

# Improving DSP Productivity by Reduction of Processing Operations using EBA Technology

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## Introduction



Fig. 1: GMP-manufacturing facility

### GMP-Biomanufacturing Challenges

Increasing productivity is a major challenge for multipurpose plants manufacturing biopharmaceuticals. Reducing the number of operational units is one important method of increasing productivity which has several effects:

- Elimination of process steps decreases losses associated with handling materials and thereby increases yield.
- Simpler processes are more cost effective to run, but also to develop
- Capital expenditure is reduced as less hardware equipment is required.
- Operational expenditure is reduced by nature of the increased yield and/or increased throughput for a given facility operation.
- Increased throughput relates to the flexibility and or efficiency of a production facility depending on it's primary function.
- A simpler process also removes the burden of QA/QC to the manufacturing process, a major factor is overall costs.

### Solutions for increasing productivity

Beside the current trend using disposables, implementation of technical solutions reducing the number of operational units is further improvement increasing process productivity and facility flexibility.

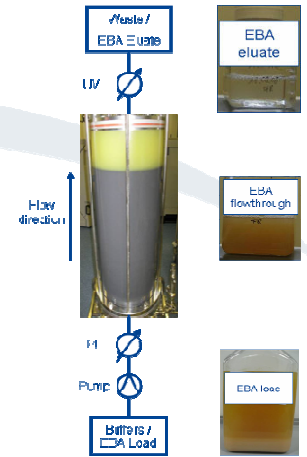


Fig. 2: EBA operational set-up

## Implementation of New Technology: Expanded Bed Adsorption (EBA) Chromatography

The EBA technology has been implemented for manufacturing of a chimeric protein (fab fragment + effector molecule). Process starts with high-cell-density *E. coli* fermentation with secretory expression. The process needed adaptation for next clinical phase manufacturing.

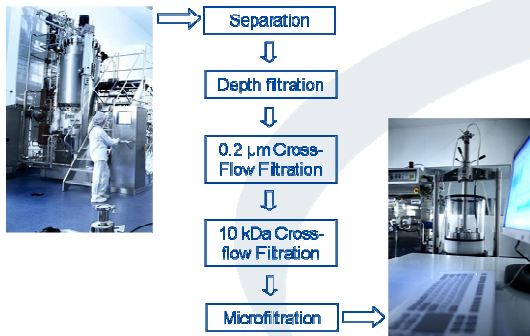


Fig. 3: Primary recovery steps of current GMP-process

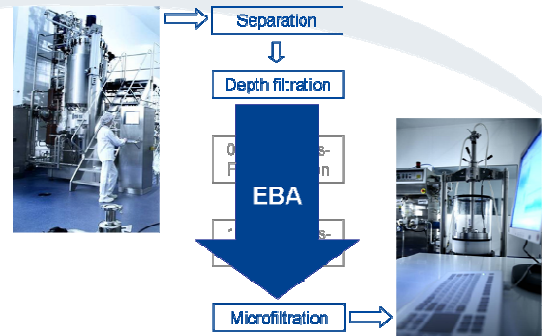


Fig. 4: Primary recovery of future GMP-process incl. EBA

## Results and Discussion

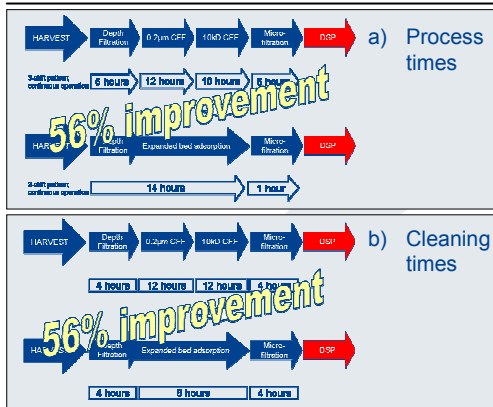


Fig. 5: Improvement in processing and cleaning cycle times

The implementation of EBA technology with "Streamline SP" resin in the case mentioned above led to a significant improvement of the process by reducing process and CIP times without a negative impact on process yields. As a direct result the utilisation rate of the multipurpose facility by the respective project is reduced.

As the number of process steps has been reduced, efforts for additional work like QC testing and QA record review were lowered as was the consumption of process media like WFI, steam, buffers etc.

These initial results could even be optimised by using "Fastline SP" resin, as the process yield in total purified product per fermenter volume could be increased 1.8-fold.

In total this case shows, that by using EBA technology results could be achieved which led to an increase in process robustness, well matching state of the art quality requirements for filing of the dossier.

At the same time increase in yields and productivity led to a significant decrease of Cost of Goods for final purified drug substance.