Modular Construction of Biopharma Manufacturing Facilities

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Agenda

❖ Changes in the Industry
❖ Future Needs
❖ The Past does not Fit
❖ The Current is not Optimal
❖ What’s Needed
❖ Scenarios which Underline the Needs
❖ Examples of the Possible
❖ Thinking outside the Box
Changes Redefine Facilities

- Increasing process intensification either due to expression rates or new processing modes reduce facility footprint

- Regulatory view is changing and supporting agile, efficient and flexible manufacturing platforms

- New manufacturing sites are asked to be multi-product/purpose sites to be able to utilize capacities in most effective way

- Regenerative/personalized medicines require specific processing systems in accordance with any possible logistic hurdle and robust containment needs
Future Trends

❖ Aging population on the rise with further needs for capacities to avoid stock-outs/drug shortage

❖ Rising middle class in different countries require in-country/for country manufacturing capacities

❖ Changing viral and microbial diseases require fast response possibilities utilizing new technologies and deployment methods

❖ Capacity planning requires robust timeline and cost budgets to be able to foresee future construction projects

Have you experienced cost overruns in facility projects? If yes, by roughly how much?

- 1 - 5%
- 5 - 10%
- 15 - 20%
- 20 - 25%
- 25% or more
Process Intensification

From large scale stainless steel to medium volume single-use to low volume continuous processing

- De-risking
- Higher flexibility
- Faster turn-around
- Closed systems
- Advanced PAT

- Closed system
- Capacity flexing
- Process step reduction
- Process control
Past Facilities may not fit New Needs

- High CAPEX (>$500M)
- Long time-to-run (3-4y)
- Product dedicated
- Inflexible/non-scalable
- Extensive qualification needs
- Difficult containment
- Difficult to clone

Change is Needed
“Until now, modular facilities have reproduced traditional architecture with regard to embedding utilities piping and HVAC ducts in the interspace between the physical module limits and the suspended ceiling making refurbishment, if required, extremely complicated.

The new approach is to segregate pre-assembled modules into laboratory and utility modules, which are designed such that they permit even simpler and faster construction, qualification, validation and maintenance, respectively....”

*Alan Pralong (2013)*
What’s Needed

✓ Speed
  • Abbreviated design phases
  • Time-to-built/Time-to-run
  • Adoption of new technologies

✓ Agility
  • Scaling up- and down w/o interruption of existing processes
  • Rapidly deployed in multiple locations (in-country/for country)

✓ Efficiency
  • Higher yield per footprint
  • Faster turn-around/set-up time
  • Multi-product runs (parallel)
  • Infrastructures for multi-purpose use
Scenario: Compression & Diversification

e.g. 10,000L bioreactor transition to multiple 2,000L systems
Scenario: SUT Implementation

Single-use technology processes create flexibility & speed, but...

...is only as flexible as the surrounding infrastructure!
Scenario: Multi-product/-tenant

Shared services and/or better utilization of the assets
Scenario: Precision Medicine

The question of centralized or decentralized (hospital, cancer center, local based, logistics hub, airport location) is still debated (needle to needle logistics for example)

- Centralized (hub)
- Decentralized (hospital or cancer center)
Possibility Example: MAb Processing

Built off-site → Assembled on-site to a facility, example JHL China

Courtesy: GE
Possibility Example: MAb Processing

Built off-site → Assembled on-site to a repurposable, multi-product/-process cleanroom infrastructure, example iCON

4 x 2,000L mAb delivered in 12 months

Courtesy: IPS, G-CON Manufacturing Inc.
Possibility Example: MAb Processing

Central manufacturing suite
- Cell culture through viral filtration
- Closed processing via aseptic connections
- Reduced personnel and maintenance

Area classification
- Closed processing allow most operations to occur in ISO 9

In-line and at-line testing
- Enhanced process control, detection and response

Amgen Singapore Site:
- “Ballroom” layout
- Single-use process technology
- Far reduced foot-print
- New cleanroom classification due to functionally closed processes
Other Example Cases – Off-site Box in Box

Pediatric gene therapy – 14 units – 8 months
Phase 2 – 10 units – 5.5 months

Bioprocess site – 10 units – 10 months

Aseptic filling site – 4 units – 10 months

Other Projects:
Bioprocess – 8 units – 8 months
CAR T – 1 unit – 3.5 months
CAR T – 3 units – 7 months
Gene therapy – 8 units – 6 months
Gene therapy – 14 units – 6 months

All systems run through a Factory Acceptance Test before delivery
Case Study – Rubius

- Rubius is focused on manufacturing red blood cells to make medicines to treat patients with rare diseases
- Had really aggressive timelines in order to support the patient population
- Recognized that a modular approach was going to provide the greatest benefit; needed a partner that had flexibility and ability to adapt

  - A total off-site, prefabricated cleanroom space of 6,500 sq. ft., including corridors was delivered in a record time of 6 months. The infrastructure was prequalified before it was shipped.
  - Rubius was 9 months ahead of their production planning due to this execution
Case Study – Rubius (Video)
Rethinking – Facility Catalogue ?!

We select Process Equipment from a Catalogue, can we do the same for Facilities in future?

Yes
(at least cleanroom infrastructures)

Creating Unit Operations

Standardizing Platforms

Predesigning Structures

Courtesy G-CON Manufacturing Inc.

Courtesy IPS

Courtesy M+W
Rethinking – Facility Catalogue ?!, cont.

We select Process Equipment from a Catalogue, can we do the same for Facilities in future?

The Benefits

- Abbreviation of Design Phases
- Known Qualification Tasks
- Cloning of Training & Procedures
- Set Timelines & Scopes
- Regulatory Familiarity
Conclusion

➢ Current, prevalent facility/process designs become outdated and strain to meet pressing industry requirements and application needs

➢ Many “tools in the toolbox are available”, but legacies still prevail

➢ Cost per sq.ft is as much an erroneous cost measurement as the initial investment thinking of stainless steel equipment versus single-use process technologies

➢ Multi-product/multi-purpose facilities become a prevalent request to gain capacity utilization

➢ Facility deployment requires much faster (< 1 year built) and possibly clonable
Thank You!

“The arrogance of success is to think that what you did yesterday will be sufficient for tomorrow”

William Pollard