Insights from a Former Regulator

Andrew Hopkins

Director of Compliance

AbbVie

PDA Parenteral Drug Association

2023 Annex 1 Workshop Series (Singapore)

CONNECTING PEOPLE SCIENCE AND REGULATION®

Regulatory updates and trends

- Annex 1 (and links to other medicinal products)
- Trends/Expectations
- Challenges

- CTR (Annex 13) effective 2022
- Part IV (Implementation date 22 May 2017
- Annex 2 A (PIC/S)
- Annex 1 (Effective 25 Aug 2023 except Lyo)

- 8.123 Lyophilizers and associated product transfer and loading/unloading areas should be designed to minimize operator intervention as far as possible. The frequency of lyophilizer sterilisation should be determined based on the design and risks related to system contamination during use. Lyophilizers that are manually loaded or unloaded with no barrier technology separation should be sterilised before each load. For lyophilizers loaded and unloaded by automated systems or protected by closed barrier systems, the frequency of sterilisation should be justified and documented as part of the CCS.

Annex 1 (history and main focusses)

- Started in 2014 (really 2012)
- International group including (TGA/ USFDA/ PMDA/ Taiwan FDA)
- Update to give more explanation of current expectations !?
- Introduction of new structure (Classification versus routine monitoring, utilities section, monitoring all together with APS (toolbox concept)
- Introduction of QRM – key element of this is Contamination control strategy (but concept is throughout the document)
- Larger document
- And no, PUPSIT is not new!!!!!!
- Why? - To make sure what we do is safe

Annex 1 (links to other products)

- Scope is open for use for other products (Low Bioburden, Creams and ointments even OSD etc.)
- Non mandatory – but still need to explain what we mean when we use terminology
- E.g. Use a grade A, with grade C background for a low bioburden BDS. Need to explain our rationale, what we include and what we do not include


Annex 1 and ATMPs
• Does Annex 1 apply?

Annex 1 (links to other products)

Annex 1 and ATMPs

- Does Annex 1 apply?
- Part IV of EU GMP specifically states that none of the other GMPs apply (Unless otherwise stated)
- However, some inspectors have stated they will use Part 1 and Annexes as “interpretative” documents
- For PIC/S, Annex 2A is written for ATMPs and states that other parts of GMPS apply

Annex 1 (Trends)

Annex 1, EMA guidance on sterilization of medicinal products, CFR 211.113, USFDA Aseptic guidance 2004

- All have one main overall aim, minimizing contamination risk
- Emphasizing the need to look at Facility, equipment and process design to do this (not, “it is all ok because we did a risk assessment, and the monitoring is great!!!!!!!”):

  “The effectiveness of the aseptic process should be determined through process design, adherence to the pharmaceutical quality system and process controls, training, and evaluation of monitoring data”

  “9.35 APS should not be used to justify practices that pose unnecessary contamination risks”

Annex 1 (Trends)

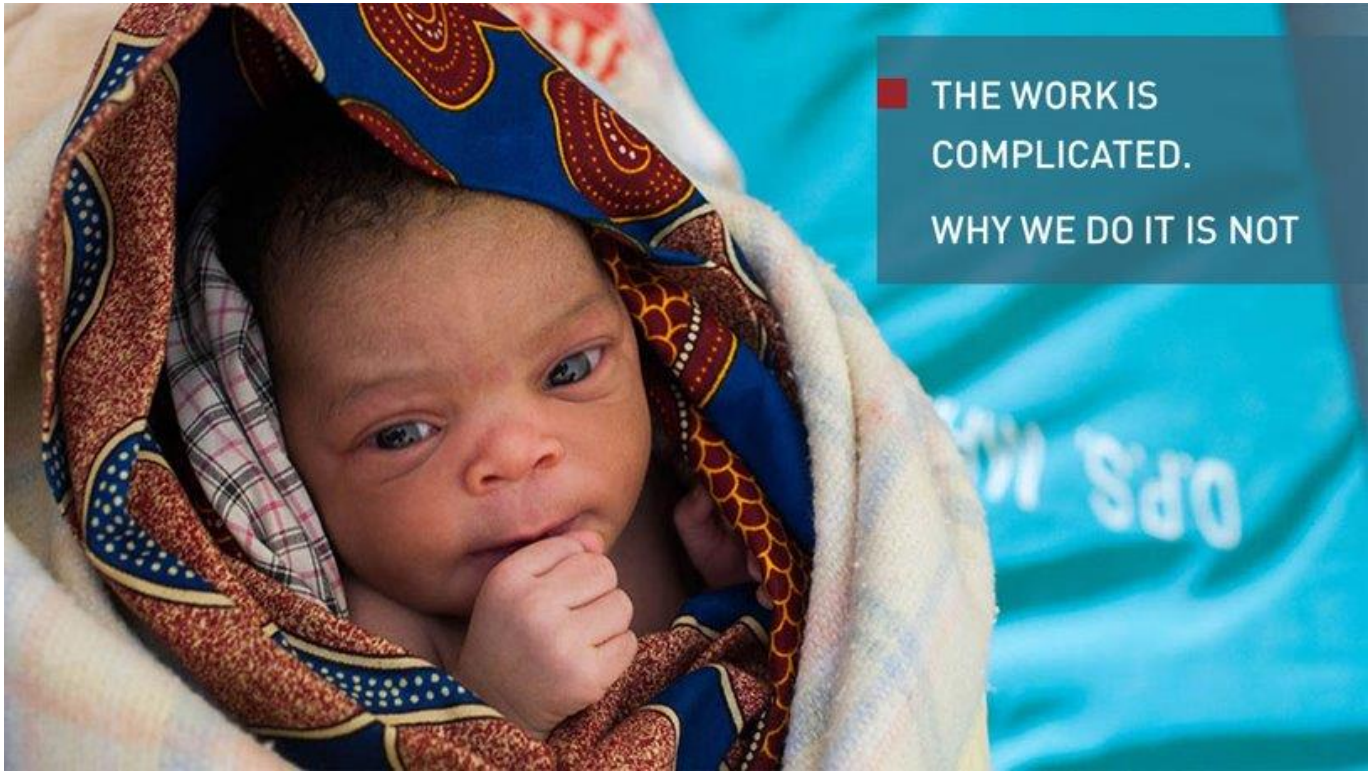
Recent conference experience

"4.3 Restricted Access Barrier Systems (RABS) or isolators are beneficial in assuring required conditions and minimizing microbial contamination associated with direct human interventions in the critical zone. Their use should be considered in the CCS. Any alternative approaches to the use of RABS or isolators should be justified."

Annex 1 (Other challenges)

- Appropriate application of QRM need to show an understanding and justification of all we do – Background of Isolator through to design of the EM system
- Knowledge Management (Industry and Regulators)
- Critical and unbiased thinking
- Keeping up with new technologies
- Less reliance on monitoring

"In the first instance, QRM priorities should include appropriate design of the facility, equipment and processes, followed by the implementation of well-designed procedures, and finally application of monitoring systems as the element that demonstrates that the design and procedures have been correctly implemented and continue to perform in line with expectations. **Monitoring or testing alone does not give assurance of sterility."**



Source: BMGF, via WHO

Thank you for listening

Any questions?