Single-chain Fragment variables (scFv) are the light and heavy chain components of the variable part of a classical antibody. Compared to monoclonal antibodies (mAb), the fragment lacks the Fc region, which means that no killer cell activation is triggered by the fragment [1]. This prevents the body's immune response, which is undesirable in some applications, for example in diagnostics or the inhibition of certain proteins [1]. To shorten the time to market of this highly-promising biologic while comply to the regulation, a QbD-based process development accompanied by predictive model seems to be the most feasible option [2].

For the downstream of the fragments, the absence of the Fc region means that the Protein A chromatography obligatory in the IgG platform process cannot be used for capture due to a lack of affinity. As an alternative to Protein A chromatography, Protein L chromatography or IMAC (Immobilized metal affinity chromatography), based on histidine-tagged-scFv, has been developed by various working groups.

In the production of mAb, ion exchange chromatography (IEX) or continuous processes such as iCCC have also been evaluated as alternatives to Protein A chromatography, which allow a much more economical process design [2]. The scFv has alternating regions of positive, negative and uncharged regions on its surface, which allows separation using the IEX. In addition to IEX, multi-modal chromatography seems to offer a greater selectivity than IEX, cutting operating costs, as the following purification steps are simplified [3].

In this talk the different possibilities of capturing are discussed based on experimental and model data to show the different possibilities of process design. The experiments and methods for selecting a chromatography are presented. Furthermore, model parameter determination for the design of a validated rigorous model are presented. The different capturing steps are compared by means of common technical and economic key figures.
For product qualification as well as process control a PAT-based APC-concept will be presented. Simplifying process development by greatly reducing analytical efforts while simultaneously enabling advanced manufacturing approaches such as continuous manufacturing, as demanded by regulatory institutions such as the FDA.

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