PUPSIT: Embracing the New Challenge in GMP Manufacturing

A Bio Farma Case Study

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PDA Implementation of CCS & PUPSIT Workshop 2024

Regulation
—what we need to know

"The integrity of the sterilised filter assembly should be **verified by** integrity testing before use (pre-use post sterilisation integrity test or **PUPSIT**), to check for damage and loss of integrity caused by the filter preparation prior to use…

EU GMP Annex 1
Point 8.87

"One of the sterile **Drug Product** process control:
Sterilizing filter integrity-tested before **(PUPSIT)** and after use, as required

PDA TR 90
Point 4.2

Regulation

—what we need to know

point, diffusive flow, water intrusion or pressure hold test. It is recognized that PUPSIT may not always be possible after sterilisation due to process constraints (e.g. the filtration of very small volumes of solution). In these cases, an alternative approach may be taken providing that a thorough risk assessment has been performed and compliance is achieved by the implementation of appropriate controls to mitigate any risk of a non-integral filtration system. Points to consider in such a risk assessment should include but are not limited to:

In depth knowledge and control of the **filter sterilisation process**

In depth knowledge and control of the **supply chain**

In depth **process** knowledge

Challenges

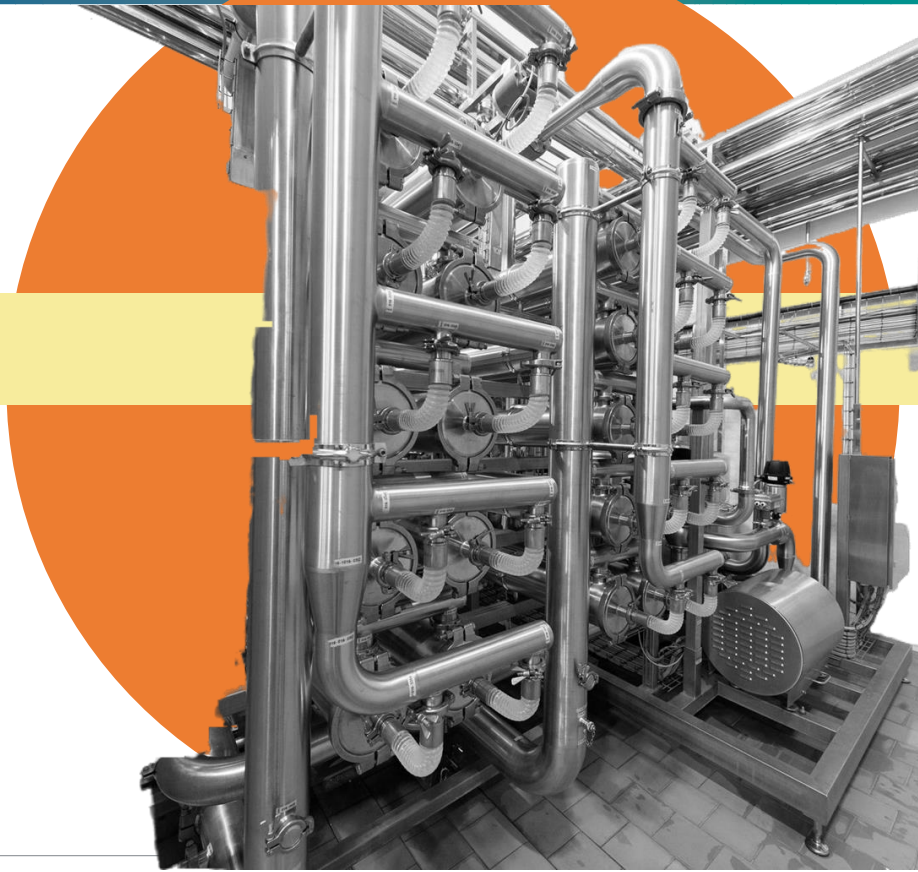
—discovering the difficulties

Facility Design

- For existing facilities with fix piping system → need to conducted **major renovation**
- Implications of renovation: room qualification; aseptic process simulation; process validation

Challenges

—discovering the difficulties



Utilities

- Is there any **use point of compressed air?**
- If there's any CA use point, integrity testing should be performed in accordance with point 8.88 of the EU GMP Annex 1

Challenges

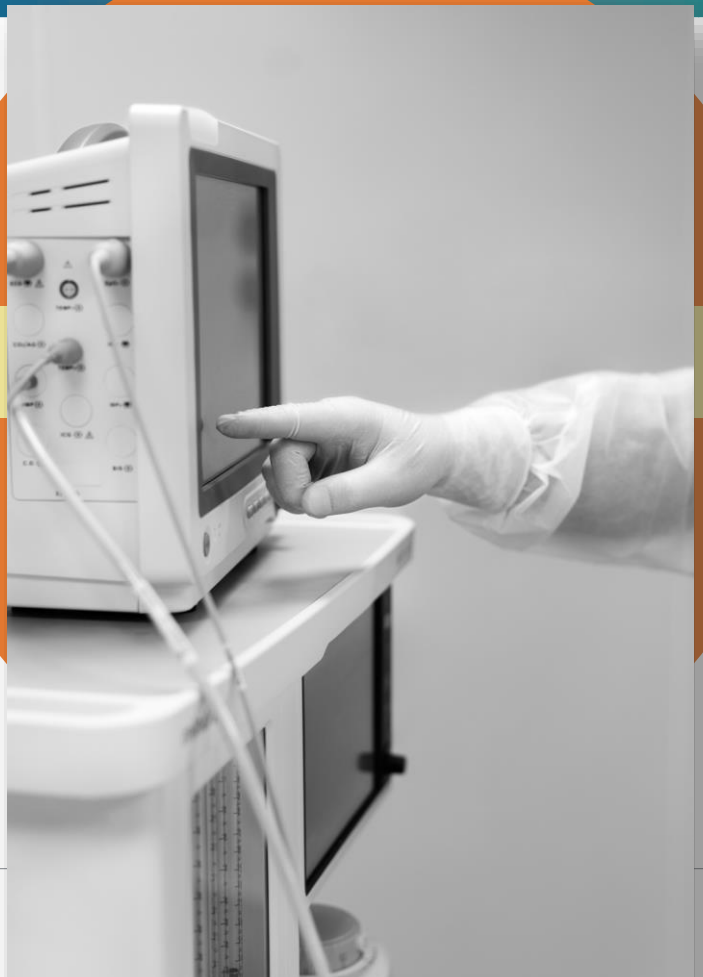
—discovering the difficulties

Wetting Agent

- WFI
- Medium
- Product
- How long will the filters be exposed to the wetting agent?
- Considering to perform preliminary study

Challenges

—discovering the difficulties



Temperature

- What kind of sterilization method is used for the filters?
- For SIP → considering the **risk of filter pore enlargement**

Case Study

—what Bio Farma currently do

Flexible Hoses

- Should be able to endure pressures >50 psi

Validated Wetting Agent

- Products and WFI

Preliminary Study

- Wetting agent medium
- Result: satisfactory

Next Plan

- Validation using medium

Drug Substance (DS)

Case Study

—what Bio Farma currently do

Drug Products (DP)

Fixed Pipe System

- Redesign process
- Determined parameter
- Preliminary study: filter flaw masking; result OK

New Facility

- Already implemented
- Already conducted APS
- Result: satisfactory

Thank you!

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