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

Industry & Technology Trends

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)

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http://www.process-worldwide.com/engineering_construction/plant_design/sterile_and_clean_room_technology/articles/346233/

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

http://www.sartorius.com/en/products/bioprocess/single-use-bioprocess-bags/

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!

http://www.sartorius.com/en/products/bioreactors-fermentors/single-use/biostat-str/

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Challenges

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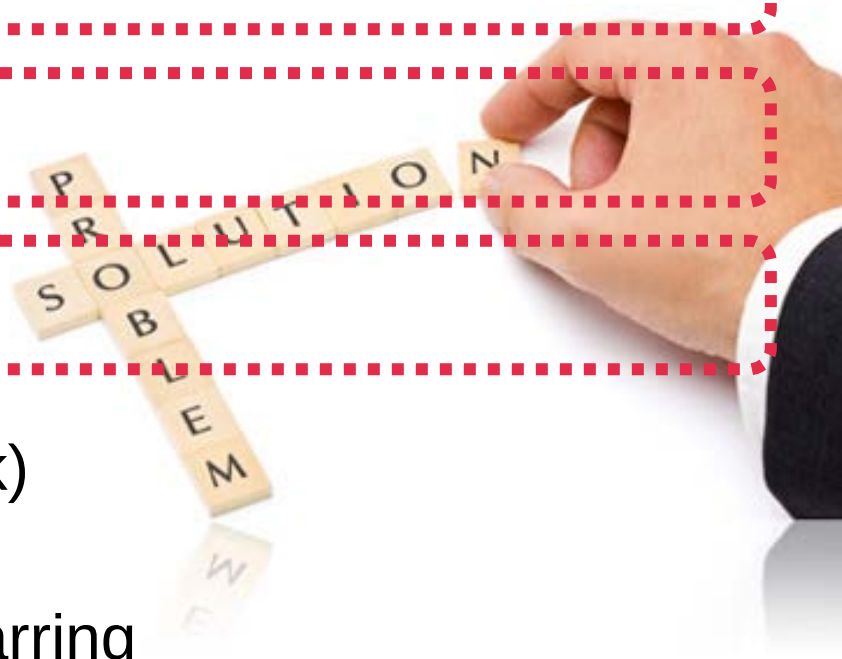
Conflicting agendas & Challenges

- 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

Conflicting agendas
GMP VS Biosafety

Bio safety

GMP

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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 technolgy / 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://advancedscientifics.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

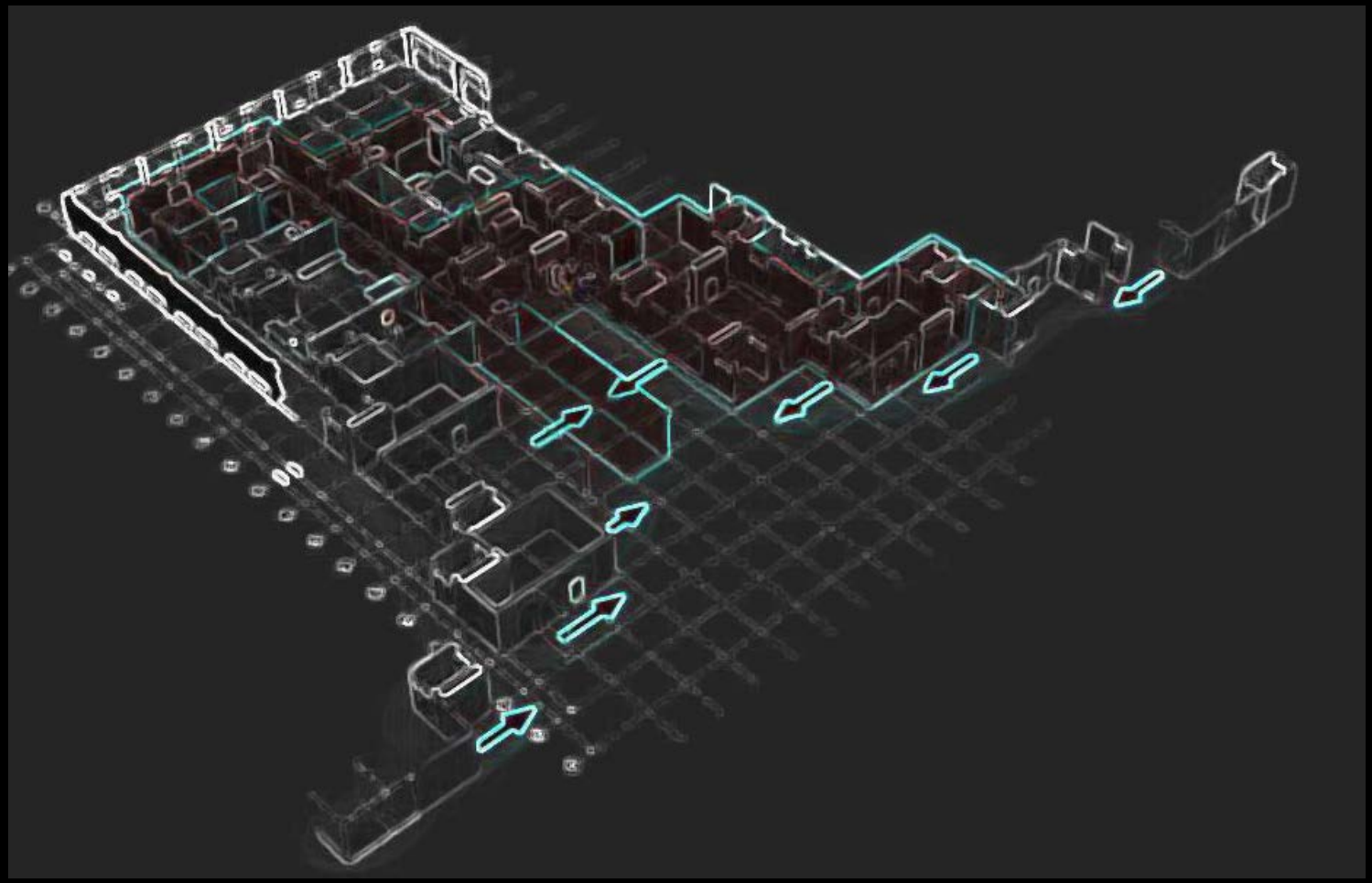
Removing complexities

- 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



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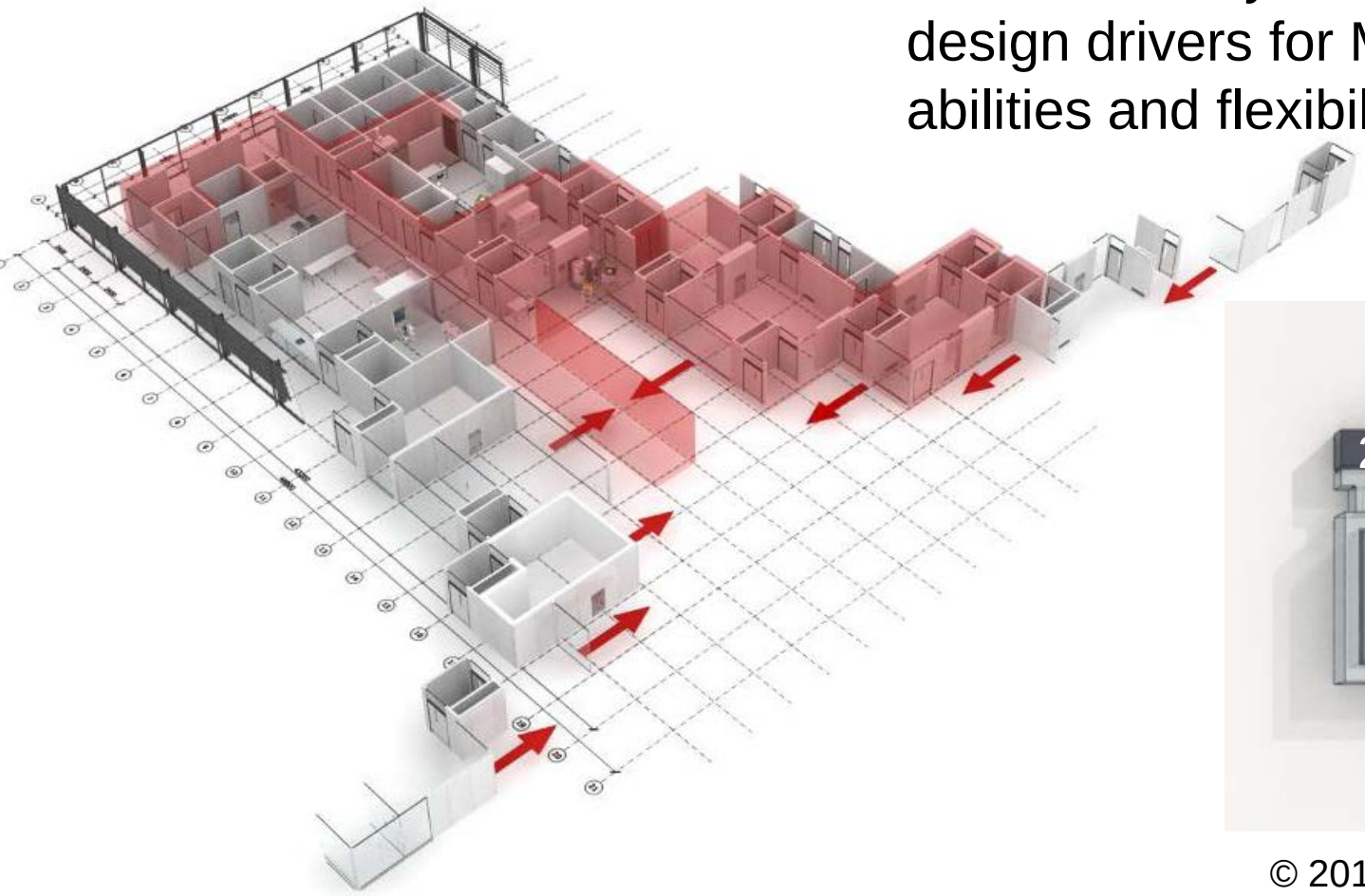
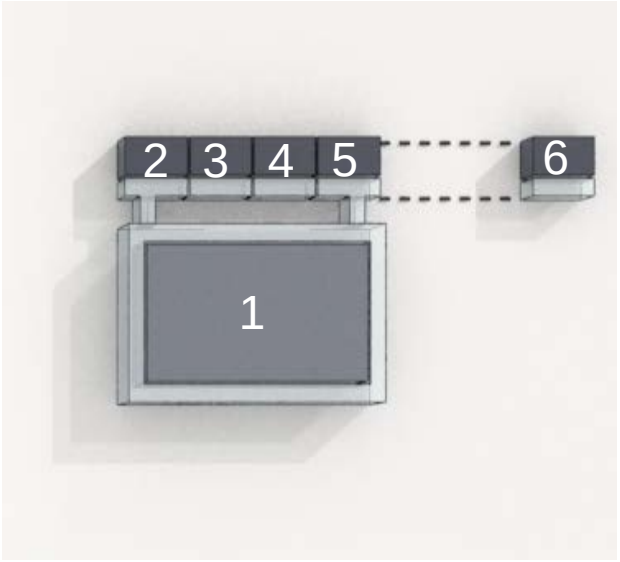
The modular approach / “generic” facility

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





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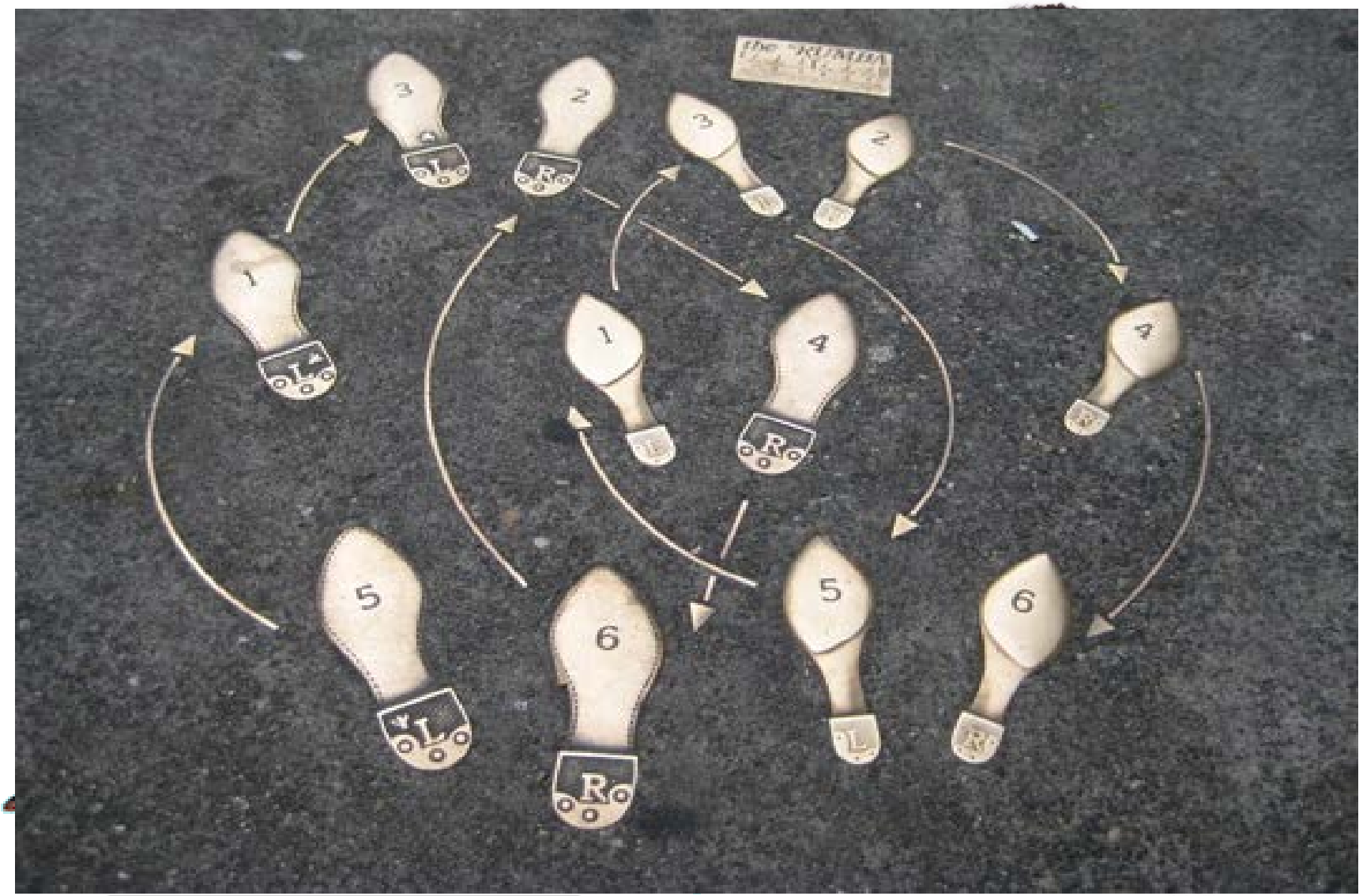
Dance floor ..... Process Design



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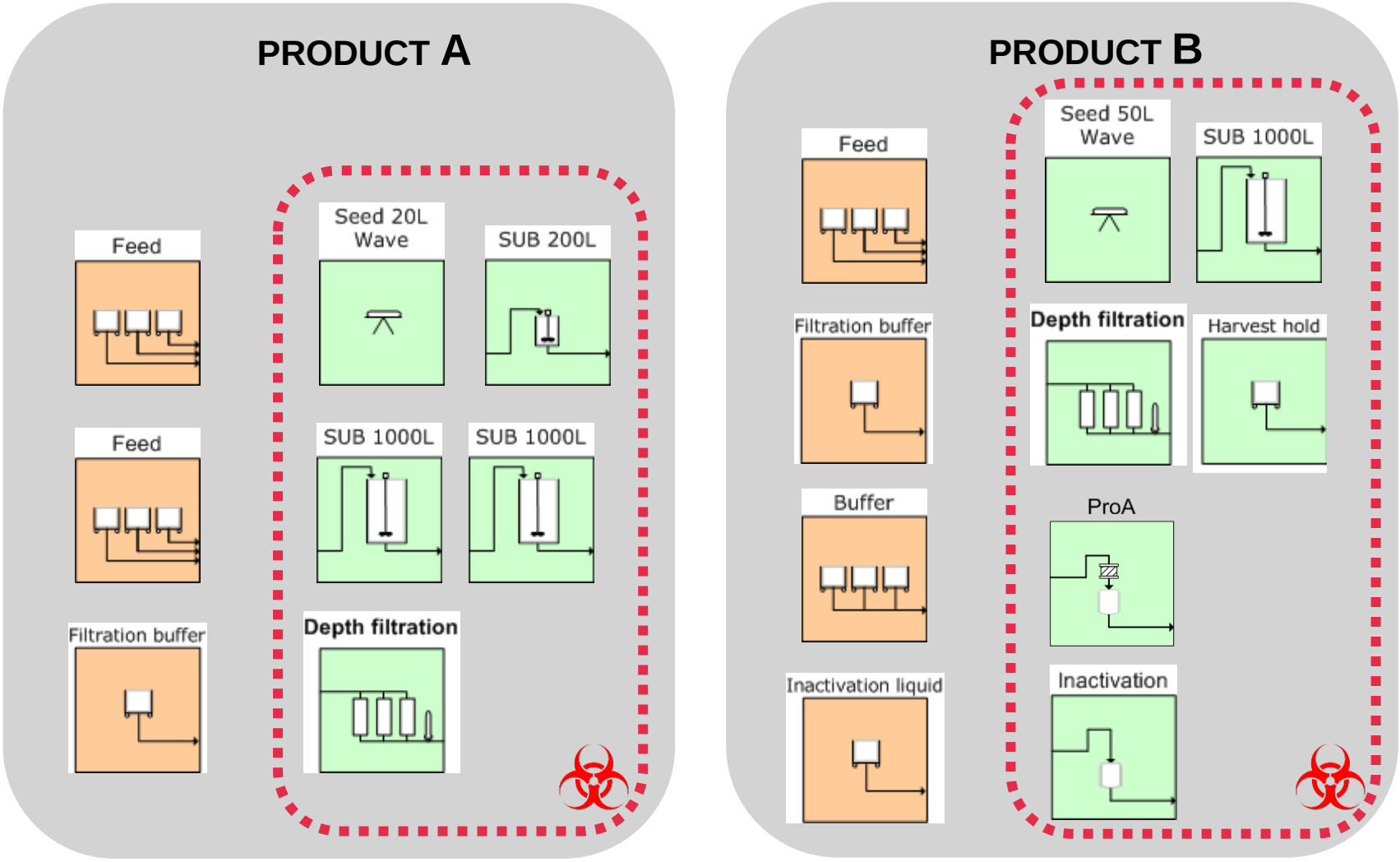
Dance floor ..... Process Design



3D views of concept facility – high containment

3D views of concept facility – high containment

3D views of concept facility – high containment

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Summary & Conclusions

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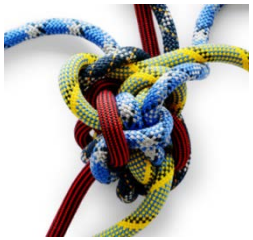
In Conclusion

SU technology can be used in high containment facilities

BUT

Biorisk must be evaluated carefully

- 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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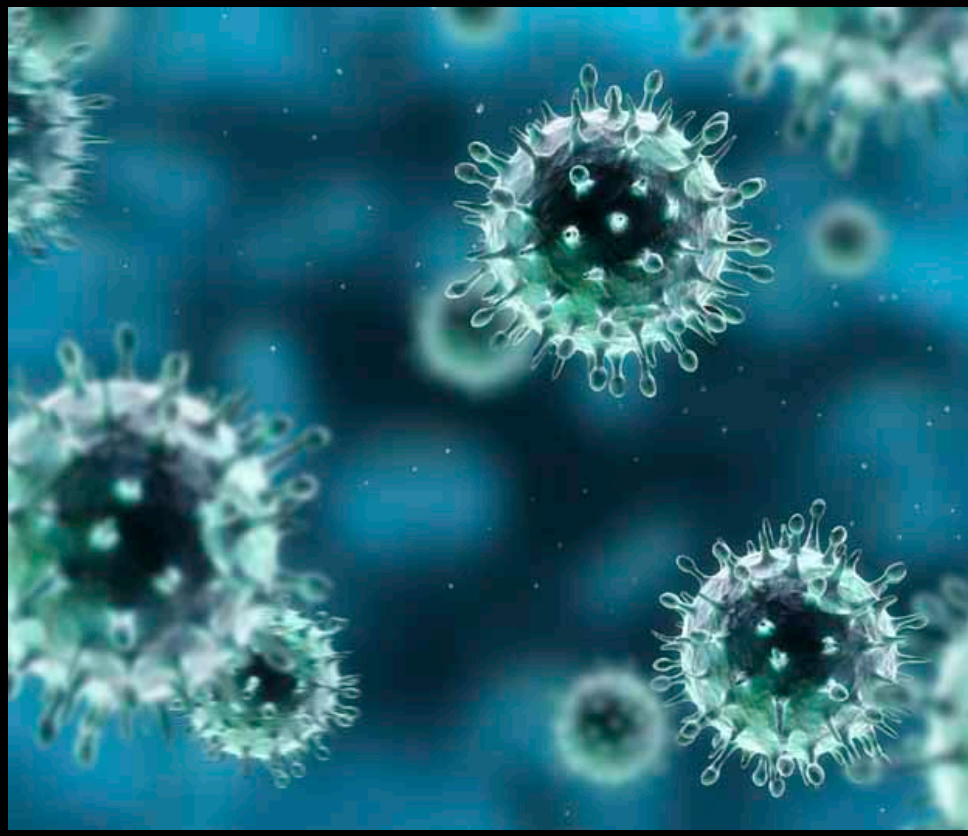

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