Trends and Challenges in Large Scale Vaccine Production in High Containment Environment

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Presentation Overview

• Industry & Technology trends in Vaccine production

• Challenges

How to Manage Conflicting Agendas with Vaccine Facility and GMP Design in high containment when using Single Use technology?

• “Generic” Facility Design examples

• Summary & Conclusions
Upstream manufacturing suite with 100% mobile, single-use and ready-to-use manufacturing equipment - the modular design of Rentschler's new production facility was awarded the 2012 Facility of the Year Award. (Picture: Rentschler)
Vaccine manufacturing – technology trends
Pilot, launch and production scale

• **Multi-product facilities** – moving towards high containment

• Increasing **recombinant products**

• **Modular approach** – effective facility structures

• Enabling technologies for **faster production**

• Acceptance of **single-use technologies**

• Reduction of logistic/support functions – **focus on the core process**
Vaccine facilities - Design Drivers

• Biological containment (BSL1, BSL2, BSL3, BSL4)

• Minimize risk for cross contamination (GMP requirements)

• Controlling Quality

• Fast-track requests / Manufacturing flexibility

• Adaptability to changes in the market / products / Efficient pandemic solutions (vaccines)

• Controlling investment costs / Time to market
Single Use Technology
From Stainless Steel towards Single Use

Single Use technology is not a new thing & Size really matters……!

- Single use technology has been known and used for many years - mostly in smaller scale

- Now single use technology is used more frequently at large scale –1000+ liter bags!
Challenges
Conflicting agendas & Challenges

- GMP vs Biocontainment (high containment)
- Waste management
- Primary barrier integrity
- Multiproduct (flexibility / Biorisk)
- Open knowledge sharing / Sparring
- Authorities – experience with SU in high containment
Conflicting agendas
GMP & Biosafety

Bio safety

GMP

KEEP IN

KEEP OUT
Conflicting agendas
GMP VS Biosafety

Bio safety

GMP
Conflicting agendas
GMP VS Biosafety

At low biorisk – GMP *normally takes* precedence

At higher biorisk – Biosafety *should* take precedence
Solid waste handling challenges

Objective:

• Ensure full inactivation of SU systems
• Use process that can be approved and validated

=>

• Incineration
• Autoclaving
• Reverse polymerisation (limited experience, new technology / looks promising for this)
Integrity of Single Use systems

• Main risk with SU is leaks

• Transport and handling can induce leaks

• In-situ integrity testing has long been sought for ensurence of sterility (product safety)

• Will increase safety for staff too
Integrity testing of Single Use systems

Helium Integrity Testing (HIT™) @ ATMI

http://www.atmi.com/lifesciences/products/bpv/hit.html

Sterile air Integrity Testing – directly before use @ user

http://advancedscientifcics.com/lifesciences/insite-inflation-and-integrity-test-system
Challenges

Biorisk & Barrier considerations

Event: Large Spill / leak from SU bag

Change of primary barrier....

Spill from SU equipment

Aerosol generation
Large Scale Vaccine production
Effects of single use technology

Removing complexities

• Cleaning flow of equipment is minimized

• Lower cross contamination risk (batch/product)

• Faster start up of production (plug & play)

• Low start up cost

• Facilitates multi product manufacturing

• Fast batch change over

Adds to complexities

• Validation of waste inactivation of SU equipment

• Solid waste flow and quantity is increased

• Increase of raw material complexity (logistics)

• Spill handling / Spill risk

• Process room may have to act as primary barrier (spills)

• Large volume in plastic bags
“Generic” Facility Design Examples
The modular approach / “generic” facility

- No tailor-made process rooms
- Generic facility Design supports design drivers for Multiproduct abilities and flexibility, etc.

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Dance floor ..... Process Design
Dance floor ..... Process Design

PRODUCT A

PRODUCT B

Feed

Seed 20L Wave

SUB 200L

SUB 1000L

Filtration buffer

Depth filtration

Feed

Seed 50L Wave

SUB 1000L

Filtration buffer

Depth filtration

Buffer

ProA

Inactivation liquid

Inactivation
3D views of concept facility – high containment
3D views of concept facility – high containment
3D views of concept facility – high containment
Summary & Conclusions
In Conclusion

• Single use technology results in less complexities related to production and GMP processes but adds to more complexities related to Biorisk.

• Large volume single use technology in high containment facilities may result in process rooms that will have to be designed as the primary barrier to mitigate biorisk.

• The pharmaceutical industry should embrace more open knowledge sharing related to Biorisk discussions in high containment facilities.
Thank you for your attention!

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