

Beamex

Calibration White Paper

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Calibration in the pharmaceutical industry

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Pharmaceutical Operations

The pharmaceutical industry produces products that directly affect the life of the majority of the billions of people that inhabit the Earth. As such, a seemingly small mistake or failure could adversely affect the health of thousands of people. Regulators in the pharmaceutical industry recognize these stakes and have implemented various regulations to ensure the integrity of pharmaceutical processes and, hence, the safety and efficacy of the pharmaceutical products on which billions of people rely.

Individuals who are not directly associated with the pharmaceutical industry should take note because some aspects of these regulations are being adopted in the process industries. Therefore, it would be pragmatic to use equipment and adopt practices that either meet or can easily be upgraded to meet pharmaceutical requirements.

Some high-volume pharmaceuticals are often manufactured using continuous processing techniques; however, pharmaceutical manufacturing is typically performed in batches. As such, these processes typically incorporate many pressure and temperature measurements such as local indicators (gauges), transmitters and switches. Many of these measurements are at extreme conditions such as may be found in an autoclave. While there may be some flowmeters, batch processes typically incorporate weighing instruments to implement material additions. Some processes involve clean rooms where the measurement of low differential pressures is important.

Process measurements can be critical to ensure product quality. Calibrating instruments properly in a timely manner is an important aspect of ensuring that a pharmaceutical product is manufactured properly. Calibration documentation can be used to verify that calibrations have been performed properly prior to producing products. Should there be a problem, this information may prove to be a key factor in determining when, where and/or how an error was made. Therefore, governing bodies tend to regulate the type of information collected and the time interval between calibrations.

Manual Documentation of Pharmaceutical Calibrations

Whereas specific regulations may vary somewhat around the world, the underlying design premise behind calibration requirements is to ensure that instrument calibrations are

performed correctly. Traditionally, this meant generating a paper trail of calibration information including its time, date, test equipment, as-found data, as-left data, and the like.

However, this is only the “tip of the iceberg”. Calibration must be performed according to approved written procedures and the calibration records must be maintained for a certain period of time. Each instrument should have a master history record, a unique identity, calibration period, and calibration error limits. Product, process and safety instruments require that they be physically tagged and sometimes color-coded. The performance of calibration standards should be more accurate than the instrument being calibrated. The calibration of the calibration standard must be documented and performed periodically. Using calibration standards that are traceable to national and international standards is required. Additional documentation pertaining to the technician and his/her qualifications and certifications to perform calibrations would also be needed to be able to demonstrate that the individual has been trained and is qualified and competent to perform the calibrations.

In most countries, these instrumentation requirements must be implemented within in the general context stipulated by 21 CFR Part 211 (Current Good Manufacturing

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Practice for Finished Pharmaceuticals). Among many other requirements, all instruments must be fit for their purpose and a documented change management system must be in place.

Pharmaceutical companies complied with these requirements by writing calibration information on paper forms that they developed for this purpose. Despite conformance with the regulations, paper documentation was both cumbersome and prone to human error. Simply put, it is not difficult to make mistakes when calculations are

performed manually and most dates, times, measurements, calculation results, and the like are written by hand.

Electronic Documentation of Pharmaceutical Calibrations

Electronic documentation systems that do not require any paper were developed to overcome these disadvantages and reduce the amount of time technicians spend in complying with documentation regulations. However, electronic records do not inherently contain signatures that identify the person performing a calibration. Therefore, 21 CFR Part 11 (Electronic Records; Electronic Signatures) addresses the additional issue of ensuring the documentation of these people.

Electronic calibration systems for the pharmaceutical industry that conform to the 21 CFR Parts 11 and 211, such as Beamex's CMX calibration software and MC5

Fortunately, there are calibration systems that are specifically designed to operate safely in rugged environments and hazardous locations.

Multifunction Calibrators, can be integrated to provide automated documentation with less human intervention. This results in fewer human errors, improved work quality, and improved efficiency that can directly affect profit. Moreover, locating the original electronic records in one database can not only reduce paper records into traceable electronic records with a history of change management, but can also turn the calibration system into a powerful repository of decision-making history that can be used to improve calibration procedures. Versatile security settings and multilevel user accounts help to ensure the security and integrity of the system and track authorized and unauthorized database actions.

Calibration Solutions for the Pharmaceutical Industry

Instruments designed to measure flow, level, pressure,

temperature, and other variables are generally used to monitor and control pharmaceutical processes. In some applications, it is practical to remove these instruments and calibrate them on the bench. This is generally not the case so many instruments are calibrated in the field. Fortunately, there are calibration systems that are specifically designed to operate safely in rugged environments and hazardous locations.

A typical calibration process is illustrated in the figure below where the calibration master schedule identifies an instrument that needs to be calibrated and downloads the appropriate calibration data into a technician's handheld calibrator. After entering his/her username and password, the technician performs an automated "As Found" calibration. If the instrument does not pass calibration (as determined by the downloaded information in the calibrator), the technician can calibrate the instrument and perform an automated "As Left" calibration. Data from both calibrations are stored in the handheld calibrator to be uploaded to the database where it is documented.

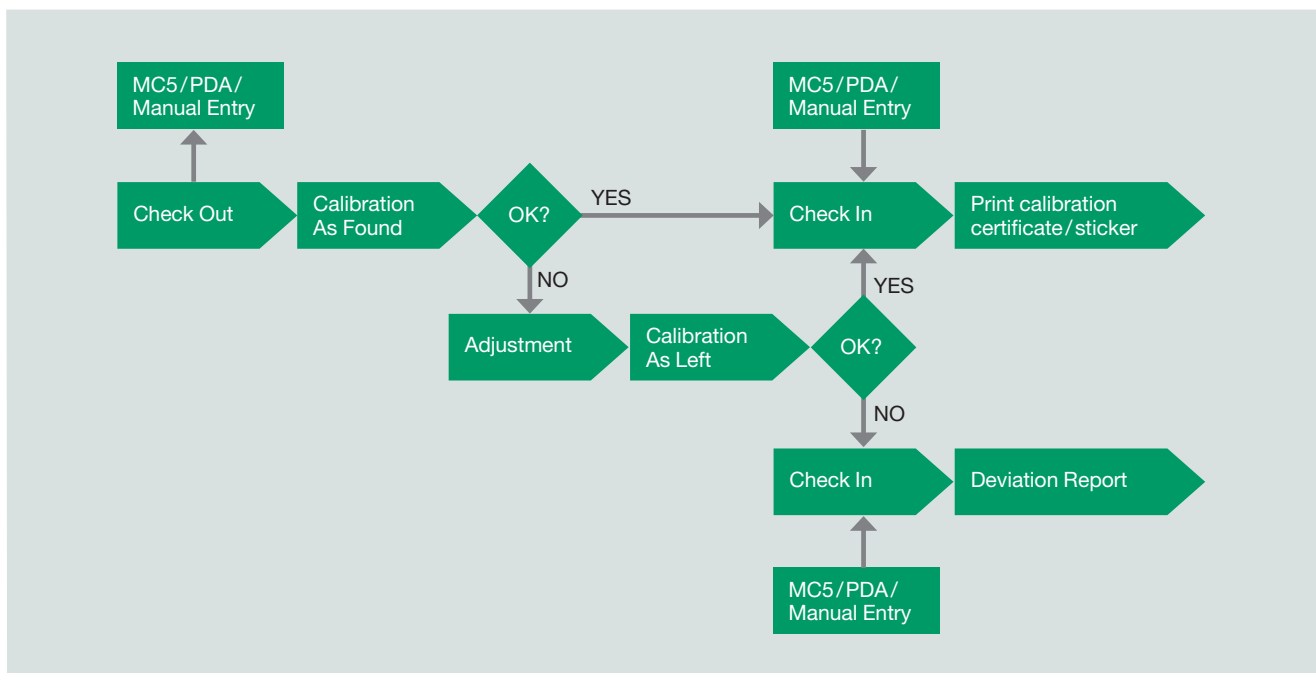
The Beamex CMX software integrates calibration management by allowing efficient planning and scheduling of calibration work. It not only alerts you when to calibrate,

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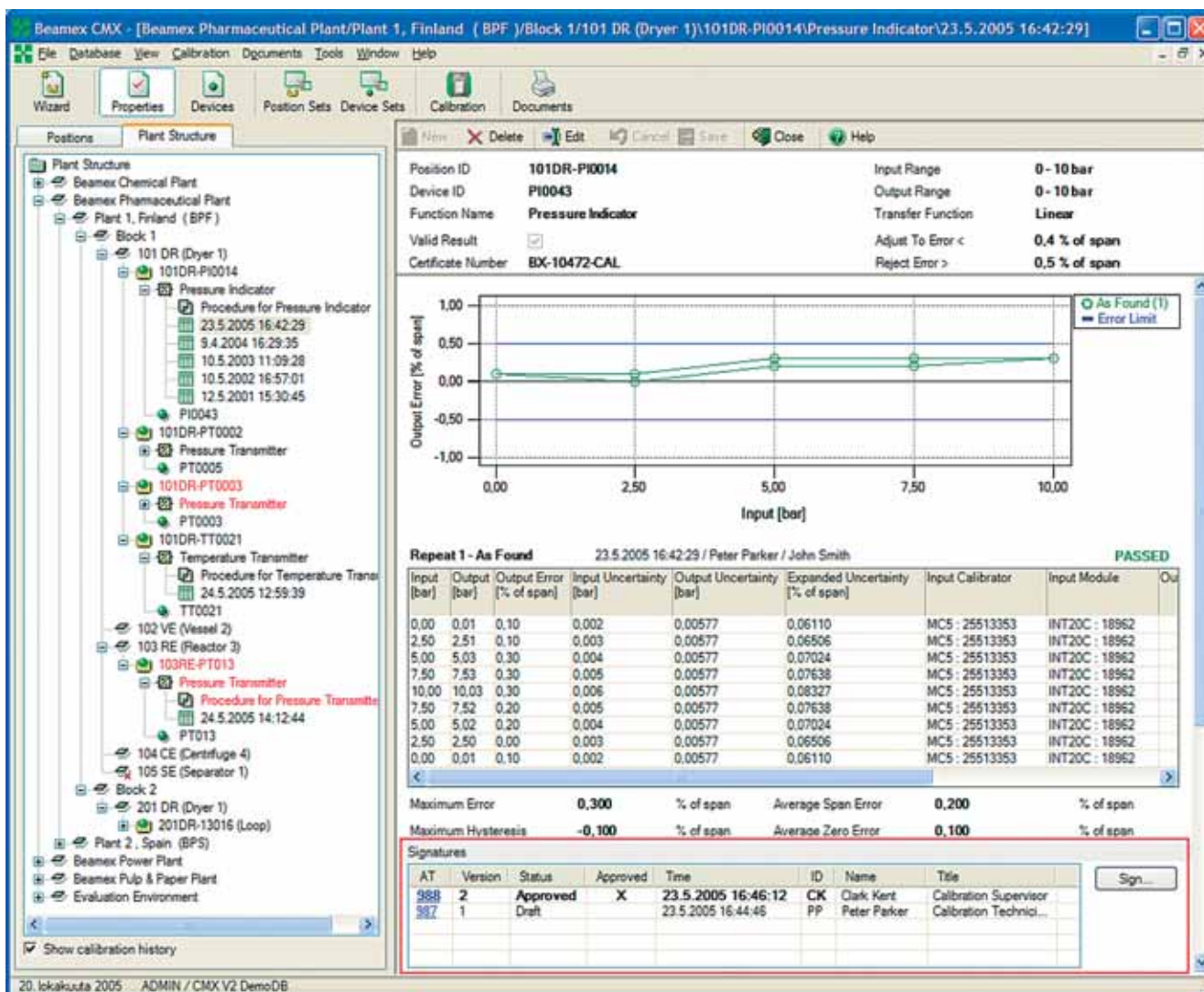
but also automatically takes data, creates documentation, adheres to cGMP regulations (21 CFR Parts 11 and 211), and tracks calibration history. This software generally makes calibration work faster and easier and is designed to integrate into management systems such as SAP/R3 and Maximo.

The Beamex MC5 is a portable multifunction calibrator that has modules that can accommodate wide ranges and many types of pressure, RTD, thermocouple, voltage, current, pulse, and frequency measurements.

The Beamex MCS100 modular calibration system is a test bench and calibration system for workshops and laboratories, which incorporates the functionality of the MC5 and can measure/generate additional parameters such as precision



Calibration process in a pharmaceutical company with the Beamex calibration system.



CMX's change management complies to FDA requirements (21 CFR Part 11 Electronic Records and Electronic Signatures).

pressures. The ergonomic design and modular construction allow the user to select the necessary calibration functions in a cost-effective manner.

Summary

Here are a few points to remember:

- Automated electronic calibration and electronic documentation save time and are less prone to human error than are manual calibration and paper documentation.
- Electronic documentation allows all calibration information to be located in one database for easy access and use.
- Proper calibration and its documentation are important for maintaining the safety and efficacy of pharmaceuticals.
- Portable Beamex calibrators for hazardous locations are designed for use in virtually all pharmaceutical plants.
- Beamex software follows the guidelines of 21 CFR Parts 11 and 211 and makes calibration and its documentation easy.

Beamex products for the pharmaceutical industry:

- MC5 Multifunction Calibrator
- MC5-IS Intrinsically Safe Multifunction Calibrator
- CMX Calibration Management Software

Beamex services for the pharmaceutical industry:

- Installation and training
- Validation services (CMX calibration management software)