Evolution of GMPs and Why They Are Particularly Important for Sterile Manufacturing

Andrew Hopkins

Senior Director

Lachman Consulting

PDA Parenteral Drug Association

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- Evolution of GMP
- Annex 1 Specifics
- How can we evolve
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Brief History of GMP

- For a long time GMPs have evolved reactively:
  - Sulphanilamide (USA)
  - Thalidomide (Europe)
  - Devonport (UK)
  - Eye drops (Worldwide)

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Evolution of GMP

- Generally, a very conservative industry
- Fear of the regulators but the regulator has evolved and wants a dialogue
- ICH 9, 10 etc……
- QRM principles have driven the update of GMPs since 2010?
- Quality Maturity Measurements
- Empowering us (but with great power comes great responsibility)

Chapter 1 principles applying QRM

Quote from an ex colleague

“ Don’t do anything stupid ”

Chapter 1 principles applying QRM

Quote from an ex colleague (second thoughts)

“ If you must do something stupid, don’t do it again! ”

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Annex 1 Specifics

QRM

- It is pushing Design not monitoring. Using good knowledge and scientific principles

Contamination Control Strategy

- This naturally leads to the Contamination control strategy. This is the evolution of QRM for microbial contamination control.

Multiple elements

- This requires the right people with the right knowledge, right attitude and to be honest

New Technology

- The CCS is a dynamic process. Has multiple input points:
  - QMS, monitoring and outward looking

Annex 1 Specifics

"The manufacture of sterile products covers a wide range of sterile product types (active substance, excipient, primary packaging material and finished dosage form), packed sizes (single unit to multiple units), processes (from highly automated systems to manual processes) and technologies (e.g. biotechnology, classical small molecule manufacturing systems and closed systems). This Annex provides general guidance that should be used in the design and control of facilities, equipment, systems and procedures used for the manufacture of all sterile products applying the principles of Quality Risk Management (QRM), to ensure that microbial, particulate and endotoxin/pyrogen contamination is prevented in the final product."

Annex 1 Specifics

"2.1 The manufacture of sterile products is subject to special requirements in order to minimize risks of microbial, particulate and endotoxin/pyrogen contamination. The following key areas should be considered: "

- "i. Facility, equipment and process should be appropriately designed, qualified and/or validated and where applicable, subjected to ongoing verification according to the relevant sections of the Good Manufacturing Practices (GMP) guidelines. The use of appropriate technologies (e.g. Restricted Access Barriers Systems (RABS), isolators, robotic systems, rapid/alternative methods and continuous monitoring systems) should be considered to increase the protection of the product from potential extraneous sources of endotoxin/pyrogen, particulate and microbial contamination such as personnel, materials and the surrounding environment, and assist in the rapid detection of potential contaminants in the environment and the product. "

Annex 1 Specifics

- "2.1 The manufacture of sterile products is subject to special requirements in order to minimize risks of microbial, particulate and endotoxin/pyrogen contamination. The following key areas should be considered"

- "ii. Personnel should have adequate qualifications and experience, training and behaviour with a specific focus on the principles involved in the protection of sterile product during the manufacturing, packaging and distribution processes."

Annex 1 Specifics

- 2.2 Processes, equipment, facilities and manufacturing activities should be managed in accordance with QRM principles to provide a proactive means of identifying, scientifically evaluating and controlling potential risks to quality. Where alternative approaches are used, these should be supported by appropriate rationale, risk assessment and mitigation, and should meet the intent of this Annex. 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.

Annex 1 principles applying QRM?

“ Don’t contaminate the product ”

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How can we evolve?

- 20 years ago, open processes, still using archaic micro
- In first instance knowledge management
- Open and honest assessment of risk
- Now: RABS, Isolators Robotics, closed? (whats next?)
- But, Caveat Emptor!
- “not all that glistens is gold”!
- New technology: Filling and monitoring
- Rapid micro: Sterility tests, Monitoring real time, predictive tools?

How can we evolve?

- **Q:** What's next: Training?
- **A:** Can't carry on with the same old ways. Need to look at new and innovative approaches. Video, VR/AR
- Can't continue with "Read and understood"

- **Q:** What's Next: monitoring?
- **A:** Real time data: Equipment, facilities, utilities and products?

- **Q:** What's Next: Data analytics?
- **A:** Real time data with predictive interpretation. Machine learning, AI?

- **Q:** What's next, ongoing dialogue?
- **A:** Talking to the suppliers and the regulators!!!!!!!

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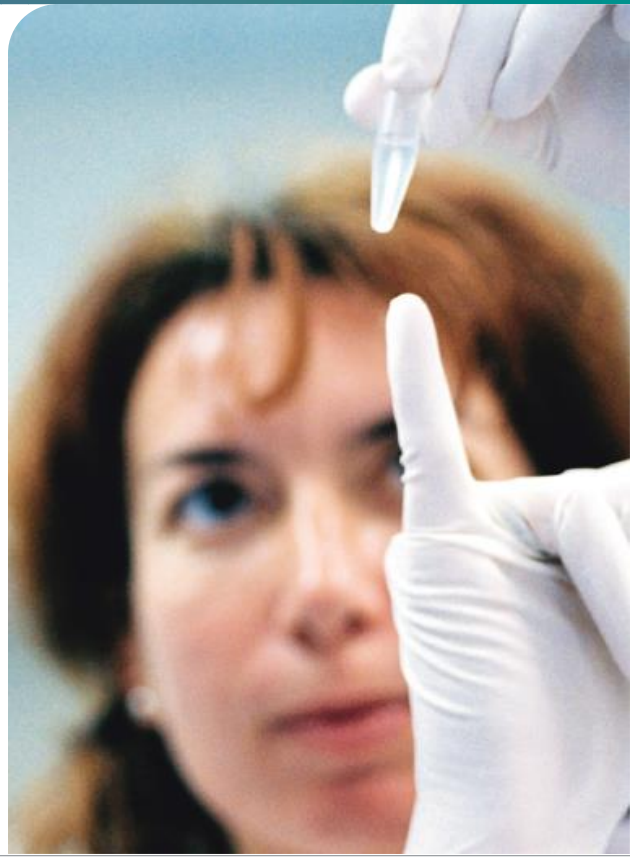
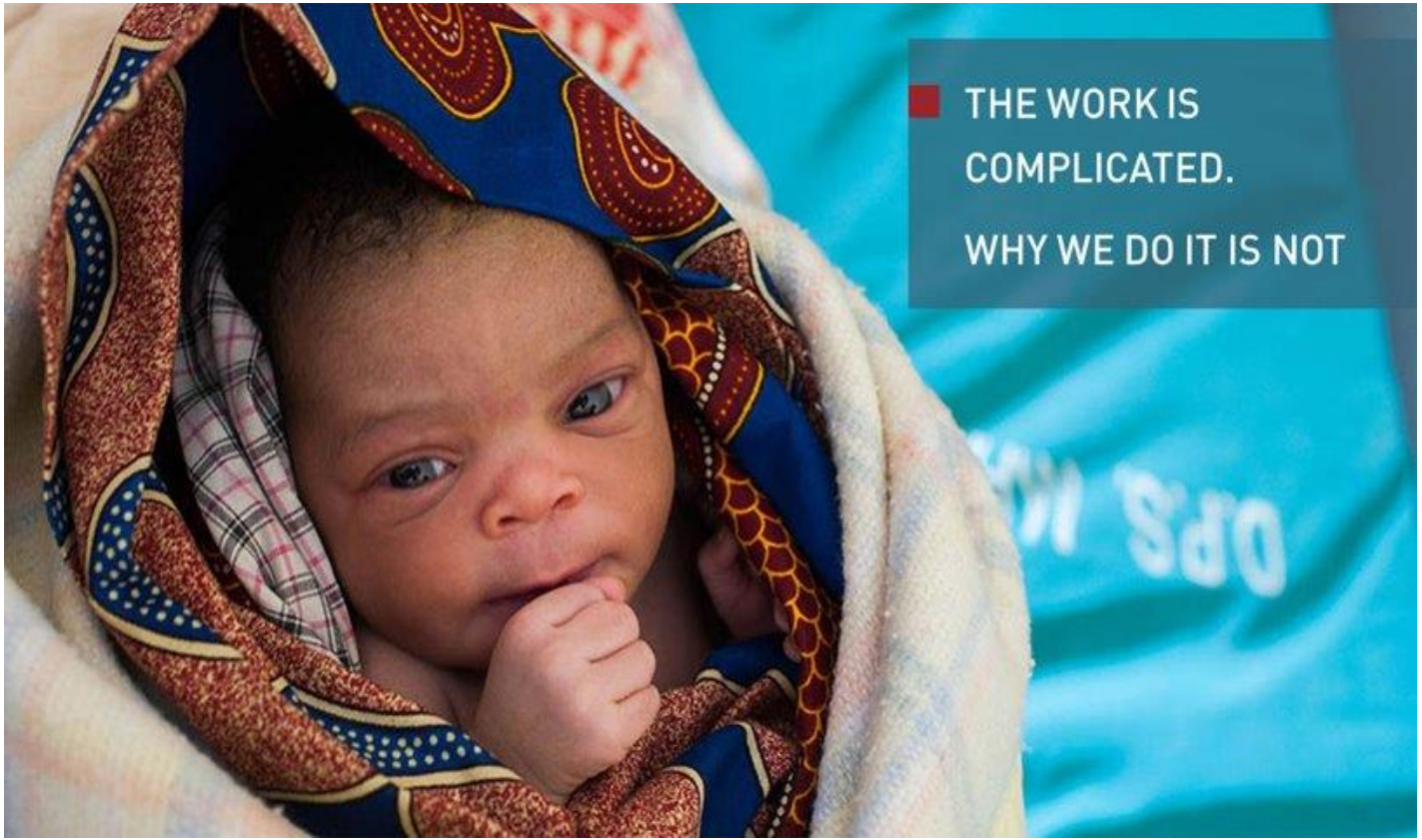
Summary

- Very conservative as an industry
- Regulations tend to be reactive
- QRM is trying to give us “freedom”
- With great power comes great responsibility
- We need to evolve (equipment, monitoring and training)
- We need to talk to each other (even to the regulators)
- We need to ensure that the patient is “in the board room” so that our decisions are always patient centric





Source: BMGF, via WHO

Thank You!