A Global Technology Roadmap for Biopharmaceutical Manufacturing: An Update from BPOG

Philip McDuff (Biogen)

Presentation to ISPE Facility of the Future Meeting 2016
Agenda

- Who is BPOG
- **What is a Technology Road Map:**
  Introduction to the Biopharmaceutical Industry Collaboration
- Why a Road Map is needed. Why now…
- How is the Map Created: The Methodology
- **Now:** Overview of key roadmap content to date
  - Market trends & business drivers
  - Biomanufacturing scenarios
  - Initial process modelling results
- **When:** Next Steps
Who is BioPhorum Operations Group (BPOG)

Industry collaboration that brings together 33 bio-manufacturers, collaborating in six phorums to accelerate the industry

<table>
<thead>
<tr>
<th>AbbVie</th>
<th>Alexion</th>
<th>Amgen</th>
<th>AstraZeneca</th>
<th>Bayer</th>
<th>Biogen</th>
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<tr>
<td>Bristol-Myers Squibb Company</td>
<td>COOK</td>
<td>Dynavax Technologies</td>
<td>Eisai</td>
<td>Ferring Pharmaceuticals</td>
<td>Fujifilm</td>
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<td>Genentech</td>
<td>Genzyme</td>
<td>GR</td>
<td>Immunogen, Inc</td>
<td>Ipsen</td>
<td>Janssen</td>
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<td>Lilly</td>
<td>Lonza</td>
<td>MSD</td>
<td>Merck</td>
<td>Pfizer</td>
<td>Regeneron</td>
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<td>Novartis</td>
<td>Novavax</td>
<td>Novo Nordisk</td>
<td>Roche</td>
<td>Samsung</td>
<td>Sanofi</td>
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<td>Shire</td>
<td>Takeda</td>
<td>UCB</td>
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6 Phorums covering all aspects of operations and accelerating biopharma industry’s journey to maturity

- **Drug Substance, Fill Finish, Development Group and IT Phorums**
  - Accelerate the way the industry delivers near term results making best practice development and implementation faster, cheaper and smarter

- **Supply Partner Phorum**
  - Strategic focus on the wider supply chain needs of the industry; defining, developing & implementing solutions
  - Focus on business processes/systems & culture

**The focus for this presentation**

- **Technology Roadmapping**
  - Revolutionise the way the industry develops longer term transformational manufacturing and technology capabilities
  - Focus on longer term strategy & 10+yr time horizon, defining needs, difficult challenges and potential solutions

**BPOG manages the linkages to ensure**

- Decisions are made at the right time, at the right place by the right people
- Linkages are made visible to avoid redundancy
- Synergies are leveraged through effective coordination

**Regulatory Interactions Group**

- Engage and align with Health Agencies in the design and adoption of advances in manufacturing
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What is a Technology Road Map?

An industry technology roadmap is –

a *dynamic and evolving collaborative technology management process*

For:

- determining precompetitive critical needs and drivers,
- identifying technology and/or manufacturing targets, and
- assessing/modeling potential solutions
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Why is a Technology Roadmap needed for the Biopharm Industry?

*Complex industry has traditionally held back innovation…*

- Complex global regulatory environment
  - Multiple jurisdictions
  - Varying requirements
- Biomanufacturers are risk averse
  - Delays in approval have major impact
  - Uncertainty around product comparability between scales and process changes
  - New technology may not be adapted because of perceived risks to program
  - Everyone wants to be a Fast Second!
- Biomanufacturers and Suppliers develop technologies in isolation
- Technology standardisation usually only occurs after the technology is launched
- Suppliers find it difficult to innovate
  - Have different end user requirements; company to company
  - Risk-reward balance is poor
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Following the Lead from other Industries.....
Using method from University of Cambridge’s Institute for Manufacturing

Semiconductor Industry

NASA
### Technology Roadmapping Steering Committee

**Biopharmaceutical Company Members**

- Abbvie
- AstraZeneca
- Bayer
- Biogen
- Fujifilm
- GSK
- Immunogen
- Janssen
- Lonza
- Lilly
- Merck MSD
- EMD Serono
- Pfizer
- Roche
- Sanofi
- Shire
- Takeda

**Supply Partner Members**

- GE Healthcare Life Sciences
- Kaiser Optical Systems
- Millipore Sigma
- Novasep
- PM Group
- Sartorius Stedim
- Thermo Fisher Scientific

- Developed a strong Steering Committee
  - Required decision making
  - Driving roadmap
  - Subject matter experts access

- Diverse participants
  - 17 biomanufacturers
  - 6 supply partners recently joined (and growing)
  - Academics & regional centres, e.g. MIT, AMBIC, CPI, SEDB, NIIMBL

- Over 130 people involved globally
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High level Technology Roadmap structure and approach

Industry Trends
- Business Drivers
  - Payer pressure on cost
  - Diversification of product groups
  - In region manufacturing
  - Personalised medicine

  | Speed | Cost | Flexibility | Quality |

Biomanufacturing scenarios
- Drug Substance – Large scale stainless steel
- Drug Substance – 2K scale SUS Continuous USP
- Drug Substance – 2K scale SUS Batch USP
- Drug Substance – <500L scale Continuous

Enabling Technologies
- Process Technologies
- Inline Monitoring & Real time Release
- Modular & mobile
- Automated Facility
- Knowledge Management
- Supplier Partnerships
Evaluating Biopharmaceutical Market Trends

New product classes
- Personalised medicine
- New Treatment Modalities
- Advances in Systems Biology
- Payer pressure on cost of drugs
- Rising Costs of Drug Development
- Biosimilars Competition
- Clinical Failures

Market growth
- Volume/year/drug
- Number of drugs supplied
- Global reach and emerging markets

Strength of Sales (Biologics)
- Robust Pipelines
- Emerging Markets
- In-region manufacturing requirements
- Complex Global regulatory environment
- Demand Forecasts

Cost
- Payer pressure
- Biosimilars
- Cost of clinical Failure

Uncertainty of approvals and sales
- Social/Political Perceptions
- Market Share
- Dose Requirements

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Clinical Failures
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- Market Share
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Rising Costs of Drug Development
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Collective Brainstorming by Industry Experts
The team have focused on 4 biomanufacturing scenarios

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Typical Products</th>
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<tbody>
<tr>
<td>1 Stainless Steel &gt; 10K, Batch – Batch /Continuous</td>
<td>Mab’s, Mab Fusions, rec Proteins,</td>
</tr>
<tr>
<td>2 Disposable ~ 2K, Continuous – Semi Continuous / Continuous</td>
<td>Unstable Products e.g. Factor VIII, Therapeutic Enzymes, Viral Vaccines, Allogenic Cell Therapy</td>
</tr>
<tr>
<td>3 Disposable ~2K, Batch – Semicontinuous/Batch</td>
<td>Mab’s, Mab Fusions, rec Proteins, Viral Vaccines</td>
</tr>
<tr>
<td>4 Disposable &lt; 500L, Continuous - Continuous</td>
<td>Biologics on Demand, Bioproduction at Bedside, Typically recombinant proteins and viral vaccines in microbial systems. Cell/Gene Therapy</td>
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</tbody>
</table>
## Cross Industry Collaboration = Substantial Benefits

<table>
<thead>
<tr>
<th>Roadmap Team</th>
<th>Vision</th>
<th>Benefit</th>
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</table>
| Process Technology            | Process Intensification                                                | • Reduction in facility size  
|                               | Continuous Processing                                                  | • Reduced capital investment  
|                               |                                                                        | • Speed to market  
| In-line Monitoring and Real-time release | Process control and assurance of product quality | • Flexibility for smaller patient populations  
|                               | Global regulatory testing standards, advanced process control strategies and raw material characterization. | • Speed  
|                               |                                                                        | • Reduced cost  
| Modular and Mobile            | Manufacturing systems using ‘plug and play’ standard designs            | • Tighter product and process control  
|                               |                                                                        | • Reduced cost of quality  
|                               |                                                                        | • Enables real time release  
| Fully Automated Facility      | Scale up from development to manufacturing in a fully automated facility. | • Eliminate $Bn’s of inventory  
|                               |                                                                        | • Product released 1-2 days after mfg  
|                               |                                                                        | • Reduce quality costs  
| Supplier Management           | Technology development partners for our industry                       | • Scalable capacity  
|                               |                                                                        | • Manufacturing process available in weeks rather than years.  
| Knowledge Management          | E2D integrated knowledge of product and process technology              | • Consistent high product quality  
|                               |                                                                        | • Reliable supply  
|                               |                                                                        | • Reduced time to market  
|                               |                                                                        | • Innovative supply partners  
|                               |                                                                        | • Industry needs delivered faster and better  
|                               |                                                                        | • Speed to market  
|                               |                                                                        | • Cross-product learning  
|                               |                                                                        | • Efficiency throughout product lifecycle  

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Modeling bio-manufacturing scenarios can identify areas for technology innovation

- **Approach to modeling (using the BioSolve Software)**
  - Identify areas of opportunity for improvement within a given scenario / facility type.
  - Compare performance between options within a scenario or between scenarios relative to a given metric
    - e.g. compare estimated Cost of Goods using different process formats
  - Process parameter sensitivity analysis
  - Identify bottlenecks in throughput and breakpoints in technology strategy/selection.
  - Evaluate the technology improvements proposed by the roadmap teams

![Scenarios](image-url)
Roadmap teams are developing the strategic technology needs, challenges, and potential solutions (Draft - Illustrative)

<table>
<thead>
<tr>
<th>Unit Operation</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4A</th>
<th>Scenario 4B</th>
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</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>Bioreactor Volume</td>
<td>SS &gt;10kL BXR</td>
<td>Disposable 2kL BXR</td>
<td>Disposable 2kL BXR</td>
<td>Disposable &lt;500 BXR</td>
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<tr>
<td></td>
<td>Bioreactor Mode</td>
<td>Batch</td>
<td>Continuous</td>
<td>Batch</td>
<td>Continuous</td>
</tr>
<tr>
<td></td>
<td>DSP Mode</td>
<td>Batch/Continuous</td>
<td>Semi-continuous/Continuous</td>
<td>Batch/Semi-continuous</td>
<td>Continuous</td>
</tr>
<tr>
<td></td>
<td>Facility Design</td>
<td>Segregated suites/Large footprint</td>
<td>Moderate footprint/Ballroom</td>
<td>Moderate footprint/Ballroom</td>
<td>Small footprint/Ballroom</td>
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<tr>
<td></td>
<td>Processing</td>
<td>Low Bioburden</td>
<td>Closed</td>
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<td>Product</td>
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<td>mAb and other CHO TPs</td>
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<td></td>
<td>Comment</td>
<td>Adaptsions on current facility</td>
<td>Continuous protein production through</td>
<td>High titer batch USP processes to match</td>
<td>Highly productive deployable facilities</td>
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<tr>
<th>(Metric1)</th>
<th>CoG</th>
<th>2019</th>
<th>2022</th>
<th>2026</th>
<th>SCENARIO(S)</th>
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<tbody>
<tr>
<td>(Metric2)</td>
<td>Quality</td>
<td></td>
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<td>All</td>
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<tr>
<td>(Metric3)</td>
<td>Speed</td>
<td></td>
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<tr>
<td>(Metric4)</td>
<td>Flexibility</td>
<td></td>
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**NEED**
Improved reliability of current in-line sensors

**CHALLENGE**
The current process parameter sensors are still not reliable and some of them need offline recalibration during the process. The number of the ports in the bioreactor are limited. The disposable sensors reliability getting better, but still have room to improve.

**POTENTIAL SOLUTION**
Reliable and robust sensors (pH, DO, CO2, T) without recalibration/correction during the process, forming sensors, Disposable sensors; multifunction sensors.
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### Roadmap plan through to publication

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<tr>
<th></th>
<th>2016</th>
<th>2017</th>
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<td>Face to face meetings</td>
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<tr>
<td>Review points</td>
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<tr>
<td>Steering committee contribution</td>
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<tr>
<td>Roadmap Team activity</td>
<td></td>
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<tr>
<td>Industry stakeholder engagement</td>
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<tr>
<td>Communications</td>
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#### Face to face meetings
- TR03 – Roadmap team meeting (12-14 Apr’16)
- TR04 – Finalising the roadmap (20-22 Sep’16)
- TR05 – Implementation planning and Industry Response

#### Review points
- 1. Summary document review
- 2. Detail document review
- Freeze document
- Publish

#### Steering committee contribution

#### Roadmap Team activity
- Overview: Market Trends, Product Classes, Business Drivers, Scenarios, Modelling
- Summary: Vision, Map, Scope, Linkages
- Detail: Needs, Challenges, Solutions
- Challenges, Solutions
- Review to clarify focus, linkages & spot gaps
- Preparation for TR04: List top points to add value, issues, debating points
- Final modifications and input from industry stakeholders
- Implementation planning and industry response
- Detail review followed by final changes to document

#### Industry stakeholder engagement

#### Communications
- BPI conference
- ISPE Article
- CASSS
- BPI article
- BPI article

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**ISPE.org**

Connecting Pharmaceutical Knowledge

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Two year cycle of roadmapping - example

2016
- TR04: Finalising the roadmap, Sep’16
- TR05: Implementation plan & Industry Response, Apr’17

2017
- TR06: Industry response and Roadmap production, Oct’17
- TR07: Industry response & Roadmap production, Apr’18

2018
- TR08: Industry response & Roadmap production, Oct’18

Roadmap 1st Edition
- Articles
- BPI Conference, Oct’16
- Publish May’17
- CASSS
- BIO

Comms, planning, industry response & review
- BPI Conference, Oct’17
- CASSS Articles & conferences
- BIO
- BPI Conference, Oct’18

Feedback
- Scope & scenarios
- Teams & basic roadmap
- Detailed roadmap

Next roadmap 2nd Edition
- Edits, revisions and progress updates to existing roadmap
- New modalities and product groups
- Disruptive technologies
- Adjacent process areas

Publish 2019
Thank You!

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