

# Integration of aqueous two-phase extraction for the manufacturing of biologics

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Up to now, there has been a significant progress solving most problems of continuous bio manufacturing. In downstream processing, continuous operations are known, but their implementation is still lacking at production scale. Up-stream cultivation technology on the other side has already created and, in part, implemented some solutions, e.g. perfusion technology<sup>1</sup>. Substantial improvements have been made in particular regarding the productiveness by the means of product titer through increased cell densities and longer cultivation times. However, this has also led to an increase of product related impurities and to higher challenges for the subsequent clarification and capture operations. Taking into account the paradigm shift towards the design of continuously operating dedicated plants at smaller scale – with or without disposable technology - for smaller patient populations, because of new indications or personalized medicine approaches, the rising need for new, innovative strategies for both clarification and capture technology becomes clear<sup>2-5</sup>. Aqueous two-phase extraction (ATPE) is by now considered to be a feasible unit operation, e.g., for the capture of monoclonal antibodies or recombinant proteins. However, most of the published work so far investigates the applicability of ATPE in antibody processes in lab-scale and for the most part only as a capture step. In contrast to this, approaches for the integration of ATPE as a combined harvest and capture step into a downstream process are shown in this talk. Additionally, a model is applied that allows early-on prediction of settler dimensions with high prediction accuracy. Finally, a reliable process development concept, which guides through the necessary steps starting from the definition of the separation task to the final stages of integration and scale up is presented. This talk will also shortly address a total process integration of continuous upstream and downstream as well as innovative devices e.g. for membrane supported ATPE. New purification steps like continuous precipitation and iCCC are discussed as well.

## References

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