Paving the Road towards Real-Time Release Testing

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Director, Life Sciences Consulting, Emerson
Mission of BioPhorum’s Technology Roadmapping Phorum

To accelerate industry innovation

..using a dynamic and evolving collaborative technology management process to focus an industry community by consensus on strategy over a 10 year time horizon

Determine precompetitive needs & drivers

Identify technology & manufacturing targets

Assess potential solutions

Coordinate implementation projects


- The result of two years effort by the Steering Committee and six enabling technologies roadmap teams
- 8 documents covering a 10 year outlook with >400 pages of content
- 4764 downloads (as per May 2018)
First Edition Technology Roadmap Vision

**Market Trends & Business Drivers – The Why**

<table>
<thead>
<tr>
<th>Cost pressure</th>
<th>Uncertainty</th>
<th>Market Growth</th>
<th>New Product Classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Payer pressure</td>
<td>Regulatory approvals</td>
<td>Emerging markets</td>
<td>Non-mAbs, ADCs</td>
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<tr>
<td>Biosimilars</td>
<td>Demand variability</td>
<td>Global reach</td>
<td>Gene therapy</td>
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<tr>
<td>Development</td>
<td>Competition</td>
<td>In region manufacture</td>
<td>Cell therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cost</th>
<th>Flexibility</th>
<th>Speed</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>-90% manufacturing cost</td>
<td>-90% changeover</td>
<td>-70% build time</td>
<td>10x robustness</td>
</tr>
<tr>
<td>-90% CAPEX</td>
<td>Demand response</td>
<td>-80% lead time</td>
<td>-90% cost of quality</td>
</tr>
</tbody>
</table>

**Biomanufacturing scenarios – The What**

1. Large-scale Stainless Steel Fed Batch
2. Intermediate-scale Single-use Perfusion
4. Small-scale <500L Portable Facility
5. Small-scale <50L for Personalized Medicine

**Scale**

- Distributed

**Enabling Technologies & Capabilities – The How**

<table>
<thead>
<tr>
<th>Process Technologies</th>
<th>Modular and Mobile</th>
<th>Automated Facility</th>
<th>Knowledge Management</th>
<th>Supply Partnership Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 90% CoGs</td>
<td>- 70% build time</td>
<td>- 50% Facility Build Speed</td>
<td>- ↓ Cost of process development</td>
<td>Safe, innovative supply chains:</td>
</tr>
<tr>
<td>- 90% process investment</td>
<td>- 75% ↓ CAPEX</td>
<td>- 50% ↓ OPEX costs from current</td>
<td>- ↓ Cost of quality</td>
<td>- ↓ Time</td>
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<tr>
<td>Process Intensification &amp; combination of unit operations</td>
<td>Quick to configure &amp; scale</td>
<td>Agile, high quality, and robust biomanufacturing</td>
<td>- Time to introduce a change to an existing process ↓ to 1 Month</td>
<td>Partnerships with quality built in</td>
</tr>
<tr>
<td>Continuous processing technologies coupled with advanced process control</td>
<td>Standard designs</td>
<td>Plug and Play</td>
<td>Cost of Non-Quality ↓ to 2% of operating costs</td>
<td>Standard working, integration and real time Electronic Data Exchange</td>
</tr>
<tr>
<td>Enhanced In-Line Monitoring</td>
<td>Streamlined validation</td>
<td>Open data standards</td>
<td>Efficient tech. transfer</td>
<td>Shared Planning</td>
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<tr>
<td>Indirect and Multivariate Sensors</td>
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<td>Integrated knowledge</td>
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<tr>
<td>Multivariate Analysis and Predictive Modeling</td>
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<td>Quality throughout lifecycle</td>
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**Technology Roadmapping**
In Line Monitoring and Real-time Release Project
“Reduce the need for release testing through implementation of RTRT/ILM”

Project Goal & Vision
Produce a prioritized list of CQAs and in-process controls (Upstream to Drug Substance) in order to inform the industry of the CQAs that should be targeted for a transition to in-line, on-line or at-line monitoring

• Rationale and business case will accompany each analytical candidate for conversion
• User Requirement Specifications (URS) will be developed for the selected measurements
• Identify attributes with the highest impact on quality, cost and speed business drivers
• Paradigm shift focus
  • Real Time Release Testing

<table>
<thead>
<tr>
<th>Biomanufacturers</th>
<th>Supply Partners</th>
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<tbody>
<tr>
<td>AstraZeneca</td>
<td>Emerson</td>
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<td>Biogen</td>
<td>GE Healthcare</td>
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<td>GSK</td>
<td>Pall</td>
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<td>Lonza</td>
<td>Sartorius Stedim</td>
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<td>Roche</td>
<td>Innovation Hubs</td>
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<tr>
<td>Sanofi</td>
<td>A*Star</td>
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</table>
• mAb process
• Batch mode
  • Continuous to be factored in later
  • Specific single use aspects not included

• Inline monitoring and Real Time Release Testing (RTRT)
  • Inline monitoring for better process control
  • RTRT includes both release of final drug substance and process intermediates for further processing
    • In-time Release Testing probably more adequate (doesn’t have to be real time testing)

Incremental vs paradigm shift
### Matrix components

#### Steps (unit op's)
- Seed scale up
- Production bioreactor
- Harvest
- Protein A capture
- Viral inactivation
- CEX B/E polishing
- AEX FT polishing
- Virus filtration
- Formulation
- Bulk-DS Filtration / Fill

#### Quality attributes
- Aggregation
- Charge Profile
- Deamidation
- DNA Conc
- Fragmentation
- Glycation
- Glycosylation profile
- HCP Conc
- Non-glycosylated heavy chain
- Oxidation
- Protein A Conc

#### Cell culture parameters
- Amino Acids
- Ammonia
- Antifoam Concentration
- B-D Glucan
- Cell Viability
- CO2
- Exit Gas Composition
- Galactose
- Glucose
- Glutamate
- Glutamine
- IgG titer
- Insulin
- Lactate
- Metals (Cu, Mn etc.)
- Methotrexate
- MSX
- Nutrients, metabolites, & CO2
- Osmolality
- pH, DO (bioreactor)
- Viable Cell Density
- Yeast Proteins

#### Downstream control
- Conductivity
- Flow
- pH
- Pressure
- Turbidity
- UV 280nm, 300nm, etc

#### Safety and other
- Endotoxin
- Microbial Safety
- Virus Safety
- Appearance (color)
- Bulk-DS Concentration
- Cell-based potency assay
- Density
- Potency/Binding: Antigen binding, Fc functional testing; FcgR, C1q and FcRn binding.
- Product Concentration
- Product Mass (Volume * Conc)
- Visible and Sub-visible Particles
- Volume / Mass / Level
<table>
<thead>
<tr>
<th>Attributes</th>
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</thead>
<tbody>
<tr>
<td>Step Attribute Matrix</td>
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</table>

Scope

Step Attribute Matrix

Current & Desired state

Ranking

URS & Business Case

Steps (unit op’s)
### Measurement type (use of data)

<table>
<thead>
<tr>
<th>Measurement type</th>
<th>Description</th>
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<tbody>
<tr>
<td>In-process test</td>
<td>Testing of an attribute, but don't take any action on this (\rightarrow) just good to know</td>
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<tr>
<td>In-process control</td>
<td>Testing of an attribute between steps (\rightarrow) needed for final release</td>
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<tr>
<td>Release testing</td>
<td>Final testing of DS according to specs</td>
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<tr>
<td>Release and stability</td>
<td>Final testing of DS according to specs</td>
</tr>
<tr>
<td>CPV monitoring</td>
<td>Demonstrating process consistency over life cycle</td>
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<tr>
<td>Process Control (feed-forward/backward)</td>
<td>Used to control the process (e.g. pooling criteria)</td>
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### Testing mode

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<tr>
<th>Mode</th>
<th>Description</th>
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<tr>
<td>Off-line</td>
<td>The sample is removed, isolated from, and analyzed in an area <strong>remote</strong> from the manufacturing process</td>
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<td>At-line</td>
<td>The sample is removed, isolated from, and analyzed in <strong>close proximity</strong> to the process stream</td>
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<tr>
<td>On-line</td>
<td>The sample is <strong>diverted</strong> from the manufacturing process, and may be returned to the process stream</td>
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<tr>
<td>In-line</td>
<td>The sample is <strong>not removed</strong> from the process stream. Can be invasive or non-invasive</td>
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</table>
Current State

- Measurement type
- Testing mode
- Time to result (includes offline waiting time)

Desired State

- Measurement type
- Testing mode
- Time to result (includes offline waiting time)
- Desired frequency (time between data points)
**Step/attribute ratings**

- **Q**: improves quality
  - Reduces variability
  - Improves product quality
- **R**: critical for real time release
  - Final drug substance
  - Process intermediates for further processing
- **C**: Need for change
  - How problematic are current methods?
  - How badly do we need to change these

**Ratings**

- **Q**: 1 or 2
- **R**: 1 or 2
- **C**: 1, 2, or 3

**Ranking**

- Weighted ranking
- SME ranking
- Rationalization
- Prioritization of steps/attributes

*Note: Focus for ranking is faster release of product*
Mapping the Highest Priority Cases

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<tr>
<th>Unit op</th>
<th>Aggregation</th>
<th>Amino Acids</th>
<th>Antifoam Conc</th>
<th>Bulk DS conc</th>
<th>Cell Viability</th>
<th>Charge Profile</th>
<th>Deamidation</th>
<th>DNA Conc</th>
<th>Endotoxin</th>
<th>Fragmentation</th>
<th>Glucose</th>
<th>Glycation</th>
<th>Glycosylation</th>
<th>Heavy chain</th>
<th>Heavy chain</th>
<th>Metabolic Stability</th>
<th>pH (DSP)</th>
<th>Concentration Product</th>
<th>Mass</th>
<th>Mass + Conc</th>
<th>Turbidity</th>
<th>Viable Cell Density</th>
<th>Virus Safety</th>
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<tbody>
<tr>
<td>Seed scale up</td>
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### Mapping the Highest Priority Cases

- **The Production bioreactor has a lot of unmet needs**
  - Some of them are incremental improvements, but put together they can make a big difference
### Mapping the Highest Priority Cases

#### Unit operations

<table>
<thead>
<tr>
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<th>DNA Conc</th>
<th>Endotoxin</th>
<th>Fragmentation</th>
<th>Glucose</th>
<th>Glycation</th>
<th>Glycosylation profile</th>
<th>HCP Conc</th>
<th>Insulin</th>
<th>Lactate</th>
<th>Metals</th>
<th>(Cu, Mn etc.)</th>
<th>Microbial Safety</th>
<th>glycosylated heavy chain</th>
<th>Oxidation</th>
<th>pH (DSP)</th>
<th>Product Concentration</th>
<th>Product Mass (Vol * Conc)</th>
<th>Turbidity</th>
<th>Viable Cell</th>
<th>Density</th>
<th>Virus Safety</th>
</tr>
</thead>
</table>

#### High priority (36)

- Aggregation
- Amino Acids
- Antifoam Conc
- Cell Viability
- Charge Profile
- Deamidation
- DNA Conc
- Endotoxin
- Fragmentation
- Glucose
- Glycation
- Glycosylation profile
- HCP Conc
- Insulin
- Lactate
- Metals
- (Cu, Mn etc.)
- Microbial Safety
- glycosylated heavy chain
- Oxidation
- pH (DSP)
- Product Concentration
- Product Mass (Vol * Conc)
- Turbidity
- Viable Cell
- Density
- Virus Safety

#### Medium priority (18)

- Bulk DS conc
- Cell Viability
- Charge Profile
- Deamidation
- DNA Conc
- Endotoxin
- Fragmentation
- Glucose
- Glycation
- Glycosylation profile
- HCP Conc
- Insulin
- Lactate
- Metals
- (Cu, Mn etc.)
- Microbial Safety
- glycosylated heavy chain
- Oxidation
- pH (DSP)
- Product Concentration
- Product Mass (Vol * Conc)
- Turbidity
- Viable Cell
- Density
- Virus Safety

#### Lower priority (12)

- Aggregation
- Amino Acids
- Antifoam Conc
- Cell Viability
- Charge Profile
- Deamidation
- DNA Conc
- Endotoxin
- Fragmentation
- Glucose
- Glycation
- Glycosylation profile
- HCP Conc
- Insulin
- Lactate
- Metals
- (Cu, Mn etc.)
- Microbial Safety
- glycosylated heavy chain
- Oxidation
- pH (DSP)
- Product Concentration
- Product Mass (Vol * Conc)
- Turbidity
- Viable Cell
- Density
- Virus Safety

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Protein A capture can be improved

- Protein A capture
- CEX B/E polishing
- AEX FT polishing

but the polishing steps (CEX B/E and AEX FT) have more to gain
Mapping the Highest Priority Cases

<table>
<thead>
<tr>
<th>Unit op</th>
<th>Aggregation</th>
<th>Amino Acids</th>
<th>Ammonia</th>
<th>Antibody Conc</th>
<th>Bulk DS conc</th>
<th>Cell Viability</th>
<th>Charge Profile</th>
<th>DNA Conc</th>
<th>Endotoxin</th>
<th>Fragmentation</th>
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<th>Non-glycosylated heavy chain</th>
<th>Oxidation</th>
<th>pH (DSP)</th>
<th>Product Concentration</th>
<th>Product Mass (Vol * Conc)</th>
<th>Turbidity</th>
<th>Viable Cell Density</th>
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<tr>
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Microbial safety #1
- Subject of a separate BPOG project

Product concentration and
Product mass common need
for all chromatography steps
- Better UV monitoring?
### Mapping the Highest Priority Cases

| Unit op            | Aggregation | Amino Acids | Antifoam Conc | Bulk DS conc | Cell Viability | Charge Profile | Deamidation | DNA Conc | Endotoxin | Fragmentation | Glucose | Glycation | Glycosylation profile | HCP Conc | Insulin | Lactate | Metals (Cu, Mn etc.) | Non-glycosylated heavy chain | Oxidation | pH (DSP) | Product Concentration | Product Mass (Vol * Conc) | Turbidity | Viable Cell Density | Virus Safety |
|-------------------|-------------|-------------|---------------|--------------|----------------|----------------|--------------|-----------|-----------|------------|-------------|---------|-----------|-----------------------|-----------|---------|---------|----------------------|---------------------------|-----------|---------|----------------------|-----------------------------|----------|---------------------|------------|
| Seed scale up     |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Production bioreactor |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Harvest           |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Protein A capture |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Viral inactivation |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| CEX B/E polishing |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| AEX FT polishing  |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Virus filtration  |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Formulation       |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |
| Bulk-DS Filtration / Fill |             |             |               |              |                |                |              |           |           |             |            |         |           |                       |           |         |         |                      |                          |           |         |                      |                             |          |                     |            |

Better cell culture process control in seed train and production bioreactor
### Mapping the Highest Priority Cases

#### Quality attributes in focus
- Charge profile
- Aggregation
- HCP

#### Unit operations and quality attributes

| Unit op                  | Aggregation | Amino Acids | Ammonia | Antifoam Conc | Bulk DS conc | Cell Viability | Charge Profile | Deamidation | DNA Conc | Endotoxin | Fragmentation | Glucose | Glycation | Glycosylation profile | HCP Conc | Insulin | Lactate | Metals (Cu, Mn etc.) | Microbial Safety | Non-glycosylated heavy chain | pH (DSP) | Product Concentration Mass (Vol * Conc) | Turbidity | Viable Cell Density | Virus Safety |
|-------------------------|-------------|-------------|---------|---------------|--------------|----------------|----------------|--------------|-----------|-----------|---------------------|---------|-----------|----------------------|----------|----------|---------|----------------------|------------------|------------------------|-----------|----------------------|-------------|
| Seed scale up           |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Production bioreactor   |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Harvest                 |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Protein A capture       |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Viral inactivation      |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| CEX B/E polishing       |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| AEX FT polishing        |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Virus filtration        |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Formulation             |             |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
| Bulk-DS Filtration / Fill |           |             |         |               |              |                |                |              |           |           |                    |         |           |                      |          |          |         |                      |                  |                        |           |                      |             |
High priority case example: Charge profile

**Current state**

Production bioreactor
- Release testing – Offline/At-line – 3 hours

Protein A
- CPV monitoring – Offline – 3 hours

Viral inactivation
- CPV monitoring – Offline – 3 hours

CEX B/E
- CPV monitoring – Offline – 3 hours

AEX FT
- CPV monitoring – Offline – 3 hours

**Desired state**

Production bioreactor
- In-process test – Online/Inline - <30 min
- Improves quality – Critical for RTRT

Protein A
- In-process test – At-line/Online – <5 min

Viral inactivation
- In-process test – Offline/At-line – 1 x pool/batch

CEX B/E
- Process control – Inline – Continuous
- Improves quality – Critical for RTRT

AEX FT
- In-process test – Offline/At-line – 1 x pool/batch
High priority case example: Charge profile

Current state

Production bioreactor
• Release testing – Offline/At-line – 3 hours

Protein A
• CPV monitoring – Offline – 3 hours

Viral inactivation
• CPV monitoring – Offline – 3 hours

CEX B/E
• CPV monitoring – Offline – 3 hours

AEX FT
• CPV monitoring – Offline – 3 hours

Desired state

Production bioreactor
• In-process test – Online/Inline - <30 min
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Protein A
• In-process test – At-line/Online – <5 min

Viral inactivation
• In-process test – Offline/At-line – 1 x pool/batch

CEX B/E
• Process control – Inline – Continuous
  Improves quality – Critical for RTRT

AEX FT
• In-process test – Offline/At-line – 1 x pool/batch
Top Ranking Attributes

1. **Glucose** – Production Bioreactor

2. **Aggregation** – CEX Bind & Elute

3. **HCP** – Anion Exchange Flow Through

4. **Cell Viability** – Seed Scale Up and Production Bioreactor

5. **Viable Cell Density** – Seed Scale Up and Production Bioreactor

6. **Charge Profile** – Production Bioreactor, CEX Bind & Elute

7. **Glycosylation Profile** – Production Bioreactor

8. **Amino Acids** – Production Bioreactor

9. **Titer/Product Concentration** – Protein A

10. **DNA** – Anion Exchange Flow Through

Note: Does not include microbial or virus safety – this is already a prioritized focus of separate workstream.
### Mapping the highest priority cases
Work in progress – pending final prioritization

<table>
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<tr>
<th>Unit op</th>
<th>Aggregation</th>
<th>Amino Acids</th>
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Conclusions and future outlook

What we learned

- Complex task
  - Bridging upstream – downstream - formulation
- Value of industry-wide horizontal and cross-functional team
  - Multiple end users
  - Mix of end-users and suppliers

Next steps

- Industry feedback
- Business case development
- Develop URS for high priority cases

The main goal is to enable a paradigm shift towards Real-Time Release Testing
Acknowledgements
The following people have generously contributed their time and energy to this project:

Annika Kleinjans (Roche)
Andre Choo (A*Star)
Ben Wilkes (Lonza)
Christian Grimm (Sartorius Stedim)
Edita Botonjic-Sehic (Pall)
Joanna Pezzini (AstraZeneca)
John-Paul Smelko (Biogen)
Justin Beller (Lonza)
Michalle Adkins (Emerson)
Reed Harris (Roche)
Rick Lu (AstraZeneca)
Stacey Traviglio (Biogen)

Udayanath Aich (Sanofi)
Vakhtang Loladze (GSK)
Victor Saucedo (Roche)
Bela Green (BioPhorum)
It is the clear policy of BioPhorum that Biophorum and its members will comply with all relevant anti-trust laws in all relevant jurisdictions.

All BioPhorum meetings and activities shall be conducted to strictly abide by all applicable antitrust laws. Meetings attended by BioPhorum members are not to be used to discuss prices, promotions, refusals to deal, boycotts, terms and conditions of sale, market assignments, confidential business plans or other subjects that could restrain competition.

Anti-trust violations may be alleged on the basis of the mere appearance of unlawful activity. For example, discussion of a sensitive topic, such as price, followed by parallel action by those involved or present at the discussion, may be sufficient to infer price-fixing activity and thus lead to investigations by the relevant authorities.

Criminal prosecution by federal or state authorities is a very real possibility for violations of the antitrust laws. Imprisonment, fines or treble damages may ensue. BioPhorum, its members and guests must conduct themselves in a manner that avoids even the perception or slightest suspicion that antitrust laws are being violated. Whenever uncertainty exists as to the legality of conduct, obtain legal advice. If, during any meeting, you are uncomfortable with or questions arise regarding the direction of a discussion, stop the discussion, excuse yourself and then promptly consult with counsel.

The antitrust laws do not prohibit all meetings and discussions between competitors, especially when the purpose is to strengthen competition and improve the working and efficiency of the marketplace. It is in this spirit that the BioPhorum conducts its meetings and conferences.
Supplier Interactions Policy v3.0

The BioPhorum Operations Group (BPOG) facilitates a cross industry collaboration process for Biopharmaceutical developers and manufacturers with the aim of accelerating the rate at which the biopharma industry attains a mature and lean state benefitting patients and stakeholders alike. Collaboration modes include best practice sharing, benchmarking, joint-solution development to common challenges, definition of standards requirements and formation of collective perspectives to mutual opportunities and regulatory guidelines.

Biopharmaceutical developers and manufacturers recognize the legally enforceable duties they have including the responsibility to control the quality of materials from their suppliers. From time to time BPOG-facilitated collaboration requires, and benefits from, supplier interaction.

Suppliers are providers of supply chain materials such as chemicals, glass, components, excipients, and media. They are also providers of process equipment such as single use systems, engineering parts and consumables. BPOG-facilitated supplier interactions may involve: harmonizing manufacturer requirements and communicating these to suppliers; seeking feedback on proposed standards; gaining opinions and ideas related to business process improvement; use of problem solving tools; and gaining support for new ways of working.

The ultimate goal of the BPOG collaboration is to strengthen competition, assure product quality and protect patient supply.

The purpose of this document is to set out the principles and policies that BPOG follows to ensure that BPOG-facilitated supplier interactions are conducted in the correct and appropriate way to meet all legal and business compliance requirements.

Underlying Principles and Policies

**Competition Laws**
All supplier interactions will comply with anti-trust and competition laws and have regard to BPOG’s anti-trust compliance statement

**Member responsibilities**
Individual biopharma companies are responsible for defining their requirements of suppliers.

**Innovation and commercial interests**
All supplier interactions will recognize and respect the need for suppliers to innovate and pursue their own commercial interests.

**Intellectual Property**
All supplier interactions will respect suppliers’ intellectual property rights.

**Confidentiality / Non Disclosure**
All supplier interactions will take into account, respect and encourage compliance with confidentiality and non-disclosure agreements.

**Equal Treatment**
All suppliers will be treated equally

**Communication**
These principles, policies and procedures will be communicated to BPOG members and suppliers whenever supplier interactions are planned or are taking place.

**BPOG responsibilities**
- It is the responsibility of BPOG Directors to ensure that these principles and policies are upheld and procedures are in place to support them.
- BPOG will educate and train its staff so they understand and follow these principles and policies and are able to communicate them when needed.
- BPOG documentation will reference or directly include relevant parts of the Supplier Interaction Policy.
- BPOG will establish and maintain records to demonstrate compliance with these principles and policies.
Introduction

The BioPhorum Operations Group (BPOG) is a cross industry collaboration with the aim of sharing best practice in the area of Operational Excellence.

Participation in BPOG is restricted to authorized member company representatives as described in the Principles of Membership Agreement.

While sharing information is central to the process of this collaboration, it is important to understand what information is appropriate to share. Our companies have a great deal of confidential information and intellectual property that should not be shared within BPOG.

This document seeks to guide the reader so that the individuals and companies involved follow the correct code of conduct and problems are avoided.

It is the clear and stated intention of BPOG that the Group and its activities are conducted at all times in full compliance with relevant completion/anti-trust rules.

Responsibilities

It is the responsibility of every person who participates in a BPOG event or sharing activity to make sure they are aware of what information is appropriate to share.

Furthermore, all participants are responsible for vetting any information to be shared via their company’s public disclosure review processes and that all information shared is free of any “Confidential” stamps or markings.

The key contact (L2) for each member company should ensure confidentiality and that IP issues are highlighted to their colleagues and all applicable company policies regarding external collaboration and public disclosure are adhered to.

The BPOG facilitators are responsible for reminding all participants of their obligations with respect to information sharing.

Sharing information

The following list is representative of the types of disclosures commonly allowed by corporate policies. BPOG participants should review their company policies to ensure they are in compliance prior to any disclosures. Information in the following areas is typically allowed:

- Operational excellence best practice models
- Management approaches and philosophies
- Organizing and planning ways of working
- Non-product or process specific generic operating procedures
- Information in the public domain
- Information provided by suppliers which would ordinarily be shared with customers
- Non-product or process specific generic engineering or technical information relating to process equipment
- General learning and ‘context’ conclusions from QA and Regulatory activity

Information from the following areas is typically prohibited by corporate policies

- Product related information
- Product related process data which constitutes intellectual property
- Specific audit or regulatory inspection findings or observations
- Product specific analytical methods
- Specific cost numbers where a market advantage may result or a supplier might be disadvantaged
- Information that is marked as confidential by the member company or a supplier
- Price information of any type
- Proprietary information including intellectual property and patented processes and equipment

BPOG event participants should direct all questions regarding information disclosure to their L2 BPOG representatives or corporate legal departments.
Back-ups