

VIRUS REDUCTION FILTRATION IN CONTINUOUS BIOPROCESSING: CRITICAL FLUX CONCEPT FOR VIRUS BREAKTHROUGH

Dharmesh Kanani, Teva Branded Pharmaceutical Products R&D, Inc
Dharmesh.Kanani@Tevapharm.com

Mi Jin, Teva Branded Pharmaceutical Products R&D, Inc

Rong Fan, University of Arkansas

Fu Namila, University of Arkansas

Ranil Wickramasinghe, University of Arkansas

Xianghong Qian, University of Arkansas

Key Words: Virus Reduction Filtration, Monoclonal Antibody, Critical Flux, Downstream Process

Virus reduction filtration is an integral component of virus clearance strategy in modern biologics production processes. Continuous bioprocessing and process intensification are the buzz words in biopharmaceutical industry due to benefits of cost savings from higher productivity, operational flexibility and better product quality. A typical batch process operates virus reduction filters at constant pressure to maximize the throughput within one shift of process time constraint. However, continuous bioprocessing would demand constant low flux virus reduction operation over extended duration to address the complications of frequent filter switching. Due to relaxation of process time constraint, continuous bioprocessing allows better utilization of filter capacity (L/m^2). However, there is limited understanding around the virus breakthrough mechanism and associated critical process parameters. This poses an interesting question how to define end point for virus reduction filtration while utilizing most of the filter capacity for low fouling feed. What is the effect of flux, differential pressure and total viral particle load on virus clearance performance of commercially available viral filters? Is there a critical flux for viral reduction filters below which they are susceptible to significant virus breakthrough ($LRV < 4$) and if yes, how sensitive it is to filter's property and other process parameters? This study explores the effect of flux, differential pressure and total viral particle load on viral clearance performance of three commercially available filters. These filters are selected to cover the wide range of filter permeability and membrane material. The viral clearance study was performed both in the presence and absence of products.