Current risk mitigation technologies such as H2S, UV-C, and gamma irradiation are useful, however not always easy to implement and are not cost effective. Size exclusion based filtration is the preferred technology for viral contamination, as it is an inert membrane. Viral contamination is often measured using a filter and viral content is often compared to a standard 0.1 µm filter to determine the level of contamination. In this study, filter costs are in the range of $3 – 4/L media filtered to process a 350 L batch of media. The viability was > 95% for both filters.

2. New Virosart® Media

The Virosart® Media filter mitigates virus contamination risk prior to the addition of nutrients plus other additions into the bioreactor system and has been developed for chemically defined cell culture media. The Virosart® Media filter is an asymmetric polyester ultrafiltration module with 20 nm pore size rating that exhibits high capacity (1000 L/m²) at 20 psi in 4 hour filtration time for filtration of cell culture media while providing a 4 LRV (log10 reduction value) for small non-enveloped viruses and a 6 LRV for large enveloped viruses.

3. Small Scale Filtration: Study 1

This study was performed to determine the filter capacity for cell culture media at the lab-scale. Two runs were performed with the Virosart® Media module to compare the filter capacity of Genentech’s chemically defined media with and without poloxamer. Poloxamer is a non-ionic surfactant which is used in cell culture media to protect cells from stressful shear conditions in bioreactors. The addition of poloxamer may help preserve high cell growth and viability which may be compromised without its use.

4. Mid-scale Filtration: Study 2

The lab-scale results were confirmed by processing 350 L of Genentech’s media containing poloxamer through the Virosart® Media mid-scale module (0.3 m², part number: 3V2--28-GVGFL). The media was prefiltered using a Sartopore® 2 XLM (0.1 µm) pre-filter. The filtration was then performed and operated at a constant flux of 300 L/MH using a Wilson Marina pump. The Virosart® Media filtered media was then sterile filtered into a sterile bag and stored at 2-8°C until used for the cell growth study (Study 3) as the media filtration was not performed under sterile conditions. The cost effective filtration of the media post Virosart® Media would not be used.

5. Cell Growth Studies: Study 3

A study was performed to compare the cell growth profiles using filter produced by Virosart® Media filter (Study 2) versus a standard 0.1 µm filter. Filters from these filters were used to culture the cells across 8 passages using shake flasks. A standard CNO cell line was used to inoculate the duplicate shake flasks. The viable cell concentration (VCC) and cell viability were recorded during each cultivation.

6. Economic Analysis

The cost effective filtration of cell culture media is feasible with Virosart® Media filter and mitigates the risk of viral contaminations of cell cultures. In this study filter costs are in the range of $1 – 3/L. The viability was > 95% for both filters.

7. Summary and Conclusion

The results presented herein demonstrate that the Virosart® Media filter had high capacities and good process economics for the media being tested. The presence of poloxamer had a negative effect on the capacity of the Virosart® Media filter. However, approximately 1000 L/m² of chemically defined media containing poloxamer could still be filtered with a Virosart® Media in little less than 4 hours for both the lab scale mid-scale media.

Growth studies comparing virus filtered media and standard filtered media (0.1 µm) in shake flasks showed no differences in growth or viability. Although the Virosart® Media membrane shows no impact on cell growth and cell metabolism in the system studied, we recommend users perform cell growth evaluations under their specific culture conditions.

In this study, filter cost is in the range of $1 – 4/L, media may be lower for media which do not contain poloxamer or where larger process times are used.