

DEVELOPMENT OF SCALE-DOWN MODELS FOR VALIDATION OF INTEGRATED CONTINUOUS VIRUS FILTRATIONS

Julie Kozaili, Asahi Kasei Bioprocess
Julie.kozaili@ak-bio.com
Scott Lute, FDA, CBER
Sarah Johnson, FDA, CBER
Daniel Strauss, Asahi Kasei Bioprocess

Key Words: continuous virus filtration, validation, scale-down model

Continuous bioprocessing is becoming more widely adopted in biomanufacturing. While much progress was achieved in upstream processes and downstream chromatography and viral inactivation steps, there is little data published on continuous virus filtration (VF). As continuous manufacturing leads to changes in processes, facilities and equipment, these factors need to be considered within the VF design space. Additionally, since the choice and performance of a virus filter is generally dependent upon the outputs from upstream unit operations, the filter may experience load solutions with fluctuating protein concentrations, salts and impurities, consistent with a chromatography step elution profile. Understanding how continuous processing impacts the performance of a virus filter can lead to developing both integration and validation strategies. In this work, we designed scale-down virus filtration models to investigate the impact of extended process times and dynamic product streams present in continuous manufacturing. We performed long-term PP7-spiked virus filtrations using Planova 20N and BioEX filters. The results show that Planova 20N and BioEX virus filters are capable of effectively (> 4 log) removing bacteriophage PP7 when run for up to one week continuously. Creative methods were successfully implemented in order to overcome long-term PP7 stability and pressure fluctuations. Additionally, both the 20N and BioEX filters were able to successfully process a mock elution peak of increased protein, salt, and bacteriophage concentrations with only an increase in filtration pressure observed during the higher protein concentration peak. Effective virus removal was achieved even under challenging PP7 particle loads (>9.5 logs total). These experiments demonstrated that small-scale viral clearance studies can be designed to model a continuous viral filtration step with specific process parameters. Both Planova 20N and BioEX filters were shown to be robust with respect to extended processing times and fluctuating elution peaks. The integration of continuous virus filtration into continuous biomanufacturing processes is therefore applicable and adaptable; it remains largely process-dependent. Further validation strategies may include mimicking multiple elution peaks in series to allow for a better characterization of the pressure limit of these filters in a continuous setup.