LIGHTHOUSE
WORLDWIDE SOLUTIONS

ApexZ and Laboratory Information Systems (LIMs)

Automate Your QC Micro Data Collection and Management

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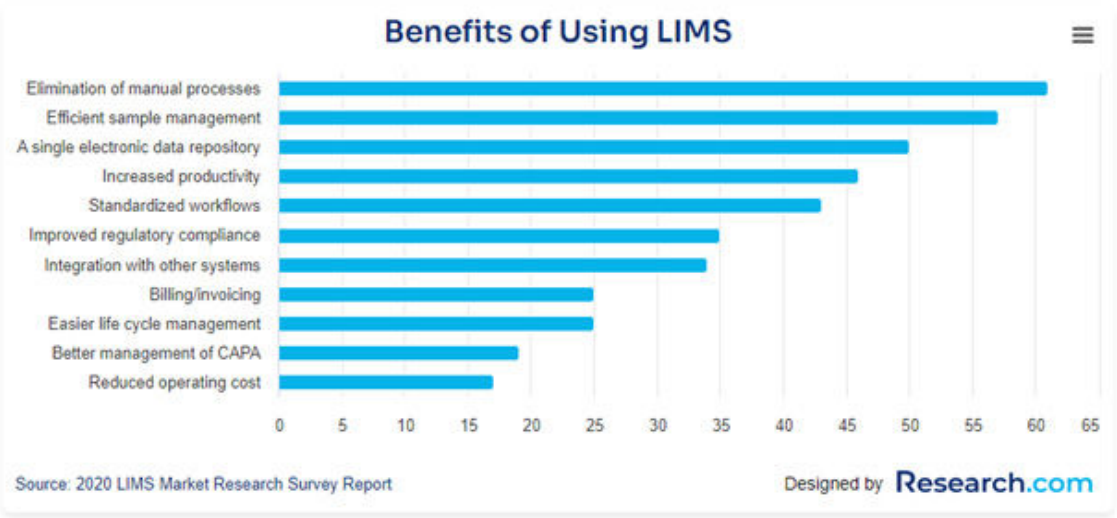
Overview

A Laboratory Information Management System (LIMS) is a software-based solution designed to enhance laboratory productivity and efficiency by managing data related to samples, experiments, workflows, and instruments. It automates and streamlines laboratory operations, ensuring data integrity, compliance, and efficient data management.

Key points:
LIMS Overview
Popularity in Big Pharma
Advantages of LIMS
Sample Handling
ApexZ
Risk-Based Approach and Data Integrity
Implementation Examples
Benefits of Transitioning to Digital Systems

Why LIMS is Gaining Popularity in Big Pharma

In the pharmaceutical industry, especially within big pharma companies, the adoption of LIMS is driven by the need for more efficient, accurate, and compliant laboratory processes where data integrity and quality are the main goals. Old paper-based data management systems are not capable of handling efficiently today's Environmental Monitoring (EM) data loads that are generated from the manufacturing facility.



Here's how LIMS is transforming pharmaceutical quality control (QC) microbiology data collection:

1. **Automation and Efficiency**: LIMS automates data collection and management processes, significantly reducing the time and labor involved in manual data entry. This automation minimizes errors, reduces redundancies, and speeds up laboratory workflows.

2. **Regulatory Compliance**: LIMS systems help pharmaceutical companies comply with stringent regulatory requirements such as FDA's 21 CFR Part 11 and ALCOA+ principles (Attributable, Legible, Contemporaneous, Original, Accurate, plus Complete, Consistent, Enduring, and Available). These systems provide electronic records and signatures, audit trails, and validation processes to ensure compliance.

3. **Data Integrity and Security**: By digitizing sample collection and data management, LIMS ensures data integrity and security. This is crucial for maintaining accurate records and meeting regulatory standards. LIMS systems track every interaction with a sample, ensuring that data is reliable and traceable.

4. **Operational Scalability**: LIMS provides the flexibility to scale operations efficiently. As pharmaceutical companies grow and their laboratory needs evolve, LIMS can easily integrate new instruments, workflows, and processes. This scalability supports both current and future laboratory needs, enabling companies to adapt quickly to new challenges and opportunities.

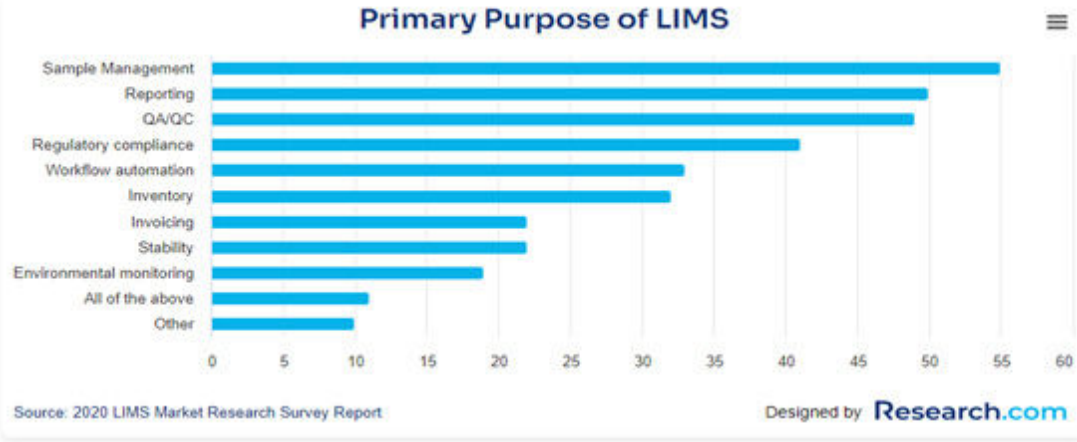
5. **Cost Savings**: Transitioning from paper-based systems to LIMS can lead to significant cost savings. Paper-based systems are slow, error-prone, and labor-intensive, leading to high operational costs. In contrast, LIMS reduces these costs by automating processes, minimizing errors, and improving overall laboratory efficiency.

Sample Handling in Big Pharma

A large pharmaceutical facility typically processes thousands of samples per day. Managing this volume with a paper-based system is not only inefficient but also increases the risk of errors and data loss. In contrast, a LIMS can handle high sample volumes with ease, ensuring that all data is accurately captured, stored, and accessible for analysis and reporting.

Interesting Facts and Statistics

- The global LIMS market is growing rapidly, driven by the increasing need for laboratory automation and data management. It is estimated to be worth over $1 billion and growing at an annual rate of 12-14%.
- Implementing a LIMS can reduce laboratory turnaround times by up to 50%, significantly speeding up the Batch release process.
- LIMS systems can integrate with a wide range of laboratory instruments, enabling seamless data collection and management across diverse laboratory



The ApexZ Portable Airborne Particle Counter was first introduced in 2017 and it has been further developed and enhanced to make your particle count data collection experience more robust, secure, and easy with workflows and SOPs built into the user interface color touchscreen. On its initial release the ApexZ was the most technologically advanced smart particle counter available. The ApexZ was the first smart particle counter to offer seamless connectivity into IT system networks, providing secure file sharing. With Active Directory and LDAP your ApexZ management and integration enables efficient security management and an API that allows seamless integration into 3rd party devices and systems such as LIMs. (*ApexZ is the only particle counter on the market with an API interface).

ApexZ technologically advanced with advanced features for LIMs integration

The ApexZ uses an Application Programming Interface to connect to LIMs systems over WiFi or wired connections. With the most advanced self-diagnostics on the market the ApexZ validates every particle count data record. If there is an issue within the data collection process the ApexZ will mark the data as Bad Data.

"The ApexZ was designed by the Pharmaceutical Industry for the Pharmaceutical Industry"

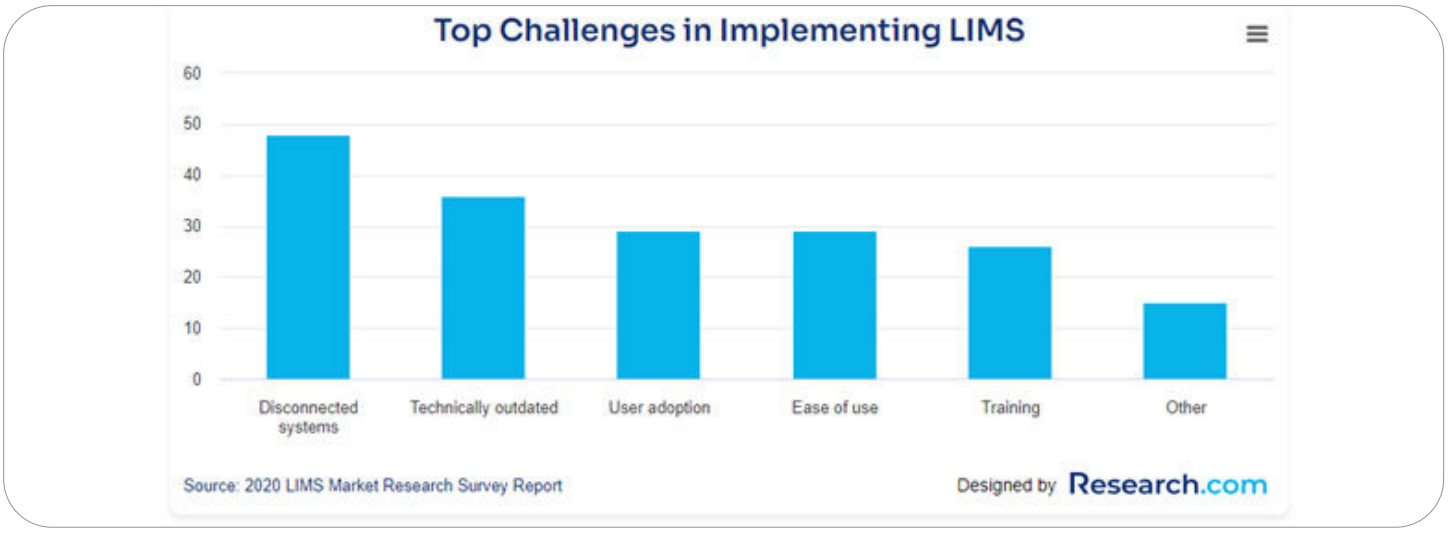
What is an API?

In the context of the integration of electronic devices such as the ApexZ, an **API (Application Programming Interface)** is a set of rules, protocols, and tools that allows different software applications or electronic devices to communicate with each other. APIs define the methods and data formats that applications or devices can use to request and exchange information.

Here are a few key points about APIs:

1. **Standardized Communication**: APIs provide a standardized way for devices and applications to communicate, ensuring interoperability between different systems.
2. **Abstraction**: APIs abstract the underlying implementation details, allowing developers to use the functionality without needing to understand the internal workings of the device or software.
3. **Reusability**: APIs enable the reuse of software components, making development more efficient and consistent.
4. **Scalability**: APIs facilitate scalability by allowing new features and services to be integrated with existing systems without significant changes to the underlying infrastructure.
5. **Security**: APIs can include security measures, such as authentication and authorization, to control access to resources and ensure secure communication.

In electronic devices, APIs are commonly used to enable communication between different components, such as sensors, actuators, and control systems, as well as between the device and external applications or cloud services. For example, an API might allow a smart thermostat to communicate with a home automation system or enable a mobile app to control a wearable fitness tracker. In our case the ApexZ API allows a standard, secure and scalable connection to many LIMs systems on the market.



In summary, adopting a LIMS in your pharmaceutical facility and using the ApexZ API will streamline your QC microbiology particle count data collection, ensure regulatory compliance, improve data integrity, and lead to significant cost savings and operational efficiencies as well as offering a proven and reliable connection from the ApexZ to the LIMs. This allows a company to totally move from inefficient and error prone, slow paper-based systems to a digital LIMS which is a strategic investment that will enhance your QC Micro data collection performance and productivity. All this allows for faster decision making and more reliable batch releases.

LIMs Manage End to End QC Data Sample Lifecycle

Most LIMs on today's market include a comprehensive suite of functions to manage the entire EM/QC sample lifecycle, such as:

- Field data collection systems that integrate into Particle Counters and other sampling devices
- Automatic action and alert notifications
- Supervisory dashboard to track progress
- Automated data collection system with data integrity built into the process (21CFR11, ALCOA+)
- Reporting, trending and visualization of operational and regulatory information
- Faster decision making on reliable Batch releases
- Digital database of QC EM sample data and retrieval ability in minutes

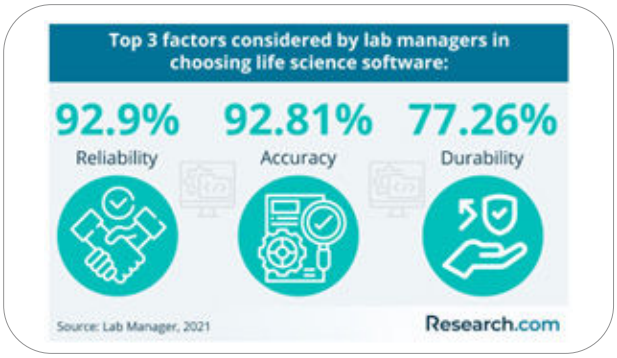
LIMs systems also can integrate with other standard monitoring equipment such as air samplers, total organic content (TOC) meters, and endotoxin devices, for direct data acquisition.

LIMs Offline Capabilities

Most LIMs use wireless technology for the paperless collection, processing and tracking of EM/QC samples. Some LIMs offer offline capabilities to enable technicians to work even if a disruption to your wireless network connectivity occurs. All cached information is automatically synchronized with the LIMs Server Data Repository. The solution is 21 CFR Part 11 compliant for technical requirements and serves as the complete system of record for all information.

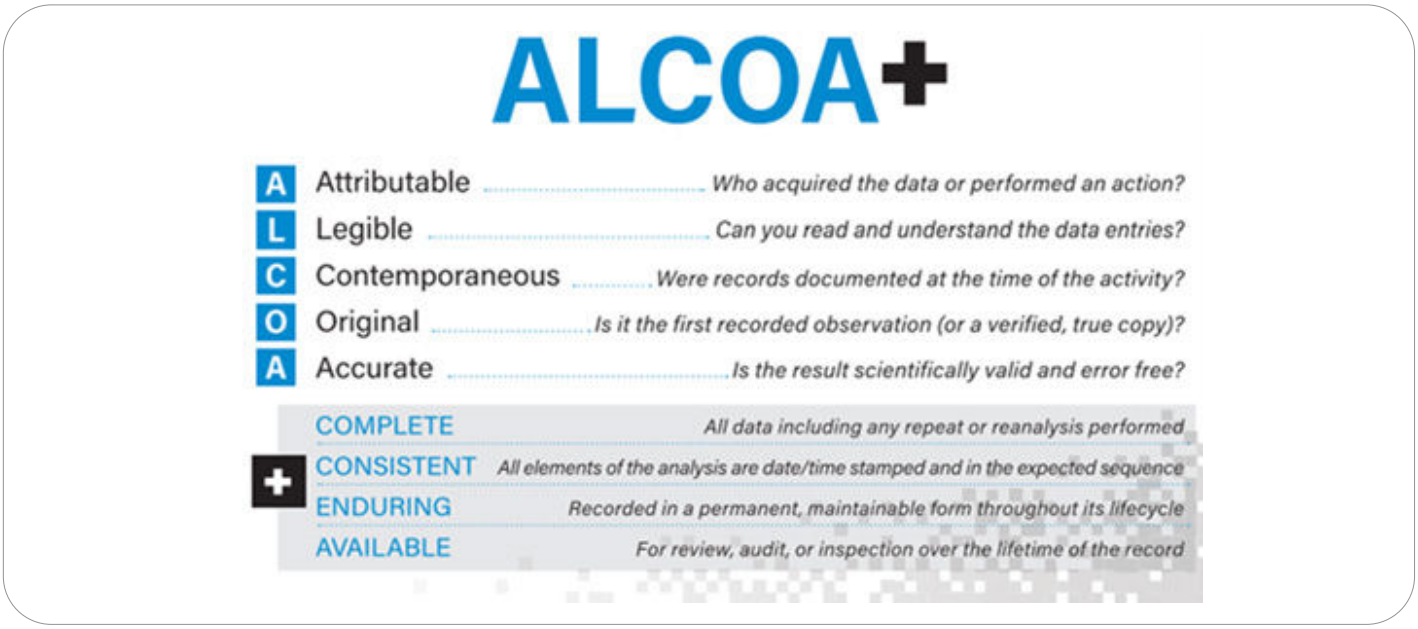
LIMs Features and Benefits

- Eliminates paper records, data reconciliation and batch data entry
- Administrative tools define parameters that govern system operation and security
- Flexible, user-friendly planning and scheduling tools ensure compliance with QC guidelines and SOPs
- Automated workflow engine enforces compliance with SOPs and manages the entire sample lifecycle
- Robust reporting and trending package produces accurate and meaningful analyses



What is Data Integrity

- "Refers to maintaining and assuring the accuracy and consistency of data over its entire life cycle and is a critical aspect to the design, implementation and usage of any system which stores. Processes or retrieves data" (HPRA)
- "Data is recorded exactly as intended, and upon later retrieval, the data is the same as it was when it was originally recorded" (MHRA)
- "The degree to which a collection of data is complete consistent and accurate" (FDA)



What Forms Does GMP Data Take?

Data integrity requirements apply equally to paper and electronic data

- Paper – lab books, logbooks, worksheets, spreadsheets, printouts etc.
- Paper records would need to include:
    1. Metadata and Data
    2. Audit trails
    3. Results and system setting files

At a sufficiently high precision to recreate the original tests. Retention of electronic data is more economic, more efficient option that the paper4 based system.

LIMs Case Study #1 MODA©

MODA© was developed by Lonza over 10 years ago. MODA© has 3 platforms that integrate together. The MODA® Platform addresses the issue of paper records associated with batch records, QC forms and logbooks, long cycle times for review/ approval activities, deviations for missing entries, incorrect entries, calculation errors and incorrect workflow decisions as well as moving from paper based records to digital records.

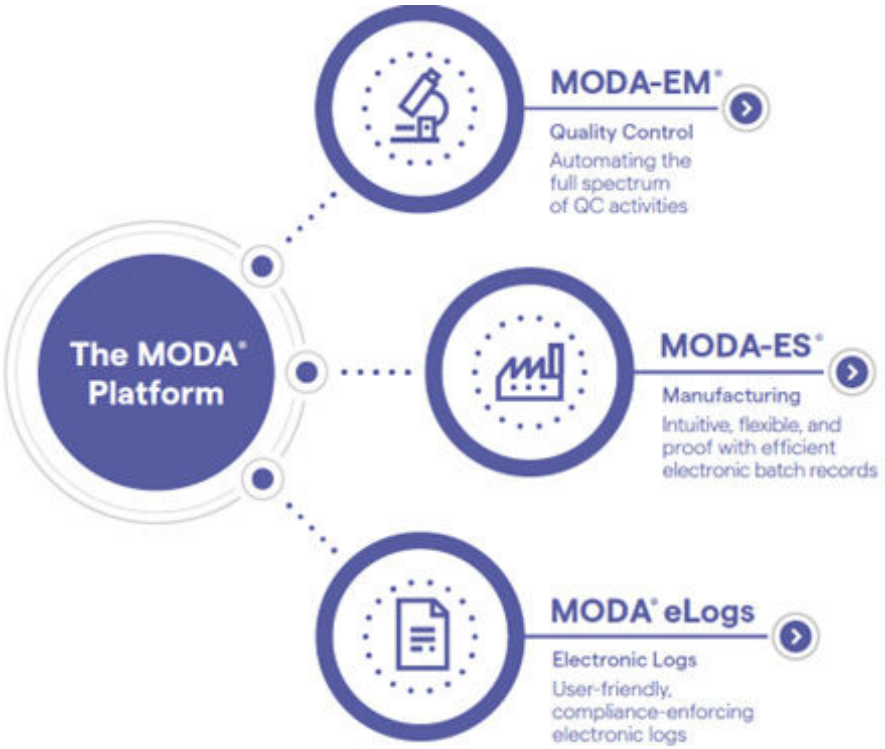
1. **Moda EM ™**

Is a Mobile Data Acquisition system with a combination of specialized cleanroom hardware and software that connects to field monitoring devices like the ApexZ and other instruments where QC EM sample data is required to be sampled from the facility to verify and record environmental conditions in various cleanrooms along the lifecycle of the end product.

MODA-EM® Software easily integrates with commonly used instrumentation and media found in manufacturing facilities, specifically production and laboratory areas.

"The ApexZ has been used in multiple Big Pharma MODA© LIMs projects and has a proven track record of seamless and reliable connectivity both wired and over WiFi".

The MODA-EM® Module is a regulatory-compliant paperless solution that automates QC processes. Users can easily manage and report on the full spectrum of EM and QC information — including surface, air, personnel, compressed gas, and product testing.



2. **MODA-ES© is an alternative to MES**.

Manufacturing Execution Systems (MES) are often too expensive and inflexible for many companies. The primary purpose of an MES is to track and document the transformation of raw materials into finished products in real time. It captures data from various sources, including machines, sensors and operators, to provide accurate and up-to-date information about the status of production activities. MODA-ES® Module offers an affordable, modular, and easy-to-configure alternative to MES.

The system is designed for easy configuration rather than customization, featuring an intuitive interface that allows manufacturing technicians to build workflows. It includes areas for data recording, instructional text (with hyperlinks to SOPs), electronic signatures, and drag-and-drop workflow setup.

The MODA-ES® Module enables quick deployment and lowers total ownership costs. It allows companies to reuse existing validated processes, reducing the need to create new ones. Its flexible standard methods enable manufacturers to process similar products without building and validating new processes.

3. **MODA® Electronic Logs**

The MODA® eLogs Module maintains electronic logs for seamless task execution, scheduling, reviewing, and record-keeping. This user-friendly, compliance-enforcing system is a powerful starting point for your digital transformation.

- Intuitive — a smooth, app-like user experience. Easy to navigate, with minimal training needed
- Enforced compliance — enforce SOP-compliant workflows for right-first-time data collection
- Improved data integrity — time-stamped audit trails, electronic signatures, and protection against use of out-of-calibration equipment ease the path to regulatory compliance
- Configurable and flexible — configure and build out workflows based on your company's needs and capabilities. Easily update workflows when processes change
- Seamless end-to-end operations — Smoothly integrates with other MODA® Platform Modules and external systems for automatic scheduling, logging, and tracking
- Reduce deviations — automatically schedule logs after equipment and room use with enforced tracking of status and state to ensure manufacturing occurs with only released areas
- Real-time data access — easily search data for quick investigations and decision making. All logs for one piece of equipment together to understand the full picture

ApexZ connected to MODA-EM

Environmental Monitoring Data Life Cycle

The selection of monitoring location points requires a good deal of knowledge on the semiconductor process. Here is a general overview of locations that should be monitored. The environmental monitoring (EM) data life cycle in pharmaceutical sterile manufacturing encompasses several key stages, ensuring that the manufacturing environment remains within controlled parameters to prevent contamination. Here's an outline of the typical data life cycle:

1. **Planning**:
   - o Defining Monitoring Program: Establish protocols and procedures for sampling, including locations, frequency, and methods.
   - o Risk Assessment: Identify areas with potential contamination risks and prioritize them.

2. **Sampling**:
   - o Sample Collection: Gather samples from defined locations using appropriate techniques (e.g., air sampling, surface sampling).
   - o Sample Transport: Ensure samples are transported to the laboratory under controlled conditions to prevent degradation or contamination.

3. **Analysis**:
   - o Testing: Perform microbiological and particle count analyses using validated methods.
   - o Data Recording: Accurately record all test results, including any deviations or anomalies.

4. **Data Review**:
    - Trend Analysis: Review data trends over time to detect patterns or changes in the environmental conditions.
    - Investigation: Conduct root cause analysis if out-of-specification (OOS) results or trends are observed.
5. **Reporting**:
    - Documentation: Compile reports summarizing the monitoring data, including any corrective actions taken.
    - Compliance: Ensure all documentation meets regulatory requirements (e.g., FDA, EMA).
6. **Action**:
    - Corrective Actions: Implement measures to address any identified issues or trends.
    - Preventive Actions: Establish preventive strategies to mitigate future risks.
7. **Review and Improvement**:
    - Periodic Review: Regularly review the monitoring program for effectiveness and compliance.
    - Continuous Improvement: Update protocols and procedures based on review outcomes and regulatory updates.

Risk-Based Approach

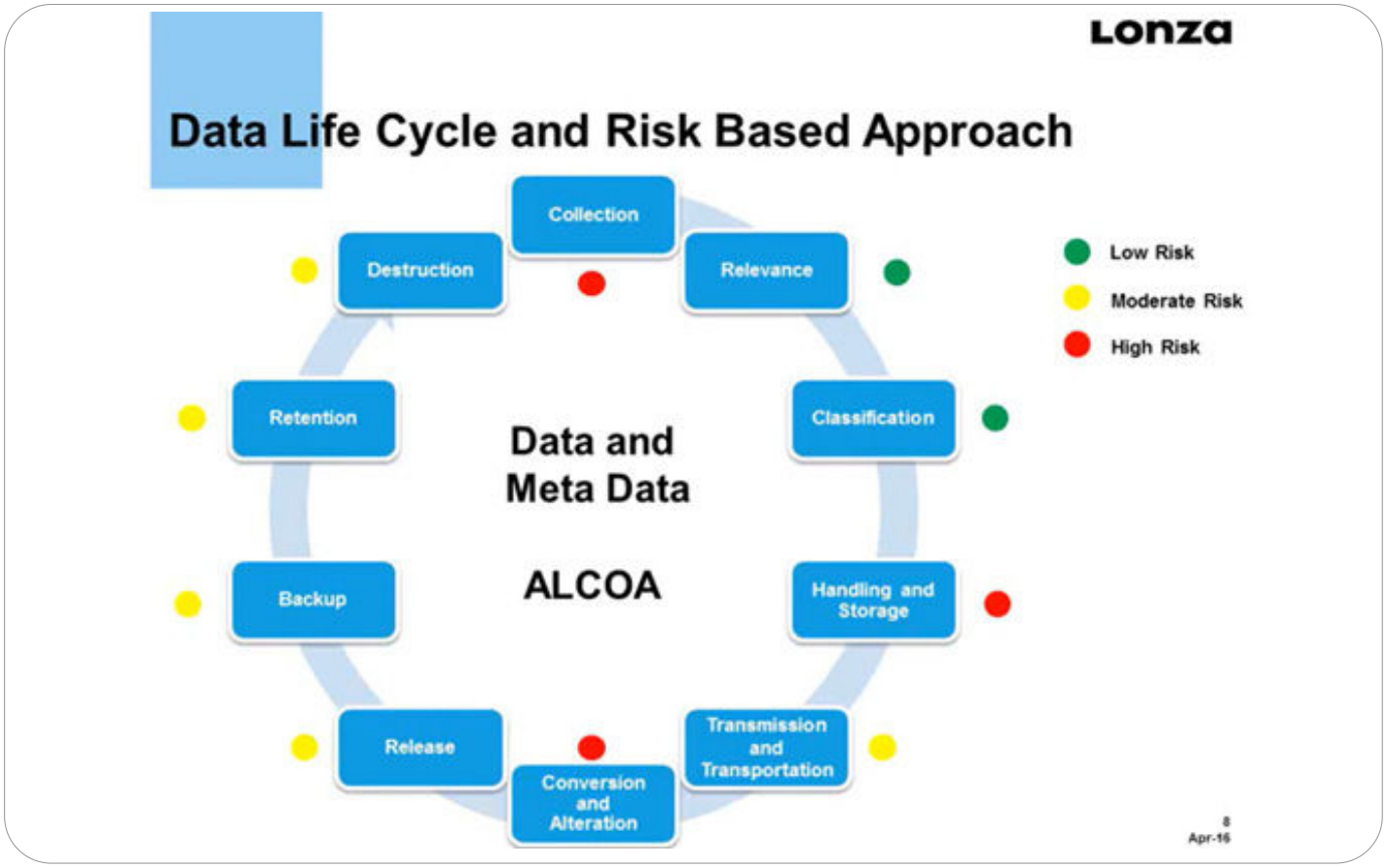
A risk-based approach prioritizes environmental monitoring efforts based on the potential impact on product quality and patient safety. This approach involves:

1. **Risk Assessment**:
    - Identifying Critical Areas: Focus on areas where contamination poses the highest risk, such as aseptic processing zones.
    - Severity and Probability Analysis: Evaluate the severity of potential contamination and the likelihood of occurrence.
2. **Risk Mitigation**:
    - Control Measures: Implement controls to reduce identified risks (e.g., HEPA filtration, restricted access).
    - Monitoring Adjustments: Adjust monitoring frequency and methods based on the risk level.

Types of EM Testing

A risk-based approach prioritizes environmental monitoring efforts based on the potential impact on product quality and patient safety. This approach involves:

- Surface Bioburden
- Viable Air Sampling
- Personnel Monitoring
- Disinfectant Testing
- Mold Monitoring
- Particulate Testing – API interface with ApexZ Portable Particle counter
- Water Bioburden
- Water Nitrates
- Endotoxin
- TOC/Conductivity
- Routine HEPA Filter Testing - using ApexZ Portable Particle Counter
- Gas Sampling



3. **Continuous Risk Management**:
    - **Dynamic Adjustments**: Modify the monitoring program in response to changes in processes, equipment, or regulations.
    - **Risk Communication**: Ensure all stakeholders are aware of risk levels and mitigation strategies.

Most At-Risk Data Points with Respect to ALCOA+

ALCOA+ principles (Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, and Available) ensure data integrity throughout the data life cycle. The most at-risk data points in EM include:

1. **Sample Collection Data**:
    - Attributable: Ensure the person collecting the sample is identifiable.
    - Legible: Ensure all handwritten entries are clear and readable.

2. **Analytical Results**:
    - Accurate: Ensure all recorded results are accurate and free from errors.
    - Original: Maintain original records and prevent alterations.

3. **Data Entry and Recording**:
    - Contemporaneous: Record data at the time of activity, not after.
    - Complete: Ensure all relevant information is captured, including metadata like date, time, and conditions.

4. **Data Storage and Retrieval**:
    - Consistent: Ensure consistency across all data entries and documents.
    - Enduring: Store data in a manner that prevents loss or degradation over time.
    - Available: Ensure data is readily accessible for review and audits.

In pharmaceutical sterile manufacturing, maintaining stringent environmental monitoring is crucial for ensuring product safety and compliance. By adhering to the EM data life cycle and employing a risk-based approach, manufacturers can effectively manage potential contamination risks. Ensuring data integrity through ALCOA+ principles further supports regulatory compliance and continuous improvement in the monitoring process.

Process and Workflow Before MODA©

Workflow (Viable and Non-Viable data collection)

- 140k EM samples per year
- Sampling scheduled manually
- Analysts enter the clean area and label media plates manually
- Analysts use a portable particle counter and manually sample the cleanroom environment
- All results are captured in a paper based system
- Original source data for particulate samples are on thermal paper
- Test records are stored in binders for media plate reading and particle count data
- Paper records are kept for a set period of time based on internal SOPs
- When results were reported, 165 different spreadsheets were utilized to trend for each sample type, by classification and building.
- Microbial IDs were entered into a separate database for EM data
- Microbial IDs were trended separately
- Particle Count data was transcribed into excel database
- Analysts reported Alerts and Actions via email to management
- Excursions were highlighted in excel spreadsheets during the reporting process

Challenges with a manual process:

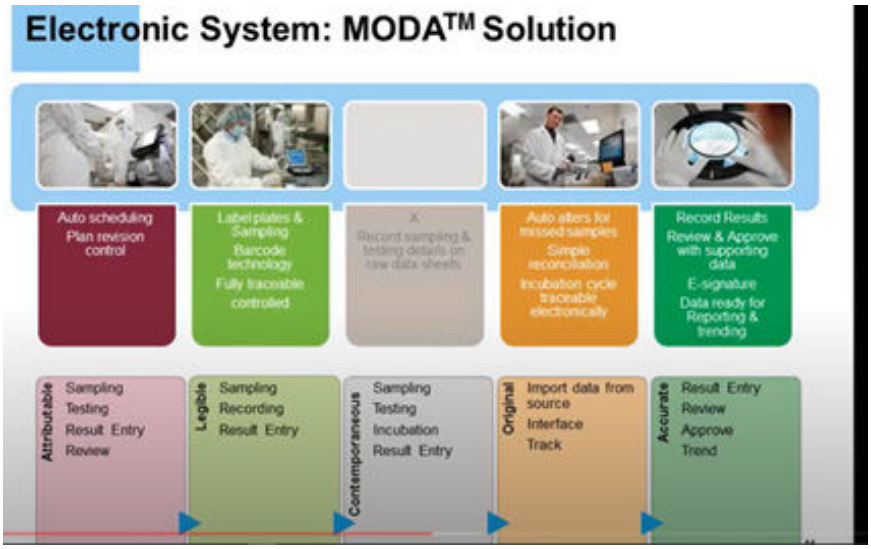
- Schedules require an additional headcount
- Handwritten sample labels
- Reconciliation of schedules vs samples received
- Reconciliation of incubated samples vs samples taken
- Manual transcript of particle counts and air sampling data
- Open to human transcribing errors
- Manual calculations for results
- Reliance on personnel to recognize excursions
- Manual reporting of excursions
- Misspelling of microbial IDs when manually entered
- Incubation times tracked manually
- Media inventory hand counted weekly

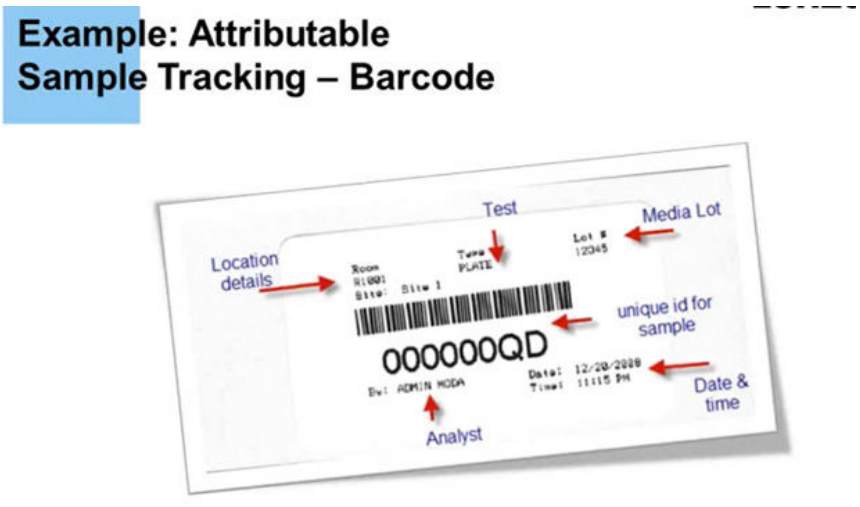
Paper-Based System – What Could Go Wrong?

- **Manual scheduling of Routine Environmental Monitoring**
  - Missed Sampling Events
- **Forms printed from document control system for daily use**
  - Forms can be reprinted
  - Type of paper used/material transfer of forms may introduce contamination
- **Sample labels printed from uncontrolled word document**
  - Type of paper used/material transfer of forms may introduce contamination
- **Non-Viable data & printouts**
  - Missing sample data or wrong sample configuration (Recipe)
  - Transcription error from printout to form
  - Missing or incomplete copies
- **Manual comparison to Alert/Action limits**
  - Missed excursion/investigations
- **Documentational Errors**
  - Missing documentation
  - Illegible handwriting

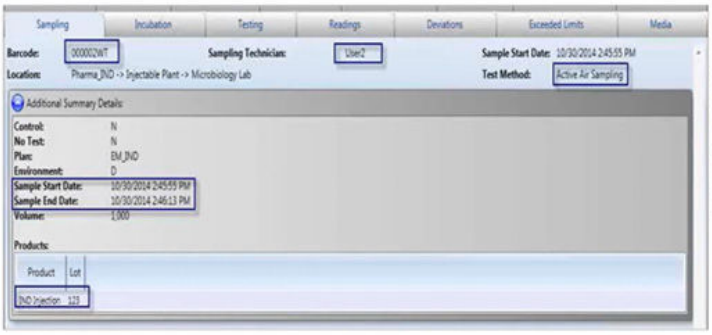
Process and Workflow Using MODA©

- Auto scheduling plan for EM monitoring
- Electronic Signatures of personnel carrying out samples
- Micro plate labels are auto generated and scanned with a barcode reader
- Particle Counter integrated into MODA EM system all data recorded digitally
- No more paper-based records required
- Alert and Action limits easily identified visually
- Both viable and non-viable data available on one system all data imported from source
- Record review and data trending results are more efficiently viewed and approved

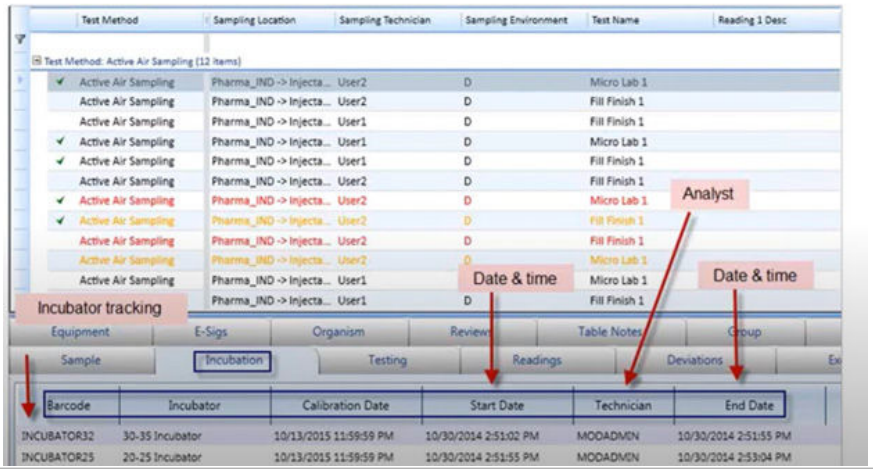




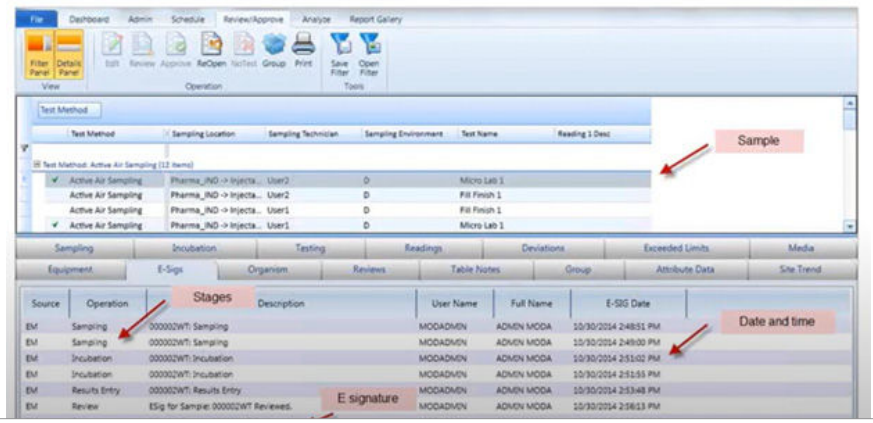
Example: Contemporaneous Data Capture through FDC



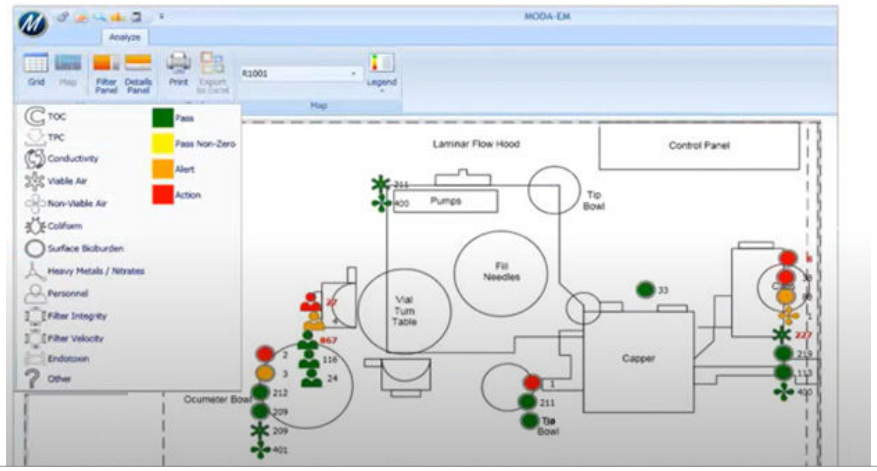
Example: Incubation Cycle Tracking



Example: Attributable Data in Each Stage of Sample Processing



Example: Visual Intelligence Portal



What are the Requirements for a Paper-Based System?

Workflow

- Sample barcoding
- Minimize or eliminate paperwork
- Linkage of consumables and equipment to sample
- Upload sample data from laboratory instruments including the ApexZ
- Digital Data export and trending
- Field sampling device to integrate laboratory instruments
- Cost savings and opportunities for efficiencies

Compliance

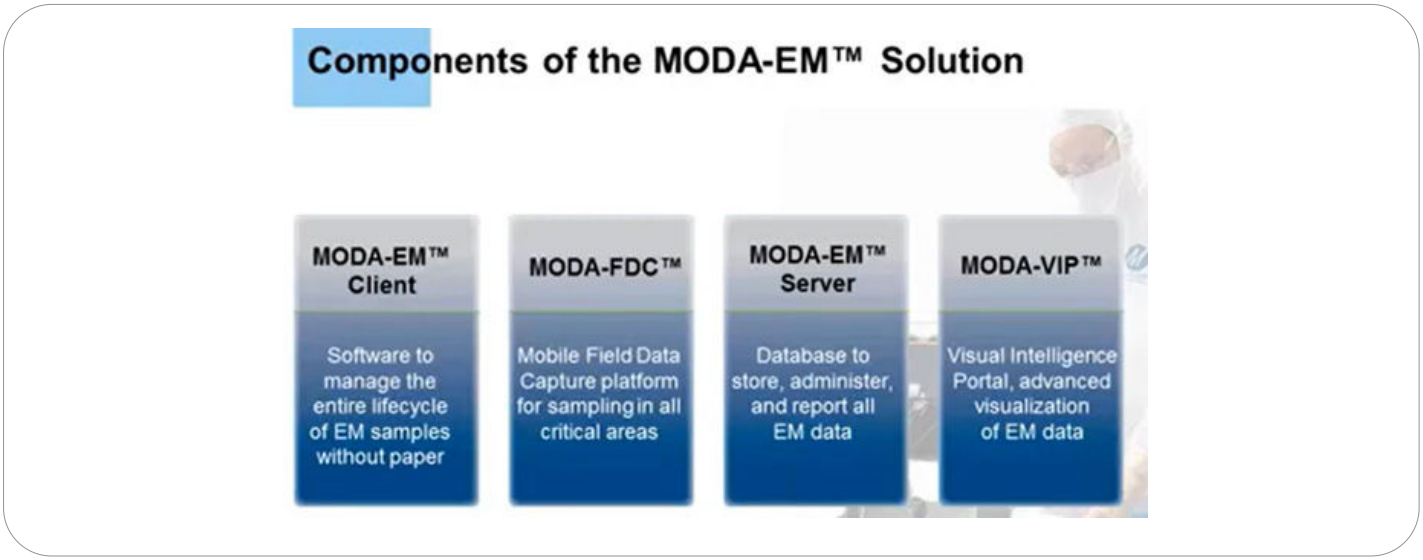
- No paper files or printouts
- Electronic signatures
- Audit trail
- Deviation flagging and notification
- Trend Reports and room visualization of sample locations and status

Key System functionality of the MODA ApexZ EM paperless solution

- Record of sample result for all types of EM sample types
- Barcode sample of location and user ID
- Chain of custody
- Testing workflow
- Tracking and control
- Results entry
- Action/Alert handling
- Approvals
- Trending and Reporting
- Generation of Compliance reports
- Track status of Instruments, materials and controls
- Visual based status of each room sampled
- Streamlined Batch release based on Data Integrity

New efficiencies realized with the paperless solution

- Scheduling takes place once a year for most samples
- Sample maps available in system for users to access
- Barcode scanning allows for greater accountability and traceability
- All materials and associated calibration are tracked to a sample instrument. Expired calibration will not be used to make samples
- Greater visual on data integrity and data quality (ALCOA+)
- Media use can be tracked by the system and reports can be easily generated
- Total Particulate samples are auto calculated to cubic meter when uploaded to system
- Conductivity acceptance criteria by temperature is calculated
- Multiple Alert levels may be applied to a test type (Mold v Bacteria)
- Trends by number of excursions in X amount of time may be configured
- Notifications are sent when samples are near expiration at any stage
- Users are notified of excursions via email
- Reports are produced for any data set in minutes
- Users from other departments given “read only” access to aid in lot release process
- Positive feedback given by regulators on reporting systems and controls



Report Generation

The MODA solution offers more than 40 standard, professionally formatted reports.

- Reports are out of the box pre-validated
- Layout of gallery is configurable by the end user
- Customer specific reports can be created and dropped into gallery

Quality Impact

- Timely and thorough data analysis for EM process
- Faster execution of root cause analysis
- Stricter adherence to validated SOPs
- Real time alerts
- Elimination of manual Data Transcripts
- Improved audit management

Productivity Impact

- Relocation of employees to other value-added tasks
- Significant reduction of re-work
  - Scheduling and sample collection reconciliation
- Electronic Data Capture vs Manual
  - Non-viable particle counters
  - LAL and TOC instruments
  - Sterility and ID instruments
- Faster reconciliation of corrective action events

Impact on Dependent Groups

- **Quality Assurance**
  - Near real time access to actionable information
  - More comprehensive view of EM/Utility process
  - Reduction of CAPA activities due to enforced workflow
- **Operations**
  - Accurate sample schedules
  - Alert system for missed tasks
  - Complete chain-of-custody from sample processing
- **IT**
  - Minimal system support required changes driven by business
  - Lower cost of ownership

Conclusion

Adopting a LIMS and integrating it with devices like the ApexZ particle counter significantly enhances QC microbiology data collection in pharmaceutical manufacturing. It ensures regulatory compliance, improves data integrity, and offers considerable operational efficiencies and cost savings, making it a strategic investment for pharmaceutical companies.

Want to learn more?

Going Paperless in the Cleanroom - LWS Applications (golighthouse.com)

Expand Your Knowledge

Lighthouse Worldwide Solutions offers comprehensive and industry standard-setting options for both possibilities, designed to meet your needs, abide by regulations, and keep your cleanroom clean.

For more information on monitoring for contamination in cleanroom applications visit our knowledge center for the most comprehensive library of cleanroom monitoring applications, webinars, tech papers and more:

www.golighthouse.com/en/knowledge-center/