VAISALA / APPLICATION NOTE

8 Steps to Validating/Mapping a Chamber

Periodic mapping of conditions within environmental chambers is critical for compliance in FDA-regulated applications, where validation of conditions such as temperature, and sometimes humidity, is mandated. [1, 2, 3, 4, 5] *This application note recommends some options to help meet cGMP requirements for validation projects. Note: we refer to probes, sensors, data loggers interchangeably within this application note. These are broad guidelines only, and most recommendations are based upon using data loggers as the sensing device.*

Validation in 8 Steps

- **Step 1** Write a plan
- **Step 2** Check equipment & documentation
- **Step 3** Confirm device operation
- **Step 4** Set up the data loggers
- **Step 5** Place the data loggers
- **Step 6** Periodically check the progress
- **Step 7** Retrieve and store the data
- **Step 8** Report the findings

Step 1 Write a Validation Plan

First, define the objective of the validation in writing, creating an outline of the methods to be used, and list any anticipated barriers. In most cases, these three items will form the bulk of the validation protocol. Below there are several questions, the answers to which will ideally be in writing as part of the Validation plan.

What regulations and requirements must you comply with?
Start with a review of those listed in the quality guidelines of the facility (i.e. CFRs 210, 211, etc) and scan for recent changes or updates. Although many regulatory bodies mandate temperature mapping of controlled spaces, they do not specify any particular method so the onus is therefore on us to document and provide justification for our mapping procedures.

How many data points do you need to monitor/map?
This number will vary based on a number of factors, including environment, temperature/RH range, application, but a typical number of units used to map small chambers can include:

- Nine (9): In most cases, this is the bare minimum of sample locations within a chamber (with the exception of very small bench-top applications). This comprises two layers of four loggers, one near each corner and one logger in the center. Or,

- Fifteen (15): three layers of four loggers one near each corner and one logger in the center.

- Or, four or five loggers per shelf.

Where will each data logger be placed?
Spacing the loggers in an evenly distributed grid is recommended, however, it's also important to monitor the worst-case locations within a chamber for heat-loss and/or air

movement. Monitoring the corners of the chamber and near any openings/pass-throughs will cover most worst-case locations; however shelving/racking within the chamber may require the identification of additional worst-case locations. Place a sensor at or near the control sensor for the temperature control unit, and any alarm sensors within the chamber.

What is the chamber load?
Will the mapping take place with the chamber empty, as for an Operation Qualification (OQ), or full of product, as for a Performance Qualification (PQ)? For most pharmaceutical and biotechnical applications, both tests are important. Consider how OQ and PQ might affect the process. As well, some regulatory bodies[2] mandate the use of maximum and minimum loads during the validation process. An empty chamber can be considered the minimum load and is usually the worst-case for temperature fluctuations within the chamber.

Tracking air temperature inside the chamber Vs. interior product temperatures:
Tracking interior product temperatures, such as the temperature inside a solution bottle, is sometimes considered more meaningful as it insulates the data against minor disturbances such as periodic door openings and closings.

What parameters will you measure?
Should the chamber be mapped for temperature only? Or temperature and relative humidity? If there is any plan to store products with humidity sensitivities, then the chamber should be mapped for relative humidity as well as temperature.

How frequently will take readings?
Typical sample rates are once every minute or once every five minutes, however, as with most other aspects of validation, be prepared to justify sample rate and include that rationale in the plan and/or protocol.

How long will the mapping study be?
Again, it varies and justification may be required. Typical study lengths are 24, 48, or 72 hours. Occasionally facilities map for one week, one month, or even longer. For laboratory scale chambers and walk-in chambers, 24-72 hours can be sufficient. However for larger scale projects (i.e. a temperature controlled warehouse) where the temperature can be influenced by the temperature outside the facility, longer studies may be required. Larger scale chambers may also require studies during summer and winter months depending on the seasonal temperature variations at the facility's location.

What will the duration be?
Pre-determining a test schedule will allow the validation technician to set all data loggers to simultaneously start and stop collecting data at the same time.

How frequently will testing be repeated?
While some industries only require an initial qualification, some require that temperature mapping be repeated on a regular basis. Once again, review any applicable regulations and be sure to document the intended test frequency in the validation plan/protocol. Generally, while the initial qualification will usually include mapping of the empty chamber and the loaded chamber, subsequent re-qualifications only require mapping of the loaded chamber.

What additional tests may be useful?
In most cases regulatory bodies only require validation of an empty chamber and a loaded chamber. However, other types of tests may provide valuable information. Two common tests that many companies find useful are:

- *Temperature Recovery Study* – This study uses the same number of probes in the same locations as the mapping study, and a measurement interval of 15-30 seconds. With the chamber temperature stabilized and data loggers recording data, the door to the chamber is opened for a period of time that is typical for normal operation of the chamber (1 minute for laboratory scale chambers, up to 5 minutes for large walk-in chambers used in shipping/receiving areas) and then closed. Data collection continues until the chamber returns to specified operating range. This test shows that product temperatures are not adversely affected during normal operation of the chamber.

- *Insulation Thermal Conductivity/ Temperature Change Study* – This study also uses the same setup as the mapping study, with the same measurement interval of the mapping study. With the chamber temperature stabilized and data loggers recording data, power is removed from the temperature control unit for the chamber. Data is usually collected for a 12-hour period. This study provides information on how long the chamber remains within the specified operating range in the event of a power failure. Data from this study can be used to help determine if product is adversely affected following a power failure, as well as for developing procedures for transferring product to a different chamber/facility in the event of failure.

Many of these questions may already be answered by past practices, protocols, or SOPs.

Step 2
Check Equipment & Documentation

In a GMP environment it is essential to ensure that the equipment being used to perform any chamber qualification is not only appropriate for the job but in good working order.

Two considerations:

- *Have the loggers been validated for this type of application?* Ideally the equipment manufacturer will provide an IQ/OQ validation protocol expressly for this purpose.
- *Are the sensors currently in calibration?* Check the Calibration Certificates (also provided by the manufacturer). The validation software should also show calibration date information, often stored the memory of each device. If using thermocouples, a pre- and post-calibration is required. For NIST-traceable calibrated data loggers, no pre- and post calibration is required.

Step 3
Confirm Device Operation

Check for damage before use. The facility may have an SOP that covers this type of check. If not, there are several ways to ensure proper operation. For example, if the data loggers have been stored together and set to "wrap" (take readings on a continuous "sliding window" basis), simply transfer the information collected by the data loggers to a PC and compare the readings from the various data loggers. If the loggers have not been stored together, another way to confirm their function is to place the loggers side by side for a short time and compare the readings. To minimize the risks of using any equipment that might have drifted out of calibration, there are several possible ways to check calibration.

There may be obvious signs of problems such as measurement readings that vary widely from the norm. If the environment has been stable, look for chemical contamination that may have corrupted the sensor measurements. Or if the logger has been dropped, physical damage in the form of a broken circuit may be the cause. For less obvious causes of out-of-cal performance, a quick accuracy check can be performed without sending the loggers to a calibration lab. Simply compare the logger(s) to other calibrated (NIST-traceable) data loggers or a NIST-traceable instrument for a reference. Finally, comparing any suspect loggers to an accepted reference standard (such as an ice bath or saturated salt solution environment) is another "sanity check."

Step 4
Set Up the Data Loggers

- Set up the test start and stop times within the mapping software as well as the sample intervals and the logger descriptions;
- Use a delayed start time to ensure sufficient time to set up and place all the data loggers, and to allow the chamber to stabilize before data collection begins;
- Configure the same start and stop time for all the data loggers. Synchronizing the start/stop times will eliminate the collection of extraneous data;
- Set a sample interval that is appropriate to the application. Again, a typical "safe" sample interval might be once per minute;
- Set a meaningful data logger description for each of the data loggers. For example, each data logger might have an ID that describes its location in the chamber.

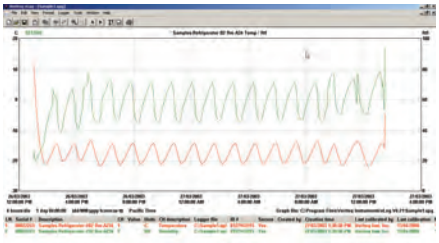
Step 5
Place the Data Loggers

Place the sensors in the chamber according to the validation protocol, or according to a diagram or grid. The interior of the chamber can be photographed to show both logger and product placement. If using probe sensors (rather than just loggers with internal sensors), it is important to ensure that they are not in contact any surfaces within the chamber.

Be sure to also place a data logger outside the chamber to monitor ambient temperature, or both ambient temperature and relative humidity. Failure to do so may invalidate the results as exterior temperatures can sometimes significantly influence interior performance. Place this outside data logger away from areas of undue temperature influence such as an outside wall, a heat-generating piece of equipment, near a window, or in a high traffic area.

Step 6
Periodically Check the Progress

If possible, it's a good idea to check the study results periodically to ensure that the mapping is progressing as expected. As an example, a typical validation protocol may call for the validation technician to establish when the temperature in the chamber stabilizes or to verify operation throughout the course of the study. Using a "flat cable" can allow for periodic checks of the data for one logger without disturbing the chamber.



Step 7
Retrieve and Store the Data

Once the study is complete, to transfer the data from each data logger to a PC. Customize the filename format to make it easy to track files and relate them to the deployment. It is recommended that the software be set to automatically include the following information in each file name: serial number of the data logger, time and date of the data download, and user description of the data logger. Most validation software will provide files that are tamper-proof and secure in order to meet the FDA's electronic record requirements of 21 CFR Part 11. Each file must be uniquely identified, allowing users to relate each printout to the original data logger files.

Step 8
Report the Findings

The results of the mapping study can be reported in several different ways:

- All data logger files can be plotted on one graph to show the variances in different parts of the chamber.
- Or, a "raw data" printout of all readings and associated times and dates can be printed to support the above graph.
- Or, data can be exported to Excel to facilitate further reports.

It is important in the report to identify the maximum, minimum and average temperatures recorded at each data logger location. In some cases it is also valuable to include the Mean Kinetic Temperature at each location. This information is valuable in identifying any hot or cold spots within the chamber, as these are the locations where sensors for continuous monitoring and alarms should be located [3].

References

1 U.S. Pharmacopeia: Good Storage and Shipping Practices <1079> USP 32-NF 27

2 MHRA: Rules and Guidance for Pharmaceutical Manufacturers and Distributors, 2007.

3 Health Canada (Guide-0069) Guidelines for Temperature Control of Drug Products During Storage and Transportation

4 EU European Commission Annex 15 Guide to Good Manufacturing Practices

5 FDA CFR 21 211.142

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