

## SINGLE-USE PRIMARY CAPTURE TECHNOLOGY WITH THE PROMISE TO DELIVER NEW STANDARDS FOR THE ECONOMICS, CONVENIENCE AND RELIABILITY OF MAB BIOPROCESSING

Oliver Hardick, Puridify / UCL, United Kingdom  
Oliver@Puridify.com

Will Lewis, GlaxoSmithKline, Stevenage, United Kingdom  
Daniel G. Bracewell, University College London, United Kingdom

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Product capture chromatography has been crucial in the process development and manufacture of mAb therapeutics over the past 20 years, and in particular Protein A affinity. Chromatography is a step that has had a lot of process development time attributed to getting packed beds to perform to their maximum capability and most of the optimisation stems from limitations of the inherent media and its pack form, such as mass transfer & pressure drop limitations, channeling and bead-wall support effects. The limited throughput that this media offers has prevented this unit operation from being economically accessible in a single-use format.

Here we present 3 case studies of work using this a novel nanofibre adsorbent which takes the well-developed performance characteristics of chromatography utilising the same chemical base materials and process infrastructure and delivers a productivity improvement of 50-fold while maintaining product CQAs. This huge throughput advantage enables the drug manufacture to choose whether they want to reduce this unit process size such that the chromatography cartridge's lifetime (in terms of cycles) can be exhausted over a single batch, with the aim of making in single-use operation economically feasible, or whether they want to trade that off with operating their unit operation in a significantly reduced time period.

The goal of this is not just to reduce COGs associated with chromatography, but to enable new overall processing strategies to be employed giving drug manufacturers greater flexibility in their choice of operations and thereby maximising the productivity of new and existing drug manufacturing facilities.

The work presented here explores the physical properties that enable this high productivity operation and discusses the resulting product characterisation and process considerations. The industrial suitability of the nanofibre technology has been tested across a 1,000x increase in scale. Initial development work focused on high-throughput screening studies on the Tecan liquid handling system (10-50 $\mu$ L) and lab scale (125 $\mu$ L-1mL nanofibre volume). Run times of less than 3 minutes allowed the impact of key process parameters on quality attributes such as host cell protein and product concentration to be quickly optimised.

This work was then scaled to a pilot purification of a 50L CHO cell culture in a single batch. In this initial feasibility study, using a 10mL prototype housing unit, a productivity of 460g/L/h was achieved, with a recovery yield over 90%. A 3-log reduction in host cell proteins was also maintained over 200 cycles, and the Protein A leaching was less than 7ppm.

The use of smaller, pre-packed, nanofibre units, could potentially replace the preparative columns used in the protein capture stage increasing facility flexibility and reducing validation costs as part of a fully disposable processing chain.

