Is your facility ready for an EMPQ?

ENSURE THE SAFETY OF PHARMACEUTICAL MANUFACTURING

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Introduction

Ensuring the safety of manufacturing pharmaceutical products relies heavily on demonstrating and maintaining control of the manufacturing environment.

In addition to chemical or physical impurities, manufacturers must establish procedures which ensure that products are safe and free from contamination by microorganisms. In many cases, if microorganisms are present, they could potentially lead to harmful effects on patients.

A well-designed environmental monitoring (EM) program allows manufacturers of both non-sterile and sterile products to observe trends in microorganism presence and to identify sources and routes of contamination. The goal of the program is to ultimately prevent future occurrences and ensure patient safety.

Regulations Helping Manufacturers

There are a number of guidelines from regulatory bodies which provide clear guidance for sterile product manufacturing and somewhat less clearly defined guidance for non-sterile production environments.

In either case, regulatory guidance has been established to ensure safe production of pharmaceutical products. For instance, EU Annex 1 and USP <1116> provide guidance on microbiological control and monitoring for sterile products inclusive of training, establishing a sampling plan and sites, and data evaluation. ISO-14644-1 cleanrooms and associated controlled environments provides more specific information related to particle counts.

ISO-14644-1 Dictates:

- The requirements to design, validate, and operate a cleanroom
- Information on the selection of sample locations and establishes requirements for air cleanliness and classification based on particle count recoveries
- Formulas needed to determine how many non-viable particle counts are required to qualify a cleanroom space for all ISO classifications
- Criteria established for particle size ranging from >0.1 micron to >5.0 micron

Additional literature from non-regulatory organizations, such as PDA's TR 13 Fundamentals of an Environmental Monitoring Program, also provide helpful strategies for establishing effective and efficient EM programs.

The EMPQ Process

An important step in developing a robust EM program is performing an Environmental Monitoring Performance Qualification (EMPQ). An EMPQ utilizes a multi-phase approach to collect data and establish long term, ongoing environmental monitoring.

Data generated represents the cleanliness of the facility and the ability for manufacturing processes to operate within the intended room classifications. Performing an EMPQ correctly is critical because an ill-prepared EMPQ execution could lead to downtime and higher costs.

The EMPQ is most successfully performed when a well-written plan is created. With the current standards in place, there are no regulations on how long an EMPQ should last, but experts recommend three days of static and dynamic testing, each, for viable and non-viable particulate testing.

STEP 1: BASELINE

Each EMPQ program begins with a baseline performed after the facility construction is completed and an initial cleaning regimen of the space has occurred. Azzur Consulting Services is a resource for cleaning validation master plans and partners with Azzur Labs to perform cleaning validations and disinfectant efficacy studies.

STEP 2: STATIC TESTING

Once the initial cleaning is completed, static testing is conducted. During static testing, there are no people present in the room except for the sampling technician(s); however, all the equipment is on.

STEP 3: DYNAMIC TESTING

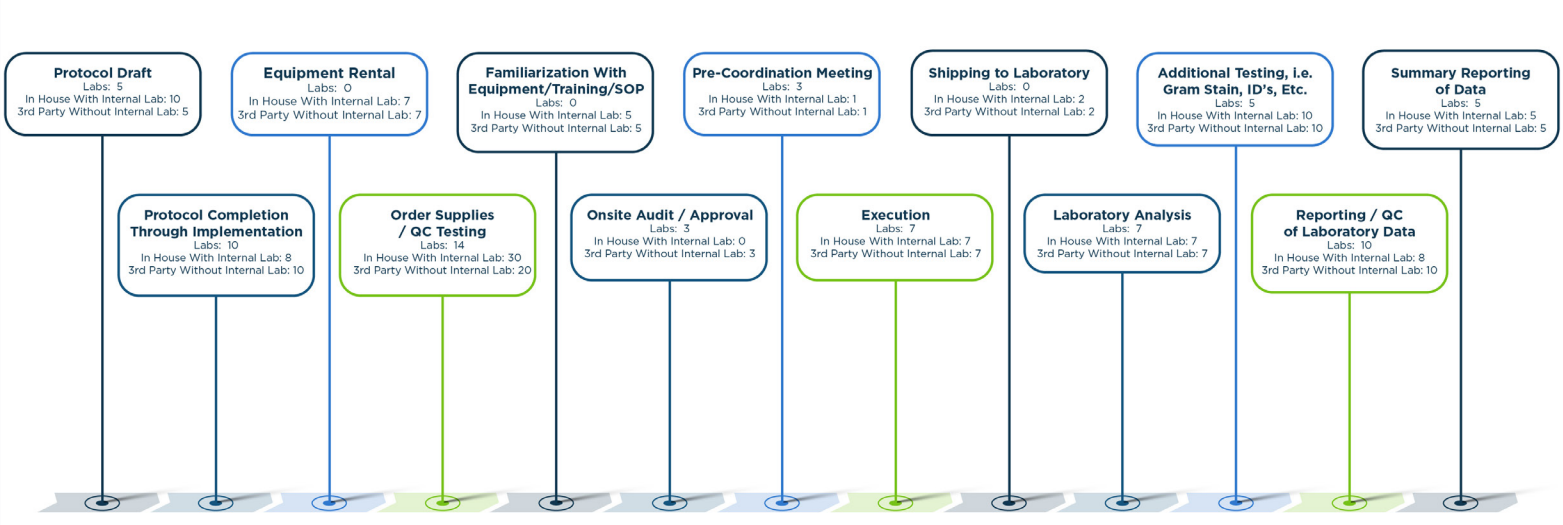
After three days of static testing, another cleaning is performed and the EMPQ moves onto three days of dynamic testing with people, processes, and equipment running.

The EMPQ Timeline

The entire length of the process is based upon the size of the facility, number of rooms, number of samples, and the number of employees the client has available.

To minimize downtime, utilizing weekends and holidays is often recommended. Considering all these aspects, it is reasonable to estimate that a full EMPQ could take between one to four months to complete. An example timeline for the stages of an EMPQ is shown below.

As shown in the figure, the time associated with each phase is dependent upon the resources and experience available. We have found that the EMPQ can proceed faster when a lab such as ours, with their own equipment, trained sampling technicians, and experienced laboratory staff, performs the EMPQ compared to when the EMPQ is conducted entirely in-house by organizations that need to invest in people and equipment.



While EMPQ is simple on the surface, the EMPQ activity requires extensive coordination between multiple groups within and among organizations.

Time is important, as speed to market is critical for product release. If feasible, performing the EMPQ on consecutive days is beneficial but does require additional approvals and coordination. Site leadership must ensure that sampling technicians have access to the building on the weekend, and staff must be on site and available on days when dynamic testing is occurring. Depending on the number of rooms being qualified, this could require a significant number of individuals.

Is Your Facility Ready?

Aside from the granular technical aspects of EMPQ planning – selecting media types, identifying the sampling locations, ensuring air samplers are calibrated and qualified, and creating maps for sampling technicians to follow - there are more high-level questions that should be answered before undertaking an EMPQ.

- **Are owners for the processes within the EMPQ defined?**
  Ensuring all involved know their roles and responsibilities will expedite decisions, reviews, and execution.
- **Is there agreement from all stakeholders on the required condition of building during EMPQ and when to start?**
  Clear alignment of building readiness is required to prevent resampling.
- **Has there been an on-site visit by any external contractors/consultants prior to the start?**
  Getting eyes on site will often reveal problems that need to be addressed prior to the beginning of the EMPQ.
- **Is the cleanroom in "ready" condition with furniture, instrumentation, and machinery installed and building monitoring systems fully operational?**
  If an EMPQ is performed prior to the room being ready, it will have to be redone after everything is installed.

Once these strategic questions are answered, the more tactical ones can now be addressed. At Azzur Group we have years of experience ensuring the EMPQ process proceeds smoothly from start to finish.

We've even prepared a detailed EMPQ Preparedness Checklist which outlines some of the most important items that need attention prior to starting any EMPQ.

How to Get Started

The process of beginning an EMPQ can seem like a significant task. However, if it is broken down into smaller parts, it is more easily accomplished.

We recommend familiarizing yourself with the existing regulations, paying close attention to recent changes that have occurred, performing risk assessment if necessary, and alignining with the management team on the goals and timeline for the EMPQ. Below, we outline seven key considerations to help move from EU Annex 1 2009 and comply with the current EU Annex 1 in 2023.

1: KNOWLEDGE

Support the collective knowledge management efforts to improve and update codified knowledge found in documents and databases.

2: GAP ANALYSIS

A gap analysis of changes between different versions of the Annex 1 should be performed at site-level, ensuring Quality Risk Management (QRM) is included in all aspects of the manufacturing process.

3: IMPROVEMENTS

Sites with the current barrier technologies (isolator and RABS) will require process improvements to meet new requirements.

4: CLEANROOM UPDATES

Cleanroom processes and practices, such as gowning, may require changes depending on the previous interpretation and implementation of the Annex 1 requirements.

5: TRAINING

Cleanroom operators should recieve aseptic training, gowning qualifications, and assessment on the relevant manufacturing processes regularly.

Additionally, all personnel entering cleanrooms should have access to training in hygiene, cleanroom best practices with summative assessments.

6: REVIEWS

Evaluate the impact of the Annex 1 changes to the aspects of the Contamination Control Strategy (CCS) with an ongoing periodic review of the Performance Qualification System (PQS).

7: CLEANROOM ASSESSMENT

Assess cleanroom design, qualification, and validation as they relate to the personnel and material flow to ensure current practices meet new requirements.

As always, you can connect with leading industry experts who can help accelerate your EMPQ execution. With years of experience, organizations like Azzur Group, can help you get to market faster while ensuring safe product manufacturing. For more resources on the topic of EMPQ, visit our website.

About Azzur Group

From Discovery to Delivery™, Azzur Group provides the life science community full life-cycle solutions for all of their GxP needs.

From Azzur Cleanrooms on Demand™ facilities, to our labs, training centers, and consulting offices across the nation, Azzur Group helps organizations start, scale, and sustain their growing enterprises. With nearly four decades of service to the life science community, we have become a trusted partner to the world's leading pharmaceutical, biotechnology, medical device, and healthcare companies, as well as their supply chain.

For more resources on this topic, or to learn about solutions Azzur Group provides to organizations in the life science community, visit azzur.com/services/laboratory-services/environmental-monitoring-and-performance-qualification.

About the Authors

About the Author: Todd McEvoy

Todd has 20 years of hands-on experience with complex scientific output, lab training, and management. As VP of Lab Testing Services, he oversees all aspects of the Azzur Group laboratory business line including P&L management, development and implementation of new testing and technology, and training and coaching of employees.

Prior to joining Azzur, Todd served as general manager of an analytical laboratory specializing in method development and problem solving for the specialty chemical and polymer markets. Todd is an editorial advisory board member for Lab Manager Magazine, as well as a Youth Association Coach for basketball in South Parkland, PA.

About the Author: Erin Thane

Erin Thane is a Senior Director Global Operational Excellence for Azzur Group. Starting out as a microbiologist working in a GMP contract testing lab, she has many years of experience working for various pharmaceutical clients at all stages of the EM program implementation.

She has written various risk-based SOP's, designed training programs and consulted with clients in setting up appropriate action plans for exceeded limits. Currently, she is focusing on helping Azzur Labs expand country-wide and enjoys the traveling opportunities this affords and the training of new colleagues.

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