

SINGLE-USE EQUIPMENT

MICROFILTRATION

Effective cell removal

Ralph Daumke, Filtrox AG, St. Gallen, Switzerland

FILTRDISC BIO SD is a high performance single-use microfiltration system for removing cells and cell debris from fermentation broth.



Clarifications of fermentation broth and cell homogenate are one of the most important steps in downstream biotech processes. Optimised fermentation processing leads to dramatically increased cell densities, accompanied by new challenges in clarification. Standard current technologies (centrifugation, depth filtration and membrane filtration) are no longer able to handle the high particle loads in an economical way.

Membranes are very cost intensive, and their scale up is impractical, as the required footprint for standard depth filtration increases with particle load. Centrifugation – an application in which mechanical stress is applied to cells – increases the turbidity through fine particles that have to be removed further downstream through separation and purification. Alternatively, a depth filter with higher capacity per area can solve these issues.

Alluvial filtration is a well-established method in pharmaceutical industries. Until recently, however, it was not used for cell separation as it was unavailable as a scalable and disposable system that fulfilled all validation requirements. FILTRDISC™ BIO SD is the first depth filter using the advantages of the alluvium technology in a disposable format, and is scalable from lab to industrial-size filtration.

Applications

FILTRDISC™ BIO SD is a filtration system that removes particles (e.g. cells, bacteria, yeast) and other turbid matter (e.g. activated carbon) from process liquids like fermentation broths or cell homogenate. The system is completely disposable. Single-use components reduce cross-contamination risks, eliminate cleaning validation efforts and reduce downtime during

module changes. Single-use methods are an ideal choice for contract manufacturers (CMO) and other operations that have a high frequency of product change. All systems can be delivered sterilised (gamma irradiation).

For alluvial filtration, the pharma grade DE (Celpure®, an Advanced Minerals brand) can be provided from FILTROX in single-use transfer bags. The fermentation broth or cell homogenate is mixed with DE in a bioreactor or mixing bag and then pumped over the filter unit. The DE and the cells/cell debris form a filter cake, extending the system's filtration capacity and preventing early blocking of the filter media. After filtration, the remaining liquid in the bag can be pumped over a FILTRDISC™ BIO SD 5" capsule to recover the last drops of the valuable liquid. After both filtrations have been carried out, the module and the capsule can be removed for disposal.

FILTRDISC™ BIO SD is also very useful for applications like active carbon removal or the filtration of highly toxic solutions.

Performance

The turbid matter in a cell broth is made up of cells, the feed and other degraded ingredients in homogenate from cell debris. Tests with *E. coli* bacteria (cell density 6.6×10^6), *Pichia* yeast (density 4×10^7) and cell homogenate were carried out to evaluate feasibility and obtain orientation values for this system. In every case, turbidity after filtration with 5" FILTRDISC™ BIO SD capsules was lower than it is after a standard centrifugation procedure.

Results from the 2" capsule trial filtration with *E. coli* could be directly used to filter a 600L batch without any other intermediate steps. For the production scale, a FILTRDISC BIO SD 16" double module was used. Reusable stainless steel supporting shells allow users to fill the FILTRDISC™ BIO SD bags homogeneously and protect them against pressure shocks. The heavy larger modules can be tilted horizontally to allow easy discharge of used bags. All DISCSTAR® BIO SD housings (except version 12K) are delivered with a separate trolley for module discharge. A pressure gauge is installed on the top of the support system. ◀