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ALTERNATING FLOW FILTRATION AS AN ALTERNATIVE TO INTERNAL SPIN FILTER BASED PERFUSION PROCESS: IMPACT ON PRODUCTIVITY AND PRODUCT QUALITY

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The application of an alternating flow filtration (ATF) system adapted to a stirred tank bioreactor as an alternative to internal spin filter was studied using CHO cells producing a fusion protein. As expected, it was possible to reach higher cell densities (maximum 50 x 10^6 vs 20 x 10^6 cells/ml) and achieve longer runs with the ATF device (50 days vs 30 days), since it is known that this cell retention device is less affected by fouling. Even tough specific cell yield was similar for both systems; volumetric production of the reactor using the ATF was almost 70% higher than the production achieved using the internal spin filter due to higher cell density and a two fold increase in the perfusion rate. Taking into consideration that it was observed certain degree of retention of the product at the end of the run we assume that this difference in the volumetric production could be even higher working with a bigger pore size or changing the hollow fiber cartridge around day 35. The later can also have a positive impact on the length of the process increasing the average daily production and overall yield. Cell specific perfusion rate was optimized for both the internal spin filter and ATF. A lower rate was achieved for the ATF, resulting in a harvest with a higher product concentration, which supposes a benefit for downstream processing.

Several quality attributes were studied, including misfolded, clipped forms and product glycosylation profile. Differences between both systems were detected only for glycosylation profile, resulting in a decrease of fucosylated glycoforms.

These results constitute valuable data for the optimization of recombinant protein production in perfusion processes since a two fold increase in the chronological productivity of a production facility could be easily achieved as long as downstream scale up is possible.