LEVERAGING AN INTEGRATED DATA PLATFORM TO ADVANCE PROCESS UNDERSTANDING AND ENHANCE CONTINUED PROCESS VERIFICATION (CPV)
BIOLOGIC MEDICINES ARE BECOMING MORE HIGHLY ENGINEERED AND MORE DIVERSE

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<tr>
<th>Small Molecules</th>
<th>siRNAs</th>
<th>Therapeutic Proteins</th>
<th>Monoclonal Antibodies</th>
<th>Fusion Proteins</th>
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<tbody>
<tr>
<td>BITE Antibody Constructs</td>
<td>Bispecific Antibodies</td>
<td>Peptides</td>
<td>Peptidomimetics</td>
<td>Bioengineered Lm immunotherapy</td>
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<td>Oncolytic Immunotherapies</td>
<td>Antibody Drug Conjugates</td>
<td>CAR T Cells</td>
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Batch/Fed Batch
- Product quality drivers
- Supply requirements
- Financial considerations

Continuous
- Product quality drivers
- Supply requirements
- Financial considerations

Next Gen Mfg
- One size does not fit all

Appropriate manufacturing technologies can be matched to modalities to deliver to the Quality Target Product Profile
THERAPEUTIC DIVERSITY REQUIRES A FLEXIBLE MANUFACTURING NETWORK

- Flexible modular platforms leveraging disposables
- Large steel based plants & platforms
- Low productivity labor intensive processes

~80% size reduction

MoF Facility 120k sq ft

Conventional Facility 750k sq ft

AMGEN
Pioneering science delivers vital medicines
Regardless of modality or manufacturing platform, the process development objective remains the same.

- Reliability
- Quality
- Modality independence
- Speed and Agility
- Start with Attributes
- Data insights

**Process and Attribute Understanding**

**Target Product Profile**
- Attribute driven process development

**Product Quality Attribute Assessments**
- Process understanding ensures reliable supply through consistent performance

**Quality Target Product Profile (QTPP)**
- Process designed to robustly achieve QTPP
FLEXIBLE MANUFACTURING INCLUDES A NEW APPROACH TO PLATFORMS

WITH **ONE MODALITY**

1 x Platform  ➔  1 x Manufacturing

WITH A GROWING NUMBER (n) OF MODALITIES

n x Modalities  ➔  n x Platforms  ➔  n x Manufacturing
However, modular platform approaches introduce new unknowns

**With one modality**

- Consistent raw materials
- Prior knowledge assets
- Mature technologies
- Sources of variability well understood

**With a growing number (n) of modalities**

- Complex and new raw materials
- New sources of variability
- Emerging technologies
- Fewer prior knowledge assets

Enabling successful manufacturing requires better ways to prospectively identify and manage variation.
EVEN TRADITIONAL MANUFACTURING APPROACHES GENERATE SIGNIFICANT AMOUNTS OF DATA

> 500 QC entries

> 2000 Batch Record Entries

> 500 million Continuous data points

Challenge: Holistically monitor & control variance throughout the process
Multiple sources of data and information are available however it can be challenging to exploit them.
COMBINING TECHNICAL INFRASTRUCTURE WITH BUSINESS KNOWLEDGE ALLOWS FOR BETTER INFORMATION IN DECISION MAKING

The Challenge: Different data at different sites on different systems

IS Infrastructure Investment

The Outcome: Accessibility and aggregation of data to drive innovation

The Impact:
- Actionable data analytics
- Product and process insights
- Differentiated processes and products
The Enterprise Data lake contains many data sources that can be combined to maximize access to a range of data sources (structured and unstructured).
CAN WE LEVERAGE PRIOR KNOWLEDGE TO PREDICT FUTURE PROCESS CAPABILITY?
A systematic approach to determining sources of process variation based on prior knowledge allows for purposeful process design.
RAW MATERIALS CONTINUE TO REPRESENT A CHALLENGING SOURCE OF INPUT VARIABILITY

Investment in data infrastructure enables access to data and knowledge allowing rapid identification of correlations between raw materials and process performance
PERFORMANCE PREDICTABILITY REQUIRES USE OF DEVELOPMENT DATA AND AGGREGATED RELEVANT PRIOR KNOWLEDGE

Ppk predictability improves with additional data. Bayesian statistics can leverage prior knowledge to supplement development data using a science-based approach.
CONCLUDING REMARKS

Modular platforms are an enabler of a biology first, modality independent strategy.

Manufacturing operations generate significant amounts of data such that it can be difficult to determine sources of process variation.

Investment in solutions to store and access enterprise data allows us to maximize our prior knowledge and even predict performance capability during early development.
All difficulties are easy when they are known.

QUESTIONS