34f Redundant Filtration Sizing and Scale up in Sterile Filtration Applications

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Filtration is commonly used for sterilization of protein therapeutics in the biopharmaceutical industry. Recent guidance provided by the FDA for aseptic processing of sterile drug products (1) mentions the use of redundant filters (two filters in series or tandem configuration). Redundant filtration can be beneficial because it minimizes the risk of expensive product loss and batch rejection even if one filter fails during sterile filtration.

This study presents design principles for filter sizing in redundant filtration based on the gradual pore-plugging methodology. A mathematical model using key filtration performance parameters, such as Vmax and initial filter resistance Ro, obtained from single filtration experiments, was developed to assess the impact of the additional filter on filter sizing. Functional tests were performed at bench and manufacturing scales with product streams of varying plugging characteristics to qualify the model. Data from these tests and from existing manufacturing runs were used to identify scale up model parameters. Predictions were generated to optimally scale up redundant filters for products based on batch size and processing time. Manufacturing data was evaluated against the model predictions. The results from these tests showed agreement between empirical data and model predictions. Thus a rational approach was developed to guide filter sizing and scale up of redundant sterile filtration unit operation in the manufacture of protein products.

References: 1. Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice, Food and Drug Administration, September 2004