MHRA
Regulating Medicines and Medical Devices

Parenteral Manufacturing
Annex one a Regulatory Perspective

Medicines and Healthcare
Products Regulatory Agency

Annex 1

Scope

- History and Background
- Process of revision
- Why update
  - General opinions
  - Personal viewpoint
- Summary

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History and Background

- The original version was revised in 1996, 2003, 2005, 2007 and 2009 however there has not been a complete review of the document since it was originally issued
- Since the original issuance and the revisions there have been changes in technologies and significant changes in GMP consequent to the adoption of the ICH Q9 and Q10 guidelines.

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History and Background

- In 2012 The German Authorities (ZLG) issued a concept statement to the EMA's IWG proposing revision of the Annex and a subsequent request was made to PIC/S for support in updating
- 2014 PIC/S Working group was set up and started work in August.
- September 2014 a draft concept paper was re-issued to IWG (by the MHRA) supporting the update.

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Process of revision

- Combined working group (PIC/S and EMA) with a task of assessing the requirements of revision:
  - Update of Question and answer document
  - Revision of the Annex
  - Complete re-write

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Process of revision

- Combined working group with a task of assessing the requirements of revision:
  - Understand Industry concerns
  - Understand Regulatory concerns

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Process of revision

- Draft Concept paper proposed at EMA IWG September.
- Following regulatory comments issue for public consultation

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Why update - General opinions

- New Issues
  - Monograph on WFI
  - Biofilm

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Why update - General opinions

- Better clarification
  - EM how often (especially lower grade areas)
  - What does “Grade A Air supply” mean

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Why update - General opinions

- Ambiguities?
  - Microbiological limits “these are average values”
  - Freeze Drying Para 34 (Grade A or in sealed trays under B) conflicts with para 116 (A at all times

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Why update - General opinions

General points for discussion

- ISO 14644 5.0µm or not?
- Closed systems
- Small batch product such as ATMPS
- Facility
  - Isolators?
  - RABS ?

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Why update - General opinions

General points for discussion

- Filter integrity testing pre use post sterilisation
- Scope – Also applicable to Non sterile manufacturing?
- Bioburden sampling

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Why update My opinions

- People still don’t understand so need more guidance

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Why update - My opinions

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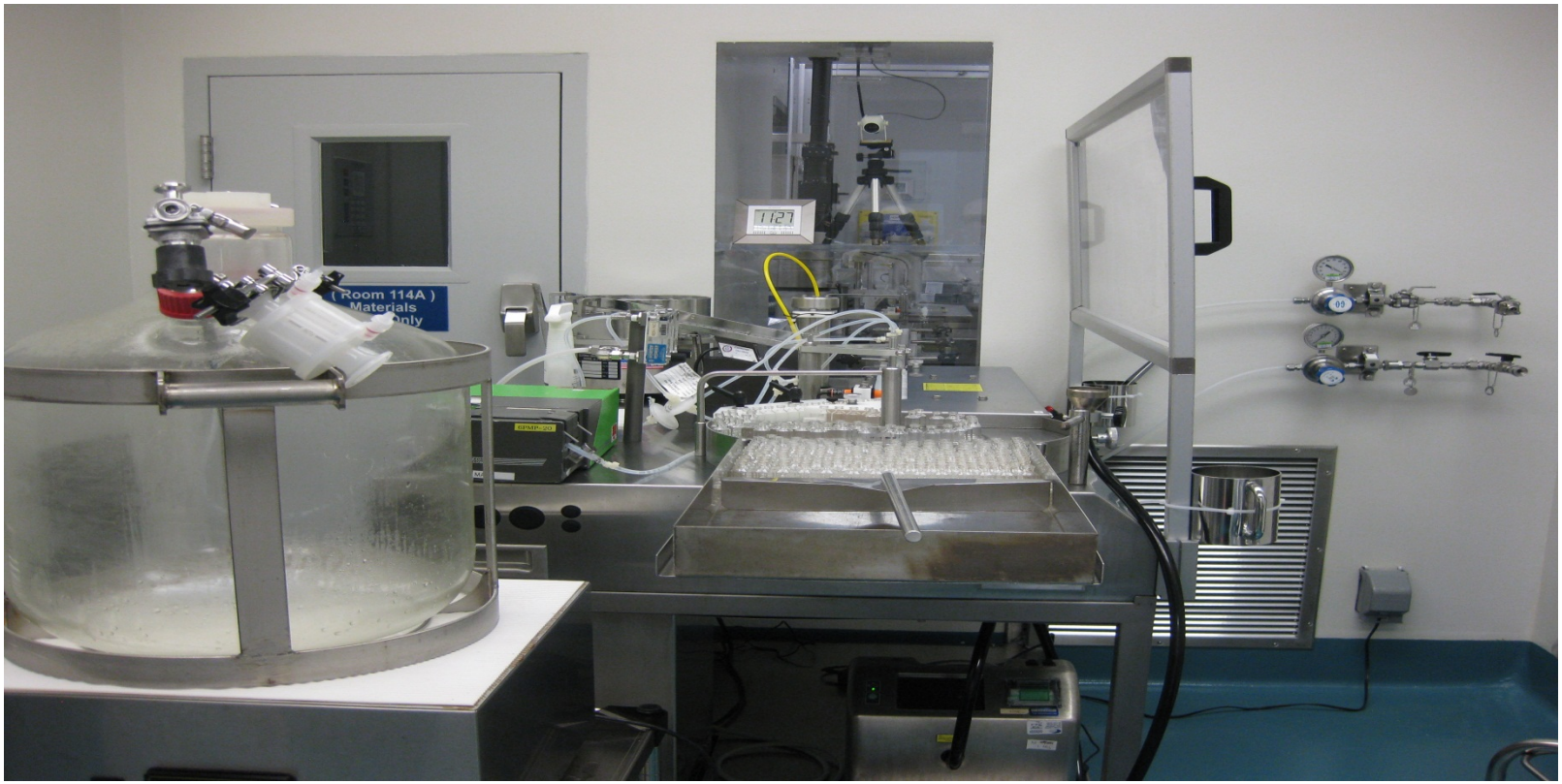
Why update - My opinions



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Why update - my opinion(process design)

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Design of the facility and processes (autoclave load)

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Why update My opinions

- Losing technical skill level
- New and emerging countries where the knowledge has not yet evolved (learning by deficiencies)
- New and emerging technologies
- Areas not covered
  - Media fills, small batches, APIs Campaigns?
  - New BFS technology
  - Closed systems

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Summary

- There are lots of reasons why Annex 1 needs updating
- It is going to happen
- Will be a shared project from PICS and EMA

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Thank you for Listening

Any Questions?

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