LABFISH
CLINICAL TRIAL SUPPLIES

WE ARE DEDICATED TO QUALITY –
SUPPLIES FOR CLINICAL TRIALS

EXPLANATION SHEET

TOPIC

CALIBRATIONS IN THE CONTEXT OF GOOD CLINICAL PRACTICE AND GOOD MANUFACTURING PRACTICE

It is essential to provide a **valid calibration** for all equipment used during a clinical trial to ensure the confidence in the generated test results. Furthermore, documented calibrations are a requirement set by both the FDA and the EMA laid down in guidelines for Good Clinical Practice (GCP) as well as Good Manufacturing Practice (GMP).

It falls under the responsibility of the Monitor to verify that the investigator at the site "has adequate [...] resources [...] and [that they] remain adequate throughout the trial period". Furthermore, the Monitor needs to determine "whether the investigator is maintaining the essential documents." [ICH GCP 5.18.4].

These resources include the equipment used.

Whenever a clinical protocol defines parameters, it is necessary to verify that the equipment used provides the correct results by performing a calibration before using the equipment.

EQUIPMENT INCLUDED IN THE VERIFICATION

THIS INCLUDES EQUIPMENT LIKE

- Refrigerators, freezers and incubators (storage temperature)
- Temperature Monitoring Devices (TDM) (Temperature data loggers)
- Centrifuges (speed / g-force and temperature)
- Blood pressure devices
- Ergometers (power)
- Infusion pumps (volume, flow rate)
- Balances / medical scales (weight)

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INFORMATION

⟶ LABFISH'S IN HOUSE CALIBRATION FACILITY

- LABFISH runs an own in house calibration facility for temperature calibration in the range of -80°C to +50°C, medical refrigerators, freezers, incubators, temperature data loggers as well as centrifuges.
- Calibrations are a central part of our ISO9001 quality management system.
- At LABFISH, we have more than 20 years of experience in calibrations so we know our instruments very well and can share our knowledge.
- Our in house facility also allows us to react immediately to any customer requests, very valuable when things need to go fast.

⟶ RECALIBRATIONS

The initial calibration of a device before using it in a clinical trial is an essential step. However, just like we know it from our car, it is just as important to repeat the calibration in certain intervals to ensure that the device continues to work within its specifications.

⟶ INTERVALS FOR RECALIBRATION

The interval for recalibrations usually will be derived from Good Clinical Practice and similar guidelines and/or set by the manufacturer. The user should always carefully check which regulations apply in the specific application context. Also, the required confidence in the data obtained may require shorter intervals.

In our experience, a recalibration period of 1 year is a generally accepted interval for a wide range of equipment.

⟶ LEGAL REQUIREMENTS

Regulations and recommendations vary between different types of equipment as well as between different countries.

Local national regulations like the MedizinprodukteBertreiberVerordnung (MPBetreibV) are binding for Germany and Austria and provide strict intervals of calibrations (Messtechnische Kontrolle - MTK) or safety checks (Sicherheitstechnische Kontrolle - STK) of a range of medical devices.

In the context of clinical trials, the most common devices covered by the MPBetreibV are clinical thermometers, blood pressure monitors, ergometers, infusion pumps and ECGs.

⟶ ADVANCED CALIBRATION: TEMPERATURE MAPPING – FOR IMP STORAGE UNITS

Temperature Mapping is a calibration technique applied to refrigerators, freezers and incubators and is used mainly in the context of storing Investigational Medicinal Products (IMP) under defined storage temperatures.

The underlying idea of temperature mapping is to document that the storage temperature is maintained within the complete storage area over an extended time span.

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CASE STUDY

CASE STUDY - PRACTICAL EXAMPLE FOR TEMPERATURE MAPPING

At first glance, it may appear a triviality and – beyond that – self-evident, that displayed temperature of, for example, a medical refrigerator should match the temperature within the refrigerator inside the given tolerances.
However, temperature distribution depends heavily on the instrument model itself as well as variations between the same type of instrument. Furthermore, the way and the quantity with which the refrigerator is loaded has a massive effect on the temperature distribution. Each type of refrigerator has its own characteristics and the apparent rule that the bottom of a refrigerator is the coldest area is often simply wrong. The real situation can only be assessed through a temperature mapping.

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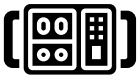

For a temperature mapping, usually **nine calibrated precision temperature data loggers** are placed into the refrigerator: four in each corner of the top layer, one in the middle and four in each corner of the bottom layer, thereby spanning the complete volume of the storage area. Depending on the setup, the refrigerator may additionally be loaded with dummy packets of the IMP and a door opening event may be simulated. The temperature is then recorded for a minimum of 24 hours, the data retrieved and evaluated.
A comprehensive calibration protocol drawn up. Once the refrigerator has passed the temperature mapping process, it is ready for storing the medication.

The storage temperature of course needs to be continuously monitored with a calibrated temperature data logger during storage.

SERVICE

LABFISH offers the temperature mapping service before shipment.
For particularly demanding application, LABFISH also offers the Installation Qualification / Operation Qualification (IQ/OQ) Service which is performed on site.

RESOURCES

1. EMA (European Medicine Agency): ICH Guidelines for Good Clinical Practice E6(R2) Sections 5.18.4, 8.2.11, 8.2.12, 8.3.6, 8.3.7
2. EU GMP (Chapter 3)
3. FDA 21CFR606.60
4. FDA 21CFR820.72
5. FDA 21CFR211.68
6. Medizinproduktebetreiberverordnung (MPBetreibV)

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