Cytovance Biologics
a Hepalink Company

Case Study

Development of a Drop-In Purification Step for the Removal of Aggregates from an Antibody Therapeutic

Benefits of Case:

- Reduced aggregate level in large scale manufacturing downstream process from very high to undetectable levels
- Simplified downstream purification process by eliminating the collection of fractions and the need for stat assays during manufacturing operations
- Improved robustness of downstream purification process

Background and Challenge:

- The client was engaged in large scale cGMP manufacturing operations at a major CMO
- The client's product contained high levels of aggregate following an affinity capture step. Subsequent chromatography steps reduced the aggregate level to acceptable levels but product losses were encountered in elution buffers, and stat in-process assays. The process was not robust. CMO did not want continue manufacturing product under current conditions.
- The client desired to improve the purification process efficiency by introducing either an aggregate disassociation step followed by purification or an efficient protein aggregate removal step compatible with large scale biopharmaceutical manufacturing.

Strategy:

- Evaluate chemical disassociation of the aggregate followed by product purification
- Evaluate chromatography resins for efficient removal of the aggregate

Development Data:

- Conditions were established to disassociate the product aggregate with chemical treatment but the biological activity f antibody was reduced
- A single drop-in chromatography step was developed that reduced aggregate levels to undetectable levels with essentially no product loss
- The new process step was compatible with the existing purification process; i.e. no modifications to existing process were required
- Limits for key process parameters were established
- New chromatographic process step was successfully scaled and transferred to major CMO

Value for the Client:

- Manufacturing process for antibody therapeutic was significantly improved and streamlined
- Aggregate levels were reduced to undetectable levels
- The need for collection and stat analysis of chromatography fractions was eliminated
- New process step eliminated downstream process bottleneck
- Significant strategic business alliance was facilitated with elimination of manufacturing issues