WHITE PAPER

JRI
By MMS group
Beyond the measure

Clean Room 2026: building a compliant, auditable and sustainable environmental monitoring program

From EU GMP Annex 1 and ISO 14644-5 to operational best practices: critical parameters, EMS architecture, metrology and lifecycle qualification.

Critical Parameters

EMS Architecture

Metrology

Lifecycle Qualification

EXPERTISE IN THE SERVICE OF YOUR CRITICAL ENVIRONMENTS

Table of Contents

Introduction p. 03
- From Regulatory Compliance to Operational Excellence

Chapiter 1 p. 04–05
- The 2026 regulatory framework: what has changed
- CCS, GAMP 5 and Software Requirements

Chapiter 2 : p. 06–07
- Critical physical parameters: what regulations require

Chapiter 3 : p. 07–08
- Building a robust, risk-based monitoring plan
- Alert Limits, Action Limits and Common Errors

Chapiter 4 : p. 09–10
- Calibration: One of the First Things Auditors Verify
- Risk-Based Calibration Strategy

Chapiter 5 : p. 11–15
- Technology and Architecture: Choosing a GMP-Compliant EMS
- Equipment Integration & Data Integrity ALCOA++
- Wireless or Wired Sensors: Choosing the Right Architecture or Both
- Continuous Real-Time Particle Monitoring: Critical, Yet Rarely Implemented
- JRI MySirius: From Monitoring to Automated Batch Review

Chapiter 6 : p. 16
- From deployment to sustainability: a lifecycle approach

Chapiter 7 : p. 17–18
- Three JRI deployments, three field lessons

Conclusion p. 19–20
- JRI and the MMS Group: global expertise for controlled environments
- The Future of Predictive Environmental Monitoring

Calibration: One of the First Things Auditors Verify

INTRODUCTION

From Regulatory Compliance to Operational Excellence

A cleanroom cannot be judged by its visible appearance. It relies on the **documented and continuous** control of its environmental conditions, and on the ability to provide proof of this at any time, to any auditor.

This evolution has accelerated over the past three years. The revision of **EU GMP Annex 1**, applicable since August 2023, has made environmental monitoring a pillar of contamination control. In parallel, the revision of **ISO 14644-5 in 2025** has transformed local recommendations into documented, justified and auditable requirements.

In June 2024, the FDA issued a warning letter to a sterile drug manufacturer due to major gaps in its monitoring programme: absence of trend analysis, uncalibrated sensors and untraced data. In an aseptic filling line, the cost of a lost batch typically ranges from **$200,000 to several million dollars.**

This white paper provides

2026 Regulatory framework
What has changed and its concrete implications

Critical parameters
What regulations require to be monitored

Robust monitoring plan
Risk-based, auditable and sustainable

GMP-compliant EMS architecture
Selection criteria and best practices

> A cleanroom is not judged by its visible appearance. It relies on **the documented and continuous control** of its environmental conditions, as well as on the ability to provide proof of this at any time, to any auditor.

This evolution has accelerated over the past three years.

The revision of **EU GMP Annex 1**, applicable since August 2023, has made environmental monitoring a cornerstone of contamination control. In parallel, the revision of **ISO 14644-5 in 2025** transformed local recommendations into documented, justified and auditable requirements.

CHAPTER 1

The 2026 Regulatory Framework: What Has Changed

ISO 14644, Annex 1, GAMP 5 - A normative series to be read as a whole

ISO 14644-1 (2015)

Air cleanliness classification based on particle concentration (ISO classes 1 to 9). The 2015 revision replaced the 95% UCL calculation with a sampling point table, increasing the number of required samples.

ISO 14644-2 (2016)

Monitoring and quality control to maintain classification in operation. It defines requalification frequencies and the requirements for a continuous, risk-based monitoring plan.

ISO 14644-3 (2019)

Test methods for qualification and requalification: HEPA/ULPA filter integrity (PAO test), particle counting, airflow measurements and differential pressures.

ISO 14644-5 (révisée 2025)

Daily operations. It requires a structured **Operational Control Programme (OCP)**: every operational decision must be justified by a formal risk analysis. Best practices left to local discretion are no longer sufficient.

Grade (at rest)	ISO 14644-1 equivalent	Maximum requalification frequency
Grade A	ISO 5 (≥ 0,5 µm)	6 months
Grade B	ISO 5 at rest / ISO 7 in operation	6 months
Grade C	ISO 7 / ISO 8	12 months
Grade D	ISO not defined	12 months

These frequencies are regulatory maximum. A risk analysis (Contamination Control Strategy) may justify shorter frequencies depending on process criticality.

CCS, GAMP 5 and Software Requirements

Annex 1 Revised - The CCS at the Heart of the System

A structured system linking all contamination risks on a site, the CCS covers 16 domains defined by EU GMP Annex 1: facility design, HVAC, personnel, gowning, raw materials, containers and closures, processes, equipment, utilities, cleaning and disinfection, environmental monitoring, pest control, waste management, preventive maintenance, change management and outsourcing.

The monitoring programme is no longer a standalone activity: it becomes an element of proof of the CCS, and its results must be explicitly incorporated within it.

Requalification - Controlled Frequencies

Any significant modification (HEPA filter replacement, HVAC adjustment, configuration change) requires immediate requalification, regardless of the periodic schedule.

GAMP 5, 21 CFR Part 11 and Annex 11 - What Regulations Require from EMS Software

GAMP 5

Documented lifecycle for any software used in a GxP environment: specifications, qualification, acceptance testing, maintenance. An EMS software not validated according to GAMP 5 (GAMP 5 being the applicable reference framework) produces data with no probative value during an inspection.

21 CFR Part 11 & EU GMP Annex 11 & ALCOA++

Individual access control, complete and unmodifiable activity log, immutability of measurement data, secure archiving and traceable electronic signatures.

JRI-MySirius

Designed and validated to meet all these requirements, with SaaS cloud or on-premise deployment according to the site's cybersecurity constraints.

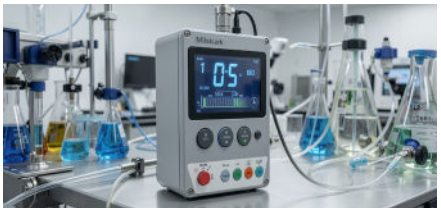
CHAPTER 2

Critical Physical Parameters: What Regulations Require

Temperature - A 2°C deviation can invalidate a batch

Temperature influences both the stability of sensitive products, microbial growth and the reliability of measuring instruments.

- Grade A/B (ISO 5) : 18 to 22 °C, tolerance ±1 °C
- Grade C/D (ISO 7/8) : 20 to 25 °C, tolerance ±2 °C
- Microelectronics (ISO 4/5) : controlled to ±0,5 °C



Humidity - A parameter often checked second, but never secondary

Target ranges in pharmaceutical environments: 40 to 60% RH for Grade A/B zones, and 40 to 65% RH for Grade C/D zones.

- Above 60% RH: microbial proliferation, HEPA filter degradation
- Below 30% RH: problematic static electricity

Differential Pressure — The barrier protecting critical zones

Differential pressure (ΔP) between adjacent zones prevents the migration of particles and micro-organisms towards the cleanest spaces.

- Annex 1 threshold: 10 to 15 Pa minimum between two adjacent zones
- Any drop triggers an immediate alarm and a documented investigation

Non-viable particles

Non-viable particle counting is a key regulatory indicator. In Grade A, continuous monitoring is required to immediately detect any drift.

Viable surveillance

Microbiological monitoring includes aerobic collection, sedimentation, surface sampling and personnel monitoring.

CO2, O2 and air velocity

CO2, O2 and air velocity complement the control system for controlled zones, according to the risk analysis and room usage.

ⓘ The fundamental rule is simple: the parameters to be monitored must derive from a formal risk assessment, not from a default approach. This is an explicit requirement of ISO 14644-5:2025 and Annex 1. A parameter not deemed critical by the risk analysis does not need to be monitored; conversely, a parameter identified as critical must be monitored, even if it does not appear in the usual lists.

JRI Expert Advice

In the field, we frequently encounter two opposite extremes: an overloaded monitoring plan that creates alarm saturation, or a plan that is too light, leaving critical zones without sufficient protection.

In both cases, the cause is the same: a plan built by habit or analogy, without formal risk analysis.

Our recommandation:

Before any deployment or revision of a monitoring programme, carry out a **thermal and hygrometric mapping** of each zone, under «at rest» and «in operation» conditions, to identify gradients, unstable zones and truly representative locations.

It is these experimental data, not empirical rules, that must underpin your plan. **One well-positioned sensor is worth more than three poorly placed ones.**

CHAPTER 3

Building a Robust, Risk-Based Monitoring Plan

An environmental monitoring plan (EM plan) translates regulatory requirements and risk analysis into concrete operational decisions.

1

Parameters to monitor
Defined and justified by risk analysis

2

Measurement locations
Determined from airflow studies and mappings

3

Acquisition frequencies
Continuous, high-frequency or periodic according to grade and risk

4

Alert / action limits
Defined for each parameter, with metrological justification

5

Response procedures
Investigation, product impact assessment, CAPA

6

Requalification frequencies
Compliant with ISO 14644-2 and Annex 1

Alert Limits, Action Limits and Common Errors

Alert limits vs. action limits

The distinction between alert limit and action limit is one of the most frequent errors in existing programmes.

Alert limit (non-critical alarm)	Action limit (critical alarm)
First level Meaning: Signals an unfavourable trend.	Second level: Meaning: Indicated a potentially non-compliant situation.
Threshold: Generally set at 80% of the specified limit.	Threshold: Specified limit.
Response: Triggers and investigation and a preventive corrective action.	Response: Requires immediate action, product impact assessment and a batch release or quarantine decision.

ⓘ Trend analysis is an explicit requirement of Annex 1 (2022), not an optional best practice. Collecting monitoring data without analysing it constitutes in itself a non-conformity. The JRI MySirius trend analysis module automatically generates control charts, detects progressive deviations and triggers early alerts.

The 5 most impactful errors during an FDA or EMA inspection

Undetected sensor drift
A sensor whose calibration has expired produces apparently normal data, but with no metrological value.

Alarm saturation
A poorly configured system generates a flood of spurious alarms that operators end up ignoring, masking genuine critical drifts.

Static monitoring plan
A plan defined during initial qualification and never revised no longer reflects operational reality.

Unstructured documentation
Records scattered across heterogeneous formats make audit preparation time-consuming.

Absence of link between monitoring and batch release
An action limit exceedance not assessed for its product impact constitutes a gap directly targeted by the revised Annex 1.

CHAPTER 4

Calibration: One of the First Things Auditors Verify

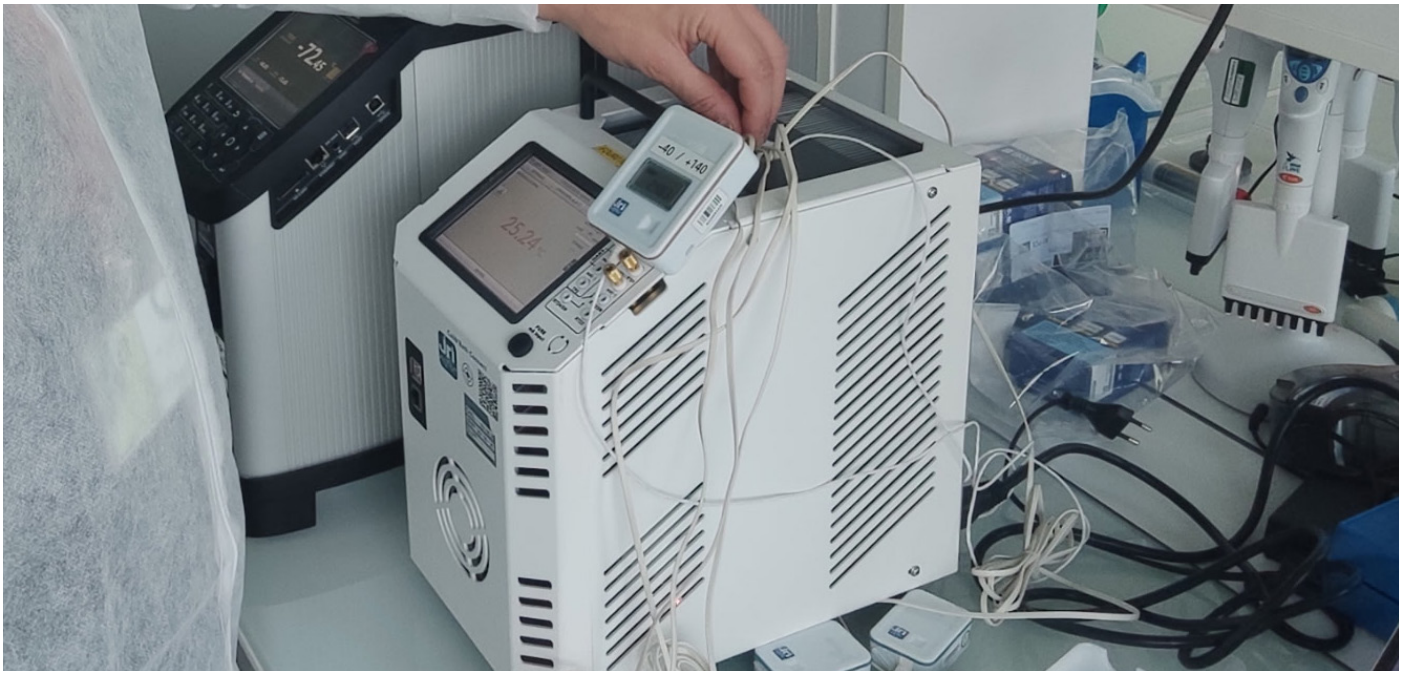
Calibration and Documentary Evidence

Calibration consists of establishing the relationship between a measuring instrument and a reference standard.

Key point: calibration does not necessarily imply adjustment. A certificate without as-found (before intervention) and as-left (after intervention) results has no probative value. Metrological traceability must link each instrument to SI units, up to national standards.

What a GMP-compliant certificate must contain:

- Unique instrument identification (ID, serial number, location)
- Traceability to SI units explicitly stated
- Identification of the reference equipment used
- As-found and as-left results
- Clearly defined acceptance tolerances (MPE)
- Measurement uncertainty (according to criticality level)
- Calibration date and next due date
- ALCOA++ compliance (since 2018, 10 parameters): Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, Available, Traceable via inviolable audit trail



Risk-Based Calibration Strategy

Decision factor	ISO 17025 accredited calibration (COFRAC/BELAC or equivalent)	Traceable calibration
Impact on product quality	Direct, linked to batch release	Indirect, for support monitoring
Patient risk	Measurements that may affect patient safety	Low risk
Data usage	Compliance decisions, regulatory submission	Trending, early alert
Instrument examples	Grade A/B T° probes, ΔP transmitters, particle counters	General CO2 sensors, humidity Grade C/D
Audit evidence	Accredited ISO 17025 certificate required for storage; traceable calibration sufficient in production and laboratory	Traceable certificate sufficient if justified

ⓘ Important : in pharmaceutical production and laboratory environments, an ISO 17025 accredited service is a prerequisite for storage activities.

Based on an analysis conducted by the JRI ISO 17025 accredited laboratory on 2,500 digital probes (study signed by Rémi Moreau, May 2025), 95.8% of instruments showed a drift of less than ±0.2°C and 99.3% a drift of less than ±0.3°C. These data make it possible to optimise calibration intervals: some instruments require a shorter frequency, others can benefit from a justified extension, reducing the overall metrological burden without compromising compliance.

-196°C to +1000°C

Calibration range

The widest in JRI laboratory history

±0,037°C

Measurement uncertainty

Among the lowest levels on the market

2000+

Certificates / month

Issued by the JRI ISO 17025 accredited laboratory, recognised in more than 100 countries via ILAC MRA

100+

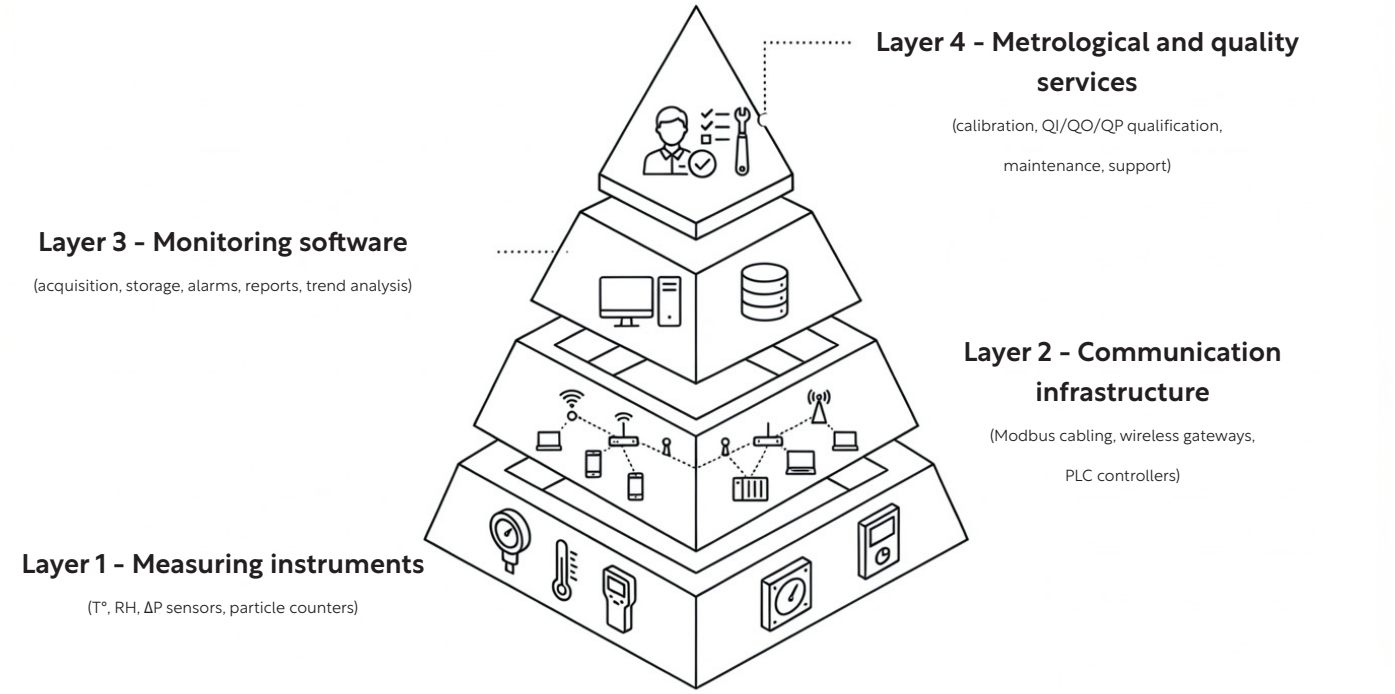
Countries covered

Via the ILAC MRA mutual recognition agreement

CHAPTER 5

Technology and Architecture: Choosing a GMP-Compliant EMS

A GMP-compliant EMS relies on four interdependent layers. The most common mistake is to reduce the project to the hardware layer alone, the sensors, underestimating the three other layers, which account for the majority of costs and compliance challenges.



Communication Technology Comparison for Cleanroom

Criterion	LoRaWAN	RF 868 MHz	WiFi 2,4 GHz	Filaire Modbus
Industrial range	Up to 3 000m	200 to 500m	30 to 100m	1 200m maximum
Obstacle penetration	Excellent	Good	Poor	N/A
Battery life	3 to 5 years	2 to 3 years	Less than 1 year	N/A
Interference sensitivity	Very low	Low	High	Faible si installation correcte
Ideal for	Large warehouses and multi-zone sites	Laboratories and medium industrial sites	Small connected spaces	ΔP transmitters, particle counters

Equipment Integration & Data Integrity ALCOA++

Integrating Existing Equipment - Saving Several Hundred Thousand Dollars

In most modernisation projects, the facility already has equipment in place. Systematically replacing it is neither necessary nor economically justified.

The JRI MySirius platform natively integrates particle counters from the market's leading manufacturers via Modbus RTU/TCP gateways, without hardware modification:

Climet | **PMS** | **Lighthouse** | **Beckman Coulter** | **...**

Data Integrity - ALCOA++ Principles Applied to an EMS

Attributable
Each data item is associated with an author identified by individual named account

Legible
Records are legible and intelligible

Contemporary
Data is recorded at the moment it is generated

Original
Preserved in its original form with its metadata

Accurate
Data is accurate and verified

Complete
No missing or truncated data

Consistent
Consistency across different systems and records

Enduring
Data retained for the entire applicable retention period

Available
Accessible at any time throughout the retention period

Traceable
Inviolable audit trail on all actions

JRI-MySirius also natively integrates bioaerosol samplers, with airflow monitoring and start/stop management. The MySirius roadmap includes manual entry (or via LIMS interface) of CFU counts and micro-organism identification.

ⓧ An Excel spreadsheet or any non-validated system cannot satisfy these requirements, regardless of the intrinsic quality of the data it contains. GAMP 5 validation of the EMS software is the sine qua non condition for the probative value of data produced.

Wireless or Wired Sensors: Choosing the Right Architecture or Both

There is no universally superior technology. The best EMS architecture is often mixed, provided one fundamental rule is respected: **the wireless solution must be proprietary.**

The unique advantages of each technology

Wireless sensors

Deployment without construction work, positioning flexibility, ideal for hard-to-access areas or listed buildings. Battery life of 2 to 5 years depending on the technology. Reduced installation costs.

Wired sensors (Modbus)

Measuring instrument connected by cable to a supervision system. Reliable, battery-free, range up to 1,200 m. Ideal for fixed critical measurement points

Why proprietary wireless is essential?

- Integrating wireless sensors from a third-party manufacturer into a third-party EMS software is a recurring source of disappointment in the field: always partial and limited integration of probe and associated wireless receiver functionalities, no control over the technical sustainability of the offer, lack of integrator expertise on operational issues encountered during wireless network deployment in industrial environments.

With JRI MySirius, JRI wireless sensors, receivers and supervision software are designed and maintained by the same actor. This native integration guarantees full exploitation of functionalities, control of the technical roadmap and end-to-end operational support.

- JRI MySirius is based on a 100% proprietary wireless architecture — sensors, receivers and software designed and maintained by the same actor — combined with native wired Modbus integration for critical equipment. It is this coherence that guarantees the performance and sustainability of your EMS.

Continuous Real-Time Particle Monitoring: Critical, Yet Rarely Implemented

Particle counting is one of the most demanding parameters to monitor continuously. Today, continuous real-time measurement remains uncommon in the field, even though EU GMP Annex 1 makes it an explicit requirement for Grade A zones.

Why continuous real-time particle counting is under-deployed?

Cost and installation complexity
Isokinetic particle counters require precise positioning, controlled airflow and integration into the supervision network.

Confusion between spot measurement and continuous monitoring
Manual counting during qualification does not replace continuous monitoring in operation. Annex 1 clearly distinguishes between the two.

Insufficient air volumes
Counters measure in L/min (28, 50 or 100 L/min) while regulatory limits are expressed in particles/m³. A minimum 1 m³ sample is required for documented compliance.

Absence of EMS integration
Many counters operate standalone, without a link to the supervision system, preventing trend analysis and automatic traceability.

What an integrated EMS enables

ⓘ Did you know? JRI MySirius natively integrates particle counters from leading manufacturers (Climet, PMS, Lighthouse, Beckman Coulter) via Modbus, without hardware replacement. Data is centralised, timestamped and integrated into trend analysis.

1 m³ sampling
The EMS drives the counter to reach the minimum regulatory volume, regardless of the measurement rate.

Rolling windows
Continuous monitoring is carried out via rolling windows, in accordance with ISO 14644 and EU GMP Annex 1 expectations.

Alert and traceability
Any limit exceedance triggers a critical alarm, a documented investigation and an automatic link to the batch currently in production

JRI MySirius: From Monitoring to Automated Batch Review

The review of environmental production conditions is today one of the most time-consuming tasks for quality teams. JRI MySirius automates this process and highlights failure points before they generate deviations.

Real-time monitoring
All critical parameters (T°, RH, ΔP, particle counting) are acquired continuously, timestamped and linked to the current production batch.

Automatic exceedance detection
As soon as a parameter crosses an alert limit (non-critical alarm) or action limit (critical alarm), MySirius triggers the alert, documents the event and identifies the potentially impacted batch.

Trend analysis and early drift detection
The trending module detects progressive drifts before they reach regulatory limits. Control charts are automatically generated for each parameter and each zone.

Automated batch report
At batch closure, MySirius automatically generates the environmental production conditions report, ready for quality review and release. What previously took several hours is completed in a few minutes.

✓ Field result: across JRI deployments in the pharmaceutical industry, the time spent reviewing environmental conditions during batch release has been reduced by 75% on average. Quality teams focus on deviation analysis, not data collection.

ⓘ The link between production batch and environmental conditions is an explicit requirement of the revised EU GMP Annex 1. An EMS that cannot establish this link automatically and traceably constitutes a documentary gap during FDA and EMA inspections.

CHAPTER 6

From Deployment to Sustainability: A Lifecycle Approach

The qualification of a controlled environment follows a progressive logic, governed by GMP and ISO 14644. It is not limited to commissioning: it is part of the entire lifecycle of the installation.

VALIDATION & QUALIFICATION

QC/DQ
Verify the design: applicable functional and technical requirements.

QI/IQ
Confirm correct installation.

QO/OQ
Validate system operation under intended conditions.

QP/PQ
Demonstrate continuous performance in real operation.

Mapping: admissible evidence in audit

A cleanroom mapping only has value if it is carried out under representative conditions of use.

10-year sustainability: the 4 key areas to anticipate

- Hardware maintenance: breakdowns and equipment replacement
- Metrology: calibrations and probe rotations
- Requalifications: regulatory changes and team training
- Software: updates and historical data compatibility

ⓘ **JRI Expert Advice - Alert thresholds: a metrological decision, not an IT one**

Alert and action thresholds are defined by the quality manager based on mapping data (mean ± 3 sigma), with sufficient margin before the action limit.

A well-configured threshold detects nascent drifts. A poorly configured threshold generates either alarm saturation or a false sense of compliance.

CHAPTER 7

Three JRI Deployments, Three Field Lessons

Hospital Pharmacy Unit (PUI)

Context : A hospital pharmacy preparing 30,000 chemotherapy bags per year in ISO 5 / Grade A under isolator.

Initial problem: The most critical parameter (differential pressure) was also the least monitored.

JRI solution deployed: Continuous monitoring of 100% of critical parameters: T°, RH and ΔP.

Observed results: Audit preparation reduced from 3 days to 4 hours, 2 pressure drifts detected before production impact, compliance maintained with **NF ISO 15189** certification.

Key lesson: Monitoring the most critical point first immediately changes the level of risk control.

Pharmaceutical Industry

Context: Grade A/B aseptic filling lines required to remain aligned with international regulatory requirements.

Initial problem: Bringing an EMS into compliance with **EU GMP Annex 1** and **Annex 11** without starting from scratch.

JRI solution deployed: Integration of existing equipment via **Modbus** and structuring of metrological traceability.

Observed results: Zero critical observation at the following FDA inspection, 0 expired calibration deadlines since deployment, 75% time saved on metrological documentation, 100% of particle counters integrated without replacement.

Key lesson: The value of an EMS depends as much on its architecture as on its documentary compliance.

Medical Devices - Multi-site

Context: 3 production sites for Class III implantable medical devices, certified ISO 13485 and subject to the requirements of European Regulation EU MDR 2017/745.

Initial problem: Each site saw part of the reality, but not the cross-site drifts.

JRI solution deployed: Unified real-time monitoring of 3 sites to consolidate data and alarms. et les alarmes.

Observed results: 60% time saved on notified body audit preparation, chronic thermal drift detected, HVAC reconfigured, return on investment achieved in 14 months.

Key lesson: Multi-site standardisation makes visible anomalies that an isolated site cannot detect.

Lesson 1

The most critical is not always the best monitored: integrating differential pressure had the most immediate impact on risk control.

Lesson 2

Integrating existing equipment via Modbus avoids heavy investment while accelerating compliance. The value of an EMS also lies in its architecture.

Lesson 3

Standardising tools across sites not only facilitates audits: it makes visible anomalies that an isolated site cannot see.

JRI and the MMS Group: Global Expertise for Controlled Environments

JRI designs and deploys environmental monitoring solutions for pharmaceutical industries, medical device manufacturers and healthcare facilities, throughout Europe. A member of the Metrology & Monitoring Solutions (MMS) Group, JRI relies on an ISO 17025 accredited laboratory and field teams specialised in GMP environments.

ⓘ The MMS Group (Metrology & Monitoring Solutions) brings together specialists in industrial metrology and connected monitoring. This structure enables JRI to offer complete solutions, from sensor design to regulatory qualification, including deployment and long-term maintenance.

MMS - Metrology & Monitoring Solutions

JRI Beyond the measure

Design, manufacture and maintenance of sensors, radio receivers and MySirius software.

ISO 17025 accredited laboratory. EMS deployments in France and internationally.

CIET Pharma Metrologie · Qualification

Entity specialised in qualification services (IQ/OQ/PQ), mappings and EMS deployments for the Benelux and Northern Europe markets. Field expertise in pharmaceutical environments and medical devices.

JRI TMI

Qualification and validation tools for measuring equipment.

Complementary to the EMS offering for projects requiring a complete lifecycle approach.

CONCLUSION

The Future of Predictive Environmental Monitoring

Cleanroom monitoring is entering a new phase. The 2026 regulatory framework, driven by Annex 1 and ISO 14644-5:2025, is accelerating the transition from a control logic to a preventive, then predictive approach.

2026

The regulatory framework strengthens requirements for control, traceability and investigation.

2026 - 2030

Artificial intelligence enriches environmental data analysis to automatically identify contamination sources and anticipate drifts before they impact production. JRI is fully committed to this direction.

Towards predictive monitoring

The EMS of tomorrow does not merely measure and alert: it anticipates, correlates and recommends, while remaining an independent system in control of its data.

> *Regulatory compliance in cleanrooms is never a fixed state. It relies on continuous monitoring, rigorous metrology and constant improvement of practices. With JRI, your compliance is never an achievement, but a permanent commitment.*

Ready to take your EMS to the next level?

Contact us :
info@group-mms.com | jri-mms.com