Industry Speaks: Transforming cGMP Manufacturing Facilities
Speakers

- David M. Marks, P.E. Speaker/Moderator
  - Principal
  - DME

- Thomas L. Bryant Discussion Panel
  - Sr. Director, Engineering, US
  - Sanofi Pasteur, Inc.

- Robert Torregrossa Discussion Panel
  - Associate Director Process Engineering
  - AstraZeneca Biologics

- Jeffrey Kratz Discussion Panel
  - Director of Global Engineering PM
  - Teva Pharmaceuticals

- Rich Meinel Discussion Panel
  - Director Global Engineering Technology
  - Biogen
About DME Facility Focus

- An INTERPHEX 2016 Technical Education Program.
- **Surveys**
  - Invited engineers, manufacturers, and other life sciences professionals like you to express views on the latest trends and technologies affecting our industry.
  - Two Surveys, executed Q4 2015.
    - Biopharma Facility Modernization
    - Aseptic Manufacturing Tech Trends
- **Whitepapers**, issued April 2016.
- **Presentations** with Distinguished Industry Panels.
  - Industry Speaks: Transforming cGMP Manufacturing Facilities
  - Trending Technologies in Sterile Product Manufacturing Facilities
Survey Overview
Survey Participants

**AFFILIATION**
- Biologics Mfg.: 44%
- Small Molecule Mfg.: 20%
- Consultant: 30%
- Academia: 2%
- Other: 3%
- Regulatory: 1%

**JOB FUNCTION**
- Engineering: 43%
- Manufacturing: 22%
- R&D: 19%
- Other: 6%
- Quality Assurance: 5%
- cGMP Compliance: 5%

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[Image: Facility Focus logo and INTERPHEX banner]
Triggers & Drivers: When Biomanufacturing Facility Transformation Becomes a Necessity
Why Change?

Manufacturing Modernization

- Safety
- Throughput
- Flexibility
- Sustainability
- ROI/COGS
- Reliability
- Quality
- Obsolescence
- Regulatory Compliance
- Throughput
- Safety
- Flexibility
- Sustainability
- ROI/COGS
- Reliability
- Quality
- Obsolescence
- Regulatory Compliance

INTERPHEX
Project Drivers

**Risk Drivers**
- Product Quality
- Regulatory Compliance
- Obsolescence
- Safety
- Reliability

**Opportunity Drivers**
- New Products
- Throughput
- Flexibility
- Sustainability
- ROI/COGS

Manufacturing Modernization
Opportunity Drivers

Retrofit for new product or process

1. Increase process throughput
2. Ranked 1-5
   1 = most frequent

3. Increase facility flexibility
4. Reduce cost of goods sold
5. Improve sustainability

- Consultant
- Biologics Manufacturer
- Small Molecule Manufacturer
Risk Drivers

1. Improve product quality
   - Consultant
   - Biologics Manufacturer
   - Small Molecule Manufacturer
   Ranked 1-5
   1 = most frequent

2. Achieve regulatory compliance

3. Improve reliability

4. Address obsolescence issues

5. Improve safety

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INTERPHEX
cGMP Assessment

cGMP MANUFACTURES ONLY:
In your company, what would typically trigger an internal assessment of facility or equipment compliance to current GMP standards?

- Small Molecule Manufacturer
- Biologics Manufacturer

<table>
<thead>
<tr>
<th>Category</th>
<th>Small Molecule Manufacturer</th>
<th>Biologics Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proactive periodic cGMP assessment on fixed schedule</td>
<td>38%</td>
<td>74%</td>
</tr>
<tr>
<td>Opportunistic assessment as part of planning for a GMP renovation driven by other factors</td>
<td>58%</td>
<td>63%</td>
</tr>
<tr>
<td>Quality-driven assessment when triggered by manufacturing deviations</td>
<td>67%</td>
<td>68%</td>
</tr>
<tr>
<td>Not applicable</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>4%</td>
<td>7%</td>
</tr>
</tbody>
</table>
cGMP MANUFACTURERS ONLY: What is the most frequent equipment obsolescence issue you encounter?

- Spare parts no longer available: 35%
- Vendor discontinuing support: 17%
- Better technology now available: 27%
- Automation system is obsolete: 11%
- Doesn't meet cGMP standards: 10%
Biting the Bullet:
Committing to a Facility Renovation Project
Risk Factors

Rank the risk factors associated with GMP facility renovations. (Ranked 1 - 5, where 1 = most risk)

1. Legacy facility unknowns; lack of reliable as-built design documentation.
2. Process validation and/or regulatory issues.
3. Impact of renovation on facility segregation and flows.
4. Upgrading equipment to address obsolescence or cGMP gaps.
5. Construction activities adjacent to GMP operations.
Renovation Risk Factors

Ranked 1-5
1 = most frequent

1. Construction activities adjacent to GMP operations
2. Process validation and/or regulatory issues
3. Impact of renovation on facility segregation and flows
4. Upgrading equipment to address obsolescence or cGMP gaps
5. Legacy facility unknowns; lack of reliable as-built design documentation

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cGMP Manufacturers
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Suppliers
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INTERPHEX
Risk Assessment

cGMP MANUFACTURERS ONLY: When does your organization typically execute a structured risk assessment as part of a cGMP facility renovation?

- Design qualification
- Process hazard analysis
- Process closure assessment
- Evaluating risk to concurrent cGMP operations
- Evaluating direct risks to the project
- Evaluating the risks associated with process change
- Development of process remediation scope
- Evaluation of legacy facility and equipment
Enablers:
Technologies and Trends that Provide the Best Modernization Solutions
New Technologies

What new technologies have you introduced as part of a facility modernization project?

- Process automation
  - Consultant: 56%
  - Biologics Manufacturer: 70%
  - Small Molecule Manufacturer: 56%

- Single-use / disposables
  - Consultant: 49%
  - Biologics Manufacturer: 68%
  - Small Molecule Manufacturer: 19%

- Continuous manufacturing
  - Consultant: 34%
  - Biologics Manufacturer: 30%
  - Small Molecule Manufacturer: 44%

- CIP improvement
  - Consultant: 54%
  - Biologics Manufacturer: 48%
  - Small Molecule Manufacturer: 30%

- Modular construction
  - Consultant: 34%
  - Biologics Manufacturer: 30%
  - Small Molecule Manufacturer: 19%

INTERPHEX
Obstacles to New Technology

What do you believe is the biggest obstacle to the adoption of new technologies for facility modernization?

- Industry Conservatism
- Other
- Lack of Industry Standards
- Regulatory Acceptance
- Process Development Requirements
- Process Validation Requirements
- Insecure Vendor Supply Chain

Consultant | Biologics Manufacturer | Small Molecule Manufacturer
---|---|---
5% | 5% | 0%
5% | 13% | 22%
32% | 20% | 26%
20% | 12% | 26%
32% | 22% | 45%
7% | 5% | 4%
SU Technology Challenges

BIOLOGICS MANUFACTURERS ONLY:
What has been your most significant challenge associated with manufacturing using single use technology?

- Operator Training; SS to SU Mindset
- Warehouse Space; Waste Disposal
- Compatibility 25%
- Cost 18%
- Integrity Issues 15%
- Supply Train 18%
- Other 17%
- Manually Intensive 7%
Facility Focus

Facility Flexibility

What aspect of facility flexibility do you consider the most valuable?

 Ranked 1-5
1 = most valuable

- Ability to convert between clinical manufacturing and commercial production
- Ability to easily adapt the facility to new products and manufacturing processes
- Ability to accommodate both large and small volume production requirements
- Ability to produce multiple products with quick changeover
- Ability to easily expand or repurpose manufacturing space

Ranked by:
1. Ability to produce multiple products with quick changeover
2. Ability to accommodate both large and small volume production requirements
3. Ability to easily adapt the facility to new products and manufacturing processes
4. Ability to convert between clinical manufacturing and commercial production
5. Ability to easily expand or repurpose manufacturing space

Manufacturing | Engineering | R&D

- 3% | 5% | 8%
- 19% | 27% | 37%
- 10% | 13% | 31%
- 39% | 40% | 35%
- 8% | 19% | 7%
Transforming Facilities

The Challenges Ahead
• Market & Business Drivers
• Regulatory Requirements
• Disruptive Technologies

The Solutions We Need
• Renovations Revisited
• Flexible Manufacturing
• What’s Next?
For More Information

• Attend our next DME Facility Focus session!
  – Trending Technologies in Sterile Product Manufacturing Facilities
  – Tuesday, April 26, 1:00-2:00pm, Meeting Room 1

• Acquire DME Facility Focus survey whitepapers!
  – Available at INTERPHEX: DME booth #1666
  – Available at www.dmeforlife.com/about-us/facility-focus after INTERPHEX.

• Contact Information
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