overcoming challenges to transition your raw materials

From research to clinical & commercial - biomanufacturing
The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.
Introduction

Overcoming challenges to transition your raw materials
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Industry focus areas

Supply Chain Origin

Change Control

Risk Mitigation
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Quality Services Teams

START

with the end

in mind
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Agenda

1. Start with the end in mind: Risks and long term effects
2. Challenges faced to use the right quality: Confronting the myths
3. Critical quality features to look at
4. How to work with suppliers (partners)
5. Conclusion: Key take-away
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Start with the end in mind

Quality standards differ for raw materials

1. Clinical development and phase
   - Discovery – Lower cost, less controlled materials
   - Early vs. late phase clinical trials
   - Transition to commercial manufacturing

2. Material use within biological manufacturing process
   - Upstream
   - Downstream
   - Final formulation
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Start with the end in mind

- Quality standards differ for raw materials
- Quality requirements increase for drugs approaching commercial launch

GMP Raw materials

Controlled Raw materials

Research Laboratory reagents

Viral clearance Prevents pathogens transmission

Minimum quality features

Biomanufacturing and vaccines quality requirements
Raw materials, cell lines, cell culture media
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Confronting the myths in raw material qualification

Some biopharma manufacturers have robust risk mitigation programs. However, myths still remain.

**Myth #1:** *Biotechs are critical and can make all suppliers change!*

**Myth #2:** *All GMP claims are the same.*

**Myth #3:** *Quality by Design is for the quality department.*

**Myth #4:** *Only one of us can win!*
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Confronting the myths in raw material qualification

Myth #1: Biotechs are critical and can make suppliers change
Fact Many Industrial manufacturers are not set up to meet needs of biopharma manufacturers *whatever your size*

**Industrial manufacturers could be unresponsive**
- Many of their products are not made for this regulated industry
- Volumes purchased are too low to open doors or cause change
- Quality assurance and documentation requirements for biopharma usually NOT met

**Risk assessment required**
- Critical to Quality attributes may not be compliant
- Technical support to biopharma or diagnostics applications may be non-existent
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Confronting the myths in raw material qualification

Myth #2: All GMP claims are the same
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**Fact**
Supplier claims vary

**Look for the details**
- Can supplier provide transparency to manufacturer?
- Look for defined approach to product and vendor qualification
- Biopharma manufacturer is required to confirm quality, cannot just accept quality claims

**Differing definitions**
- Some suppliers claim GMP for food and cosmetic grades
- Food Chemical Codex and Cosmetic not typically acceptable GMP quality for Biopharma use
Myth #3: Quality by Design is for the quality department.
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**Confronting the myths in raw material qualification**

**Fact**
Quality by Design is a systematic approach for development

**Systematic approach**
- Multivariate analysis
- Process analytical chemistry
- Project and knowledge management tools

**Development-flexibility within the design space**
- Investment of resources to obtain the knowledge to control the commercial manufacturing process
- Supplier may be unaware of your needs

**Quality risk management-risk based control strategy**
- Assess, control, communication and review of risks to the quality of the drug
- Improve decision making
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Raw material critical quality attributes to look at

Have you defined what makes your raw materials critical?

- Impact on impurities
- Impact on safety and/or performance
- Origin
- Impact on cost
- Availability and impact on supply
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Myth #4: Only one of us can win!
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Confronting the myths in raw material qualification

**Fact**  
Customer-Supplier partnerships work best

**Activities which generally happen in Phase II**

- Send questionnaires and specifications to suppliers
- Find potential gaps – minor & major
- Try to close gaps with existing suppliers
- Search for alternatives when gap is too important

**Finance and Regulatory Affairs do not like the costs of the “delayed effect”**

- Understanding the application
- Insure the chosen raw material is suitable
- Customer needs vs. wants
- Long-term capacity planning for availability
- Cost of raw material vs. value in use
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Raw material critical quality attributes to look at

- Control on critical parameters
- Notification of critical changes
- Cost effective
- Security of supply
- Network of reliable suppliers
- Consistent in form, quality & specifications
- Known origin: biologics crude material & manufacturing
- Origin documentation guaranteed

Develop "critical to quality attributes" based on your definition.
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Supply Chain Transparency: Where do you draw the line?
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How to work with suppliers – Research to Clinical & Commercial

RESEARCH

Drug Pipeline

MANUFACTURING

Choices, Innovation, Price

Transition

Grey Zone

Supplier challenge: Provide raw materials suitable for use in manufacturing

Need to meet regulatory guidelines
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How to work with suppliers – Research to Clinical & Commercial

Historical Approach – Raw Material Qualification

1. Research developers use easily available raw materials with established specifications

2. As drug moves into clinical trials, sourcing starts to ask for documentation of quality (Certificate of Origin, Name of Manufacturer)

3. Requests to add in quality to research-grade materials after purchase

4. For standard traded items, name of manufacturer may not even be available, and often not feasible to provide current product at a higher quality, such as GMP

Leads to FRUSTRATION and DELAYS
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Comparison of approaches

**Traditional Development**

- Focus on end product safety and performance
- Fixed process – do not change make any changes after Research
- Fixed specifications
- Work with suppliers starting phase III

**Enhanced Development**

- Systematic – understand material features and process to meet critical to quality attributes
- Supply Chain Risk Management to ensure uninterrupted drug supply
- Work with suppliers who can support you in transitioning to Clinical and comply with Regulatory requirements
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Current Supply Chain Management Requirements

Requirements of the Biopharma & Diagnostic Industry

- Management of Changes – Risk based
- Chain of Custody – Supply Chain Awareness
- Manufacturer/ Supplier Partnership
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Making a Difference

Influencing industry standards and regulations

• Thought leadership for the industry
  • Rx360
  • BPOG

• Collaborative environment
  • Biopharma manufacturers
  • Diagnostic manufacturers
  • Suppliers

• Addressing industry issues together
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Find the Right Balance

Quality

Cost

supply chain partner
contact details

Tom Beil, Quality Services
Merck KGaA, Darmstadt, Germany

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