TCAL Solutions for Pharmaceutical and Biotech Industry
Sales Tool

Industry Overview

Although many of the applications are similar between pharma and biotech, it is helpful to understand the differences between the two.

Pharmaceutical manufacturing relies on chemical-based compounds that have known physiological effects. Examples include blood pressure, respiratory, and metabolic drugs. Pharma manufacturing is similar to other process manufacturing in that raw materials are converted to a finished product through batch manufacturing processes. Process and quality control are critical to produce an effective product.

Biotech manufacturing involves the use of living organisms or substances from them to produce medicines such as cancer treatments, genetic therapies, and vaccines. The manufacturing process involves the growth of cultures in bioreactors. The product is moved from smaller vessels to larger ones as the volume increases. Maintaining accurate temperatures in the bioreactor is critical to sustaining product survival and growth.

Both pharma and biotech are regulated by government agencies such as the FDA (U.S.) and EMA (Europe). Biopharm companies who export product are required to comply with the standards of the destination country—meaning that good manufacturing practices (GMP), which drive requirements for calibration equipment, are similar from company to company and country to country.

Application 1 - Temperature Sensor Calibration

Pharma and biotech process manufacturers require accurate temperature control in order to produce products that are effective and safe. Sensors that monitor and control temperatures in bioreactors, mixing vessels, storage chambers, and fluid lines are typically calibrated every six months. Since the sensors are integrated into the manufacturing system, production is typically shut down to perform the calibrations. Temperature sources such as drywells and micro-baths are positioned on a cart or on the floor next to the sensor under test. The sensors are removed from their installed locations and immersed inside the drywell or micro-bath. Typically, three set-point temperatures are measured and compared to a reference thermometer. Adjustments to the process control system (PCS) are made using two technicians. One adjusts and monitors the PCS while the other monitors the reference thermometer readout.

Pharma sterilization chamber

Mixing vessel with sensors

Fluke solution

The Automated Test feature of the 1586A Super-DAQ allows calibration technicians to fully automate the calibration process with a single temperature source that covers the calibration range. Savings realized include improved efficiency since technicians can start a test and walk away to perform other tasks while the 1586A automatically records data once the source has stabilized—no need to check and re-check temperature source stability. The Super-DAQ can record data for multiple UUTs (as many as 40) in a single calibration batch. Fewer temperature sources may be required since tests can be run unattended. Work continues while technicians are busy with other things, breaking for lunch, or even after their shift has ended. For more information, visit the 1586A Super-DAQ Resource Center >

Recommended equipment

- For accuracy ± 0.008 °C at 0 °C using 100Ω reference PRT: 1586A Super-DAQ with High-Capacity Module
- For higher accuracy ± 0.005 °C at 0 °C using 100Ω reference PRT: 1586A Super-DAQ with DAQ-STAQ Multiplexer
- Fluke Calibration temperature sources to cover the calibration range:
  - Micro-baths: 6102 (35 °C to 200 °C), 7102 (-5 °C to 125 °C)
  - Field Metrology Wells: 9142 (-25 °C to 150 °C), 9143 (33 °C to 350 °C)
  - Ultra-Cool Field Metrology Well: 9190A (-95 °C to 140 °C)
- Secondary PRT

Customer job titles

Calibration Technician, Calibration Engineer, Metrologist, Metrology Supervisor, Instrument Technician, Lab Manager, Quality Engineer, Process Engineer, Facilities Manager, Site Supervisor

Application 2 - Chamber Mapping

Regulatory agencies require biopharm companies to demonstrate temperature accuracy and uniformity of storage chambers such as freezers, refrigerators, incubators, and ovens. Thermocouples are positioned at locations within the chamber. Temperature data is collected and analyzed to ensure that there are no hot or cold spots within the chamber which could impact product quality. Proof of data integrity (i.e. no tampering of data, dates, test setup, etc.) is required by regulatory agencies (referred to as 21 CFR Part 11 for FDA compliance).

1586A Super-DAQ collecting thermocouple data

Fluke solution

Most chamber mapping applications typically require a maximum of 16 channels and scan speeds of 10 channels/second or less. The 1586A Super-DAQ meets these requirements. The Align Channels feature of the 1586A allows the user to automatically 'zero' offsets between channels and store the offsets in the Mx+B function for each channel. This allows the user to easily measure temperature uniformity of the chamber directly without having to apply thermocouple offsets manually.

Although Fluke makes no claims to 21 CFR part 11 compliance, the security levels of the 1586A allow users who understand the regulation to protect recorded data and test files. Third party cal labs are often well versed in these regulations and will write their own procedures and claim compliance to the standard. The TCAL Business Unit is working with TQSoft to develop 21 CFR part 11 compliant software for the 1586A that will be available 2Q 2105 from Fluke.

Recommended equipment

- For accuracy ± 0.65 °C using type T thermocouple: 1586A Super-DAQ with High-Capacity Module (internal CJC at 0 °C)
- For higher accuracy ± 0.30 °C using type T thermocouple: 1586A Super-DAQ with DAQ-STAQ Multiplexer (internal CJC at 0 °C)
- TQSoft software

Customer job titles

Validation Engineer, Quality Engineer, Quality Manager, Compliance Engineer, Process Engineer

Application 3 – Freeze drying

Freeze drying or lyophilization is a process for preserving biological or pharmaceutical products by freezing the material and then reducing pressure in order to sublimate the frozen water in the sample from a solid to a gas. Similar to chamber mapping, freeze drying requires that the shelves in the process chamber of the lyophilizer be monitored and validated to ensure product quality. Thermocouples and pressure transducers are typically used to measure chamber temperature and pressure.

Freeze dryers

Fluke solution

Accuracy of the 1586A Super-DAQ using the internal High-Capacity module is adequate for most freeze drying applications. If greater accuracy is required, the 1586A with the DAQ-STAQ Multiplexer can be used. The 1586A can measure pressure transducers by converting scaled voltage or current inputs to a pressure equivalent using the Mx+B function.

Recommended equipment

- For accuracy ± 0.65 °C using type T thermocouple: 1586A Super-DAQ with High-Capacity Module (internal CJC at 0 °C)
- For higher accuracy ± 0.30 °C using type T thermocouple: 1586A Super-DAQ with DAQ-STAQ Multiplexer (internal CJC at 0 °C)
- TQSoft software

Customer job titles

Validation Engineer, Quality Engineer, Quality Manager, Compliance Engineer, Process Engineer

Application 4 – Humidity Sensor Calibration for Production Rooms

Pharma and biotech process manufacturing is done in a clean production environment. The level of environmental pollutants (dust, microbes, chemicals) is typically monitored and controlled. Humidity in production rooms is also continuously monitored since it affects product quality and worker comfort.

Humidity monitors in production rooms typically combine a transmitter and sensor. Usually, the transmitter is attached to the sensor and wall-mounted. Sometimes the transmitter is connected to the sensor using a long cable and placed in a return air duct to protect the sensor from solutions used to spray and clean production rooms.

Sensors used to monitor production room humidity need to be calibrated every 6 to 12 months. Typically a "spot-check" or one-point calibration of a wall mount transmitter is done using a handheld humidity meter such as a Vaisala HM 70 or Rotronic HygroPalm 23. One-point calibrations are quick and convenient, but are limited in value. Calibration with a handheld meter needs to be carefully managed. Temperature differences between the probe and its environment, technician body heat, and moisture from breath can all cause RH measurement errors. Further, one-point tests may cause out-of-tolerance readings when ambient conditions change.

Fluke solution

Using the 5128A RHapid-Cal Humidity Generator for a multi-point calibration gives a more reliable test and truer characterization of how a humidity sensor operates over its working range than a "spot-check" calibration with a handheld meter. The 5128A is compact, lightweight, and can be easily transported on a cart to a production room.

Customers generally want and need to leave the wall mount transmitter in place during calibration. Many models allow the sensor to be detached from the transmitter for calibration. Connect the sensor with a cable to the transmitter or to a handheld device and insert it into the 5128A chamber. Cables are supplied by the transmitter manufacturer.

Humidity measurement is extremely temperature dependent. For best results the sensor and 5128A RHapid-Cal need to be in temperature equilibrium. Select a temperature test point that matches the normal production room temperature. The 5128A chamber will quickly reach a very stable and uniform temperature environment for calibrating the sensor at different humidity points. Use at least 3 to 4 calibration points distributed across the humidity range found in the production room.

Recommended equipment

- 5128A RHapid-Cal Humidity Generator
- Grommet kit
- Extra desiccant(s) (optional)

Customer job titles

Calibration Technician, Calibration Engineer, Instrument Technician, Lab Manager, Facilities Manager, Site Supervisor

Application 5 – Humidity Data Logger Calibration

Data loggers are compact and easy-to-use recorders for monitoring humidity levels of equipment and facilities used in pharma and biotech manufacturing processes to reduce the risk of product contamination and spoilage. Equipment includes incubators, stability chambers, refrigerators, and freezers. Facilities include labs, production clean rooms and storage warehouses. These data loggers require periodic calibration.

Fluke solution

The 5128A RHapid-Cal Humidity Generator is ideal for calibrating humidity data loggers used to monitor pharma and biotech processes. To calibrate data loggers, place them directly into the 5128A test chamber and use the square, clear glass door and the shelf accessory. If the data logger display allows, it can be visually read through the clear door and compared with the 5128A reference value. Otherwise, put the data logger into "logging" mode. Then set and record the actual 5128A temperature and humidity at known points in time. The logged data is then compared against the actual 5128A temperature and humidity settings. Data loggers that are too large to fit on the shelf accessory can be placed in the bottom of the chamber. To accommodate even larger loggers, the chamber mixing insert can be removed. Using these methods to fit larger loggers may impact the mixing airflow or move the logger's sensor outside of the specified working area of the chamber. If so, it is best to use an external reference (membrane-type sensor or chilled mirror) to monitor the 5128A temperature and humidity.

Recommended equipment

- 5128A RHapid-Cal Humidity Generator
- Grommet kit
- Square clear door with shelf
- Extra desiccant(s) (optional)

Customer job titles

Calibration Technician, Calibration Engineer, Instrument Technician, Lab Manager, Facilities Manager, Site Supervisor