EU GMPs Annex 1: 2022 - New role for microbiologists on pharmaceutical aseptic processes

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Microbiological Pharmaceutical Quality Control Labs

FDA GUIDE TO INSPECTIONS OF MICROBIOLOGICAL PHARMACEUTICAL QUALITY CONTROL LABORATORIES

Note: This document is reference material for investigators and other FDA personnel.

*"Microbiological test results represent one of the **more difficult areas** for the evaluation and interpretation of data. These evaluations require **extensive** training and experience in microbiology. **Understanding** the methodology, and more importantly, understanding the limitations of the test present the more difficult issues."*

Microbiologist role in pharma industry

- The role of microbiologists in pharmaceutical development and pharmaceutical manufacturing has become more visible and important in recent years due to the Quality by Design and Risk/Science-based (ICH Q9 and Process Understanding) approaches promoted by regulatory authorities and industry.
- Microbiology, microbiological control and contamination control are indispensable in the production of sterile and non-sterile products, as well as biological pharmaceutical substances (APIs), as evidenced by multiple conference presentations and publications.
- Lack of sterility assurance is one of the primary reasons for recalls of sterile drug products, and presence of objectionable organisms is the number one reason for recalls of non-sterile products.
- The science of industrial microbiology and its applications have a large impact on microbiological and contamination-control strategies for robust and consistent processes with infrequent failures and contaminations.

"The Pharma Microbiological Function"

- Production workers engaged in contamination control or other, non-laboratory activity of a microbiological nature
- Laboratory microbiologists / analysts
- Production microbiologist /process driven
- Management with oversight: QA, QC, Manufacturing, Validation, Engineering
- Microbiological investigations for process failures or deviations in laboratory/production
- Support engineering department in cleanroom and process design
- Regulatory Investigators

Educating colleagues

- Microorganisms are everywhere
- Challenges to control product and process entry and their multiplication
- Importance of personnel activities in maintaining microbial control
- Importance of process design in maintaining microbial control
- Production personnel need to understand the need for microbiological contamination controls
- Endotoxin/pyrogens risks in the sterile products

Change in Mindset

- Philosophy should be “Quality is everyone’s business”
- Owner of EM & Micro Data?
  - *microbial and total particles environmental data should primarily owned, understood by and seen as the responsibility of QC Microbiologists.*
- Quality & Operations designed a program of awareness to ensure that:
  - *all personnel understood the impact of their actions*
  - *all personnel know the environmental trends of their area.*
- This approach is aligned with the principles of Knowledge Management as outlined in ICH Q10 (Quality System).

Microbiological EM Knowledge Management Principles

- Those that create the total particles and microbiological counts must understand their impact and be responsible for their results.
- As "the microbes don't wait", we need to utilise "Real time Quality" in Microbiology.
- Deliver results to owners ASAP to enable an immediate response via scheduled documented meetings that are an integral part of the Quality System.
- Increase everyone's general Microbiology knowledge:
  - *"Everyone making our products should be a 'Microbiologist".*

How to move forward?

Some proposals

1. EDUCATION

- Introducing pharma microbiology science in secondary school.
- Redesign university courses to include pharmaceutical microbiology courses (for example two years of specialization) with alternative microbiological methods evaluation.
- Collaboration within university and pharmaceutical/medical devices companies for master courses, thesis or training internship.
- Improve the knowledge of pharmaceutical microbiology in regulatory and inspection bodies by specific education courses and programs.
- The pharmaceutical microbiologist must be continuously scientifically updated on aseptic processes and production methods.

2. INNOVATION/RESEARCH & DEVELOPMENT

- To study/evaluate new analytical technologies of microbiology at the research and university level.
- Collaboration between pharmaceutical industries and academic bodies in the development of “state-of-the-art” microbiological process and analytical methods.
- Close relationship between technology producers, opinion leaders and pharmaceutical companies in the development of new technologies.

3. PHARMACEUTICAL/MEDICAL DEVICES COMPANIES

- Recognize the importance of the role of the microbiologist within the company by the top management.
- Redesign/rethink microbiology laboratories in order to be as close as possible to production depts.
- Innovate the microbiology laboratory with the inclusion of instrumentation/technologies in line with the times
- Include microbiologists in management roles in aseptic manufacturing departments.
- Include microbiologists in aseptic manufacturing engineering teams for new and/or revamping projects.

4. AND TO CONCLUDE

- Microbiologists must be prepared for the challenges that the new Annex 1 places before us and clearly inform senior management about the company's risks of non-compliance with the new Annex 1 from the point of view of controlling microbiological, particle and pyrogenic contamination by proposing technological, design and process solutions.

Murphy's Law of Microbiology (always valid)

"Under the most well-defined conditions of nutrients, temperature, humidity and time, microorganisms will always do what they darn well please, especially when your job depends on it"

Thank you for your attention

Q&A

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