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SCALE-UP AND SCALE-DOWN TOPICS FACING THE INDUSTRY

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Scale-up and scale-down is bringing several challenges along. We present some recent examples where these challenges occur and how extensive hardware characterization by for example computational fluid dynamics has leads to get a better understanding of the processes themselves.

The increasing implementation of small scale bioreactor systems like ambr15 and ambr250 as well as the usage of new single use bioreactors (>2-L) in parallel to established glass vessels has led to additional challenges in scale-up and scale-down. The mini-bioreactor systems, originally used for screening approaches, are going to be implemented as small scale testing systems but could also be part of validated scale down models. This means more systems and scales than before have to fit together with respect to process performance and product quality output. To be prepared for this challenge in-depth characterization and comparison of the hardware is needed. We executed an extensive study with several projects to characterize the new small scale systems and to verify their scalability to larger scale and production facility. First the hardware was extensively characterized by computational fluid dynamics. Additionally, we performed for several projects cell culture runs with the different systems in parallel to show scalability and assess the suitability of the systems for actual scale-down model.

Apart from the actual cultivation hardware, coming along with the new high performing media generations - chemically defined and well balanced - is the question of media scalability. We are assessing different online probes to characterize media preparation and to define scale-up factors for media preparation scale-up. The evaluation of these probes will be presented. However, not only online signals but also the availability of suitable small scale media preparation models is a topic to be considered.

The success of scale-up and scale-down of future processes as well as the process characterization in suitable scale-down models is one of the main challenge biopharmaceutical industry is facing. We hope to show in our case studies how knowledge-driven approaches and extensive characterization may support to be well prepared for these topics.