Risk Versus Benefit: Acceleration of CMC for Biologics/Vaccines Products

WCBP Mini Case Study

Linda Lemieux, Merck & Co., Inc., Rahway, NJ, USA

Beth Junker, BioProcess Advantage LLC, Westfield, NJ, USA

Scope

Often in development there is a balance among speed, cost, and program risk. Accelerating CMC activities to speed up clinical or commercial manufacturing can have great benefits but might cost the program in the long run. The risks associated with regulatory acceptance, repeat testing, additional studies, replacement manufacturing runs, post-approval commitments, and multiple regulatory submissions could carry a high cost if realized. Accelerating early development, if not undertaken prudently, could adversely impact late-stage development timelines.

In this mini case study we will highlight examples of product acceleration and discuss pathways that were used to mitigate the risks and gain the benefit.

Example: Multiproduct Resin Reuse

Background:

- Due to pandemic, fresh AEX and CEX resin was unavailable for GMP manufacturing of new mAb for clinical manufacturing.

Considerations:

- Delay development program until new resin available? Risks versus benefits?
- Reuse resin from a similar program? Timeline and resource requirements?
- Other options?

Example: Multiproduct Resin Reuse

Action Plan:

- Risk Assessment
- Protocol Scope
- Analytical Requirements
- Studies and Data Requirements
- Regulatory Strategy

Example: Multiproduct Resin Reuse

Questions:

- Do we have strong supportive data for a submission?
- What are the risks to regulator acceptance?
- Do we approach regulators? If so, how and when?
- What questions should we ask?

Regulatory Strategy:

- FDA Type C Meeting
- Supportive data in briefing book
- Response to comments and meeting discussion
- Modify implementation plans based on feedback
- Approach additional agencies as needed

Result: Successful implementation of multiproduct resin reuse strategy for acceleration of GMP manufacturing

Questions for Discussion

- When does the benefit of accelerating CMC activities outweigh the associated risks?
- How can the risks be effectively mitigated?
- How can we overcome internal and external regulatory barriers to accelerate product development?
- When it is prudent to proceed without regulatory input?