Sensors 4.0
The Future of Pharma Operations

Real-time diagnostics, easy network integration and verifiable measurement results are gaining ground in pharmaceutical production. What requirements must intelligent sensors fulfill to enable next-generation process technologies?

Traditional pharmaceutical manufacturing processes haven’t changed for decades. Recent FDA regulatory updates and equipment technology advancements are now promoting continuous manufacturing. These new methods require continuous monitoring to control quality and react to performance changes.

A process revolution
In traditional manual operations, a sensor captures data from a specific part of the process. For example, a tank scale measures material inventory. An operator documents and evaluates the measurement and responds appropriately if there is a problem.

In an automated process, faulty measurements can easily go unnoticed and lead to product quality issues or even safety hazards. Modern, intelligent sensors with networking capabilities provide a wealth of additional information that helps improve the efficiency, quality and safety of automated production processes.

For example, a pH sensor with integrated diagnostics can be replaced at just the right time before it fails during an expensive reaction process. Similarly, a metal detector continuously monitors critical parameters to reduce testing frequency and alert users of potential problems.
Weighing sensors in pharma
Let’s take a closer look at weighing sensors that are used in many automated processes throughout the pharmaceutical industry. For example, they are used to dose materials into reactors or to verify final product weight. These applications usually have tight tolerances and require consistently accurate measurements. Because inaccurate measurements, especially if they go unnoticed, can have a significant impact on quality and cost, continuous monitoring of sensor performance is critical. An immediate alert sent to the control system or the production manager’s mobile phone ensures rapid troubleshooting.

Integrated diagnostics
State-of-the-art automated weighing technology is based on intelligent load cells with integrated microprocessors for signal processing directly at the “working point”. This eliminates data transmission errors and improves the accuracy and consistency of measurement results. The intelligence of the load cell also allows continuous analysis of the weighing process. This means a failure or even gradual loss of performance can be identified and reported. In contrast, load cells with analog-value transmission provide, at best, a general fault message. A gradual decline in performance of a single load cell is not recognizable.

Capabilities for remote diagnostics via cloud-based systems allow for early recognition of potential issues and enable a service provider to react immediately to avoid costly downtime.

Process benefits from diagnostics
Dynamic checkweighers can add further diagnostic capabilities by monitoring the weight of each package and instigating automatic adjustment of filling systems to ensure target weights are met. Advanced data collection software also harvests live production data from product inspection equipment and makes adjustments to optimize productivity.
Continuous improvement
The ability to collect such detailed measurements and diagnostic data provides a new and improved approach to process control and optimization, which is a prerequisite for the Industry 4.0 age. Intelligent sensors pave the way for reduced downtime, faster troubleshooting, and less waste and scrap product – ensuring overall improvements in quality, compliance and productivity.

www.mt.com/ind-4-0-ph

Ensure uptime and process accuracy

Weigh modules with diagnostic capabilities
PowerMount™ weigh modules feature an integrated microprocessor that enables continuous process analysis. The weighing system will detect any gradual performance decline and initiate maintenance activities to avoid unplanned downtime and prevent inaccurate measurements.

www.mt.com/Powermount-ph
Sensors That Learn
Give You the Most Reliable Diagnostics

To maximize product quality and yield, you need to know if your sensors are performing correctly. That is why we have always made diagnostics the main focus of Intelligent Sensor Management (ISM®). And with our new version of ISM we offer a world’s first – sensors that actually learn from your processes to give you unequalled diagnostics performance.

Breakthrough Innovation
Since its launch in 2006, ISM technology has gone on to help hundreds of companies across the world increase process reliability, reduce maintenance costs and simplify sensor handling. One of the central features of ISM is its diagnostic algorithms that predict when sensor maintenance, cleaning or replacement will be required.

With our new, advanced algorithms we provide a breakthrough innovation – sensors that actually learn from and adapt to processes. This gives you exceptionally reliable diagnostics that are specific for every single process.

No more guesswork
ISM sensor diagnostics do not give you raw data that has to be interpreted: they provide easy-to-read tools that tell operators what needs to be done and when to keep sensors and your processes running reliably.

Sensor diagnostics mean you can confidently plan maintenance for when it is actually needed – neither late which can damage production, nor early when it is not required.

Keep your processes in the lead
There is a huge variation in processes found across manufacturing, so the latest ISM sensors actually adapt to the conditions they operate in. As a consequence, ISM diagnostics represent each and every process more accurately than ever before. This enables you to further optimize maintenance and calibration procedures to get the most out of your resources.

Diagnostics speed saves time
Exchanging sensors can lead to risk exposure as a measurement point is taken off-line, so a fast ramp-up that gets you back to reliable operation quickly is key. To always ensure your sensors are up and running as fast as possible, the new algorithms provide accurate diagnostics in only 24 hours.

They not only learn – they teach
In some applications, process conditions mean that it can take some time for algorithms to stabilize and give you precise diagnostics data. We have solved this by giving ISM sensors the ability to learn from other sensors that have already been used in an application. For example, when a pH probe is removed from a process and is connected to our 21 CFR part 11-ready iSense™ software, information on the conditions of that particular process can be stored as an application profile. This profile can then be transferred into a different pH sensor.

When this second sensor is installed in the same process, it carries the knowledge of its predecessor and does not need to acclimatize. And if process conditions alter, sensor diagnostics adjust themselves appropriately.
Sensor maintenance
Now diagnostics are accurate as soon as a sensor is installed and you can be sure you are conducting maintenance when it is necessary. That means you can always be certain your sensors are performing at their best.

Beyond plug and measure
With the application profile database on iSense and the ability to calibrate ISM sensors away from the process, you can build a stock of ready-to-go application specific sensors. Now you can replace a sensor at the measurement point in seconds without having to adjust the transmitter.

For today’s processes, tomorrow’s
ISM developments such as new advanced diagnostics and mobile apps that provide quick sensor checks on the go mean that ISM will remain the leading technology in analytical measurement.

“...I can transfer the knowledge of one sensor to another with just a click.”

Learn More
Sensors for your processes
METTLER TOLEDO Process Analytics in-line sensors cover pH, conductivity, gas and dissolved oxygen and many other parameters.

We offer flow-through, stationary and retractable sensor housings. Our process connections include Ingold, ANSI, Tri-Clamp, Varivent and flange.

Learn more about
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Learn More
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Preparing for EU Compliance
Tamper-Evident Pharmaceutical Packaging

EU directives 2011/62/EU and EN 16679 mandate the use of tamper-evident devices on pharmaceutical packaging to ensure product integrity and help to combat the distribution of falsified medicines. How can pharmaceutical manufacturers comply with these new requirements?

The European Union has developed further regulations to assist in combatting counterfeit medicines. Directive 2011/62/EU is entitled “Directive for prevention of the entry into the legal supply chain of falsified medicinal products,” or the “Falsified Medicines Directive” for short. A deadline of February 9, 2019 has been set for manufacturers in EU member states to implement systems to protect consumers from falsified medicines.

What is required?
First, wholesalers and authorized medicine dispensers must verify the authenticity of each individual pack. This is accomplished through serialization and aggregation technology to provide complete supply-chain visibility. Next, packages must include a device that makes it possible to detect any attempts to tamper with the outer packaging of the medication. Manufacturers that fail to comply with both of these directives will lose the right to distribute their products within the European Union.

Tamper-evident technology
There are four common methods for tamper-evident technology: gluing, special folding techniques, film wraps and adhesive seals. Many cartons are sealed by gluing, which doubles as a security feature where the seal cannot be broken without damaging the surface of the package. Folding techniques utilize box designs that feature perforations or other methods of opening that require the tearing of the box. Film wrapping is frequently used as it needs to be removed in order to open the container. As a fourth alternative, adhesive seals can be placed on the carton’s closures that must be broken to
open the package. This solution is utilized in METTLER TOLEDO pharmaceutical packaging solutions.

**All-in-one solutions**
Pharma companies can easily integrate the addition of a tamper-evident mechanism and serialized marking for complete compliance with directives 2011/62/EU and EN 16679. METTLER TOLEDO PCE solutions, such as the Datamatrix Station XMV TE, provide flexible marking, verification and tamper-evident sealing. Checkweighing technology is added in the case of the XS2 MV TE, which provides four inspection technologies in one unit.

www.mt.com/pi-xs2mvte-ph
Improved Supply-Chain Security
Aggregation Supports Verification

Aggregation supports pharmaceutical manufacturers and combats the rise of counterfeit products by improving supply-chain visibility. Aggregation technology is quickly becoming a hot topic because of its potential to ensure traceability for pharmaceutical manufacturers.

The European Union’s Falsified Medicine Directive addresses the growing danger of counterfeit medication on the market. The directive goes into effect in February 2019 and mandates complete traceability of individual packages. Wholesalers and dispensaries must establish the authenticity of package contents.

U.S. industry pressure
While there are no legal requirements for aggregation in the United States, the pharmaceutical industry is increasingly using aggregation technology to increase supply-chain security. Representatives from some of the top pharmaceutical companies in the country have made it clear they expect their contract packagers to implement aggregation in addition to manual serialization requirements as a way of improving end-to-end product traceability.

The deadline for pharmaceutical companies to implement serialization systems is November 2017. It’s therefore not surprising that manufacturers are making moves to add aggregation to their processes in order to have a complete track-and-trace system implemented.

Benefits of aggregation
In order to keep track of each individually marked package without aggregation, each carton must be scanned at every step of the distribution process. Aggregation allows cartons to be bundled together; scanning one barcode will automatically scan every carton in a given bundle. Being able to pull

Carton serialization
Bundle aggregation
Case aggregation

The steps after carton serialization are all considered part of aggregation. Depending on the manufacturer’s distribution network and scale, bundles, cases or pallets may be desired. Obviously, larger distributors will require pallet serialization while smaller ones may only require case serialization for their aggregation methods.
the complete list of cartons in a bundle means that manufacturers can identify and rectify weaknesses in their distribution chain should a carton go missing or be found in the wrong place.

Implementing aggregation
Much of the infrastructure required for aggregation is already in place for manufacturers who have achieved serialization. Aggregation adds a step to the process: mass-scanning the contents of a case and assigning an identification number to the bundles. This requires additional software and hardware, but many suppliers provide the necessary hardware and all-in-one software to handle both serialization and aggregation applications.

Free Download

Improving supply-chain security
Criminal statistics in several countries show that the production of counterfeit products is on the rise. Our white paper, Aggregation Solutions for Traceability of Products, outlines the steps you can take to improve supply-chain security in your business.

Free download
www.mt.com/pi-aggregation-ph
The term ‘Lean’ was coined in 1990 by MIT researchers studying the highly successful Toyota production system. Since then, the understanding and implementation of lean principles, also known as kaizen in Japanese, have permeated many sectors aiming to eliminate mistakes, reduce delays, lower costs, and improve the overall quality of a product or service.

Kaizen means ‘improvement’ and follows five basic principles (also known as 5S):

- **Seiri** Eliminate the unnecessary
- **Seiton** Organize/configure workspace
- **Seiso** Maintain a clean workstation
- **Seiketsu** Standardize lean processes
- **Shitsuke** Keep it sustainable

These basic concepts and techniques can also be applied to laboratory environments, where changing science, regulatory standards, technical innovations and financial pressures encourage the use of lean practices. This practical guide developed by METTLER TOLEDO explains how to cultivate a lean culture in your laboratory by sharing perspectives and good practice, including innovative technological solutions.

**Lean behavior is ubiquitous in nature**
Highly organized worker bees clean the hive cells from which they just emerged
METTLER TOLEDO’s comprehensive guide offers advice on how to implement lean techniques in the lab. These “nine steps to lean” are further enhanced by our range of METTLER TOLEDO analytical and weighing instruments, where lean-thinking drives innovation.

**The nine steps to lean**
- Housekeeping
- Value stream mapping
- Workload
- Laboratory workflow
- Performance management
- Equipment
- Skills of laboratory personnel
- Laboratory chemicals/auxiliary material
- CIP activities

**LabX PC Software –**
An integrated vision of laboratory practice

- Connects METTLER TOLEDO instruments to a single PC software
- Automatic data transfer - shortens transport and distances
- Instantly available test data stored on server - eliminates transcription errors
- Compliance module including 21 CFR part 11 - supports your lab to be regulation compliant
- Built-in Method Editor allows you to develop or customize application methods

**XPR Microbalance –**
Setting the standards in precision weighing

- Small footprint helps save workspace
- No edges and removable parts make it easy to clean
- Integrated GWP Approved quality assurance function
- Error free data transfer and full traceability
- Store methods in a custom library

METTLER TOLEDO’s comprehensive guide offers advice on how to implement lean techniques in the lab. These “nine steps to lean” are further enhanced by our range of METTLER TOLEDO analytical and weighing instruments, where lean-thinking drives innovation.
How to Ensure Data Integrity in Production
Is Your Weighing Data Audit-Proof?

Ensuring the reliability and integrity of weighing data generated across the entire pharma production chain is fundamental to regulatory compliance.

Data integrity issues often are traced back to human error. However, current weighing systems provide a range of features that help ensure process data is accurately captured and securely stored or transferred to the company’s data management systems.

Download the Data Integrity White Paper to learn more
www.mt.com/ind-data-integrity-ph