

SINGLE USE COMPACT SETTLER FOR CLARIFYING CELL CULTURE BROTH, SELECTIVE REMOVAL OF DEAD CELLS AND AFFINITY CAPTURE OF ANTIBODIES

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We have redesigned the successful “inclined settler” technology used as a selective cell retention device in mammalian cell perfusion bioreactor cultures into a more compact and easily scalable design using cylindrical and conical geometries. Through this novel settler design, we have achieved 6 – 10 x more settling area for the same footprint, compared to the traditional multi-plate or lamellar rectilinear scale up design. Using this compact settler design, we have demonstrated significant clarification of the smaller yeast *Pichia pastoris* cells in continuous harvest or settler effluent stream and high cell densities (700 – 1000 O.D.) in perfusion bioreactors operated over several months.

We have now fabricated this compact settler as a single use disposable plastic settler at 6 inch diameter scale and are planning to fabricate it in two larger sizes: 12” diameter and 24” diameter over the next six to twelve months. Recent experimental data with this compact settler as the selective cell retention device for achieving high cell densities in mammalian perfusion bioreactor cultures (operated for over a month of culture) will be presented. Our industrial collaborators are testing this device as a single use disposable device for clarification of cell culture broth from fed-batch bioreactor, for potential replacement of centrifuge for this operation.

Another exciting application of this compact plastic settler is the affinity capture of antibodies from cell culture broth directly onto protein A beads suspended inside the settler, while the cells and unbound host cell proteins are easily washed away in the settler top effluent, followed by elution, cleaning and regeneration steps on the beads suspended inside the settler. This integrated bioprocessing application can potentially replace the current unit operations of centrifugation, depth filtration and affinity column chromatography. Reproducible data from the preliminary experiments on this novel bioprocess application will also be presented.