Environmental Monitoring Systems

Eurotherm®

Digitalize environmental monitoring aiding Life Sciences regulatory compliance

Digital Engineered Solutions for Environmental Monitoring Systems adopting industry best practices.
Designed to aid compliance to FDA 21 CFR Part 11, EudraLex Annex 11, and Good Practice guidelines.

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Life Sciences regulatory compliance

Monitoring storage and production environments typically requires regulatory compliance and demands safe and effective systems to protect a pharmacy's livelihood and patient health. FDA current good manufacturing practice (CGMP) regulations make sure that a pharmaceutical "product is safe for use"[1]. EMA GMP requires that medicines "are appropriate for their intended use"[2].

Regulatory bodies including the FDA (US), EMA (Europe), CDSCO (India), NMPA (China), MHRA (UK) and ANVISA (Brazil), as well as global institutions and associations like the WHO, ISPE, PIC/S, emphasize the need for accurate measurement, data integrity, and secure recording of critical process parameters (CPP). This requirement exists for pharmaceutical laboratories and manufacturing environments.

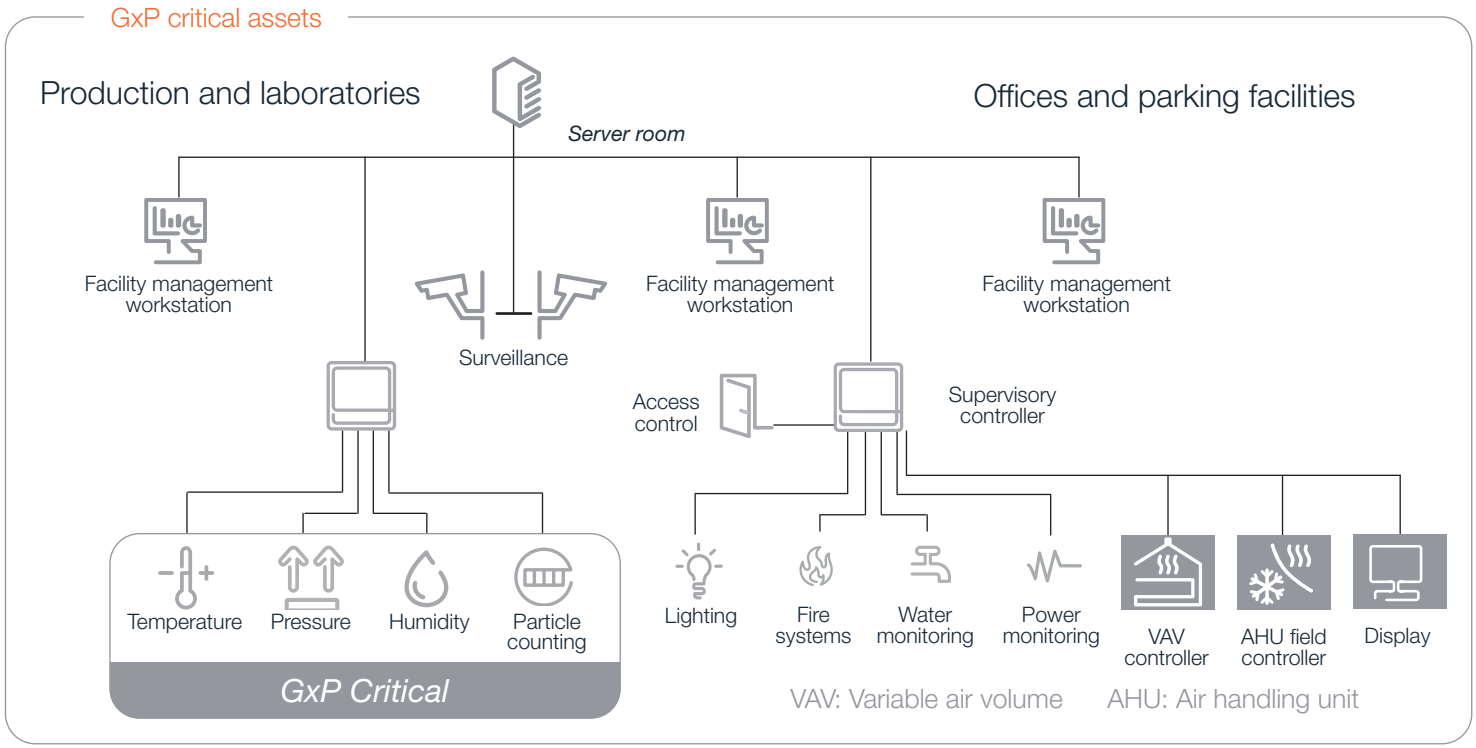
If data recording is electronic, FDA 21 CFR Part 11 and EudraLex Annex 11 apply. Recorded data should comply with ALCOA+ principles for data integrity as specified in:

- FDA 21 CFR Part 211, 68, 188, and 192
- EudraLex Vol. 4, Chapter 4, Guidelines
- EudraLex Vol. 4, Annex 17, Real time release testing and parametric release
- EudraLex Vol. 4, Chapter 4, Guidelines
- MHRA Guidance on GxP data integrity
- WHO Guidance on good data and record management practice

A traditional approach

Traditional facility management systems use a building management system (BMS) to serve GxP[3] and non-GxP areas. This choice can lead to:

- Higher CapEx for engineering, qualification, and validation
- Significant OpEx, since ongoing system maintenance and improvements may require high overheads for calibration, risk assessment, and change management



[1] **FDA current good manufacturing practice regulations.** Content as of 21 September 2020.
[2] **EMA good manufacturing practice.**
[3] GxP is a general abbreviation for "good practice" where the "x" stands for different areas of activity like: M for manufacturing, L for laboratories, D for documentation, E for engineering, C for clinical, and others.

An optimized approach

ISPE guidance[4] suggests considering the segregation of the:

- Building management system (BMS)
- Environmental monitoring system (EMS)
  The BMS includes the heating, ventilation, and air conditioning (HVAC) systems, and should be implemented following good engineering practice (GEP). In contrast, the EMS should be implemented in accordance with good manufacturing practice (GMP) required by regulatory bodies[5].

EMS implementation typically requires full qualification and validation activities.

BMS – Implemented according to GEP

- Controls the environment conditions
- Manages calibration according to engineering best practices
- Provides alarm and event management
- Provides recording and reports as required
- Delivers energy optimization and sustainability targets

EMS – Implemented according to GMP

- Monitors and records CPPs and events for manufacturing environments, critical equipment, and warehouse
- Provides warnings and alarms for conditions out of specification
- Manages calibration according to GMP requirements
- Provides electronic records and audit trail for all critical parameters
  Provides reports as specified
- Complies with electronic signature requirements (FDA 21 CFR Part 11 and EudraLex Annex11)
- Complies with data integrity ALCOA+ principles

[4] Cf. ISPE GAMP Forum Position Paper "Use of Building Management Systems and Environmental Monitoring Systems in Regulated Environment", PE S/O 2005.

[5] A list of the relevant regulations and guidance can be found in additional Eurotherm assets related to EMS.

Digitalize for sustainability and real efficiencies

Paperless environmental monitoring

There is an increasing expectation for the adoption of sustainable business practices. It follows that profitability is also dependent upon sustainability.

Choosing a digital engineered solution represents a way for businesses to be more efficient:

- Helps to reduce the cost associated with multiple paper copies and protected archiving space
- Aids employees to focus on greater value creation by saving their time
- Can make multi-location operating procedures[6] and change reports available for analysis and knowledge sharing
- Helps to ease compliance to best practices
- Represents an essential factor within a strategy to reach net-zero emissions

Digitalization

Digitalization enables greater data utilization. It removes the need for manual data processing and transcription, thus minimizing errors and favoring data integrity.

The availability of digital data and the use of digital technologies provide the necessary conditions to make informed decisions and evolve a business towards more efficiency, safety, and sustainability.

A Eurotherm Digital Engineered Solution (DES) for an EMS can make process data and environment alarms digitally available in readable format for early warnings and historical views. Visualization and analysis of this information can be obtained using graphical recorder displays, Eurotherm Data Reviewer software, SCADA HMI, historian databases, or reporting packages.

Eurotherm Store and Forward technology helps to avoid gaps in the historian database and to support the Data Integrity ALCOA+ principles. Data and contextual metadata is collected and stored at the instrument level (SCADA/HMI controller), and archived on-premises or via cloud storage.

Exception report

When “review by exception” is triggered by the batch records management system, the DES reporting function can identify out-of-specification parameters. The batch review process can be limited to only these events. This helps to release product quicker and with reduced quality control specialist involvement.

Cybersecurity

The use of digital technologies may bring business risks related to cyber threats. Every digital enterprise needs a strategy that reduces and responds to cyber threats.

An effective industrial cybersecurity strategy is typically based on a defense-in-depth approach to achieve multiple physical and digital protection layers.

The Eurotherm EMS DES uses controller and data acquisition products offering communication robustness and user access features. This helps to protect the system from being compromised by cyberattacks.

Efficiency

Systems segregation. Segregating the control system (BMS) from the monitoring system (EMS) offers a more efficient operation:

- Qualification documentation and execution challenges apply to EMS only
- Change control and risk assessment activities are not required for modification to the BMS
- Periodic and sophisticated calibration routines are limited to the EMS
- Record management is limited to the EMS critical parameter data and its contextual metadata

Dynamic reporting. Eurotherm offers a range of solutions to generate reports automatically or on-demand. Users can either adopt standard library reports or create custom reports.

Sensors. Using fit-for-purpose sensors helps repeatability, stability, and accuracy of the EMS and improves the reliability and versatility of the BMS. Duplication of sensors can also be avoided under some architectural designs.

ISPE GAMP® 5 guide: A risk-based approach to compliant GxP computerized systems

To help secure investments and simplify future plant audits, Eurotherm has developed a proven set of validation compliance documents using the ISPE GAMP 5 guidelines. Used in hundreds of installations, these templates can deliver improved confidence during the qualification execution and risk mitigation associated with a validation process. The result can be an opportunity for a reduction in time-to-market of products, as well as a higher probability to decrease CapEx and OpEx throughout the lifetime of your installation.

[6] PIC/S, Good practices for computerized system in regulated GxP environment, PI 011-3, 25 September 2007.

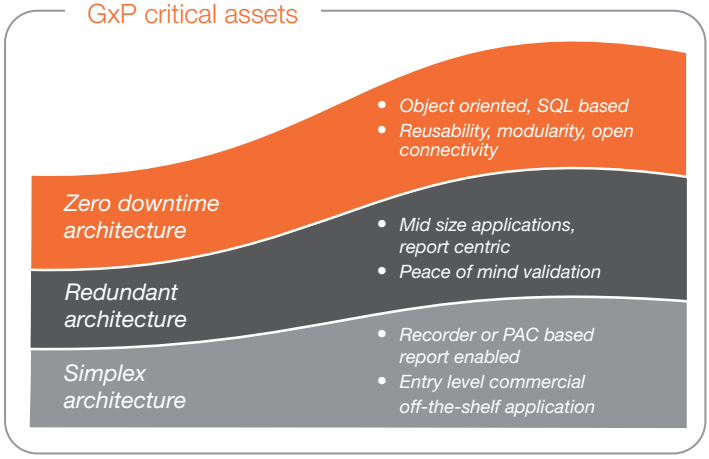
Eurotherm Digital Engineered Solutions for Environmental Monitoring Systems

From simple off-the-shelf solutions to plantwide automation and turnkey projects with full hot-swap redundancy features.

Scalable architectures from room to enterprise-level

From an entry-level architecture based on Eurotherm self-contained recorders, to a high availability architecture including redundant instrumentation, virtualized servers, cybersecure networks, and Store and Forward technology, a Eurotherm EMS DES can deliver:

- User-configurable inputs and outputs (I/O)
- Contextual metadata recorded and stored in proprietary tamper-resistant file format
- Data management supporting data integrity ALCOA+ principles
- Store and Forward technology aids integrity and reliability of electronic archiving
- ISPE GAMP category 3 dedicated function block designed according to ISPE good practice guide
- Configurable alarms (critical, non-critical, or events) with status and management (inhibition, shelfing, delay), including specific reporting displays
- Time synchronization for accurate time and date stamps at the SCADA/HMI control level
- Native and easy-to-use, redundant processor for high process availability, with hot-swap I/O
- Easy-to-read, full audit trail for user management, alarm/alert, and traceability of configuration changes (with online reconfiguration)
- Link to Microsoft® Active Directory for simplified and centralized user management
- Secure File Transfer Protocol (SFTP) client and server for enhanced cybersecurity robustness supporting a defense-in-depth cybersecurity approach
- Eurotherm Data Reviewer/Reporting/Historian/OSIsoft PI interface
- On-cloud or on-premises Historian. Thin or thick workstations with ‘Responsive Design’
- Profibus slave, Modbus master/slave, Modbus TCP communication protocols, OPC-UA capable
- Interface to third party products, e.g., particle monitoring, wireless sensors

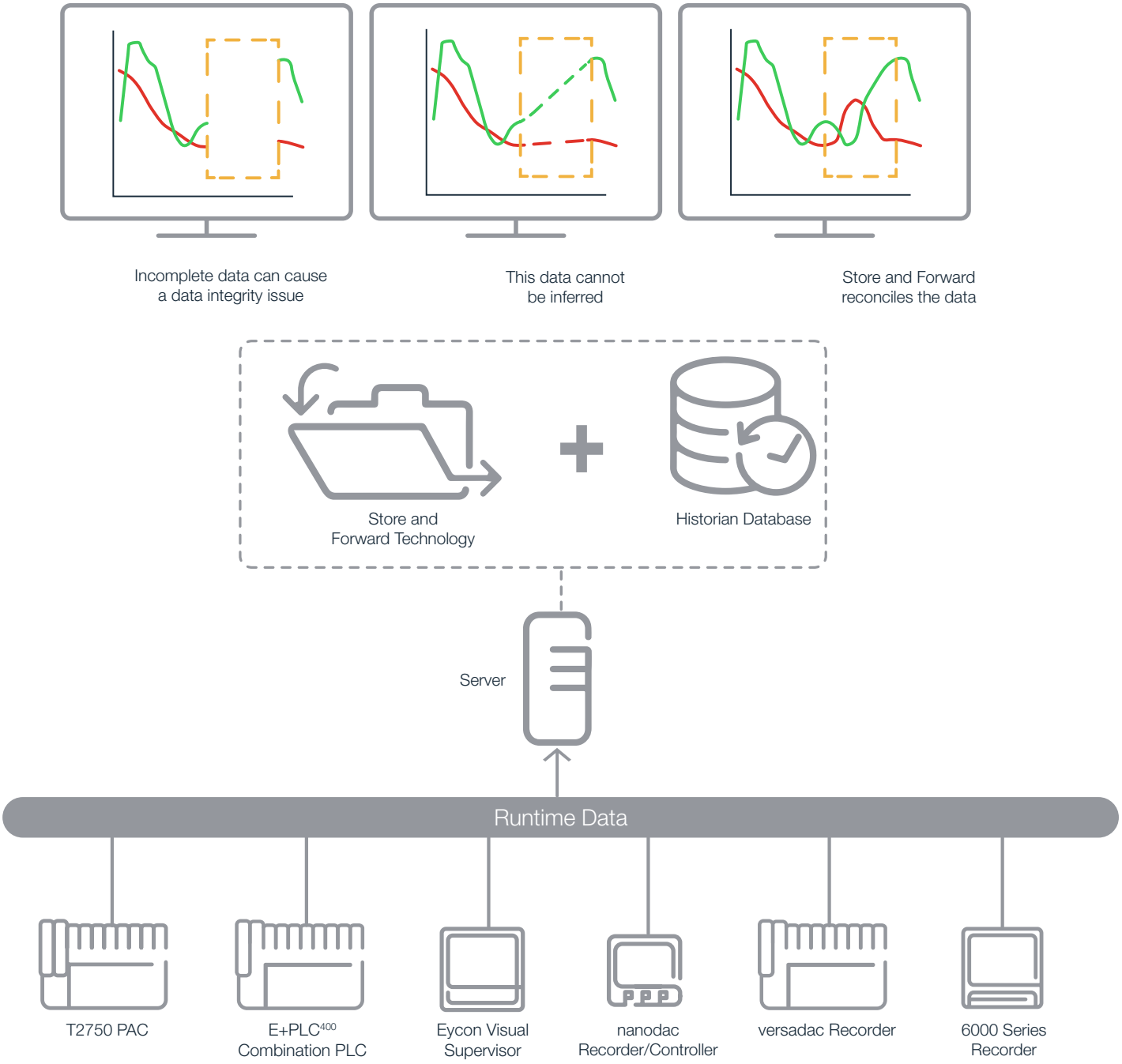


Self-healing data archiving with Store and Forward

Enhanced regulatory requirements demand that GxP critical records comply with ALCOA+ principles to maintain data integrity and quality.

As a trusted advisor to the Life Sciences industry, Eurotherm offers a range of solutions to help maintain data integrity throughout the data lifecycle. Eurotherm recording products record data at the point of measurement for archiving later, reducing the risk of data loss if the server or communications are temporarily lost.

When used in harmony with a historian database, Eurotherm Store and Forward technology aids reliability of archiving by reconciling any missing data to storage databases when communications are resumed. This supports data integrity ALCOA+ principles by providing original and attributable data that is contemporaneous, consistent, and complete.



Plug and Produce

ISPE Special Interest Groups Pharma 4.0 “Plug and Produce” vision

“A global Plug and Produce standard for end-to-end integration enables quality by design (QbD) and data integrity by design through current, new, and emerging technologies for vendor-agnostic connectivity, interoperability, and data analytics.” [7]

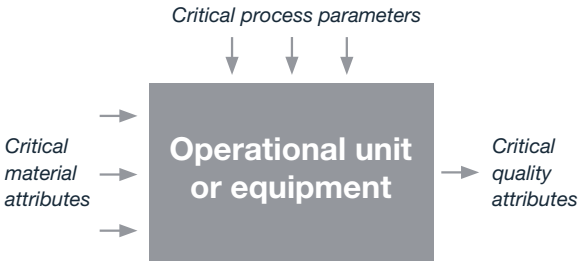
“System implementation and equipment integration are drastically simplified, significantly safer, less costly, and less risky. The user experience is substantially enhanced through increased usability, consistency, and interoperability across systems used in pharmaceutical manufacturing and its support functions, from the sensor up to the long-term data archive.” [7]

> ***By its very nature, a vision is an expression of an aspiration*** [8]

Eurotherm EMS DES embrace this vision through a flexible technology architecture that can deliver operational technology (OT) data processing, contextualized audit trail, alarm deviations, real-time process data, and historical process data. Such data is provided in a format that can serve manufacturing execution system (MES) platforms and analytics services through a range of communication protocols. Additional field measures can be added using a model-based, object-oriented approach (self-instantiation).

Quality by Design

In a QbD approach[9] product quality is continuously monitored and controlled at the earliest stages, rather than waiting for the process to end. QbD includes prior knowledge, risk assessment, process models, and design of experiments (DoE).



Pharmaceutical manufacturers need to identify, control, and validate process variables that could cause a non-compliant result. This can be accomplished by managing the quality target product profile (QTPP), the critical material attributes (CMA), the critical quality attributes (CQA), and the critical process parameters.

As defined by the process analytical technology (PAT) approach, Eurotherm EMS DES can assist in achieving manufacturing efficiencies through data measurement and root causes analysis on CPP deviations, which can produce exception reports and time-stamped evidence for the correlation of parameter behaviors at their occurrence.

System lifecycle support services

Eurotherm products are developed and manufactured under a quality management system to ISO9001:2015. Internal product software development is approved to TickITplus Foundation Level.

Eurotherm has developed a wide offer of services designed to meet the quality standards required by the Life Sciences industry.

- Project design and construction per ISPE GAMP 5 good engineering methodology
- Calibration services
- Service level agreements and global alliance agreements for improved plant efficiency

[7] Pharma 4.0 Plug & Produce Workgroup Charter (Working Draft), ISPE Pharma 4.0 Plug & Produce Working Group, 21 November 2019.
[8] ISPE GAMP RDI Good Practice Guide: Data Integrity by Design, October 2020, paragraph 2.2.1.
[9] Yu L.X., Amidon G., Khan M.A., Hoag S.W., Polli J., Raju G.K., et al. Understanding pharmaceutical quality by design. American Association of Pharmaceutical Scientists 2014 Jul; 16(4): 771–783. PMC Free Article.

Eurotherm US LLC

44621 Guilford Drive, Suite 100
20147 Ashburn, VA
USA

Phone: +1-703-724-7300

www.eurotherm.com

Contact your local sales representative

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