Table 28: Multi-product Manufacturing and Chromatography Resins

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SCOPE:

This table will discuss opportunities and challenges associated with extending resin reuse to multiple products. Chromatography resins used for purifying biopharmaceuticals are generally dedicated to a single product. For clinical manufacturing and small volume products, this can result in resin being used for a fraction of its potential lifetime.

The participants will discuss benefits and risks associated with multi-product resin reuse, data required to ensure safety of the product, regulatory considerations, impact on global filings, leveraging multi-product facility concept for resins and relevance of multi-product for single use facilities.

QUESTIONS FOR DISCUSSION:

1. How do we move forward in the future to deem chromatography resin reuse acceptable by global health authorities? What are the regulatory risks including global filings?

2. What are the risks for patient safety or product quality?

3. Can the cleaning effectiveness be sufficient to ensure none to minimal product carryover? What data would be required?

4. How do you maintain control/changeover in a multi-product facility if the chromatography column is used for different products?

5. What benefits in addition to cost savings do you see with multi-product resin reuse approach? Should the approach be applied to ProA only or all resins?

6. Does the approach add value for single use facilities?

DISCUSSION NOTES:

1. How do we move forward in the future to deem chromatography resin reuse acceptable by global health authorities? What are the regulatory risks including global filings?
   - Multi-product chromatography use would need to be proposed by industry to the FDA and/or other health authority. Possible path forward is to use strategy only for early phase clinical products.
   - Consider not using for Phase 3 development or commercial processing as more stringent expectations and additional filing details are required. Additionally, the resin lifetime is achieved for commercial products.
   - One potential strategy is to choose a column downstream in process instead of ProA (first column) where the feed stream is cleaner to reduce risk of not
removing all impurities. On the contrary, implementing for first step reduces risk due to presence of downstream chromatography steps to remove any residual product and prevent product carryover.

- Companies would have to generate data and develop strategy to support multi-product resin reuse.

2. What are the risks for patient safety or product quality?

- Companies will have to perform the risk assessment for their products. They will have to demonstrate efficient cleaning, no product/deactivated protein interactions.

3. Can the cleaning effectiveness be sufficient to ensure none to minimal product carryover? What data would be required?

- Need to consider if column should remain packed between different products or adaptor removed to allow unpacking, treating the resin, and repacking of the resin. Removal of adaptor poses risk for contamination.
- There are regulations that detail how much carryover is considered acceptable in a product for multi-use vessels. These regulations should be used as guideline in developing a process to clean columns between processing multiple products.
- The process to clean columns between multiple products should include a deactivation buffer to allow a lower risk assessment.
- If we use stronger cleaning agents on the column, there is the possibility of leached ProA over time, which may impact binding capacity.
- Every company would have to validate the process to clean columns between multiple products.
- If company wants to use the same column for multiple products, CMOs may have resin dedicated for a specific customer and use it for applicable products.

4. How do you maintain control/changeover in a multi-product facility if the chromatography column is used for different products?

- From a product bioburden perspective, it is better to keep the column packed between products and put it in storage instead of unpacking the column and putting the resin in the cold room.
- Extractables and leachables should be included in the risk assessments if pre-packed column is used to ensure material is compatible with cleaning solutions and would not contribute to impurities (leachables).

5. What benefits in addition to cost savings do you see with multi-product resin reuse approach? Should the approach be applied to ProA only or all resins?

- While cost savings are not as significant as ProA, however, there might be other benefits such as simplification of business process for resin storage, reducing risk of bioburden due to packing/unpacking. It would be case dependent and would require every company to perform assessment and weigh out risks and benefits.

6. Does the approach add value for single use facilities?

- Single use facilities do not perform cleaning validations. If the same columns are
used for multiple products, then cleaning validation will have to be completed. It might not be value added. However, companies would have to perform economic assessment for their product.