SG Conference Readout

Bruce Loxley

Senior GMP Compliance Advisor, PDA SAB Member

GSK

07/08 May 2024

PDA Parenteral Drug Association

2024 Pharmaceutical Manufacturing and Quality Conference

CONNECTING PEOPLE SCIENCE AND REGULATION®

AI/ML

- AI is a game changer concerning- not only drug discovery but helping us to work better
- Start simple – begin with a Problem statement when considering an AI solution
- Human in the Loop will still be there. The Guard and the Guide
- Data is the new Oil!
- AI is currently a little kid, but will soon become a teenager, but the parents (Human in the Loop) are still needed
- Already a lot of Regulator interest and encouragement (FDA White papers, EMA AI Initiative – Listen and Learn sessions)
- Regulators are well aware that AI will create some significant paradigm shifts

Facilities Dr Pohlhaus FDA

- Misconceptions About CGMP: “Something cannot be considered CGMP until it is widely adopted”
- “Senior managers have critical responsibility to allocate resources for production infrastructure upgrades if operations are deficient” - thereby creating *de facto* the quality culture of the organization
- ICHQ9(R1) – consider the *Lifecyle* factors – including “Oversight of Outsourced Activities and Suppliers”
- Focused on Quality Considerations for non-steriles – “Review of complaints, adverse event reports, and recalls involving objectionable contamination of non-sterile dosage forms”
- Take Home messages – (i) “At Some Point, Maintenance Will Not Be Enough”
- (ii) CGMP Means Incorporating Feasible and Valuable Changes”

Interaction with CDER–new Facilities and Technologies

- FDA will not approve a new technology; they will approve a new technology applied to a new product
- FDA since 2014 has had an emerging technologies program ETP and actively encourage interaction with industry during the submission and approvals process

- Regulatory Agencies in general are very focused on minimization of Drug Shortages – PDA Survey done on aging facilities. One key finding is that cGMP not applied to QC laboratories.
- Quality Heads – go to the shopfloor!!!!!
- Safety is a subset of Quality

Newly built facilities

- Plug and Play – modular design, SuS, easily reconfigurable
- Linear Process Flows – for ease of personnel movement but also for contamination reduction
- One modern driver in this business is to have more agile, flexible manufacturing, smaller volumes, but faster turnaround, more local manufacturing
  - Opportunities exist for Portable on Demand POD facilities therefore exist
  - However, POD is out of scope of current regulations (this is evolving discussion)
- Continuous Manufacturing is more mature concerning Regulatory impact
- ICHQ13 (Mar2023) issued, CM also covered under FDA ETP initiative

Annex 1 Implementation

- Mr Boon – PIC/S Subcommittee on Training – Working groups established on Annex 1 Implementation, also AI. Annex 1 IWG focuses on training
- Watch out for the future (pan) African Medicines Agency (AMA)!
- PIA = PIC/S Inspectors Academy is established- webs based training, and a structured curriculum for each node (steriles/nonsteriles etc) – for Inspectors and by Inspectors. Harmonized Training

Challenges in Annex 1 Implementation

- Particle losses in tubings – we must qualify the system as a whole. Annex 1 requirement detail significantly increased in 2022 revision

- Uncertainty in Industry on CCS – do I develop a new document or collate existing? For new facilities – I have no data!! How do you assess CCS effectiveness?

Micro / RMM Part 1

- Concept of Microbiological Quality Critical Attributes
- 20 WL from March 2023 to know on ophthalmic products linked to micro contamination! A lot of this was linked to “insanitary” conditions in manufacturing.
- Facility Socks!
- CCIT – FDA very willing to accept new deterministic methods for CCIT – bring them the data!!!
- CCIT – maybe 10 units are needed for testing, anything less requires statistical justification
- Lots of updates on USP endotoxin, micro and RMM monographs
- Bioburden controlled products IPT – what are the limits? What are the volumes for testing? Industry feedback indicates it would like some guidance in <1119> on Bioburden Monitoring
- RCA for issues at CMO – the MAH may need to ensure under the Quality Agreement you can get to Root Cause

Micro / RMM Part 2

- Micro Investigations – learn from case studies to avoid making the same mistakes – understand the Contaminant do the research!!! Make sure the identification is correct. Then understand points of ingress.
- “When problem solving, dig at the roots and do not just hack away at the leaves”

- CCS – PDA TR90 provides a lot of help when designing and implementing a CCS
- Like all Risk Assessments – the CCS is a living document; one that needs regular review for accuracy and effectiveness checking
- Remember that perfect smoke test photo showing Grade B surround air getting directly sucked into the RABS? Keep an open mind when assessing a CCS!

RMM Case Study

- Replacing traditional EM by biofluorescence – why not? Regulators support this!
- Real time data allows for agile response to adverse trends
- Criteria from regulators is that the method has at least equivalency or superiority to existing methods (§9.28 Annex 1)
- Cleanliness of tubing becomes critical in biofluorescence. May also be some interference from polymers, solvents etc. Equivalency / superiority demonstration by doing parallel testing in Grade A environments (Isolator/RABS)

Human Capital

- Openness Trust, OPENNESS TRUST
- Psychological safety – the Speak up Principle – best way to get employee engagement to raise issues so we can resolve them
- Nobody comes into work wanting to do a bad job – buy we are human, and we make errors
- In addition to speak up – Managers need to Listen more

- Human centric goal as part of Industry 5.0
- Sustainability is linked to development of personnel capabilities
- Resilience! Dynamic world
- Everyone is a Leader, even if it is only of Yourself!
- Managing Transition to 5.0 – Purpose/Picture/Plan/Part (played by the individual)
- New KPI = Keep People Inspired!

ICHQ12/QMM

- You tell me the highlights!

Thank You!

Thanks to the Committee, the Speakers, Moderators and PDA AsiaPac!