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5 Rules of sensor placement in validation/mapping applications

In today's global economy, drugs, biotechnology, and medical devices are shipped all over the world. To ensure these temperature-sensitive products are stored correctly, new or revised regulations have been developed in many key regions, including China, Europe, and the U.S.A. New Good Distribution Practice (GDP) regulations help to perform mapping studies to qualify storage areas. Two common questions in mapping studies are 1) where to place sensors and 2) how many sensors to use. This article discusses five rules to apply when creating a rationale for sensor placement in mapping studies.

Global regulators, including the Food and Drug Administration (FDA), the European Medicines Agency (EMA), China's SFDA, and Japan's Pharmaceuticals and Medical Devices Agency (PMDA) require manufacturers to determine if environmental parameters affect product quality and perform stability testing to determine appropriate product storage specifications. It is the job of facilities managers, supply chain managers, and validation specialists (among others) to help ensure that those storage specifications are met by mapping storage areas. Unfortunately, most regulations offer little guidance on how to perform a mapping study. For example, the location and number of sensors that are needed to qualify a given space are not dictated by the regulations; it is left to manufacturers and distributors to determine adequate sensor placement as part of their quality processes.

The GDP regulations explicitly assign responsibility for compliance to the entire distribution network. This means that a large number of previously unregulated entities must now secure their portion of the cold chain by performing mapping studies. This has created a need for information on best practices for mapping studies. The following five rules offer new mapping practitioners guidelines to creating a reasoned rationale for sensor placement in this basic and critical validation activity.

Five rules for sensor placement

There are five key considerations for determining sensor placement in your mapping studies. While every combination of environment and product specifications is unique, these rules are applicable to almost every situation.

RULE 1 — Map the extremes.

RULE 2 — Map in three dimensions.

RULE 3 — For large spaces, map storage only.

RULE 4 — Identify and address variables.

RULE 5 — If it's worth mapping, it's worth monitoring.

RULE 1: Map the extremes

To do an effective mapping, we must place sensors in the geometric extremes of the space. We must also place sensors in the locations that will experience the extremes of high or low temperatures. Mapping the extremes captures the worst-case conditions of the space and helps ensure we collect data from the entire storage space. Consider a cube. A cube comprises six planes joined at right angles. The parts of a cube include: corners, edges, sides, and the space inside. A corner is a junction of three planes, while an edge is a junction of two planes. A side of a cube is made from a single plane, and the space inside is made from zero planes **(Figure 1)**. This progression of planes (3, 2, 1, 0) can guide us in determining the extremes of this cubic space. The extremes are 3 (the corners) and zero (the space inside).

> ***Note:*** *Figuring out where to place a monitoring probe is a common challenge. If mapping identifies a hot or cold spot in the middle of a unit, it will be difficult to put a sensor there because it will preclude using the space to store products. Our goal is to find a location for the probe that will be representative of the storage conditions, yet outside of the traffic areas.*

Figure 1: Parts of cube

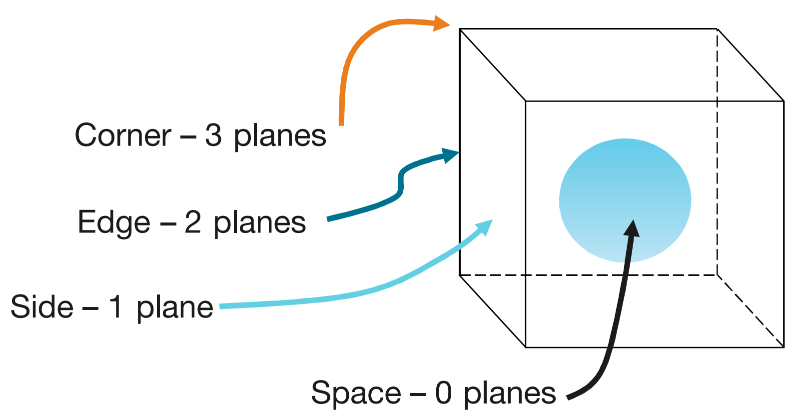
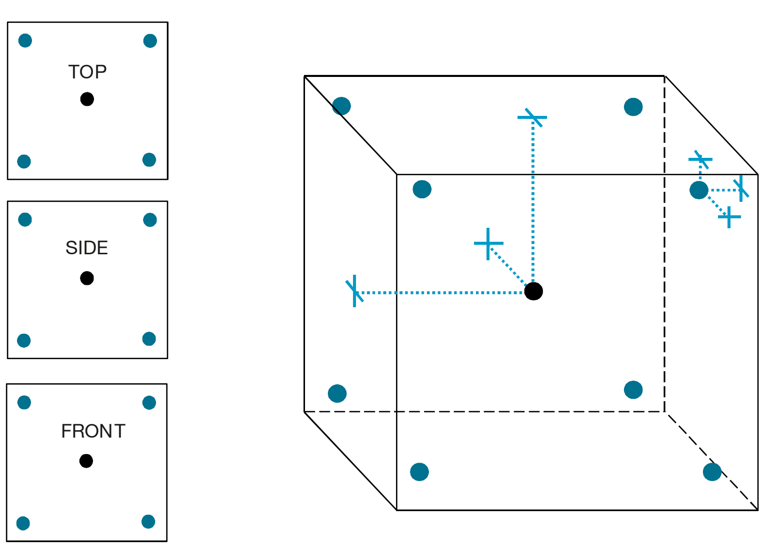


Figure 2: Corollary 1A If ≤2 m³, use 9 + 1



Let's apply this geometric map to a space with a volume of two cubic meters or less (≤2 m³), taking the corners and center into consideration. If a space is less than 2 m³, a total of nine sensors should be placed; one at each of the corners and one at the center. This is what we call Corollary 1A: If ≤2 m³, use 9 + 1 **(Figure 2)**. The +1 represents an additional sensor at the location of the controlling probe or the building monitor probe to act as a point of reference. As a reminder, ≤2 m³ (approximately 70 ft³) is the volume of almost every free-standing refrigerator, freezer, or incubator with one or two doors.

In this same ideal ≤2 m³ space, let's challenge this model to see if it captures the worst-case scenarios for the two most common challenges to temperature uniformity: Air Circulation and Heat Exchange. Let's consider air circulation first. Because the corners are bound by three planes, they should have the least air circulation. The center, which has no planes, should have the most air circulation. What about heat exchange with the outside environment? Again, the corners have three planes that allow the most heat exchange with the outside environment, and the center with no planes should be most insulated from heat exchange. Therefore, we can be confident that this model captures the worst-case scenarios for these two common challenges to temperature uniformity.

Now, suppose the space is larger than 2 m³, up to 20 m³. A 20 m³ space would be the size of a small bedroom, say 3 m x 3 m wide and 2.2 m high (10 ft. x 10 ft. wide and 7 ft. high). How many sensors do we need in this space? We already know we need nine sensors to map a space up to 2 m³, so we will use that as a starting point. From our previous analysis of a cube **(Figure 1)**; we know we still have edges and sides available for sensors. The recommended practice is to place an additional six sensors, one at the center of each side of the cube **(Figure 3)**. This gives a total of 15 sensors, and brings us to Corollary 1B: If a space is <20m³, use 15 + 1 sensors. Again, the +1 is for the controlling RTD or monitor probe. For more detail on the mapping strategies presented in Corollary 1A and 1B, refer to the ISPE's "Good Practice Guide: Controlled Temperature Chamber Mapping and Monitoring."

Our cube-based models are useful because most storage areas are cubical or rectangular in shape. Though certain room layouts may seem challenging; remember that an L-shaped room is simply a combination of two rectangular spaces. If possible, treat such a case as a single space and map the entire space at the same time. It is easier to use more sensors than it is to explain to an auditor why connected spaces were mapped separately. The only rationale that supports mapping connected areas separately is if they actually are controlled independently with different control zones on the same HVAC system.

Figure 3: Corollary 1B If ≤ 20 m³, use 15 +1

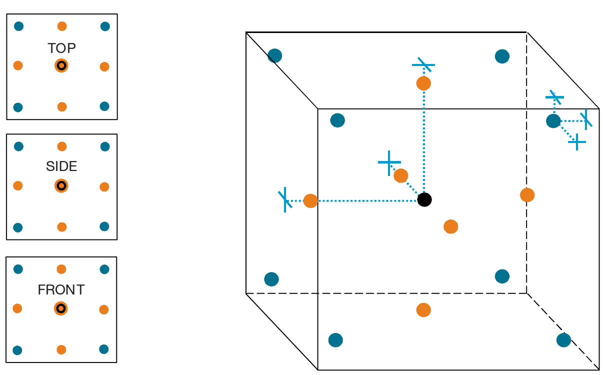
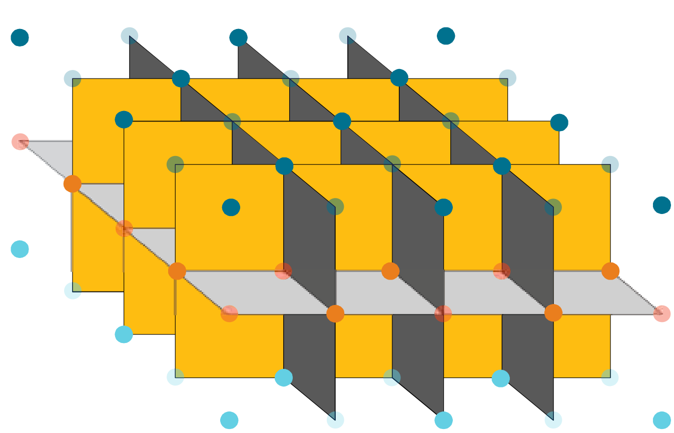


Figure 4: Corollary 2B Remove sensors if possible (faded dots = extraneous sensors)



RULE 2: Map in three dimensions

Again, let's consider the 15 + 1 diagram for volumes <20 m³. Notice that the sensors placed are inside three distinct planes, going from left to right **(Figure 5)**, top to bottom **(Figure 6)**, and front to back **(Figure 7)**. Each of these sets of planes display a single planar dimension. The three arrangements together display three planar dimensions and demonstrate what it means to "map in three dimensions."

Rule 2 is applied obligatorily when using the models presented in Corollary 1A and 1B. But what if we need to map spaces that are larger than 20 m³? This leads us to Corollary 2A: If a space is ≥20 m³, use "Stacks of 3" **(Figure 8)**. By arranging a line of three "Stacks of 3," one vertical plane of sensors can be created (a single planar dimension). By arranging multiple interlocking lines of "Stacks of 3," we can create three planar dimensions of sensors in a large space **(Figure 4)**. This is how to arrange sensors in a large space to achieve mapping in three dimensions.

The downside of applying "Stacks of 3" is that a lot of sensors are required. We can mitigate this with Corollary 2B: Remove sensors if possible. Going back to our 20 m³ cube **(Figure 3)**, using "Stacks of 3" in this space would require 27 sensors. However, we already established that we can map such a space using only 15 sensors. By removing alternating sensors in each plane, we can maintain the integrity of each plane of sensors. **Figure 4** shows such an arrangement in a larger space. Stacks of 3 have been applied: the faded dots indicate the sensors that could be removed while still retaining the integrity of mapping each plane of sensors **(Figure 4)**.

RULE 3: For large spaces, map storage only

As a space gets larger, it is not necessary to map hallways and access areas. We only need to map areas where product is actually stored, such as racks, shelves, and other storage areas. This may necessitate some procedural controls to prevent storage from occurring in the areas that were not mapped; consider implementing appropriate signage, training, and standard operating procedures for this purpose.

Rules 1 to 3 provide a model for how to place sensors based on geometry, thermodynamics, and common sense. Our model now needs to be modified to provide a mapping that represents the reality of the area to be mapped. The ISPE states this quite clearly in their Good Practice Guide: Cold Chain Management: "Additional points may be needed depending on airflow sources/characteristics, shelving (storage locations), external temperature sources, previous experience with similar units, and their thermal behavior." We must thoroughly understand the space we are mapping so we can qualify it appropriately. This is where Rule 4 applies.

RULE 4: Identify Variables

The process of identifying variables recognizes the potential heat sources or areas of heat differences in the environment to be mapped **(Figure 9)**. This will guide the final placement of sensors. The process of evaluating these variables and the resulting sensor placement choices should be well-documented so that the reviewers, auditors, and approvers of the mapping study will understand your sensor placement rationale.

Figure 5: Rule 2 Map in 3 dimensions

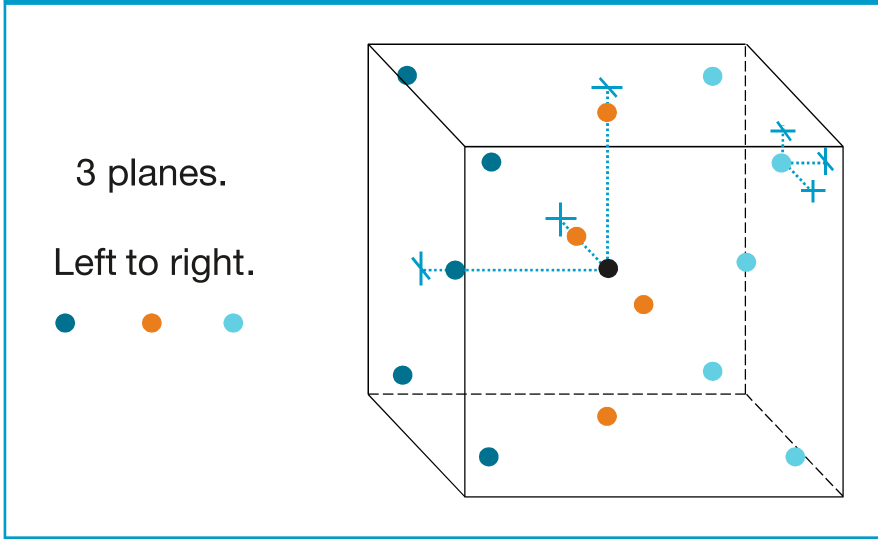


Figure 6: Rule 2 Map in 3 dimensions

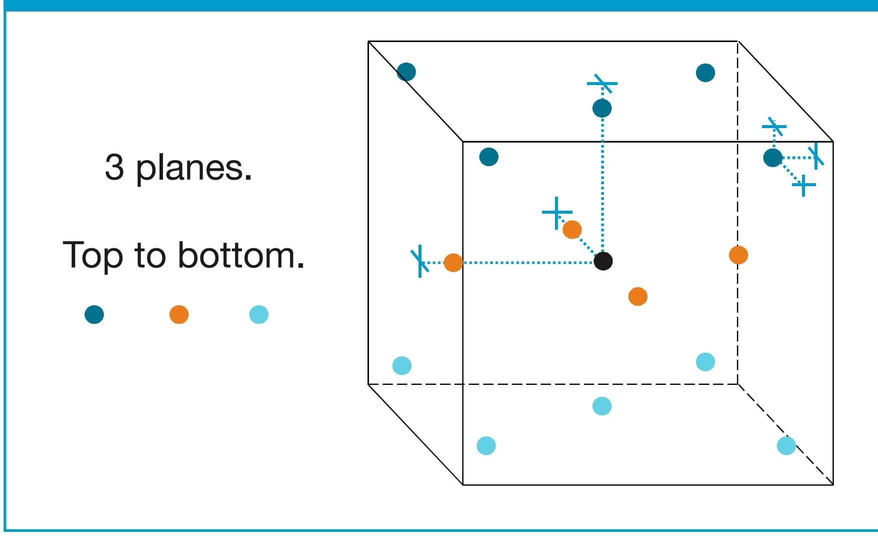


Figure 7: Rule 2 Map in 3 dimensions

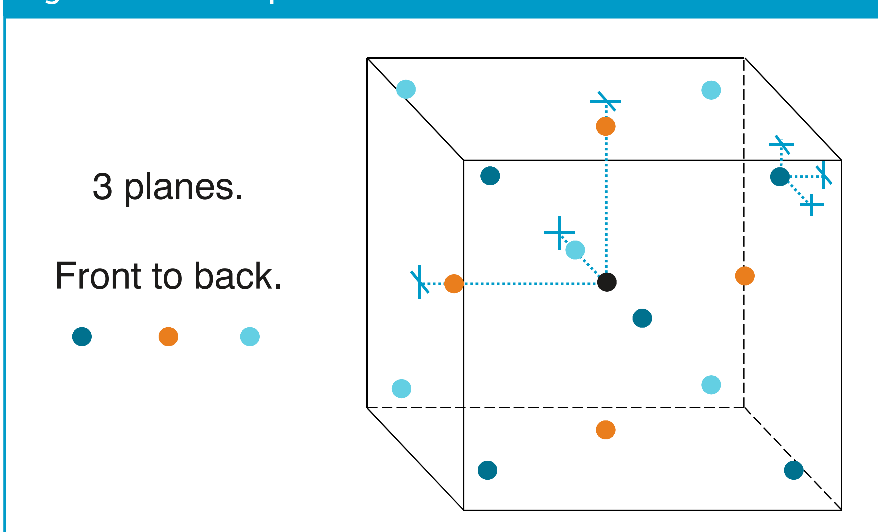


Figure 8: Corollary 2A If ≥ 20m³, use stacks of 3

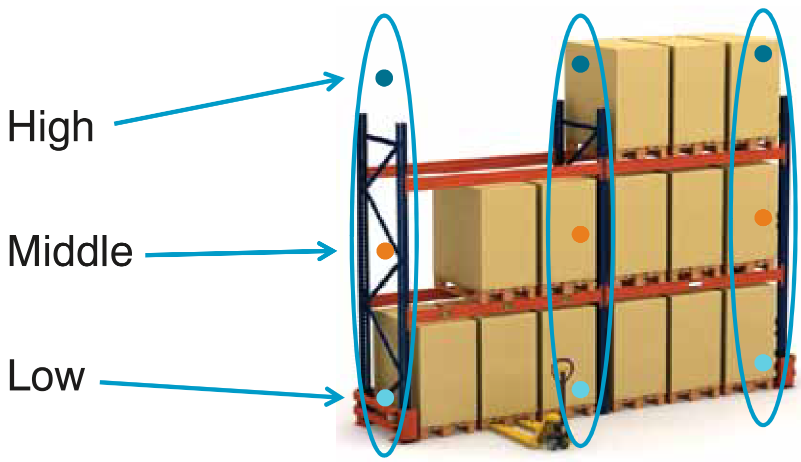


Figure 9: Common Variables

- **Volume:** As a space increases in volume, the less relative surface area it has. There is less opportunity for heat exchange with the outside environment. This will typically mean fewer sensors per unit volume.
- **Temperature differential:** This is the difference in temperature between the inside and outside environment of the space. The greater the temperature differential, the greater the density of sensors required.
- **Height:** Height allows space for heat to rise. This allows vertical gradients to form. A cool concrete floor and a hot metal roof will result in a cool-to-hot gradient from the bottom of the floor. Height also provides space to let us use “Stacks of 3.”
- **Exterior walls:** Exterior walls may allow the outside weather conditions to have an impact on the inside space. Additional sensors near exterior walls may be needed to evaluate this impact.
- **Doors and windows:** Windows can enable heating by sunlight and faster temperature exchange with the outside environment. Open doors can allow airflow. Determine when doors are open, the direction of air flow through the door, and the temperature of the air coming through the door.
- **Lighting:** In new warehouses, energy-saving lights or motion-control lights are used, and these are generally located over access areas where product is not being stored. In an old building or a re-purposed space, lighting could be an issue if it is generating heat over product storage areas.
- **Gradients:** Our sensor placement should predict the location of gradients so that they may be captured in the study, such as a vertical gradient between a cool floor and a warm ceiling. Gradients can be a good thing. For example, if there is a temperature gradient between two sensor locations with acceptable data, and there are no other sources of temperature variation between them, it may not be necessary to add a sensor in the middle. The stable gradient can give us confidence in the temperature uniformity along that axis so that fewer sensors are needed. Locating gradients in the space can inform our rationale for sensor placement.
- **HVAC vents and returns:** The HVAC system will dictate the majority of the airflow pattern in a closed warehouse. A poorly designed HVAC system may result in significant hot or cold spots. Often, the air coming out of the HVAC system is outside of controlled parameters so we should be on the lookout for product storage locations near vents.

Variables need to be identified to guide sensor placement decisions

Figure 9: Common Variables *(continued)*

- **Air circulation:** Air circulation, or the lack of it, can cause hot or cold spots to occur during heating and cooling cycles. This can be an important and difficult variable. However, it is increasingly common for large warehouses to use fans to increase air circulation. This creates a more uniform environment and decreases heating and cooling costs.
- **Control sensors:** Mapping sensors should be placed next to control sensors to allow easy correlation of mapping data to data from the control system. Remember that a poorly placed control sensor can cause the HVAC system to perform erratically if it's too close to a vent, door, or window.
- **Machinery:** Machinery and its associated charging systems can be a source of heat. While machinery is typically isolated from the product storage areas, it can also be integrated, such as automated picking systems.
- **Racks and shelving:** These items in a storage space can affect the temperature dynamics and possibly block air movement, particularly in smaller spaces. The impact of shelving in smaller controlled spaces depends on how the units are designed to cool or heat (using air movement or temperature conduction). In larger spaces like warehouses, a rack of shelving can act like a wall to block airflow, particularly when filled to capacity.
- **Traffic patterns:** Movement can change airflow. For example, the opening of doors causes temperature changes. How long are doors kept open? Does an open door allow air to flow in or out? Is the incoming air a different temperature?
- **Human factors:** People interact with the space, and in the process they may create additional variables. For instance, they may store product in the wrong spots. Document patterns and factors unique to the space.

***Note:** It is hard to guarantee that your planned mapping will occur during the hottest part of the summer or the coldest part of the winter. One solution is "Continuous Mapping." Install a dense sensor array and leave it installed as your monitoring (and mapping) system. This will require an up-front investment in sensors, but if the space is remapped frequently, labor savings will add up because extra sensors no longer need to be placed or collected for each mapping event. The seasonal mapping validation can be performed retrospectively, by selecting the appropriate week of mapping data after the hottest (or coldest) weather period has been identified.*

While this is not an exhaustive list of variables, it does outline many that should be considered when placing sensors. A more conservative point of view would dictate placing sensors near every one of these variables. However, this does not necessarily mean having to add sensors; we may be able to simply adjust the sensor grid of our "Stacks of 3" so that it accounts for the identified variables.

***Note:** If a storage chamber has shelves in a fixed location, sensors can be placed directly on the shelves. However, placing sensors on moveable shelves could lead to questions during an audit. Instead, map the entire space ignoring the current shelf locations to allow for more flexibility in your use of the space.*

Warehouse Mapping Example

Consider a large warehouse of about 40,000 m³. Variables include racks and shelving, an HVAC system, exterior walls, a south-facing wall with direct sun exposure, doors going into and out of the Shipping & Receiving area, loading dock doors, and thermostatic controls **(Figure 10)**.

Following the rules discussed, an array of sensors has been applied to the central storage area using Stacks of 3 **(Figure 11)**, shown here with blue, orange, and green dots. These Stacks of 3 are most easily seen in the FRONT and SIDE views in **Figure 11**. Where the Stacks of 3 were used, the redundant sensors were removed. This can be seen in the **Figure 11** TOP view as alternating blue and orange dots. The blue dots represent both a high and a low sensor, while the orange dots represent a middle level sensor. Then sensors were placed near the prominent temperature variables in the area: the HVAC vents, the doors to the Shipping & Receiving area, and the cool concrete floor.

These sensors provide coverage of the secondary storage shelves and near the prominent temperature variables in the area, which include the doors to the Shipping & Receiving area, and the south-facing wall. Sensors have also been placed in empty corners that are likely to be used for emergency or accidental product storage.

Finally, we address the Shipping & Receiving area, seen at the top of **Figure 11**. Shipping and receiving areas are not intended to be product storage areas, but product often spends several hours here. This sensor arrangement monitors any temperature variable effects by the loading dock doors. Additional sensors are placed at the thermostats, and outside in the shade on the North wall to capture ambient conditions, as indicated by the red arrows.

In review of this warehouse example, we have satisfied the first 4 rules. We have satisfied Rule 1 and mapped the extremes, in this case, the center and corners. In the main storage racks, we have sensors in three planes in three dimensions using the "Stacks of 3" guidance described in Rule 2. Sensors were placed in areas where products are stored to satisfy Rule 3. We satisfied Rule 4 by adjusting the sensor placement to coincide with the doors, HVAC vents, and along the southern exterior wall.

In total, 49 sensors were used, which is not very many for a space that is 40,000 m³. Remember that for a space of 20 m³, we used 15. Our warehouse is 2,000 times bigger, and requires only three times as many sensors, showing a non-linear relationship between volume and sensor number.

Figure 10: A schematic with shelving, a loading dock, an HVAC system, lighting, and other variables.

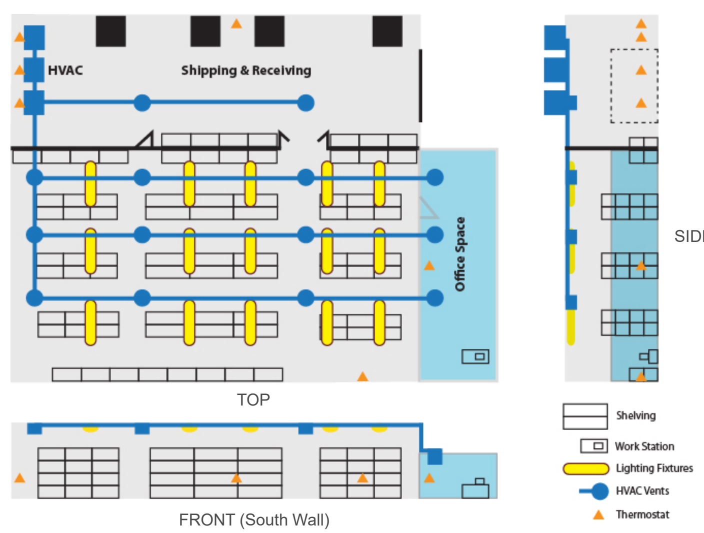
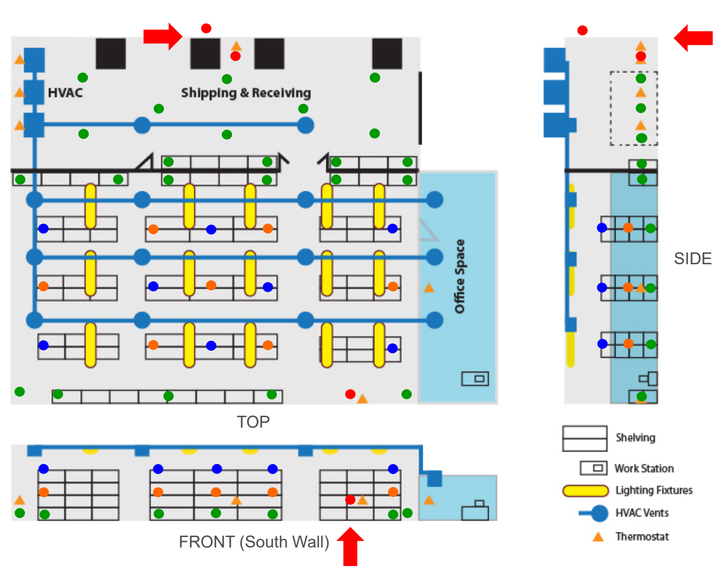


Figure 11: Sensor placement sample; sensors are green, blue and orange dots at different heights.



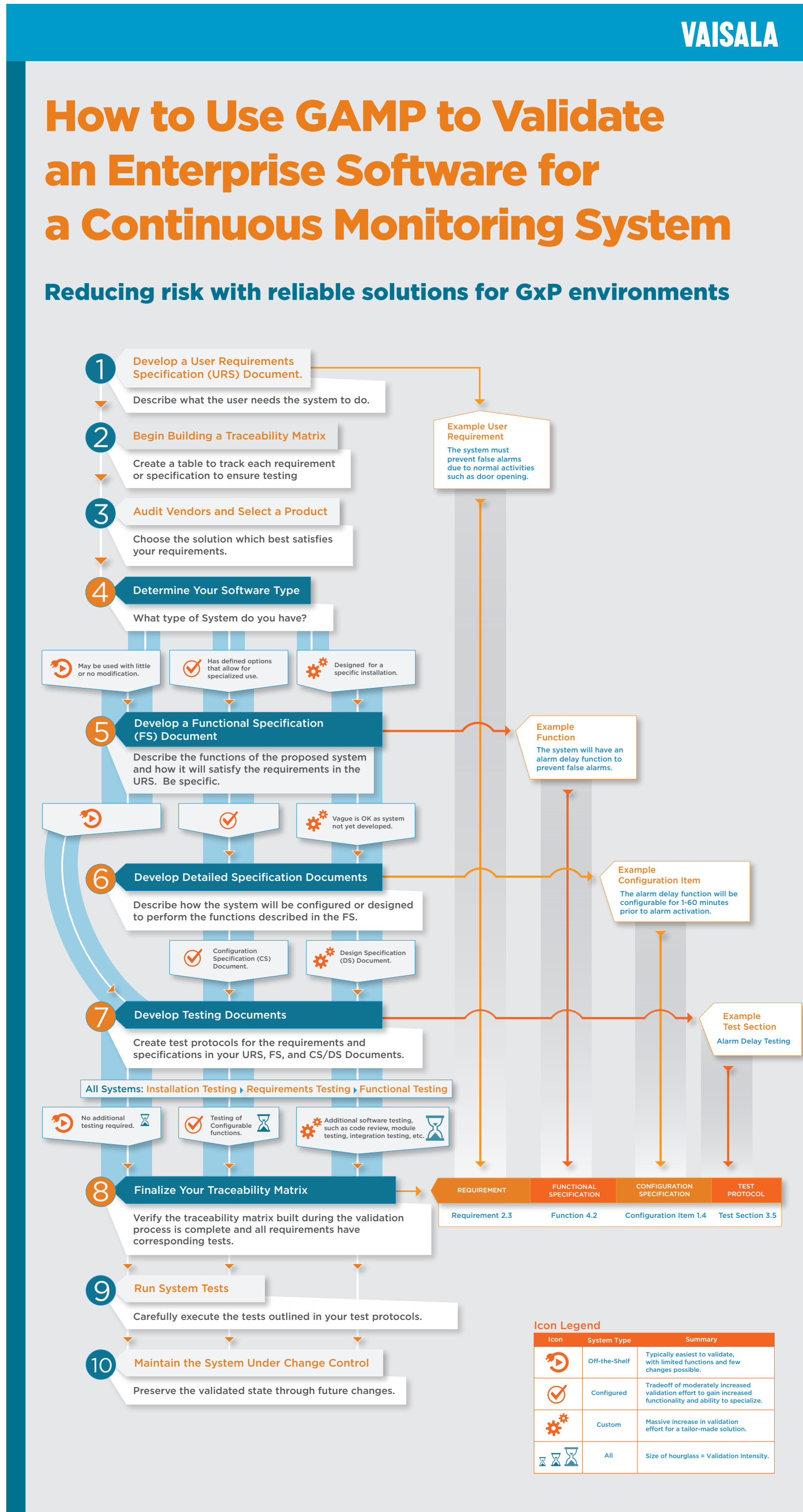
RULE 5: If it's worth mapping, it's worth monitoring

In continuous monitoring system sensor placement, we first identify the hot and cold spots, and then select a monitoring strategy to account for these known areas of concern. This may be accomplished by monitoring these spots directly, or by finding representative spots.

Next, select the right monitoring solution. With a good match between your monitoring system(s) and your Quality System, there will be less risk of non-compliance, or lost product.

Finally, validate the monitoring system to ensure that it is installed correctly and operating according to expectations. For more information on how to do this following the ISPE's GAMP process, refer to our infographic in **Figure 12**.

Figure 12: Validate your Monitoring System according to GAMP



Download this “How to use GAMP to Validate an Enterprise Software for a Continuous Monitoring System.” infographic.

Summary

Validation has always been an important element of a successful compliance strategy. The advent of regulations for Good Distribution Practices has increased the importance of mapping studies, and increased the number of entities that are expected to perform such studies.

Creating an accurate profile of storage conditions through a consistent validation program establishes that the environment is adequately understood, documented, and controlled. It also demonstrates that the environment is suitable for sensitive products and compliant with Good Manufacturing Practice.

Moreover, the information obtained from reasoned, well-executed mapping studies will inform decisions on how controlled areas are monitored continuously, making monitoring choices evidence-based. Such an approach to monitoring temperature, humidity and other critical parameters ensures that any auditor or inspector will find a shining example of environmental control when they visit your facility.

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