Roundtable Session 1 - Table 11 - Use of Chromatography Resins Across Multiple Products

Facilitator: Helen Kumagai, Genentech
Scribe: Lesley Luginbill, Genentech

Abstract

The practice of dedicating chromatography resins to a single product often leads to significant underutilization and waste in biopharma, especially in clinical manufacturing. The rising cost and supply chain vulnerability of chromatography resins, coupled with global sustainability targets, necessitate a re-evaluation of the long-standing practice of dedicating resins to single products.

Multi-Product Resin Reuse (MPRR) is an increasingly critical strategy to improve cost-efficiency, enhance manufacturing flexibility, and promote environmental sustainability. While MPRR is technically feasible—often demonstrated in manufacturing to utilize a resin's full lifecycle—the regulatory path for its full adoption remains fragmented globally. This session will explore how industry can develop robust, risk-based qualification packages for resin platforms, and how global regulators can foster a harmonized, predictable framework to accept these data, ensuring product quality and patient safety are maintained while optimizing manufacturing efficiency and environmental footprint.

This roundtable discussion will explore questions in three areas - Strategic and Business Implications, Technical and Operational Challenges and a harmonized Regulatory framework for global acceptance.

Discussion Questions

How significantly does MPRR contribute to your company's sustainability goals, and what are the measurable impacts (e.g., reduction in waste, transportation, buffer preparation)?

What are the estimated cost savings associated with implementing MPRR across clinical and/or commercial production? Any increase/decreases in logistical costs associated with resin management?

How is the resin performance and lifetime maintained after being repeatedly exposed to harsh cleaning procedures? What are the critical parameters for continuously monitoring resin performance and how are these thresholds established and adjusted?

What are the challenges and best practices for ensuring consistent and effective enhanced cleaning across different products and manufacturing sites?

What are the best practices in establishing maximum allowable carryover (MAC)? What has been your company's experience in gaining regulatory approval on MPRR?

What has been your company's experience in gaining regulatory approval on MPRR?

What key concerns have been raised by regulatory agencies in different regions?

Notes

1. Strategic and Business Drivers

The group identified several key motivators and barriers to adopting MPRR, emphasizing cost and sustainability.

- **Cost Efficiency:** Protein A (ProA) resins represent the highest ROI for reuse strategies due to their significant cost.
- **Sustainability Impacts:** MPRR aligns with global sustainability goals by reducing waste, buffer consumption, and transportation logistics.
- **Facility Suitability:**
    - **Internal vs. External:** MPRR is most advantageous when clinical manufacturing is centralized at a single internal site.
    - **Barriers:** CMOs (Contract Manufacturing Organizations) may find MPRR inappropriate due to the complexities of managing shared resin across different client projects.
- **Business Drivers:** Implementation should be driven by a clear business case where the cost/waste reduction outweighs the additional technical and quality risk.

2. Technical and Operational Challenges

Technical discussions focused on the "how-to" of ensuring resin integrity and product purity across different modalities.

Cleaning and Carryover Management

- **Analytical Sensitivity:** A major hurdle is developing methods with sufficient sensitivity (e.g., nano-range testing, 1µg/mL) to detect protein carryover accurately.

- **Maximum Allowable Carryover (MAC):** Discussion about calculating the MAC based on the maximum dose of the *subsequent* product to ensure patient safety.
    - **Note on "Ultra-Potent" molecules:** Special care and potentially different "MAC" thresholds must be established if a facility plans to use shared resin for highly active substances.
- **Enhanced Cleaning:** There is a need to demonstrate the effectiveness of cleaning across various modalities (e.g., bispecifics vs. mAbs).
- **Dead Zones:** A critical concern is ensuring no "dead zones" exist within the column or packing that could harbor residual product.

Resin Performance and Monitoring

- **Lifetime Studies:** Cycling multiple products requires trending performance over time to detect ligand stripping or resin fouling.
- **Monitoring Parameters:** * Yield is often the first indicator of resin decay.
    - Leached Protein A should be monitored not just in elution, but potentially in the sanitizing solution as an In-Process Control (IPC).
    - Cumulative contact time and "new types of alerts" should be established.
- **Physical Management:** Discussion on whether to leave columns packed between products or to unpack and store resin. Microbial monitoring (packing/storage) remains consistent with current single-product practices.

Safety and Viral Clearance

- **Virus Safety:** The existing viral safety package is generally robust enough, but controls on feedstreams are essential to prevent adventitious agent introduction.
- **Potency & Bioactivity:** Concerns were raised regarding the effect of harsh cleaning (e.g., 0.1 M hydroxide) on any residual protein left on the column—could degraded residuals impact the next product?

3. Regulatory Framework and Quality Oversight

- **Current Status:** The consensus is that while the industry is ready, the regulatory review of MPRR proposals is currently uncertain.
- **Risk-Based Guardrails:** Companies should define boundaries for implementation based on:
    - Molecule class and potency (e.g., avoiding "ultra-potent" compounds).
    - Potential Sensitivities of Patient population
    - Platform media/feedstream consistency.
- **Quality Alignment:** Site Quality expectations vary; internal Quality Assurance teams must be brought on board early to define what constitutes a "worst-case" product for validation.

- **The Technical Package:** The data package should include the following.
    - Robust carryover assessments.
    - Toxicity data for the product residuals.
    - Data on the rate of resin decay.
    - Evidence of downstream clearance capabilities.