Day 2 Readout 17th May 2023

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Annex 1 Workshop Co-Chairs

17th May 2023

PDA Parenteral Drug Association

2023 Annex 1 Workshop Series (Singapore)

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P4 - CCS

- CCS is a critical document for the site and is on the same level as a SMF/Site Policy from a hierarchical perspective.
- CCS review is recommended annually, but it should not be onerous as a lot of the inputs feeding into an approved CCS are also reviewed annually with the PQR process or management review
- Gaps, mitigation/remediation actions can be reported in the CCS, but other quality systems e.g. CAPA, may address the detail of tasks and status.
- Many companies have a CCS in development, and maybe just need to work on the holistic overarching conclusions drawing links between diverse QRAs. There are a handful of participants that have more work to do, sometimes there is a shortage of experts at the company. Recommend use of TR90 to act as guidance in your company's CCS implementation and maintenance.
- CCS also needs to look outwards upon review – consider newer modern technology developments that can further reduce risks

P5 – Personnel training, monitoring etc

- Personal hygiene is taken for granted, so we are training only on expected behaviours while factors shedding, hygiene outside site, open lesions, personal illness is not talked about enough
- SOCKS SOCKS SOCKS – Feet are dirty, some countries do not have culture of wearing closed shoes, was a request from Regulators in multiple regions, Just Do It!
- Consider contamination like an onion – layers of protection increasing towards the core
- Quality Culture was a theme – shadow of the leader, ease of raising an issue, explaining why certain tasks need to be done in a certain way (eg cleanroom behaviour)
- Micro lab personnel needs to get out into shopfloor, and understand the process – shift in expectations for microbiologists (see TR88 – The microbiologist in deviations management)
- Disqualification of operators – in the case of repeated monitoring failures, observed bad cleanroom behaviours – get HR involved and DISQUALIFY
- Annex 1 requirements need to be read – companies should become intimately conversant with what to do –a lot of points are non-negotiable

P6 – Production Technologies

- Aseptic processing success if guaranteed to a combination of good technologies but complemented by good training, behaviours, QRM, PQS. Everything working together holistically will assure patient safety
- PUPSIT is a requirement but, flaw masking is probably only possible when there is a heavy foulant liquid being filtered
- Not doing PUPSIT on basis of small volume. If the filter can be FITd, and is appropriately sized, do PUPSIT
- CCI at timepoints in Stability studies – Appropriate aging studies can replace this with appropriate QRM. However, one could consider CCI in place of sterility test, in stability testing (dependent on what has been submitted to regulatory authority)
- For CCI – lot of discussion for what "under vacuum" means from the Annex 1 requirement for testing. Also, no 100% requirement for large volume bags, but containers closed by fusion

P7 – Aseptic Process Simulation and EM

- 2004 FDA Aseptic Processing Guide states do not perform manipulations that "pose unnecessary risks". This matches Annex 1 §9.36 wording on not validating bad practices.
- Zero contamination is the limit!
- EM – it is not just one parameter that needs to be in control to show that your environment is under control. EM also only gives an indication that the area is under control.
- A drift in EM results means there HAS been an event. Companies need to be challenging again their DESIGN and their ASSURANCE measures to see what has changed, or what has proved to be deficient in ensuring control. Look again at risks analyzed (CCS).
- It's an alert LEVEL and an action LIMIT
- Lots of questions in the room on the technicalities of what and how to do tasks associated with APS and EM, reflecting the fact that we all have different products and experiences. Not one size fits all – use your QRM applicable to your situation.

Thanks!

Thanks to our speakers and sponsors for making this event possible!

Thank You