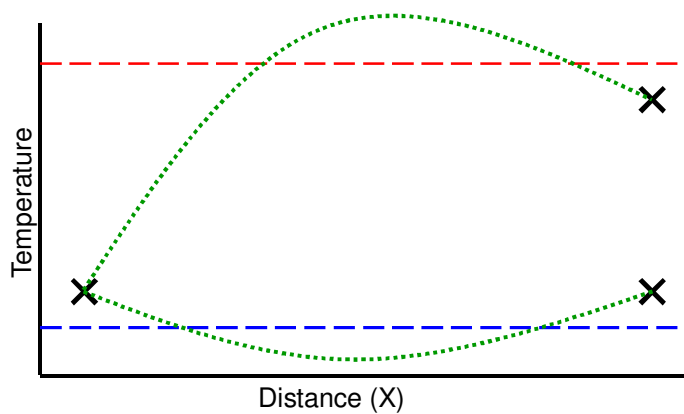




## Distance Between Points



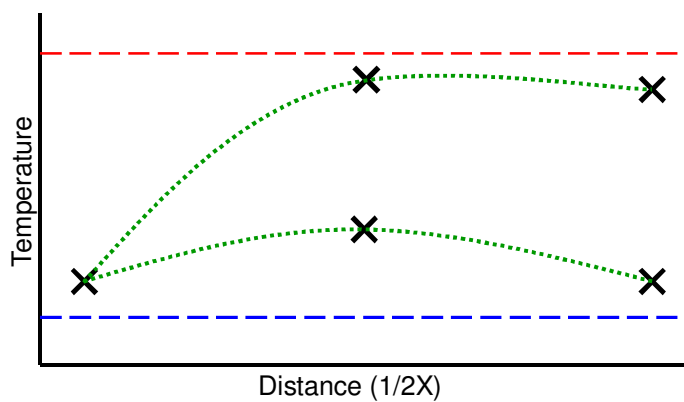
## Distance Between Points



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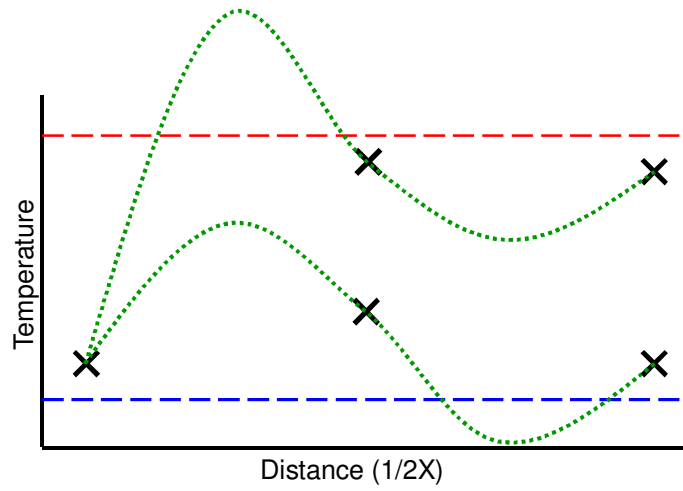
## Distance Between Points



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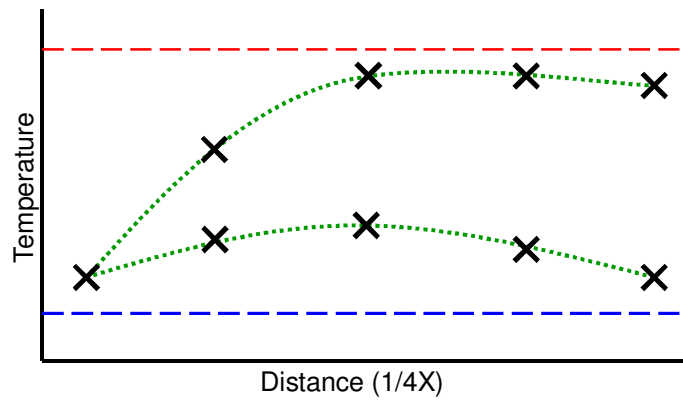
## Distance Between Points



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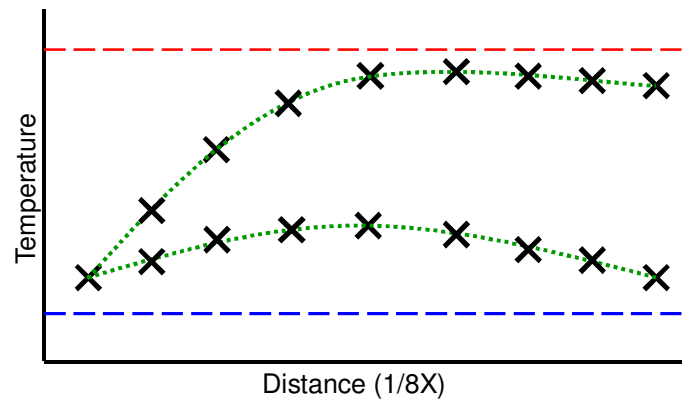
## Distance Between Points



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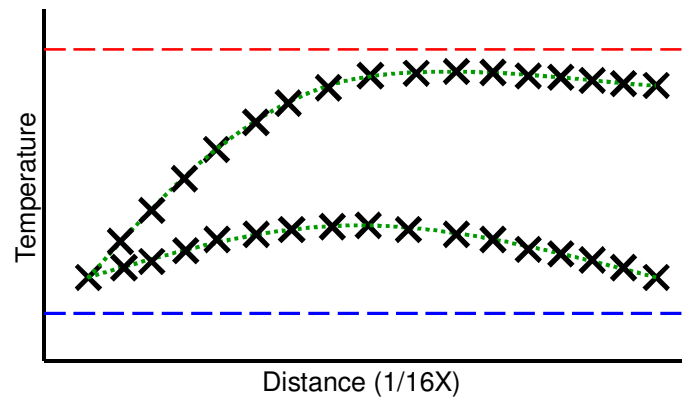
## Distance Between Points



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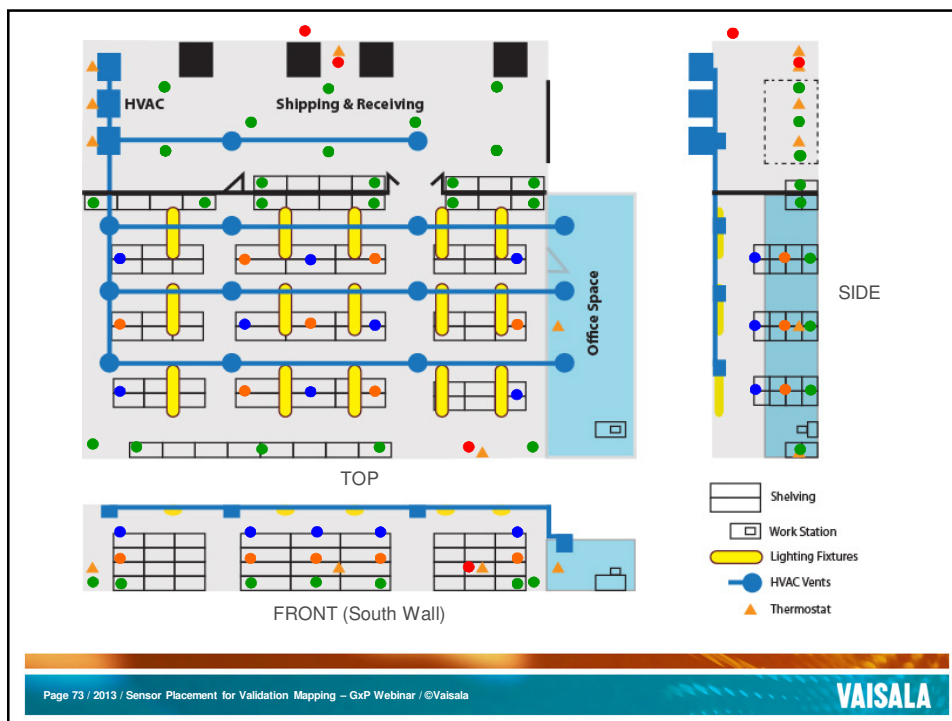
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## Distance Between Points



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## 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.**”*

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



## Rule Summary

- Rule 1 – Map the Extremes
  - Corollary 1A – If  $\leq 2m^3$ , use 9+1.
  - Corollary 1B – If  $\leq 20m^3$ , use 15+1
- Rule 2 - Map in 3 Dimensions
  - Corollary 2A – If  $\leq 20m^3$ , use Stacks of 3
  - Corollary 2B – Remove Sensors if Possible
- Rule 3 - If  $\geq 20m^3$ , map storage only.
- Rule 4 – Identify Variables
- Rule 5 – If it is worth Mapping, it is worth Monitoring



## 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)



## 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.



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## Thanks for Attending!



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