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Life Sciences Automated Environmental Monitoring Systems: Regulations and Guides

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Executive Summary

This document is a compendium of key European and North American rules and regulations governing environmental monitoring of storage and production in the Life Sciences industry

Index

Aim

This document is intended to help identify European and North American rules and regulations for environmental monitoring systems that pharmaceutical storage and production facilities must comply with.

Definitions

Building Management System (BMS) or Building Automation Systems (BAS)

A computerized system that controls, monitors, and optimizes environmental conditions through functions and facilities such as heating, air—conditioning, lighting, and security.[1]

Environmental Monitoring System (EMS)

Monitoring storage and production environments have become a crucial issue within the pharmaceutical industry. The FDA, EMA, and other regulatory bodies require effective control of process parameters: “Lighting, temperature, humidity, air contamination, and ventilation should be appropriate and such that they do not adversely affect, directly or indirectly, either the medicinal products during their manufacturing and storage or the accurate functioning of equipment”[2]. Accurate measurement and storage of room parameters are mandatory. If data recording is electronic, the methods must comply with FDA 21 CFR Part 11, EudraLex Annex 11 or country equivalent.

Critical Process Parameter (CPP)

A processing parameter that directly influences the drug substance characterization or impurity profile in or after a critical step is called a ‘Critical Process Parameter’[3]. Because of this criticality, manual or automatic records must be carefully gathered and archived.

[1] ISPE GPG: HVAC — Page 280, Appendix 13
[2] EudraLex Volume 4, Part 1, Chapter 3 — Premises and Equipment, General (3.3)
[3] ISPE GPG: HVAC — Page 281, Appendix 13

Regulatory Requirements

The criticality of the EMS is dictated by the impact of the monitored process parameters on product purity, safety, quality, and strength (cf. FDA 21 CFR Part 211 — Current good manufacturing practice for finished pharmaceuticals), not by the functionality of the EMS itself.

Environmental monitoring is described and specified by many regulations, guides, and inspections practices. This document contains a list of key references and is not intended to be exhaustive.

This list helps explain why an EMS is so important in the Life Sciences industry. There is almost no pharmaceutical production where environmental parameters are not required to be monitored.

USA Regulations

FDA 21 CFR PART 203 — Prescription Drug Marketing

Subpart D — Samples

203.32 (a) — Drug sample storage and handling requirements. Storage and handling conditions

FDA 21 CFR PART 211 — Current Good Manufacturing Practice for Finished Pharmaceuticals

Subpart B — Organization and Personnel

211.22 (a), (d) — Responsibilities of quality control unit
211.25 (a), (b), (c) — Personnel qualifications
211.28 (c) — Personnel responsibilities; related to access control

Subpart C — Buildings and Facilities

211.42 (c), (d) — Design and construction features
211.46 (b), (c), (d) — Ventilation, air filtration, air heating, and cooling
211.58 — Maintenance

Subpart D — Equipment

211.68 (a), (b) — Automatic, mechanical, and electronic equipment

Subpart E — Control of Components and Drug Product Containers and Closures

211.87 — Retesting of approved components, drug product containers, and closures
211.94 (b) — Drug product containers and closures

Subpart F — Production and Process Control

211.113 (a), (b) — Control of microbiological contamination

Subpart H — Holding and Distribution

211.142 (b) — Warehousing procedures

Subpart I — Laboratory Controls

211.160 (b - 1, 4) — General requirements
211.166 (a) — Stability testing
211.170 (b) — Reserve samples

Subpart J — Records and Reports

211.186 (b - 9) — Master production and control records
211.188 (b) — Batch production and control recipes

FDA 21 CFR PART 600 — Biological Products: General

Subpart B — Establishment Standards

600.11 (a), (e - 3) — Physical establishment, equipment, animals, and care
600.15 — Temperatures during shipment

FDA 21 CFR PART 820 — Quality System Regulation

Subpart G — Production and Process Control

820.70 (c), (e) — Production and process control

EU Regulations and PIC/S equivalents

EudraLex Volume 4 — EU Guidelines to GMP — Part I: Basic Requirements for Medical Products

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Part I (released: February 2022))

Note: PE 009/Part I content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Part I

Ch. 1 — Pharmaceutical Quality System (Jan 2013)
- 1.4 (viii) — State of control
- 1.4 (ix) — Batch release
- 1.4 (xiv) — Root cause analysis
- 1.9 (i) — Adequate facilities
- 1.10 (xi) — Equipment qualification status

Ch. 3 — Premise and Equipment (Mar 2015)
- 3.3 — General
- 3.6 — Use QRM to prevent cross—contamination
- 3.12 — Production area ventilation
- 3.19 — Storage area conditions
- 3.28 — Laboratory conditions
- 3.41 — Equipment calibration

Ch. 4 — Documentation (Jan 2011)
- 4.29 — Documents required — Procedures and records (Other)

Ch. 5 — Production (Mar 2015)
- 5.21 (ii) — Technical measures — Separate HVAC systems
- 5.21 (iv) — Organizational measures — Monitoring of air
- 5.43 — Processing operations: intermediate and bulk products

Ch. 6 — Quality Control (Oct 2014)
- 6.7 (vi) — Documentation
- 6.9 — Data recording

EudraLex Volume 4 — EU Guidelines to GMP — Part II: Basic Requirements for Active Substances used as Starting Materials (into operation: 1 September 2014)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Part II (released: February 2022))

Note: PIC/S PE 009/Part II content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Part II

Ch. 4 — Building and Facilities
- 4.2 (20) — Utilities
- 4.2 (21) — Control of environmental conditions
- 4.4 (40) — Containment
- 5.3 — Calibration
- 5.4 — Computerized systems

Ch. 18 — Specific Guidance for APIs Manufactured by Cell Culture/Fermentation
- 18.1 (15) — General
- 18.3 (31) — Cell Culture/Fermentation
- 18.5 (52) — Separate AHU

EudraLex Volume 4 — EU Guide to GMP — Revision to Annex 1: Manufacturing of Sterile Medicinal Products (released: November 2008, draft version released: February 2020)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 1 — Manufacture of sterile medicinal products (released: February 2022))

Note: PIC/S PE 009/Annex 1 content is identical to EudraLex Volume 4 — EU Guide to GMP — Revision to Annex 1 (version November 2008)

Draft version February 2020

2. Principle
   - 2.2 — QRM principles

3. Pharmaceutical Quality System (PQS)
   - 3.2 — Environmental monitoring excursions

4. Premises
   - 4.1 — Controls and monitoring
   - 4.4 — Four grades of cleanroom
   - 4.12 — Time-based separation
   - 4.13 — Doors for pass-throughs
   - 4.14 — Cleanrooms differential pressure
   - 4.16 — Indicators of pressure differences
   - 4.27 — Cleanroom qualification — airflow direction and other measurements
   - 4.29 — Cleanroom classification, Grade A,B & C (Table 1)

8. Sterilization

9. Environmental monitoring
   - 9.4 — Risk assessments
   - 9.8 — Alert levels and action limits
   - 9.9 — Adverse trends
   - 9.12 — Operating procedures in case of exceeded action limits
   - 9.13 — Batch documentation includes environmental monitoring
   - 9.14 — Non—viable particle monitoring
   - 9.15 — Limits for environmental monitoring of airborne particulate (Table 6)
   - 9.16 — Particle monitoring duration
   - 9.17 — Grade A monitoring (≥0.5 and 5 µm particulates)
   - 9.21 — Size of monitoring samples
   - 9.22 — Occasional indication of macro particulate counts
   - 9.23 — Monitoring conditions such as frequency, sampling volume, or duration
   - 9.24 — Microbial monitoring
   - 9.27 — Continuous viable air monitoring
   - 9.28 — Adoption of automated monitoring
   - 9.29 — Sampling methods
   - 9.30 — Action limits for viable particle contamination (Table 7)

10. Quality Control (QC)
   - 10.1 — Personnel training
   - 10.10 — Product batch certification

Version November 2008

General
   - 1 — Clean areas
   - 3 — Environmental cleanliness level
   - 4 — ISO 14644-1
   - 8 — Cleanroom monitoring
   - 9 — Particle monitoring
   - 13 — Particle concentration
   - 15 — Quality risk management and alert/alarm limits
   - 16 — Temperature and humidity
   - 18 — Aseptic operations

Premises
52 — Doors and warning system
53 — Positive pressure
55 — Air supply warning system, pressure recording

Processing
68 — Process simulation after HVAC changes
73 — Ambient temperature and humidity

PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 2A — Manufacture of advanced therapy medicinal products (released: February 2022)

Chapter 3 — Premises and Equipment
3.5 — Air handling units
3.7 — Pressure continuously monitored
3.8 — Pressure differential monitoring
3.10 — Particle counters
3.11 — Temperature and humidity
3.13 — Level of air monitoring
3.19 — Annex 11 is required

Chapter 5 — Production
5.18 — Pressure cascade
5.23 — Environmental control
5.32 — Controlled environment for seed lots and cell banks
5.36 — Storage temperature monitoring

Chapter 6 — Quality Control
6.10 — Batch release
6.14 — ATPM short shelf life batch certification

EudraLex Volume 4 — EU Guidelines to GMP — Annex 2: Manufacture of Biological Medicinal Substances and Products for Human Use (into operation: June 2018)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 2B: Manufacture of Biological Medicinal Substances and Products for Human Use (released: February 2022))

Note: PIC/S PE 009/Annex 2B content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 2 (November 2008)

Principle
5th paragraph — Appropriate environmental controls

Part A: General Guidance — Premises and Equipment
5 — Environmental control of contaminants
6 — Manufacturing and storage environmental classifications
8 — Multi-product facility environmental monitoring
12 — Pressure monitoring

Part A: General Guidance — Seed lot and cell bank system
41 — Controlled environment
45 — Storage temperature recording

Part B: Specific Guidance on Selected Product Types
5 — Transgenic Plants environmental conditions

EudraLex Volume 4 — EU Guidelines to GMP — Annex 3: Manufacture of Radiopharmaceutical (into operation: 1 March 2009)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 3: Manufacture of Radiopharmaceutical (released: February 2022))

Note: PIC/S PE 009/Annex 3 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 3 (November 2008)

Premises and Equipment — General
- 16 — Manufacture in controlled environmental areas
- 20 — Calibration
- 23 — Minimize environmental contamination
- 24 — Air pressure control

Premises and Equipment — Sterile Production
- 25 — Environmental cleanliness
- 26 — Pressure control

EudraLex Volume 4 — EU Guidelines to GMP — Annex 5: Manufacture of Immunological Veterinary Medical Products

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 5: Manufacture of Immunological Veterinary Medical Products (released: February 2022))

Note: PIC/S PE 009/Annex 5 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 5

Principle
- 2nd paragraph — Environment protection

Personnel
- 2 — Knowledge of Environmental protection

Premises
- 6 — Environment control
- 11 — Pressure
- 20 — Documentation for pressure gradients

Equipment
- 26 — Recording temperature with alarms

Starting Materials
- 43 — Suitable environment
- 44 — Appropriate temperature
- 60 — Storage temperature of the bulk product before filling
- 63 — Storage temperature of final containers

EudraLex Volume 4 — EU Guidelines to GMP — Annex 6: Manufacture of Medicinal Gases (into operation: 31 July 2010)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 6: Manufacture of Medicinal Gases (released: February 2022))

Note: PIC/S PE 009/Annex 6 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 6

Documentation
- 17 — Cryogenic vessels test
- 18 — Hospital tanks test

EudraLex Volume 4 — EU Guidelines to GMP — Annex 7: Manufacture of Herbal Medicinal Products (into operation: 1 September 2009)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 7: Manufacture of Herbal Medicinal Products (released: February 2022))

Note: PIC/S PE 009/Annex 7 content is to a great extent identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 7

Premises — Storage Area
4 (3 for EudraLex) — Storage conditions

EudraLex Volume 4 — EU Guidelines to GMP — Annex 12: Use of Ionising Radiations in the Manufacture of Medicinal Products

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 12: Use of Ionizing Radiations in the Manufacture of Medicinal Products (released: February 2022))

Note: PIC/S PE 009/Annex 12 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 12

Microbiological Monitoring
46 — Environmental monitoring

EudraLex Volume 4 — EU Guidelines to GMP — Annex 14: Manufacture of Medicinal Products Derived from Human Blood or Plasma (into operation: 30 November 2011)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 14: Manufacture of Medicinal Products Derived from Human Blood or Plasma (released: February 2022))

Note: PE 009/Annex 14 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 14

5. Premises and Equipment
5.2 — Environmental monitoring

6. Manufacturing
6.6 — Temperature recording

EudraLex Volume 4 — EU Guidelines to GMP — Annex 17: Real—Time Release Testing and Parametric Release (into operation: 26 December 2018) and

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 17: Real-Time Release Testing and Parametric Release (released: February 2022))

Note: PE 009/Annex 17 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 17

3. Real-time release testing (RTRT)
3.3 — RTRT strategy integration through the PQS

4. Parametric release and sterilization
4.5 — Environmental monitoring & calibration
4.7 — Required personnel experience
4.14 — Calibration should be traceable
4.15 — Calibration tolerance

EudraLex Volume 4 — EU Guidelines to GMP — Annex 19: Reference and Retention Samples (into operation: 1 June 2006)

(PIC/S PE 009 — Guide to Good Manufacturing Practice for Medicinal Products. Annex 19: Reference and Retention Samples (released: February 2022))

Note: PIC/S PE 009/Annex 19 content is identical to EudraLex Volume 4 — EU Guidelines to GMP — Annex 19

5. Storage Conditions

5.1 — According to Guidance on Declaration of Storage Conditions for Medicinal Products and Active Substances
5.2 — Accordance with the marketing authorization

North America guides

FDA Guidance for Industry — Sterile Drug Products Produced by Aseptic Processing (released: September 2004)

IV. Buildings and Facilities

First and second paragraphs
A. Critical Area — Class 100 (ISO 5) — Sixth paragraph and note 5
C. Clean Area Separation
D. Air Filtration — Second and third paragraphs
E. Design — First and last paragraphs

X. Laboratory Controls

A. Environmental Monitoring
E. Particle Monitoring

XI. Sterility Testing

C. Investigation of Sterility Positives — 3. Monitoring of production area environment
C. Investigation of Sterility Positives — 6. Production record review

XII. Batch Record Review: Process Control Documentation

First paragraph

Appendix 1: Aseptic Processing Isolators

B. Design — 3. Pressure Differential
F. Environmental Monitoring

FDA Guidance for Industry — CGMP for Phase 1 Investigational Drugs (released: July 2008)

V. Recommended CGMP for Phase 1 Investigational Drugs

C. Facility and Equipment

FDA Compliance Program Guidance Manual — Chapter 56 — Drug Quality Assurance — Drug Manufacturing Inspections — Program 7356.002 (into operation: 31 October 2017)

Part III — Inspectional

C. System Inspection Coverage — Facilities and Equipment System — Air handling units, equipment calibration, storage conditions (temperature)

FDA Compliance Program Guidance Manual — Chapter 56 — Drug Quality Assurance — Sterile Drug Process Inspection — Program 7356.002A (into operation: 11 September 2015)

Part III — Inspectional

3.3 — Inspection Approaches — Air handling systems, air pressure balance, and HEPA filtration
3.5 — Quality system — Environmental monitoring alert, alarms, and trend data. Change control for air handling systems and automated BMS
3.6 — Facilities and Equipment System — Appropriate specifications for air filtration, pressure, temperature, and humidity. Continuous monitoring with alert and alarms

3.8 — Production System — Batch record review of environmental monitoring data
3.10 — Laboratory Control System — Environmental monitoring and sampling locations

Attachment A
Environmental monitoring — Non-viable — Environmental monitoring, pressure, temperature, and humidity. Alert and alarm log.

FDA Compliance Program Guidance Manual — Chapter 56 — Drug Quality Assurance — API Process Inspection — Program 7356.002F (into operation: 11 September 2015)

Appendix A — Facilities and Equipment System
Facilities — HVAC qualification and monitoring
Process equipment — Calibration
Laboratory Control System — Calibration, adequacy of equipment and facility

FDA Compliance Program Guidance Manual — Chapter 56 — Drug Quality Assurance — Surveillance Inspections of Protein Drug Substance Manufacturers — Program 7356.002M (into operation: 1 October 2021)

PART III — Inspectional
4. Facilities and Equipment Systems — B. Facilities — (6) Facility Environmental monitoring effectiveness and adequacy

Attachment A: Consideration for Protein Drug Substance Surveillance Inspections
(4) HVAC Systems — Air pressure differential monitoring and alarming
(6) Facility Environmental Monitoring — Are EM data and trends adequate and effective? Alert and alarm management

Attachment B: Highly potent or Toxic Products
1. Process Containment — Adequate pressure differential monitoring

FDA Guide to Inspections of Sterile Drug Substance Manufacturers

III. Facility
First and last paragraphs

VI. Environmental Monitoring
First and last paragraphs

VII. Validation
Seventh paragraph

XII. Packaging
Last paragraph

FDA Guide to Inspections of Microbiological Pharmaceutical Quality Control Labs

IV. Sterility testing
Second paragraph (“The USP points out that the facilities and the environmental monitoring used should be similar to those used for manufacturing product”)

FDA Guide to Inspections of Dosage Form Drug Manufactures — CGMPR'S

Buildings and Facilities [21 CFR 211 Subpart C]

Adequate temperature, humidity, and bacteriological controls

Tablet and Capsule Products

To prevent cross-contamination, each operation should have its own air handling unit
Determine what temperature, humidity, and dust collecting controls are used by the firm in manufacturing operations.
Lack of temperature and humidity controls can affect the quality of the tablet.

Sterile Products

Air — Should be filtered to control particulates. Sterile drugs require handling under HEPA filtering and positive pressure
Environmental Controls — Specifications for viable and non-viable particulates must be established. Out-of-limits test results to be reviewed and possibly included as part of the firm's release procedures

FDA Guide to Inspections Oral Solutions and Suspensions

II. Facilities

Third paragraph — The firm should demonstrate the efficiency of the filtration of the air produced by the HVAC system

FDA Biotechnology Inspection Guide

Ascites production

A.2 — Animal quarters and cages must be kept in sanitary conditions
B.3 — There should be written procedures that describe the storage conditions for ascites

Extraction, Isolation, and Purification

F — Microbiological quality of the environment requires controls and monitoring
Processing and Filling
C — Filling should include an adequate environmental monitoring program

Environmental Coverage

A — Environmental assessment
B — Inspection approach

Health Canada GMP guide for drug products (GUI-0001, released: July 2020)

C.02.004 — Premises — Interpretation

3.f — Maintain air quality
4 — Temperature and humidity
7 — Validation Master Plan should include HVAC
11 — Quality risk management

C.02.007 — Sanitation — Interpretation

2.i — Environmental monitoring procedures — define alert and alarm limits

C.02.007 — Sanitation — Interpretation

4 — Transportation and storage conditions

C.02.011 — Manufacturing control — Interpretation

6 — Temperature excursion
17 — Check measuring devices
27. j — Manufacturing master formula
29. k — Packaged product

International harmonisation guides

PIC/S PE 005 — Good Practice Guide for Blood Establishments (released: 1 June 2021)

E. GPG for Blood Establishment and Hospital Blood Banks

1.2.10 — Validation
1.2.12 — Change control
1.3.1.1.2.2 — Adequate premises and space
3.1.2 — Premises utilities
3.1.6 — Air-control facilities
3.4.3 — Special provisions
3.5.5 — Storage conditions
4.1.3 — Equipment qualification
4.1.21 — Calibration
4.2 — Data Processing system
4.7.2 — Calibration and monitoring of equipment
7.3 — Storage conditions

PIC/S PE 008 — Explanatory notes for pharma manufacturers on the preparation of a Site Master File — Annex: Content of Site Master File (released: January 2011)

4. Premises and Equipment

4.1.1 — Description of HVAC systems

PIC/S PE 011 — Guide to Good Distribution Practice for Medicinal Products (released: 1 June 2014)

3. Premises and Equipment

3.1 — Acceptable temperature limits
3.3.1 — Environmental factors
3.3.2 — Temperature mapping and monitoring
3.4 — Equipment
3.4.2 — Calibration
3.4.3 — Alert and alarm management
3.4.5 — Calibration records for key equipment and temperature and humidity recording devices
3.5 — Computerized systems

5. Operations

5.5.1 — Storage. Medicinal protection

6. Complaints, Returns, and Product Recalls

6.3.3 — Temperature storage conditions

9. Transportation

9.1.1 — Ensure temperature conditions
9.2.2 — Handling of temperature excursions
9.2.5 — Temperature control and monitoring — Calibration
9.4.3 — Temperature-controlled containers
9.4.4 — Temperature—controlled vehicles. Temperature mapping
9.4.5 — Temperature storage conditions

PIC/S PI 005 — Recommendation on Guidance on Parametric Release (released: 25 September 2007)

Appendix I — Recommendations for a general sterility assurance system for terminally sterilized products and provisions for parametric release

5.2 — Primary focus on control of pre-sterilization bioburden — Environmental control plays a relatively small part
5.11 — The relevance of environmental control of the filling area should be evaluated and inspected accordingly

PIC/S PI 007 — Recommendation on the Validation of Aseptic Processes (released: 1 January 2011)

2. Introduction

2.3.1 — General information — The annex includes requirements, standards, and recommendations for monitoring the environment

3. Definition

Alert limits applied to environmental monitoring.
Environmental monitoring program

4. Process simulation test procedures

4.1.3 — General comments — Environmental monitoring use to detect anaerobic microorganisms

7. Environmental and personal monitoring

7.1.1 — Air Borne Microbial and Non-viable Particle Monitoring — Monitoring activity should not compromise the product quality
7.3.1 — Microbial Monitoring — Use methods identified in Annex 1 of the EU/PIC/S GMP guide

8. Staff training

8.5 — Environmental monitoring personnel should understand the risks associated with the source of contamination

PIC/S PI 012 — Recommendation on Sterility Testing (released: 25 September 2007)

8. Sterility Test Facilities

8.1.2 — Air Supply — Request for audible and visual alarms, plus recording for differential pressure monitoring

10. Environmental monitoring

10.1 — Sampling methods (active air sampling; settle plates; surface contact plates, swabs or flexible film; hand plates)
10.2 — Operational conditions
10.3 — Written procedures

ICH Q7A GMP Guide for Active Pharmaceutical Ingredients (released: 10 November 2000)

4. Buildings and Facilities

4.20 — HVAC should be qualified and adequately monitored
4.21 — Provide adequate ventilation, air filtration, and exhaust systems. Include control for air pressure, temperature, dust, microorganism, and humidity
4.40 — Dedicated air handling equipment should be employed for the production of highly sensitizing materials

5. Process Equipment

5.30 — Equipment should be calibrated according to written procedures and an established schedule
5.31 — Equipment calibrations should be performed using standards traceable to certified standards, if existing.
5.32 — Records of these calibrations should be maintained.
5.33 — The current calibration status of critical equipment should be known and verifiable.
5.34 — Instruments that do not meet calibration criteria should not be used.
5.35 — Deviations from approved standards of calibration on critical instruments should be investigated

10. Storage and Distribution

10.10 — Materials should be stored under appropriate conditions (e.g., controlled temperature and humidity when necessary). Records should be maintained.

11. Laboratory Controls

11.50 — A documented testing program should monitor the stability characteristics of APIs, and the results should confirm appropriate storage conditions.

18. Specific Guidance for APIs Manufactured by Cell Culture/Fermentation

18.15 — Appropriate equipment and environmental controls should be used to minimize the risk of contamination.

18.21 — Cell banks should be maintained under storage conditions designed to maintain viability and prevent contamination.

18.22 — Records of the storage conditions should be maintained.

18.52 — Open processing should have separate air handling units.

Conclusions

This document is intended to provide a starting point to identify which rules and regulations are referencing the various aspects of environmental monitoring of a pharmaceutical facility.

Analyzing the mentioned points, paragraphs and subparagraphs should help build a comprehensive view of North American and European inspector's expectations.

At the same time, this document can be the foundation to design and build any automated environmental monitoring solution.

For further reference, we recommend reviewing:

- “Environmental Monitoring Systems (EMS): ISPE guidance and best practices” which is a description of how the ISPE Baseline and Good Practice Guides have interpreted the regulations
- “Environmental Monitoring Systems (EMS): Requirements” which gathers the functional requirements for an automated system designed to control and monitor the critical process parameter for environmental monitoring

About the author

Roberto Zerbi is the Global Business Development Manager of the Pharmaceutical segment for Eurotherm. Roberto has spent more than 25 years at Eurotherm, covering various roles: project management, sales, marketing, nurturing partnerships with OEM machine builders, strategy, and digital innovation. His experience ranges from continuous to batch processes, covering the life cycle from detailed design to predictive maintenance. In recent years Roberto has been involved in digital transformation, the impact of innovation on business processes, Quality by Design, and risk management. He is passionate about robotics, artificial intelligence, and cognitive processes. Roberto is a member of the Alumni of the Politecnico di Milano and of the International Society for Pharmaceutical Engineering (ISPE).

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