

TROUBLE-SHOOTING MEMBRANE FILTRATION ISSUES IN ORDER TO SCALE-UP CLARIFICATION PROCESSES USED IN THE MANUFACTURING OF VACCINE CANDIDATES AGAINST INFECTIOUS DISEASES

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ABSTRACT

The primary recovery step within a manufacturing process is definitely an important stage for cellular clarification and product recovery, but remains to be an on-going challenge for the scientist. After harvesting the culture, several recovery techniques have been used to recovery intracellular proteins. Several filtration technologies (Vortex membrane filtration system, dynamic membrane filtration system, micro-filtration, static filtration, bead clarification and ultra-filtration) for harvesting and clarifying culture have been investigated and optimized. The vortex and dynamic membrane filtration system, although performing well at the bench-scale, are not scalable and cost-effective. Static filtration using a combination of depth filters is an expensive application upon scale-up. It has been found that the conventional micro-filtration method is effective in recovering proteins released after homogenization by optimizing several process conditions such as membrane chemistry, cross-flow velocity and transmembrane pressure. Other factors such as viscosity, temperature and protein concentration and morphology affect the filtrate flux of the microfiltration operation and need to be examine during process optimization and scale-up. Other simpler and more robust techniques like the adsorption of protein onto chromatographic beads and filtering off the cellular debris has been found to be more scalable and effective in protein recovery. In addition, as the beads are cleaned and re-used again, the cost of operating the batch adsorption method is lowered and the disposable cost can be reduced significantly in comparison to using depth filters to clarify the antigen. The advantages and challenges of each clarification application are discussed.