Flow and Level Instrument Verification in the Pharmaceutical Industry

Automatic verification minimizes the need for expensive instrument calibrations.

By: Ravi Shankar, Endress+Hauser

Recently, Quality Risk Management (QRM) has become a mandatory regulatory requirement for drug manufacturers. The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) publish guidelines and requirements which customers and vendors are expected to follow. Guidelines such as "Process Validation: General Principles and Practices" by the FDA and Annex 15 issued by the EMA offer input to help drug manufacturers design processes correctly.

Based on the new process validation model published by the FDA (Figure 1), validation is never finished, but is instead a process of continuous improvement. Maintenance and calibration activities of instruments are part of stage 3 in the model.

QRM is an overall and continuous process to minimize product quality risk. Instrument calibration/ verification interval definitions are part of QRM risk analysis, and guidelines for these procedures are described by the FDA and EMA accordingly. Selecting the correct instrument for the application is absolutely crucial in the design phase of the project, and the criticality of the measuring point defines the required reliability and measuring accuracy of the instrument.

ISO 9001:2008 section 7.6 requires instruments to be calibrated or verified at regular intervals. The following basic requirements have to be fulfilled:

- Calibration/verification must be traceable to a national standard
- Calibration/verification must be performed at regular intervals, and
- Calibration/verification must be documented.

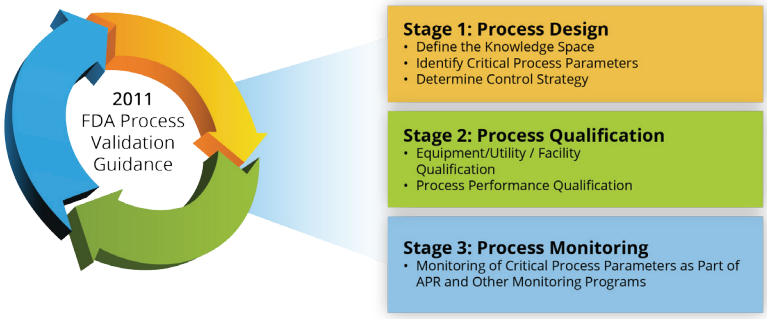

Figure 1: The FDA Process Validation Model.

Calibration and Verification

The first step in verification is to determine if the instrument is still operating within specifications before it is taken out of service for calibration. A calibration of an instrument—for example a flowmeter—involves determining and documenting the difference between the measured and the correct value.

Traceability is accomplished by a formal comparison to a standard which is directly or indirectly related to national standards. Detected deviations between the measured value and the reference value can be corrected after the calibration by adjusting the calibration factor. A calibration protocol is issued to document the findings, and recorded for possible audits.

"As left" means that after sensor cleaning and adjustment the sensor is controlled again with the same standard. The purpose is to control the sensor's performance "as it is left to the process." "As Found" means the

calibration is performed with the instrument before any adjustments are made. This requires that the instrument is functioning properly by passing all bench tests beforehand. If an instrument is determined to be faulty (fails bench tests), then an "As Found" calibration will not be performed.

Users must select the type of calibration that they are requesting. This will determine what documentation is provided as part of the calibration. The options are: Standard 2 and Standard 1 Protocols.

Standard 2 means that the calibration is traceable to NIST, but no special or additional documentation are provided, other than the standard calibration certificate. Standard 1 is the same, except only an "As Found" calibration is performed. No adjustments are made to the instrument.

A substantial number of FDA warning letters are issued because remedial action after a calibration check has been considered insufficient.

Documentation about instruments and their maintenance activities has to be filed for inspector visits. Even if a flowmeter theoretically could be operated for 25 years without calibration due to its excellent safety and reliability parameters, it would most likely trigger some critical questions during an audit if no paperwork was available to prove it remained within calibration.

Calibrations are expensive but provide very clear results for the user. Even though many instruments have proven exceptionally long-term stability which exceeds the entire lifetime of the equipment, they still have to be checked regularly to avoid legal implications. Some companies calibrate every six months.

Today, modern instruments have built-in technology to simplify compliance and verification. Several instrument vendors offer this capability, but all approach the solution in different ways. In this article, we'll use Heartbeat Technology from Endress+Hauser to illustrate how modern instrumentation simplifies calibration and verification.

	Wet calibration	Automatic Verification
Instrument check based on primary fluid	Yes	No
External testing equipment required	Yes, such as calibration rig	No
Test depth	>99%	>95%
ISO 9001:2008 compliant	Yes	Yes
Traceable	Yes	Yes
Process interruption required	Yes	No
Removal of the meter from the process	Often yes, due to the process piping design	No
Cost during the life cycle	high	low

Figure 2: Automatic verification minimizes the need for expensive calibrations.

Automatic Verification

Automatic verification is an accepted procedure. For example, Heartbeat Technology from Endress+Hauser has been tested and independently certified by the European agency TÜV. Heartbeat verification fulfills all requirements specified in ISO 9001:2008 section 7.6 and can be used interchangeably with traditional wet calibrations for traceable instrument checks.

Heartbeat Technology continuously monitors the entire signal chain for deviations within a very tight band. The failure threshold is defined by the specified accuracy of the instrument. Therefore, Heartbeat Diagnostics will trigger an alarm as soon as the sensor or instrument is no longer operating within the original specification. With automatic verification, a sensor does not have to be removed from the process until the diagnostics sound an alarm.

The entire signal chain of the instrument is analyzed for possible errors and their subsequent impact on the system and its measuring accuracy. Typically, a failure modes, effects, and diagnostic analysis (FMEDA) is used during the device design phase to identify critical components in the signal chain starting at the process-wetted parts, followed by the electro-mechanical components, the amplifier board, the main electronic elements and the outputs.

FMEDA is a systematic analysis technique to obtain failure rates, failure modes and diagnostic capability. The FMEDA technique considers:

- The functionality of each component
- The failure modes of each component
- The effect of each component failure mode on the product functionality
- The ability of any automatic diagnostics to detect the failure
- The design strength (de-rating, safety factors)
- The operational profile (environmental stress factors)

As a result, a proper safety measure has to be assigned to every critical path or component. Measures include digital signal processing and continuous loop checks with the help of internal reference components. In order for an internal component to be used as a diagnostic reference it has to fulfill special requirements such as factory traceability and exceptional long-term stability.

For the most critical circuits, independent and redundant components are implemented, reducing greatly the possibility of an undetected drift. Today it is possible to design instruments with a self-diagnostic coverage of 95% or higher (in accordance with IEC 61508).

While the Test Depth of automatic verification is not as complete as a wet calibration—95% vs. 99% (Figure 2)—it is good enough to prove to regulatory authorities that an instrument is operating correctly and does not need calibration.

Wet calibrations can, in many cases, be eliminated from the maintenance schedule without jeopardizing regulatory compliance.

Flowmeter Verification

Modern flowmeters, which operate based on a Coriolis, electromagnetic, ultrasonic, vortex or thermal measuring principle, do not have any kind of moving parts that are subject to wear. They have been tried and tested in thousands of applications and are well-known for guaranteeing highly-stable measurement results over a long period of time.

The reason for this long-term stability stems from the technologies' resistance to wear provided by the lack of moving parts in the sensor. Therefore, for these measuring principles, it is assumed that they will exhibit long-term stability if they are properly selected, sized and installed. Good engineering practice eliminates the possibility of systematic errors, such as from selecting a material that leads to corrosion of the sensor element in conjunction with the fluid to be measured.

Verification does not require fluid going through the meter (Figure 3); instead, it verifies a number of internal components (secondary variables) which are closely correlated to the flow measurement.

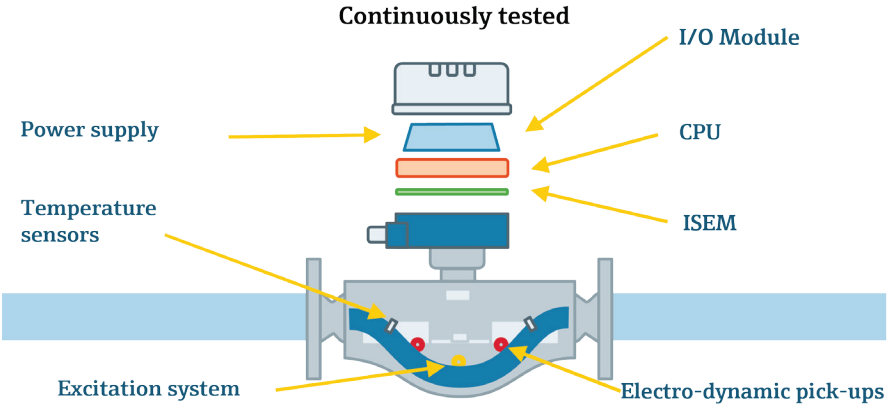

Figure 3: Modern instruments, such as this Coriolis flowmeter, can automatically verify correct operation. Any deviations will send an alarm.

During verification, the current conditions of the secondary parameters are compared with their reference values, thereby determining the device status. Verification produces a pass or a fail statement, depending on whether the assessment is positive or negative. A traceable and redundant reference, contained in the verification system of the device, is used to ensure the reliability of the results. In the case of a Coriolis flowmeter, this is an oscillator, which provides a second, independent reference frequency.

Coriolis, vortex and ultrasonic flowmeters apply time-based principles, measuring the frequency of the sensor oscillation with the help of quartz clocks as digital frequency generators.

Magmeters rely on precision voltage references to measure the voltage induced in the magnetic field of the sensor.

Flowmeters are often used for many years in industrial applications. References with long-term stability ensure that deviations due to aging or external influences are extremely improbable. However, if this should occur, it is immediately detected by the continuous monitoring system integrated in the device. This ensures highly reliable operation and, by detecting errors in a timely manner, prevents the device from working outside of the factory specifications.

This increases the safety of plant operation and ensures consistent product quality.

Level Instrument Verification

Level instruments do not need calibration as flowmeters do. Level instruments can be verified periodically without process interruption, verifying the accuracy compared to when it was installed.

For this reason, verification is vital to ensure proper operation and to provide added confidence to operators. A modern level instrument equipped with verification capabilities and its capability to conduct continuous automatic internal checks and diagnostics allows for added safety and reliability. For example, Endress+Hauser level instruments conduct more than 80 diagnostic procedures that are permanently running in the background.

Some of these internal checks include:

- Reference pulse
- Quartz synchronization
- Clock verification
- Cycle time measurement
- Supply voltage check
- Temperature monitoring
- Check sum in RAM
- Cable breakage.

As explained above, the instrument uses internal reference components to check for proper operation of various functions.

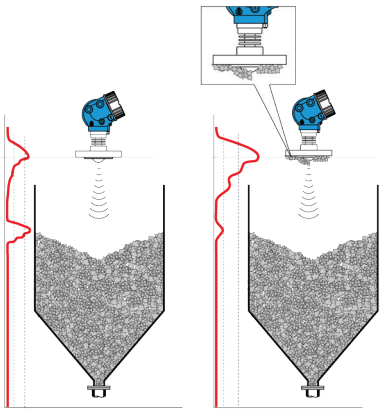

Figure 4: A radar level instrument can detect material buildup on its antenna (right).

Level instruments are also able to diagnose process problems. For example, a radar level instrument can monitor for buildup in the area around the horn—the area of the coupling signal (Figure 4)—and detect material buildup on the antenna by evaluating the quality during installation as a clean horn. A threshold can be set for build up to notify the operator before the unit would lose its echo. The notification can be from the front display and an analog or open collector output The red line in Figure 4 shows the difference in the level signal when material buildup is present.

In cases of material buildup or foam, the instrument can send an alarm message to the operator.

Paperwork for Audits

In addition to the continuous monitoring functionality running in the background, a traceable verification report about the health status of the sensor and instrument can be generated on demand. This report is produced, without the need of external devices, directly within the instrument. The operator does not have to write any results down on paper, which makes the entire process faster and consequently reduces costs. The quality of the verification results improve, as there will be fewer mistakes due to human error.

Devices with internal verification can store multiple results in the transmitter. In addition to the verification result (pass/fail) the transmitter logs the actual measured values for all tested parameters. This data can be used for tracking trends in the lifecycle of the measuring point. This allows for timely conclusions regarding the measuring point's state of health and it assists in preventing unexpected failures. Verification data may be transferred to asset management software for archiving and trend analysis.

By comparing the data from multiple consecutive verifications, trends can be detected and systematically tracked during the lifecycle of the measuring point. This allows for timely conclusions regarding the measuring point's state of health or process-specific influences on the measurement result.

Summary

Continual internal diagnostics and insitu verification capabilities reduce maintenance expenditures because calibrations on flow instruments are done only when needed and diagnostics built into the level devices along with ability to verify periodically identify problems with instruments. It leads to a better overall equipment effectiveness as it results in less process downtime for maintenance and fewer unexpected shutdowns from instrument failures.

About the Author

Ravi Shankar began his work with instrumentation more than 23 years ago. He attended Bangalore University India where he received his Bachelor's degree in Instrumentation Technology. In 1993, Ravi began his career with Endress+Hauser. He started as a sales and service consultant, where he was responsible for application sales and service coordination for major customers. From there, he went to work for Process Instruments as a sales engineer. In May 2011, Ravi became Life Sciences Industry Manager. In this capacity, he is responsible for business development and strategy for the life sciences industry.

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