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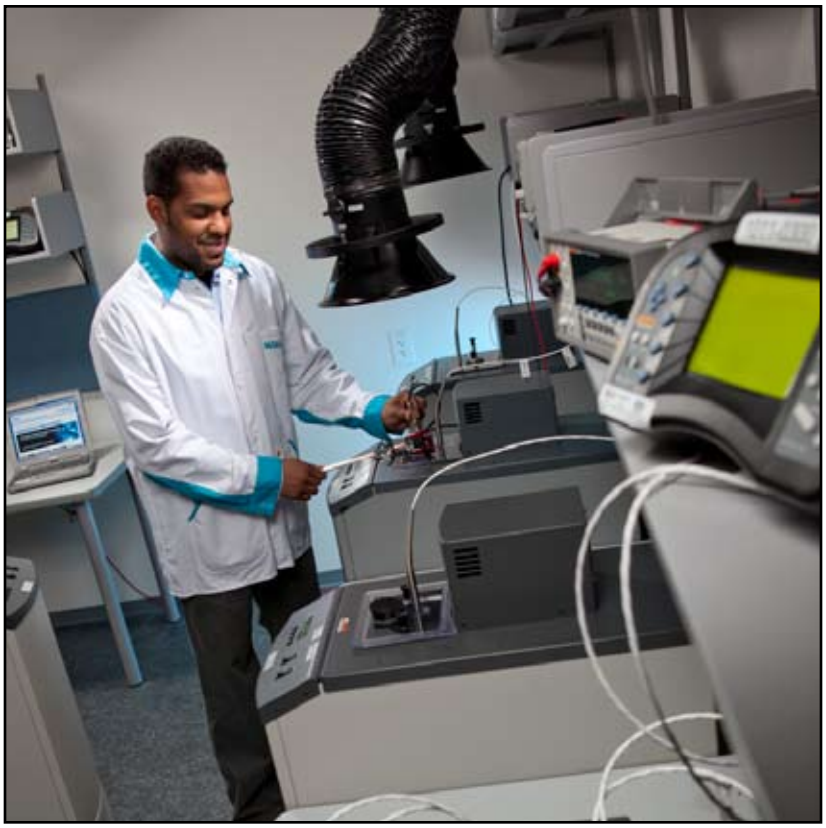

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Measurement Accuracy: The Good, The Bad and The Ugly

By Jim Tennermann

Measurement accuracy is a subjective concept applied to all kinds of measurements. Generally speaking, accuracy refers to the degree of "closeness" of the measurement to a "true value." This definition is usually good enough, but not always. The subjective nature of accuracy allows for a wide variety of claims that may technically be true, but misleading at the same time.

Let's consider this in the context of measuring relative humidity (RH). RH is expressed as a percentage, so the possible range of RH is 0 to 100%. Manufacturers of RH measurement equipment typically specify accuracy as a ± value of some percent. For example, one might say that a certain device is accurate to ± 3% RH. Due to the competitive nature of the instrumentation manufacturing business, makers of a different device may claim to be more accurate with ± 2% RH. Superficially, with all other things being equal, this ±2% device would appear to be "better." Beware, because this is not always the case and can be misleading until you dig deeper. In this article we'll look at how you start digging.

Measurement Characteristics

Accuracy specifications come in many forms. For example, accuracy may or may not include other measurement characteristics. One characteristic is the difference in the measurement value when the true value is approached from a higher value versus a lower value, otherwise known as hysteresis. If a device has a lot of hysteresis, this can be left out of the accuracy specification and justified by reporting accuracy based on measurement values that always start from a higher value (or a lower value). This may be accurate, but it is misleading because it does not address a significant element of the measurement performance.

The Concept of "True Value"

Another issue with measurement accuracy is the concept of the "true value." When a device is calibrated, it is compared to a reference standard that can be considered to be the true value. However, all reference standards embody some imperfection. There is always some variation from the true value that we hope to achieve. What if the variation in one reference standard is different from another standard? In this case, a measurement device calibrated and adjusted to one standard may achieve its stated accuracy, but when compared to a different standard, it could be out of tolerance. This is where the concept of measurement uncertainty becomes helpful.

Measurement Uncertainty

A simple (and incomplete) explanation of measurement uncertainty is that multiple measurements made in the same way with one device are never precisely the same. As a result, the measurement device is likely to provide a range of values centered on the true value or offset from it. Similarly, all reference standards vary from the true value in some way. Because the reference standard is never precisely the true value, its variation has to be considered when specifying the overall performance of any given measurement device.

When using measurement uncertainty, it is possible to say that the uncertainty (variability) of the reference standard and the process of calibration is a specific value, such ± 0.5% RH. This can be statistically combined with the instrument accuracy to arrive a range of measurement performance that is likely to be correct 95% of the time. This value is always bigger than the accuracy of the measurement device, regardless of how accuracy is defined. (Keep in mind that this is in the calibration laboratory, not in the real world.)

Additional Uncertainties

Measurement uncertainty actually applies to individual measurements. In the real world, calibration and device accuracy are not the only influencers of a specific measurement. Additional factors might include environmental conditions (different from the conditions in the calibration laboratory) operator error, inconsistent methodology between operators; and unknown additional variables. These, and other, additional uncertainties from the real world can be statistically factored in (if they are known) to the overall measurement performance. Again, the total value of uncertainty increases.

There is more. Returning to the concept of the combined calibration uncertainty and device accuracy, consider that this might vary when the value of the reference standard is adjusted to achieve multiple calibration points. For example, a generated RH value of 20% RH at 25° C may have less uncertainty than a generated value of 80% RH at 40° C. Similarly, performance of the measurement device might change at the extreme ends of its measurement range. If known, this goes into the uncertainty budget. Total measurement uncertainty almost always increases when devices are used at the extremes of their operating range.

Let's add an additional complication. Measurement uncertainty, as described above, provides a statistical probability as to how often the measurement is within specification. If this value is 95%, what about the other 5% of measurements? It's possible to use a different statistical model to achieve 99% probability, but once again, the total value of uncertainty will increase even more. In fact, this value is likely to be substantially greater than the "accuracy" that we started with, perhaps by multiples.

The takeaway here is that "accuracy" never tells the entire story about measurement performance. If measurement performance is critical, scrutinize the device and manufacturer's specifications and ask questions about anything that is unclear or seems inadequately defined.

Additional Resources

The National Conference of Standards Laboratories International (NCSL) is an international organization dedicated to measurement science and can provide you with more information. Visit: http://www.ncsl.org/

The "Guide to the expression of uncertainty in measurement" (GUM) is a good starting place for understanding measurement uncertainty. Visit: http://temperatures.ru/pdf/GUM.pdf

The Tracks of Traceability: A calibrated $2 thermometer is still a $2 thermometer

By Jim Tennermann

Everyone in the quality profession has heard the term "NIST traceable." Having calibration traceability to the National Institute of Standards and Technology (NIST) is desirable for most measurement devices. It is also enshrined as a requirement in some regulatory documents. Unfortunately, NIST traceability does not ensure measurement quality. Here's why...

National Institute of Standards & Technology (US)

NIST, a U.S. government organization based in Maryland, is the official keeper of the flame for the highest level of measurement accuracy. If you want to know how good your thermometer is, you can send it to NIST, and it will compare it to the very best temperature standards ("calibration" is simply the comparison of one device to another) and send it back with a report. Of course this isn't practical; NIST cannot calibrate the millions of thermometers that are in daily use, and the service is expensive.

This is where the concept of traceability comes in. If you have one thermometer that has been calibrated at NIST, it can become your "standard," and you can calibrate all of your other thermometers with it. All of these thermometers will have NIST-traceable calibration. This batch of thermometers can be used to calibrate other thermometers, which can in turn be used to calibrate still more thermometers. With proper documentation, all of these thermometers will have NIST-traceable calibration. Traceability requires an unbroken chain of calibrations that goes all the way back to NIST. The chain could be several calibrations long or a hundred calibrations long; it doesn't matter, as long as the chain is unbroken.

What NIST traceability is NOT

Now for the bad news: NIST traceability does not necessarily provide a reliable and high-quality measurement. Remember, calibration is only a comparison between two devices. It's possible to calibrate a $2 thermometer against the best thermometer in the world, but it's still a $2 thermometer. Imagine this scenario: You are responsible for the proper operation of a stability chamber that is actively in use. After 12 months of operation, you remove the temperature sensor that controls the chamber environment and have it calibrated. The calibration report shows the thermometer to be out of specification. Now what? In the best case, the deviation is small, and a backup thermometer functioned properly for 12 months, providing quantitative data regarding the actual chamber temperature. In the worst case, someone will have to analyze the potential effect of "out of control" temperature on the products inside the chamber. If the effect is significant or cannot be determined, this can be costly, setting back a stability study by several months.

Now for the good news: You can prevent measurement disasters. If you are responsible for a temperature measurement, start by selecting the right thermometer for the job. If you're not sure how to do this, consult a metrologist in your organization, or contact a reputable vendor of thermometers for technical assistance. Set up a calibration program for this thermometer (and make sure your calibrations are traceable to NIST). Finally, consider using a second, independent thermometer for a backup measurement.

Accreditation is the difference

Returning to NIST traceability, there are other issues to consider. First, all calibration documents should be in a format that is generally acceptable. ISO/IEC 17025 defines the key elements of an acceptable calibration document. In fact, this is a global standard for quality systems of testing and calibration laboratories. If you are outsourcing calibration, consider using a vendor that is accredited to this standard. Visit the sites of the American Association for Laboratory Accreditation (A2LA) and the National Voluntary Laboratory Accreditation Program (NVLAP) to learn more and to find firms that have accreditation.

National Metrology Institutes and International Standards

As you might imagine, other countries also have national metrology institutes (NMIs) that serve similar functions to NIST. In Canada the equivalent organization is NRC. In Mexico it is CENAM. It is entirely possible that organizations located in different countries might request calibration traceability to their own NMI. This can be particularly challenging if your own organization has operations in more than one country. But there is more good news. Many NMIs "recognize" each other. This recognition is formally organized by the Bureau International des Poids et Measures (BIPM). It does not necessarily mean that your company or your customers will freely accept calibration documents traceable to any of the BIPM signatories. However, if you see any logistical advantages, you may be able to modify your quality system to allow for this.

I have used the example of a thermometer for simplicity. NIST is the keeper of many standards—pressure, time, frequency, voltage, humidity, and many more. All traceability issues remain the same, regardless of the measurement parameter.

Capacitive Humidity Sensors: Advantages and Disadvantages

Jim Tennermann

Winston Churchill reportedly said, “Democracy is the worst form of government, except for all the others.” So it is with capacitive humidity sensors. These sensors can perform amazingly well in some environments and terribly in others. There are many benefits and disadvantages to capacitive humidity sensors. Let’s look at some of them.

Fundamental vs. Secondary

Fundamental measurement devices depend on some intrinsic physical phenomenon to provide consistent, high performance measurement. In the world of humidity, chilled mirror hygrometers achieve this by controlling the temperature of a surface so that condensation remains in an equilibrium state on that surface. The temperature of the surface is measured, yielding a very accurate dew point measurement expressed in the International System of Units. By contrast, the capacitive humidity sensor is a secondary device. It relies on a dielectric material and how that material changes as a function of relative humidity. The dielectric material can be “fooled” into responding to substances other than water vapor, and it can drift over time due for a variety of reasons. So, why doesn’t everyone use a chilled mirror hygrometer? For starters, they can be two to three orders of magnitude more expensive than capacitive sensor based devices. They are heavy, complex, sensitive to flow rates, and need regular maintenance. The tradeoff between the two technologies: users of capacitive sensors sacrifice some performance for price, simplicity and ease of use.

Simplicity

Capacitive humidity sensors are simple. They consist of two plates sandwiching a dielectric material. Each plate has a “leg” for an electrical connection. The sensor is attached to an appropriate device for measuring capacitance. What could be easier? Well, it’s not really that easy. First of all, the plates have to be permeable to water vapor or the response time of the sensor would be far too slow. The plates are typically very thin layers of metal, often sputtered onto a base material. This requires sophisticated equipment and process knowledge. Some sensors are manufactured in clean rooms to obtain uniformity and consistency. This is not simple. Furthermore, the actual change in the sensor’s capacitance is quite small over the humidity range of 10 - 90%. Electronic circuits for measuring the sensor have to be designed carefully to measure this small change, and stray capacitance has to be eliminated in all wiring that connects the sensor to the electronics. These are not issues for users, but knowledge of these details might help users understand the differences in price and performance between instruments that appear to be the same.

Contamination

All humidity sensors must be in contact with the gas that they measure. Anything in the gas that “disagrees” with the sensor can alter the sensor’s performance. For example, small oil droplets in aerosol form can coat the sensor, forming a barrier that limits water vapor permeability. Dust can accumulate on the sensor with a similar effect. The most difficult contaminants are chemicals that interfere with or change the nature of the dielectric material.

These contaminants can be sneaky. When the sensor is exposed to them, they create measurement error. In some cases, when the sensor is removed from service for calibration, the contaminants may outgas and the measurement error disappears. Other contaminants may cause permanent damage to the dielectric. Sensors from different manufacturers may react differently because of differences in dielectric material or sensor design. All sensors have strengths and weaknesses when it comes to contamination, but sorting them out is nearly impossible without direct testing. This is the nature of capacitive humidity sensors. Unfortunately, every humidity measurement technology is also subject to degradation due to contamination.

Environmental Conditions

Capacitive humidity sensors are big winners when it comes to environmental conditions. They can withstand high and low temperatures. They can measure in saturated conditions and “dry as a bone” conditions. They outperform most technologies when it comes to extremes. Clever tricks can extend the sensor performance. For example, when measuring warm and moist conditions, condensation may form on the sensor and corrupt the measurement. This can be avoided by heating the sensor prior to exposing it to warm and moist conditions. Caution: Don’t use a torch to heat the sensor. Look for a humidity instrument that has this function in the design.

In conclusion, capacitive humidity sensors are not a universal solution for humidity measurement, but they’re pretty darn close. They are suitable for the vast majority of humidity measurement applications.

Ensuring Accurate Humidity Measurement in Cleanrooms

Jim Tennermann

Every cleanroom has environmental-control specifications that define the upper and lower limits for temperature and relative humidity (RH). Pressure, flow, and contamination must also be controlled. Devices that measure RH (e.g., sensors and transmitters) play a relatively small role in cleanroom management, but their failure can cause significant problems. Operators should bear several factors in mind to ensure that sensors function properly and maintain the appropriate humidity.

Installation location

The fact that RH depends on temperature affects the placement and installation of RH sensors. For example, if only 50 mm of an instrument's 200-mm stainless-steel probe is exposed to the process air, the rest of the probe may serve as a heat sink or source, depending on its environment. Thus, the temperature of even a carefully designed humidity-sensing element can change and cause an RH measurement error that depends on the difference between the process-air temperature and the environment surrounding the exposed portion of the probe. This error is easily measured in a laboratory environment.

Because local heating can affect wall-mounted RH instruments' measurements, operators should install the devices away from equipment that generates heat. Good airflow in the cleanroom usually minimizes convective-heat problems, but warm or hot equipment radiates heat, potentially creating a temperature discrepancy and corresponding measurement error. Loop-powered devices with a 4–20-mA output dissipate some power as heat, and this dissipation could affect wall-mounted RH instruments. Some wall-mounted RH devices housed in enclosures heat themselves by several degrees and experience significant measurement errors. RH devices with short probes that isolate the humidity-sensing element from the instrument's electronics preclude this possibility.

Humidity sensors should be protected from moisture. They should be located far enough from cooling coils so that they are unlikely to be affected by entrained water droplets. The sensors also should be kept away from steam-injection or ultrasonic-humidification elements. Many RH probes incorporate filters that eliminate catastrophic errors by protecting the sensing element from water. Water can accumulate on or in the filter material, however, and create a microclimate around the sensor that results in measurement errors.

In all of the situations described above, measurement errors result from subtle factors that change over time or occur only seasonally. These situations are among the most difficult to remedy when the sensor has been installed in an inappropriate location. If the errors are big enough to create out-of-specification conditions, they will trigger service calls, calibration requests, and equipment replacement. Personnel can prevent these potentially expensive problems during the design and specification processes for RH sensors.

Accuracy

The instrument-specification process is a good time to think about the accuracy specifications of the various RH sensors available. No standard requirement for accuracy has been established, so manufacturers must consider their specific applications to determine the accuracy specifications they need.

Although they are important criteria, accuracy specifications should not necessarily be the decisive factors for RH instruments. Sensor vendors emphasize these specifications, but performance claims can sometimes be misleading because "accuracy" is a qualitative term in measurement science that includes uncertainty.

Vaisala Cleanroom facility

Long-term stability

Long-term stability is easily the most important performance characteristic of an RH instrument. Long-term stability is the instrument's ability to make accurate measurements consistently over a long period of time. Reputable vendors perform long-term tests to characterize their own devices. The results of these tests help personnel understand the sensor's baseline performance, but the performance in individual cleanrooms may be different because of the cleanrooms' unique conditions.

The most significant threat to the long-term stability of an RH instrument in a cleanroom comes from vapors from the chemicals used in cleanroom processes. Vapors cause incorrectly low RH readings in high-humidity conditions because the vapor blocks water molecules from reaching the sensor. In low-humidity conditions, vapors cause incorrectly high RH readings. Some RH devices are equipped with features that minimize the effect of chemicals. For example, a chemical-purge function heats the sensor quickly to a high temperature (e.g., 160 °C), and thus cleans it of unwanted vapors.

Conclusion

Many humidity-measurement problems in a cleanroom such as sensor drift can be anticipated and prevented with thoughtful planning. Care should be taken throughout the entire RH-instrument specification and installation processes. Correct installation location, protection from moisture and vapors, and the instrument's long-term stability should be taken into account to ensure optimal sensor performance.

Instrument Tolerances: Manufacturer vs. Process

Michael Boetzkes

Using the instrument maker's tolerance, there is often a higher risk of an "Out of Tolerance" appearing on a calibration certificate; this costs money. Consider the following scenario: You have just received back from calibration the set of temperature sensors used to monitor the warehouse. Most of the instruments have been shown to be within manufacturer published tolerances. A few of the instruments, though, are listed as out of tolerance. Now the fun starts!

What to do with OOT results

The out-of-tolerance results need to be fully documented, including a full investigation into the use history of the instruments since their last calibration. All of this is rightfully required by your Quality Management system to ensure that no product has been negatively affected by the larger than expected errors in the readings. The investigation shows that the instrument manufacturer's tolerances for the instrument are tighter than the tolerance required to monitor the warehouse. All of the out-of-tolerance points from the calibration certificates show that the readings of the instruments are within the tolerances for the warehouse monitoring system; therefore, no products have been negatively affected.

Manufacturer Tolerances v. Process Tolerances

This is a common situation that many of us find ourselves dealing with, a difference between manufacturer tolerances and process tolerances. In many cases we have selected our process monitoring instruments based on more than just the measurement tolerances of an individual instrument. We may have chosen an instrument with higher accuracy for a number of reasons, including:

- *Compatibility with existing monitoring systems*
- *Lower risk of an out-of-tolerance reading affecting products*
- *Better overall value*
- *The manufacturer was on the Approved Vendor List*

The Risks of OOT

Whatever the reason, the manufacturer-specified tolerances are often significantly tighter than our process requires. This leaves us in a situation where we have a higher risk of an "Out of Tolerance" appearing on a calibration certificate than if the instrument being used had a tolerance matching our process tolerance. This in practice is costing extra money either due to an increase in calibration costs, a shortening of calibration intervals, or an increase in investigations of out-of-tolerance conditions.

There is a potential solution which will help contain costs and will also not increase the risk of negatively affecting product quality. When sending instruments out for calibration, have the calibration laboratory use the process tolerance when evaluating for in- or out-of-tolerance. The process tolerance is typically the more relevant limit rather than the manufacturer specification. The process tolerance was established not by looking at what instruments are capable of performing, but by looking at the requirements of the process. It is this limit that tells us when product may be affected and is therefore a more relevant tolerance to ensure that the measurement instrument is meeting.

Process Limits and Calibration

Most calibration laboratories default to using manufacturer specifications when performing this evaluation. The calibration laboratory does not know what the process limits are for an instrument unless we tell them; the only information that is readily available at the calibration laboratory is the manufacturer specification. When selecting a calibration vendor, ask if they have the capability to use customer specified acceptance limits. In most cases, this should not pose a significant problem. When sending the instruments in for calibration, include the instructions for the values to use for the process limits.

Using process limits instead of manufacturer specifications provides a low-risk and low-cost mechanism for reducing the cost and effort associated to out-of-tolerance events. It provides a more relevant analysis of the calibration results and will limit the need to reduce calibration intervals in the case of equipment not meeting manufacturer specifications.

Understanding the Performance of Test and Measurement Equipment

Michael Boetzkes

Any good Quality Manager knows that assumptions about an instrument can lead to unpleasant surprises during the calibration cycle. Test and measurement equipment play a critical role in most production and development processes. These instruments are used to make decisions regarding the effectiveness of processes and to ensure product quality. It is no surprise, therefore, that the need for regular calibration of test and measurement equipment is included as part of most major quality standards and are a commonly reviewed area for auditors, whether they are from an internal department, accreditation body, or a regulator such as the FDA. Most quality systems will also define the actions that must be followed in the case of an instrument being found out of specification during a calibration. What sometimes does not get enough attention is the selection of test equipment to reduce the risk of an out-of-tolerance condition affecting the process.

Considerations in Selecting Equipment

There is a fine balance to be considered when selecting equipment. Cost is always an important consideration, but let us look at the other critical issue: appropriateness of the instrument to the process. It is critical that the instrument selected can meet the measurement requirements of the process not only on the day it is delivered new, but also for the time period between calibrations.

All measurement instruments are prone to drift over time. Unfortunately, from a process view this means there is always some risk that instruments currently in use are actually out of specification. To mitigate this risk, calibration intervals are assigned based on manufacturer specifications, process requirements, equipment history, and acceptable risk requirements.

Understanding Instrument Performance

In most cases the manufacturer's specifications are weighted heaviest when determining suitability of equipment for a process. It can be difficult to make a proper determination of an instrument's expected long-term performance because all of its specifications must be looked at to gain proper insight into its performance. It is not sufficient to look solely at the instrument's accuracy. That usually does not take into account the long-term (or one year) drift of the instrument, or may only be applicable to a narrow operating environment. Not properly understanding the performance of an instrument will lead to unpleasant surprises during the next calibration cycle.

Some instrument types and applications tend to be easier to define than others. A high-end digital multimeter used in a laboratory setting can be relatively straightforward. Many manufacturers will state 24-hour, one-week, one-month, and one-year accuracies as well as provide guidance about the effect of temperature on the readings. The behavior of these types of equipment is well known and, in the grand scheme of metrology, relatively predictable. On the other end of the spectrum are instruments such as relative humidity meters. These are used in such a wide variety of operating conditions and environments that it is difficult for manufacturers to specify the right instruments for every application. Every environment is different and could have a different effect on the sensors.

The environment will always have an effect on the function and accuracy of the sensors used in it.

Specifications: Know your reference

When looking at specifications, always check to see if all the factors are included in the stated accuracy. Many times the stated accuracy is only valid for a specific temperature range, or it may not include the calibration uncertainty, or perhaps the long-term drift is not included. It is important to take a careful look at what is and is not being included in an accuracy specification. If it does not explicitly say that long-term drift is included in the accuracy, it likely is not and must be taken into account separately.

The end-user needs to be aware of requirements of the process and how the reference equipment will support them. It is critical to gather all the information regarding an instrument before approving it for a process. The repercussions of not knowing are typically far more expensive that the initial effort.

To Wire or Not to Wire – Which Option Should you Consider?

Jon Aldous

There are many reasons why wireless sensor communications seem to be the complete panacea for a wide area monitoring system. So why hasn't wireless monitoring completely replaced the traditional wired sensor? From the impracticality of running hundreds of feet of cable throughout a warehouse, equipment continually being moved around a facility, to the physicalities of a cleanroom not allowing cable penetrations — wireless monitoring has progressed leaps and bounds within the last five years. So why hasn't wireless monitoring completely replaced the traditional wired sensor? In truth, there are times that wired systems are better, but for most scenarios, a hybrid system of wired and wireless is the ideal solution.

Common Problems in Warehouse Environments

Warehouse temperature and humidity monitoring presents the ideal scenario for wireless sensors, but there are some common problems seen in these environments. The dynamics of a typical warehouse present ever-changing barriers for wireless signals. Validation studies are typically performed on empty, half-full and full environments. This gives a confidence that the thermal and humidity levels throughout the day or seasons can be constantly met. But throw in mechanical forklifts, boxes full of foil-based packaging, and top it all with fluids, and wireless signals can be easily blocked or severely degraded. On top of this, most wireless sensors operate either in the 915MHz or 2.4 GHz license-free regions, as do WiFi access points, kitchen microwave ovens, mobile handsets and a myriad of other consumer devices.

Ensuring Wireless Monitoring Systems Operate Correctly Amid Stray Signals

Typical monitoring systems don't have to be in continual contact with the main system recording the data, which helps significantly. Most importantly, any data collected during an offline period is captured, stored and transmitted during that connection period. If data rate isn't as important as redundancy, then a number of wireless connectivity scenarios are available based on complexity and, of course, cost.

Typical wireless statistics are based on line-of-sight, anywhere between 100 to 5,000 feet (outdoors!). The line-of-sight within a closed environment is severely compromised. A sensor placed back-to-back, on the opposite side of a cinder block wall from the access point, has its signal soaked up like a sponge. Place that same sensor 20 feet further away along the lateral of that wall, and the signal has to pass through 20 feet of cinder sponge. The placement of access points and repeaters is essential to ensure complete wireless connectivity.

Wireless systems that use a mesh topology, in which the monitoring device is acting as both a measurement device and repeater, provides a fuller signal path for connectivity, but two tradeoffs are the firmware complexity and the amount of power each repeater uses. To relay signal the sensor must be on more often than if operating in normal point-to-point mode. Point-to-point mode works just like normal WiFi, a laptop-to-access point: low complexity, low power, longer battery usage, simple connectivity; but the wireless signal can be easily blocked.

Truly wireless systems require point-of-measurement power and memory. Some have a motion activated display and can send alerts via smart phones.

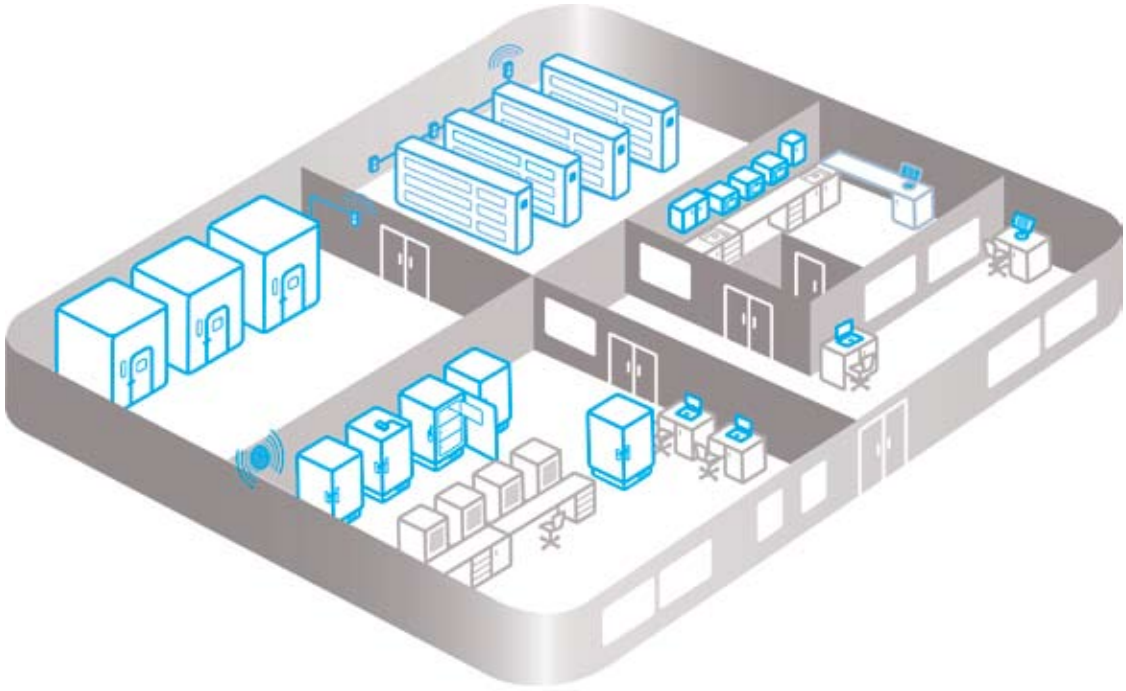
Battery Source

Does your wireless sensor use the same battery source to measure, store the data, and send the data to the access point? Depending on the criticality of your measured data, relying on the same battery source to store and send is a business decision. Most wireless sensors will report back a timeline of battery exhaustion; this can be anywhere between four and thirty-six months depending on the network topology being used, data rates, packet resends, and connection times. Having a separate battery for data collection will ensure that the data will be continually measured and stored for up to ten years – even during transmitter battery change!

To return to the original question, why haven't wireless sensor monitors replaced wired? If the monitoring system requires continual connectivity for fast data update rates and the data is being used for controlling HVAC and production, then wireless may not be the correct system. If the sensors are in locations that are hazardous, dynamic or difficult to reach for continual maintenance, a wired system may be the better option; and if the sensor requires power to operate, you should consider running wire.

Hybrid systems

A functional monitoring system should be capable of being a hybrid of wired and wireless options: a mixture of low-maintenance battery-powered wireless and of fully wired sensors. With the correct mix of infrastructure — using either WiFi or proprietary mesh networking topologies, and wired sensors — users can get the best of both worlds, and a near maintenance free system.



Most facilities benefit from a combination of both wireless and wired sensors; so long as each is used in a context that considers the strengths and weaknesses of both types of connectivity.

Tips for Responding to FDA Form 483 Inspectional Observations

Bruce McDuffee

According to the FDA document, Investigations Operations Manual (IOM), the *FORM FDA 483 INSPECTIONAL OBSERVATIONS* is intended for use in notifying the inspected establishment's top management, in writing, of "... significant objectionable conditions, relating to products and/or processes, or other violations of the FD&C Act and related Acts which were observed during the inspection." This statement and other background information can be found in section 5.2.3 Reports of Observations of the IOM. The FDA goes on to point out that these reports of objectionable conditions are made based on the judgment of the inspector. As with many government inspections, the inspector has discretion in his or her interpretation of what is "significant" and what is minor. Nevertheless, the issuance of "written inspectional observations" is required by law when an inspector finds a possible deviance from federal regulations.

Form 483s v. Warning Letters

It's likely that the day comes when your firm receives a 483; naturally you want to cooperate fully with the FDA in addressing the objectionable conditions listed therein. One thing that you should be clear about is that this is not a 'Warning Letter'; it's more like an offer to help you resolve issues and improve your quality system. To be clear on the process: the FDA *may or may not* issue a formal warning letter if you do not show that you have addressed the observations within the 483 to the agency's satisfaction. However, it's an important distinction to note that receiving a 483 does not necessarily mean you are out of compliance.

10 steps to an effective 483 response

Your 483 response needs to accomplish these three things: establish credibility, demonstrate acknowledgement and understanding of the observations and the associated requirements, and show commitment to corrective and preventive actions. Below, are 10 steps that will help you achieve these objectives:

1. Get your response in on time or early if possible. The FDA wants to see the response within 15 days, so plan your review and internal processes accordingly.
2. In the first paragraph of your response, demonstrate your understanding of and desire to comply with FDA regulations.
3. Respond individually to each item addressed on the form. Give a corrective action and time-frame for implementing.
4. Prioritize by first addressing the conditions that will most likely affect product quality.
5. Outline how and when each deficiency will be corrected.
6. Avoid talking about whose fault the issue is or how it came to be. For example, keep a positive tone and indicate how the quality system will be improved.
7. Include any reference documents, such as purchase agreements for a new monitoring system or employment agreement for a new quality manager.
8. Keep in mind that there is a formal process available for you to dispute the findings.
9. Be proactive in addressing the conditions. For example, address why the deficiencies were not detected internally and what will be done to correct this condition.
10. Seek clarification with the inspector when you receive the 483 on the spot. Be sure you understand each objectionable condition before the inspector leaves the site. Your firm may decide to seek out an industry expert if the matters seem complex or if the issues are not able to be resolved by your own personnel.

Tips on Preparing for an FDA Inspection: Are you following current good manufacturing practices?

Bruce McDuffee

If you're in the business of manufacturing drugs, medical devices, nutraceuticals, manufacturing or importing any product in the United States that must comply with current Good Manufacturing Practice (cGMP), your facility will be inspected by the U.S. Food and Drug Administration (FDA).

According to the Federal Food, Drug and Cosmetic Act, "Registered domestic drug establishments shall be inspected by the FDA at least once every two years." Under some conditions the inspections may be even more frequent, such as when a drug is being manufactured for the first time, if there have been previous problems validating a similar process, if production of a product or a new process is substantially different from past operations, or when a process is particularly complex.

What to expect in an inspection

You may or may not receive notice; inspectors have been known to show up unannounced and there is no requirement that they provide you notice. However, inspectors are not allowed to come in the back door for a quick look around the factory.

When the inspector does show up, announced or not, you should be presented with an FDA Form 482. If you are not presented with the form, be sure to ask for it. The inspector should also show an official FDA identification for your review. The form 482 clearly states what an inspector may inspect and what information is off limits:

- *An inspector may enter, observe, collect samples, interview employees, and review any records related to the production of the regulated product.*
- *An inspector cannot demand access to personnel data (except training records), financial statements, sales data (except shipment data), pricing data, or research records.*

What is the inspector looking for?

The best place to start is to read the FDA document Investigations Operations Manual (IOM). The IOM is the primary guidance document on FDA inspection policy and procedures for field investigators and inspectors. In general, they are looking for answers to the following questions:

- *Are you following cGMP?*
- *Is your staff knowledgeable and familiar with regulations and cGMP?*
- *Is documentation available demonstrating training, monitoring, and compliance programs?*

According to the IOM, the FDA will "audit and assess any available process validation protocols, activities, data, and information, whether or not completed, and report to the firm any deficiencies."

Attitude does matter

There are two ways to look at an inspection: as an intrusion and inconvenience to your normal business activities, or as a chance to tell your story and improve your systems and processes. Obviously, inspectors prefer the latter.

It's human nature to dislike an inspection of yourself or something in which you are personally invested (like a department or a company) because it usually involves some level of criticism. However, think of criticism as a good thing. In this case, it's meant to help you comply with regulations so the products that you produce are good quality, safe, profitable, and helpful to mankind.

Please Tell Me How to Map This Chamber: An 8-step guide

Bruce McDuffee

"Please tell me how to map this chamber!" This is a plea we hear at every Vaisala Good Manufacturing Practice seminar. The question deals with environmentally controlled chambers, everything from small refrigerators or freezers, to walk-in chambers or even large warehouses regulated under cGMP guidelines. Attendees who ask the question are usually more interested in how to map a chamber for maximum reliability or effectiveness as opposed to meeting the U.S. Food and Drug Administration (FDA) regulations. Like many of our answers, the first two words of our response are, "It depends." After the third seminar where this question kept cropping up, we formulated an eight-step guide document to help answer the question from an effectiveness perspective. A brief overview of that guide is presented here.

STEP 1: write a validation plan

The first step to mapping a chamber starts at the foundation — make a plan. Like all foundations, it is the most important and comprehensive step. If your foundation is poor or weak, your structure will eventually fall down. Step one poses several questions that must be asked and answered to ensure a strong foundation for steps two through eight.

Any organization subject to meeting cGMP requirements must be prepared to defend its answers or the decisions made at this stage. The questions or considerations that must be addressed include: chamber load, parameters to measure, duration of the test, what type of tests, type of equipment, placement of loggers, number of loggers, and frequency of the sample. Regulations and guidance documents from the FDA, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), The United States Pharmacopeial Convention (USP), and the International Society for Pharmaceutical Engineering (ISPE), as well as your own standard operating procedures (or others) should be consulted and referenced in your Validation Plan documents.

STEPS 2 &3: verify and document

Both of these steps involve verifying the equipment. Step two—check equipment and verify documentation—is almost as important as step one. It may seem obvious to many, but it is often assumed that equipment is satisfactory, and therefore the verification is overlooked or ignored (at your peril). The two major considerations here are calibration and validation of the testing and recording equipment.

Step three involves further verification by confirming the operation of the devices. Once again, it is not good practice to assume your devices are in working order. Verify and document.

STEPS 4 &5: setup and placement

Steps four and five discuss the setup and placement of the loggers or measurement devices. There are several ways to configure the placement, and once again, it depends on many factors. Whether you choose nine, 15, or more points to measure, you must be prepared to defend your decision in the likely event that one of your customers or someone from a regulatory agency will inquire.

STEP 6: periodic reviews

Step six requires that you check in on the progress from time to time. It is important to maintain a regular system of spot checks that spans the duration of your study.

STEPS 7 & 8: final data processing

Finally, steps seven and eight discuss final processing of the data. Step seven: retrieve and store the data, is quite important for a cGMP-regulated business. Compliance with Title 21 of the Code of Federal Regulations (21 CFR) Part 11—"Electronic records—Electronic signatures," for example, is crucial and should be ensured at this stage. Step eight: reporting is where all your careful preparation and efforts come to fruition, and you present your results in all their (and your) glory.

Download the entire guide to Mapping chambers at: http://knowledge.vaisala.com/LP=60

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Original Publication of each article

The following articles were written by four Vaisala experts between late 2011 and 2012. Each was published in a variety of publications, including:

Manufacturing Business Technology

- *http://www.mbtmag.com/articles/2011/08/accuracy-good-bad-and-ugly*

PharmaManufacturing.com

- *http://www.pharmamanufacturing.com/articles/2011/151.html*
- *http://www.pharmamanufacturing.com/articles/2011/151.html*
- *http://www.pharmamanufacturing.com/articles/2012/059.html*
- *http://www.pharmamanufacturing.com/articles/2011/121.html*

Quality Digest

- *http://www.qualitydigest.com/inside/quality-insider-article/tracks-traceability.html*
- *http://www.qualitydigest.com/inside/metrology-article/understanding-performance-test-and-measurement-equipment.html*
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