Facility Design Influences

- Industry Trends
- Importance of Stakeholders in facility design
- Pipeline
- Process Development
- Design affects operations and operational costs
Industry Trends

• Traditional Paradigm
  – Fewer, bigger reactors are better to ensure supply
  – Stainless steel will be more efficient in the long run
  – Disposables are for clinical use only
  – Owning capacity is necessary for supply security

• New Paradigm
  – More, smaller reactors are more flexible for supply
  – Disposables offer multiple benefits of speed, cost, turnaround, and flexibility for commercial supply

Industry Trends

• Experience from last 10 years:
  – Increased yields, product approval delays/failures

• Next decade
  – Focus on smaller/rare diseases
  – Biosimilars will fragment the supply for established products
  – By 2016, bioengineered vaccines and biologics will account for 23% of sales, up from 17% in 2009
    (Source: EvaluatePharma, op. cit.)

• Need for smaller, more agile capacity
Stakeholder’s Impact on Design

- Regulatory Affairs
  - Interpretation of cGMPs
- Quality (QA/QC)
  - Application of cGMPs
  - Product, Personnel Flows, etc...
- Facilities
  - Cleaning
  - Accessibility and ease of maintenance/calibration
Stakeholder’s Impact on Design

• Manufacturing
  – Single or Multiple products?
  – What is the flow of the process, personnel, etc...?
  – Single or multiple access points?

• Materials
  – Ease and flow of material movement
  – Central or Local staging
    • Warehouse
    • Inside and outside of the processing areas

Stakeholder’s Impact on Design

• It is critical that the Design Team have dedicated staff from each discipline
  – Part of their annual Objectives

• Stakeholders need to have decision making authority
Pipeline

• What influences the multi-product strategy?

• HVAC Strategy
  – Segregation of specific MFG functions

• Flows
  – Personnel, Product, Materials, Waste, etc...

• Operation paradigm
  – Area Clearance practices
    • Stakeholder buy-in for multiple product line-clearance procedures
Impact of Area Clearance Practices

Process Development

- How much process optimization occurs by the time the facility is built?
- If USP titers increase 2x
  - Facility is now out of balance
    - Use USP at 50% to keep DSP at design?
- Individual products may have different capacities
- Strategy for anticipating these changes
Continuous Processing

Example 1: Continuous upstream (perfusion), batch downstream

Example 2: Batch upstream, continuous downstream

Example 3: Continuous upstream + capture, batch downstream

Example 4: Continuous upstream and downstream

International Symposium on Continuous Manufacturing of Pharmaceuticals
Konstantin B. Konstantinov, Charles L. Cooney, May 20-21, 2014
New Technologies

• Continuous DSP
  – Direct processing of harvest material
  – Eliminates large tanks, reduces facility footprint
  – More complex operation

Continuous Process

• Continuous or fully continuous?
• Either will have a dramatic effect on facility design
  – Footprint
  – Infrastructure...
• Risk profile(s) will be different
  – Solutions to mitigate risk
  – Acceptance of Risk(s)
• Prior to implementation...
  ... stakeholder understanding is critical
New Technology Enables....

• Single-use technology enable simpler, more flexible facility
  – Reduced infrastructure demand
    • WFI systems can be smaller
    • Clean in Place not required
    • Clean steam distribution not required
    • Portability
  – Limited distribution piping
    • Primarily WFI
    • Clean steam if autoclave or special requirements are necessary
    • “Process piping” is flexible tubing!

Flexibility

• Single use bioreactors can be changed easily
  – Use 500L in same space as 2000L
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Operations Effect on Design

• What is the optimal material movement into and out of a clinical suite?
• What considerations need to be taken into account?
  – Number of Staff
  – Volume of raw materials/supplies
• What is the historical viewpoint of the organization?

• Each stakeholder’s input alters the design
Facility Design Impact on Operations

Material Airlocks

Personnel Airlock
Facility Design Impact on Operations

Design Affects OPEX

- Operational Assumptions - Floor plan
- Airlocks/Gowning practices
  - Gowning Supplies
  - Time
- Effect of late changes
  - “Hybrid” solutions
  - Project delay
Summary - Design Considerations

• Final Design requires all disciplines early involvement and ownership

• Review of multiple scenarios
  – Single vs. Multi-product
  – Clinical, Commercial
  – Operational desires

Summary - Design Considerations

• Operations and Technology Change the Risk profile...
  – Potential Loss of Product with equipment failure
    • Level of complexity
  – Common rooms, Footprint
  – Closed/Open manipulations
  – Area Clearance
  – Flow requirements
Thank You!

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