EU GMP Part I Annex 1 draft

12.11.2020

Finnish Medicines Agency
Pirjo Hänninen
10.11.2020

Content

- Schedule
- Content
- Questions??

Annex 1, manufacturing of sterile pharmaceutical products

- Annex 1 draft, second targeted consultation to industry ended in July 2020, prolonged cause of Covid
- 2000 comments https://ec.europa.eu/health/medicinal_products/consultations/2020_sterile_medicinal_products_en
- WHO ja PIC/S joint the drafting group
  - PIC/S Annex 1 second targeted concultation on-goin
  - https://picscheme.org/docview/1985

Annex 1 content

1.Scope

2.Principles

3.PQS, laatujärjestelmä

4.Premises

5.Equipment

Annex 1 content

6.Utilities

7.Personell

8.Production and Spesific tecnhologies

9.Viable and non-viable environmental & process monitoring

10.QC

1.Scope

- Provides guidance to manufacturing of all sterile products using QRM principles
  - So that microbial particulate and pyrogen contamination is prevented in the final product

2.Principles

Key areas:

- Facility, equipment and process design
- Personnel
- Process and monitoring systems

Managed according to QRM principles

CCS= **C**ontamination **C**ontrol **S**trategy

3.PQS = Product Quality system

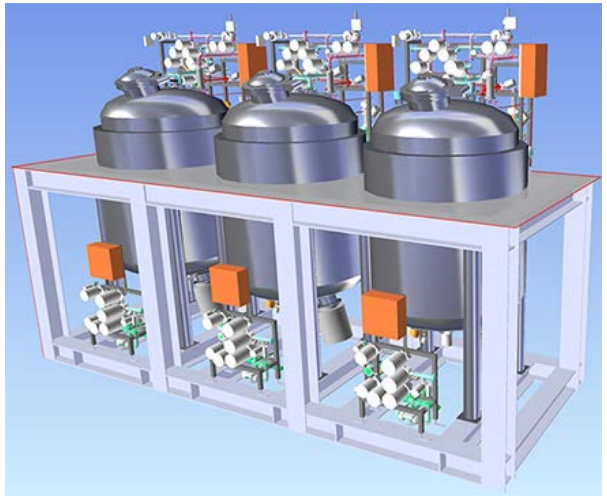
- Effective risk management system is implemented into all areas of the product life cycle
- Non-conformatives/deviations => root cause analysis, impact assessment

4.Premises

- Conducting all non-essential processes outside clean areas
- Reference to Annex 15
- Barrier technologies
- Airlock design (unidirectional flow)
- ISO 14644 implementation (selecting particle locations)
- Disinfection process should be validated

5. **Equipment**

- Highlights the separation of personnel and processes
- Written detailed description of equipment's, reviewed in CCS
- Direct and indirect parts (used in sterile process) should be sterilized



6. **Utilities**

- Direct contact to product , part of the product, contact surfaces
- Minimizing biofilm formation in water systems

Finnish Medicines Agency
Pirjo Hänninen
5.11.2020

7.Personell

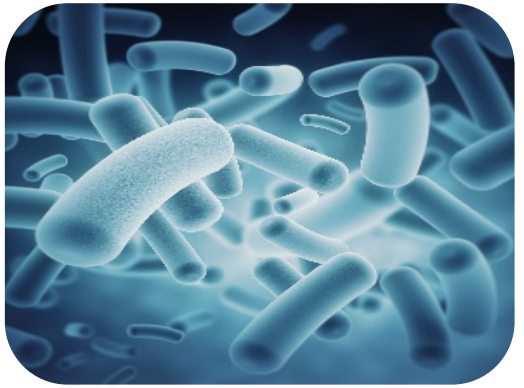
- Biggest section
- All unnecessary activities should be performed outside cleanroom areas (inspection windows etc)
- Training to everyone entering to clean area (qualification and disqualification)
- Electronical devices not allowed, unless supplied by the manufacturer
- Clean room gowning
  - Integrity
  - Goggles
  - Dedicated laundry

8. **Production and spesific technologies**

- More details to production and specific technologies
- PUPSIT (pre-use post sterilization) to all large volume products
- Terminally sterilized and aseptic processes
  - Finishing of sterile products
  - Sterilization
  - Form fill seal , blow fill seal
  - Lyofilization
  - Closed system
  - SUS- single use system

9.Viable and non-viable environmental & process monitoring

- Non viable and viable monitoring
- Aseptic process simulation
- A-grade microbes limits ;no growth



Finnish Medicines Agency
Pirjo Hänninen
5.11.2020

10. QC

- Bioburden and sterility assay samples: samples should be taken to be representative of the worst case scenario.
- Bioburden assay from each aseptic batch and assay from terminally sterilized batch (overkill) on defined
- If it not possible analyze sterility prior final release (e.g. short expiry) , risks should be identified in CCS (mitigate and minimize the risks)

Summary

- The expectation for each facility to have in place a formal, holistic contamination control strategy, focused on minimizing contamination control with respect to sterile manufacturing
- Additional requirements for cleanroom classification (beyond ISO requirements)
- A major focus on risk-based approaches
- Recommendations for the wider use of barrier technology
- A strong focus on personnel controls, such as gowning, and training

Kiitos!

Finnish Medicines Agency
Pirjo Hänninen
10.11.2020