Taking mAb purification to the next level

BIOMANUFACTURING From a processing perspective, mAbs are usually manufactured using a typical platform process that consists of three purification steps based on chromatography – and increasingly relies on membrane adsorption. German contract manufacturer Rentschler has now come up with a simplified two-step programme that is more economical, yet maintains quality and safety standards throughout the purification process.

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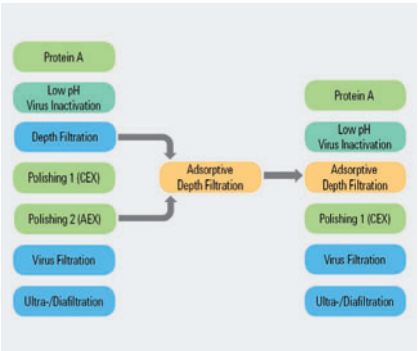
Most generic purification platforms for monoclonal antibodies and Fc fusion proteins include a Protein A affinity chromatography step and two polishing steps that employ cation and anion exchange chromatography, or membrane adsorption. The primary objective of these polishing steps is to remove process-related impurities, in particular residual host cell proteins (HCP) and DNA, as well as product-related impurities (aggregates, fragments). Moreover, each polishing step decisively contributes to process safety in direct relation to its virus removal capabilities.

Adsorptive depth filtration

While depth filtration is a widely used unit operation specifically aimed at removing precipitated particles that occur upon acidic virus inactivation, a new generation of adsorptive depth filters is also able simultaneously to remove process-related impurities. These single-use hybrid clarifiers contain a Q-functional anion exchange (AEX) hydrogel media that is integrated with a fine-particle bioburden reduction membrane. Rentschler has now set up a shortened purification process for mAbs that capitalises on this hybrid function, allowing users to skip the AEX-based polishing step (see above). The new two-step purification platform has been shown to increase overall yields of the target drug substance, while at the same time maintaining high product quality, process safety and robustness.



Novel two-step downstream process for mAb purification when applying adsorptive depth filtration.

Removing viral contaminants and process-related impurities

Rentschler has tested different adsorptive depth filters for their ability to remove process-related impurities and viral contaminants, including the functionalised non-woven Emphaze™ AEX Hybrid Purifier (3M, USA). All virus clearance studies in the test employed enveloped X-MuLV (Xenotropic Murine Leukemia Virus) and small non-enveloped MVM (Minute Virus of Mice). Both model viruses are negatively charged at neutral or basic pH, and both putatively bind to the positively charged surface of a filter membrane.

The study demonstrated significant virus removal by anionic adsorption, with samples reaching log reduction values (LRV) of 2.0-5.0 for X-MuLV and 2.5-7.0 for MVM – comparable to values achieved by classic AEX-based polishing steps. The viral clearance potential of the Emphaze™ AEX Hybrid Purifier by electrostatic retention could moreover be viewed as an orthogonal method for the currently adopted virus filtration step, which is based on size exclusion. Adding adsorptive depth filtration to the shortened two-step antibody purification process (Protein A, CEX) removed process-related impurities like HCP and DNA as effectively as the classic three-step process (Protein A, CEX, AEX), while overall product yields rose.

The process simplification has allowed Rentschler to be more economical in its mAb purification platform, while improving overall process safety and yield. ■

Picture: Rentschler Biotechnologie