Sample storage

Guidance for cold storage temperature mapping

Many agencies that audit laboratories require temperature maps of all areas where samples may be stored to verify that temperatures in those areas meet the applicable acceptance criteria. Temperature mapping is accomplished by placing thermal sensors in predetermined locations within a sample storage unit and recording the temperature at each location. A temperature map of a freezer can indicate whether it is performing according to the manufacturer's specifications, help identify suitable sample storage space, and provide data to guide placement of sensors for continuous monitoring.

Have detailed requirements for temperature mapping been set? The answer is no. While this is unsatisfactory to laboratories that want a "one size fits all" protocol that will work for any application, other laboratories enjoy having the freedom to choose a scientific, risk-based approach to sample storage. Although various agencies around the world have issued guidelines to help laboratories and businesses better understand their requirements, there is no universally applicable temperature mapping method. Most businesses in a given industry benchmark themselves according to how mapping is performed in that industry. This is usually accomplished by referencing publications like the ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients (APIs) [1]. While the ICH Q7 guide describes good manufacturing practices (GMPs) that apply to API storage and distribution, it does not provide specific instructions on how to determine whether storage temperatures are appropriate and adequately controlled.

Organizations like the U.S. Food and Drug Administration (FDA), the International Society for Pharmaceutical Engineering (ISPE), and the U.S. Pharmacopeia (USP) have also issued guidelines for manufacturers [2-5]. USP chapter 659 provides specific test acceptance criteria that pertain to the storage, packaging, and distribution of active ingredients, excipients, and medical products [5]. The following description of a USP-compliant freezer appears in the Temperature and Storage Definitions section of USP chapter 659: "A place in which the temperature is controlled between –25°C and –10°C (–13°F and 14°F). It is noted that, in some instances, articles may have a recommended storage condition below –20°C (–4°F). In such cases, the temperature of the storage location should be controlled to ±10°C (±50°F)."

Although there are many ways to map temperatures in a freezer, a few basic practices can help mapping practitioners avoid common problems. The following guidance is intended to help novice and experienced practitioners properly set up mapping tests that best reflect the conditions in their laboratory freezers. We describe testing problems we regularly encounter in the field that can skew results and cause tests to fail. Our goal is to offer customers practical advice based on field experience and customer feedback that will help them perform robust and repeatable mapping tests. While we do not cover every detail related to performing mapping tests, we discuss important aspects of testing that can cause problems and how these problems can be avoided.

Steps to take before purchasing a freezer

Establish your requirements

If you intend to use your freezer for storage at different temperatures, confirm that it is designed to satisfy your testing criteria prior to purchase. You should also consider the primary requirements of your in-house quality team, customers, and regulators. Verify that the freezer you intend to purchase can satisfy each requirement before placing the order. You can do this by checking the specifications listed in the technical data sheet (TDS) for the freezer or reviewing the manufacturer's end-of-line testing results. Keep in mind that factory test results may differ from your test results due to differences between setup parameters. We recommend asking your sales representative about testing a demo freezer using your protocol.

Select the right freezer

Selection of the most suitable freezer for your storage needs is the most important thing to consider before thinking about installation and testing. There is nothing worse than purchasing and installing a freezer, only to discover that it is the wrong freezer for your application. You will have already spent a considerable amount of time and money, and returning a freezer and ordering a replacement is a time-consuming process. We recommend communicating your test acceptance criteria to our sales personnel before you select a freezer so that we can assist you in finding the right product.

Determine the path the freezer will take from the dock to its designated location

Carefully measure the entrance to your laboratory and the space you have allotted for the freezer before you order it. We have observed several instances in which purchased freezers did not fit through laboratory doors.

Ensure the designated location is environmentally suitable before installation

Make sure the average temperature in the area where you intend to place the freezer will not cause inadequate performance. The final location for a freezer is often determined before it is ordered, and utilities and other environmental conditions have already been qualified. Prior to purchasing a freezer, confirm that the proper temperature can be maintained in the selected location and that the additional heat load can be accommodated.

Best practices for optimal performance

Adhere to the manufacturer's installation instructions

Following the installation instructions of the manufacturer will help ensure that you put your freezer in a location where it will operate properly. Proper installation will also contribute to successful qualification and temperature mapping.

Establish your testing protocol

Purchasing the right freezer is only a first step. Knowing how to test it is critical for successful qualification and release for use. While some laboratories can perform in-house testing of their freezers, others require testing by a third party. Enlisting Thermo Fisher Scientific services can help ensure that your freezer is set up correctly using a proven test method. If problems are encountered during setup or testing, we can resolve them immediately or expedite any repairs or adjustments that may be needed.

Ensure test sensors are positioned correctly and documented accurately to get reproducible results

Documentation should include an accurate diagram with precise sensor location measurements. Taking photographs of the sensors after installation can provide additional documentation.

- When test criteria require sensors to be placed in the air, be sure the sensors do not touch any surfaces. A probe that touches the walls or door of the freezer may give you an inaccurate reading.
- Insert sensor wires into the freezer through an existing port whenever possible and close any gaps with putty or another type of temporary insulation. If the sensor wires are routed through the door gasket, situate them in a way that minimizes gaps. It is acceptable to use temporary insulation to seal the gaps, which can be as simple as covering them with tape.

Dial in the freezer for best performance

Once the freezer display indicates the set point has been reached, confirm that the unit has stabilized before collecting data. Stabilization typically requires two on/off cycles. Set up the reference test equipment as specified in your protocol and determine whether the trend is centered around the set point.

- Center the temperature trend on the desired temperature, –80°C for example, before starting the test. Set the offset to move the trend higher or lower using the freezer controller. This will not affect peak variance in most cases. Once the trend is centered, you may begin collecting data. This process will enable you to utilize the entire range specified in your acceptance criteria. It will also enable optimal freezer operation and allow you to take full advantage of your monitoring system alarm limits.
- If you are using a simulated load, make sure it can be situated in the freezer without displacing the sensors. This will allow you to compare the data recorded when the chamber is loaded to the data you collect when it is empty. Make sure there is no contact between the sensors and the simulated load. A sensor that comes into contact with a simulated load can give inaccurate readings that may cause test failure.

Document activities in real time

It is important to document as you perform the test to ensure that entries are accurate and available for future reference.

In the event of failure, consult the protocol for appropriate next actions

A Thermo Fisher testing team can quickly identify problems and begin troubleshooting immediately. On-site testing saves time and money and can help ensure that your freezer will be operational in an expedient manner.

Conclusion

The purpose of this white paper is to help you better understand what cold storage temperature mapping entails. This information should serve as a starting point as you implement your temperature mapping process and reinforce some of the basics for those who do it every day. If you have questions about cold storage mapping, please contact your Thermo Fisher sales or service representative.

References

1. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (2000) Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients: Guidance for Industry.
2. U.S. Department of Health and Human Services (2016) Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients: Guidance for Industry.
3. International Society for Pharmaceutical Engineering (2021) Good Practice Guide: Controlled Temperature Chambers 2nd Edition.
4. International Society for Pharmaceutical Engineering (2019) Baseline Guide Vol 5: Commissioning and Qualification 2nd Edition.
5. U.S. Pharmacopeia (2017) <659> Packaging and Storage Requirements.

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