Dual sourcing of primary packaging components in biopharma manufacturing: A case study

Tim Schultz, BS, MBA
Merck & Co., Inc., Rahway, NJ, USA

Abstract

- The biopharmaceutical industry has weathered multiple challenges over the past 4 years. One of the major pressure points that manufacturers of parenteral products have had to overcome is supply chain issues – namely with **primary packaging components**. Biopharma manufacturers must consistently act and react to such market pressures
- This poster will discuss how our company has challenged some of the "status quo" in the sterile primary packaging component space; in particular, we will discuss how we have updated our governance system to address bringing sterile products to market in ways that can be more nimble and effective – **including dual-sourcing of suppliers of primary packaging components** – ultimately bringing life-saving medicines and vaccines to our patients faster and more reliably

Objectives

- To understand the unique challenges of single-sourcing and dual-sourcing **primary packaging components** for parenteral products
- To address the "status quo" present in many of our companies – that is, going to market with a single primary packaging component image
- To explain the risks of going to market with a single primary packaging component image
- To identify ways to mitigate the risks of being single-sourced, including internal governance strategies

Case study

Background

- Multiple Merck Manufacturing Division (MMD) projects, both technical and strategic, indicated that dual-sourcing of primary packaging components (PPC) is required in the sterile Drug Product space
- MMD leadership request was to evaluate the Merck network and develop mitigations to address PPC dual-sourcing across all modalities
- Global Technical Operations created a steering committee that requested an overview of the landscape for PPC duality projects (active, proposed) as well as a definition of success and consolidation of opportunities in large molecule (LM) and small molecule (SM) products
- MMD leadership requested an overview of the PPC duality landscape for pipeline products to support development of a governance document as well as principles to allow for exceptions to that document

Summary of the PPC landscape for inline and pipeline products

- Inline products are predominantly **single-sourced for elastomers and cap/seals**
- Broad subset of inline products that are **dual-sourced for glass** (dependent on site and image, LM vs SM, internal vs external)
- Pipeline products are predominantly **single-sourced for elastomers and cap/seals**; in addition, these are mainly **single-sourced for glass**
- Review mitigations, developed in collaboration with Merck Research Laboratories, Sterile Drug Product Commercialization, Packaging Commercialization, Supplier Development & Performance Management, Procurement, and Global Tech Ops (LM and SM)

THE LEGACY SYSTEM INTRODUCED POTENTIAL UNINTENDED RISK TO SUPPLY

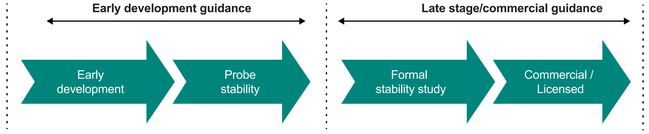
Drivers for a second supplier

Political	Business	Environmental	Technical-Development
Unforeseeable **world events** that impact supply (eg, EU gas supply risks)	Supplier **economic concerns** (eg, financial risks, downsizing, buyouts, catastrophic events)	Locations within environmentally **sensitive areas** (eg, North American earthquake zone)	Protection against **technical and/or supply** issues (eg, unsuitable component, **long lead times**)

- Dual-source strategy not only **mitigates the above risks**, but the strategy also benefits pharmaceutical companies through **increased business and quality engagement**, as well as protection against potential supplier retaliation

Opportunities to fortify duality for pipeline products are captured in *Technical Guidance Document*

Previous state:



No requirement for PPC duality

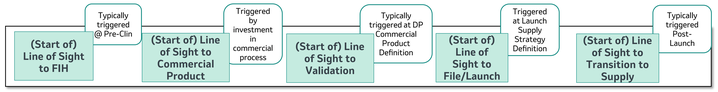
Requirement for PPC duality often **negated by exception** with single approval

Proposed additions:

- Design in PPC duality upstream in the drug product life cycle
- Align the Exception process by stage gates
- Approval by committee for the Exception process and re-evaluation at stage gates or milestones – Tactical Execution Governance and Tactical Execution Governance + Value Chain Governance
- Develop principles to govern the Exception process; eg, technical/supply readiness, program strategy, cost, etc
- Generate awareness of Technical Guidance Document through expanded reviews and engagement with key leaders to ensure duality is recognized and endorsed at appropriate forums

Product life cycle and governance structures

Commercialization stages



Strategic governance review

Tactical execution governance milestones

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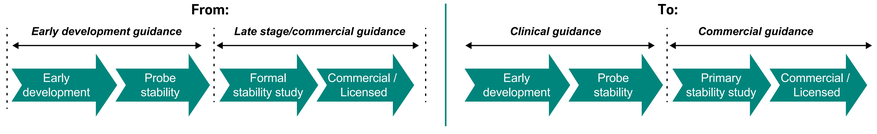
Chris Roberts: MMD Global Science Technology Services
Stephen Conway: MMD Packaging Commercialization
John Haines: MMD Value Chain Management
Allen Templeton: MRL Preclinical Development
Caroline McGregor: MRL Analytical R&D

Revisions to *Technical Guidance Document* created a paradigm shift for the organization



1. One image **MUST** utilize the defined Merck Standard PPC
2. There is **NO** requirement to establish a second PPC supplier
3. Exception process required **single** approvals

1. All images **MUST** utilize the defined Merck Standard PPC
2. A second supplier **MUST** be established for PPC utilized in FSS or post-licensure studies
3. Exception process required **single** approvals

1. One image **MUST** utilize the defined Merck Standard PPC
2. A second supplier **MUST** be established for PPC utilized in clinical programs
3. Exception process requires **Tactical Execution Governance** approval

1. All images **MUST** utilize the defined Merck Standard PPC
2. A second supplier MUST be established for PPC utilized in PSS or in FSS supporting post-licensure changes
3. Exception process requires **Tactical Execution Governance** and **VCM** approval

Completed significant revisions to *Technical Guidance Document* to better position pipeline products

Status	Proposed revisions
✓	Design-in PPC duality upstream in the drug product life cycle
✓	Aligned the Exception process by Development and Commercialization stage gates
✓	Approval by committee for the Exception process and re-evaluated at stage gates or milestones – Tactical Execution Governance and Tactical Execution Governance + VCM
✓	Developed principles to govern the Exception process; eg, technical/supply readiness, program strategy, cost, etc
✓	Expanded reviews and engagement with key leaders to ensure duality is recognized and endorsed at appropriate forums (Merck Research Laboratories, Merck Manufacturing Division, Global Procurement, Supplier Development, Global Tech Ops, etc)

Selection of PPCs

Selection of appropriate PPCs is a critical decision: Technical, strategic, quality, and business elements must be considered when determining the final image

Principles for component selection:

	Product/Market Level Segmentation (rank on Company's prioritization matrix)
	Use of standardized PPC (leverage known technical/supply capabilities, economies of scale)
	Clinical considerations • Program probability of success • Technical constraints of PPC (eg, non-standardized lyophilization vials) • Availability of drug substance • Speed to market
	Commercial considerations • Location of primary stability batch fills – site-agnostic GMP facility (including all GMP sites) • PPQ batch fills utilizing matrix approach for PPC • Availability of drug substance • Assessment of volume projections/LROP vs analytical/stability testing costs

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