

# A New Orbital-Mixed 2L-12L Single Use Bioreactor for Cell Culture Scale-Up and Bulk Protein Production

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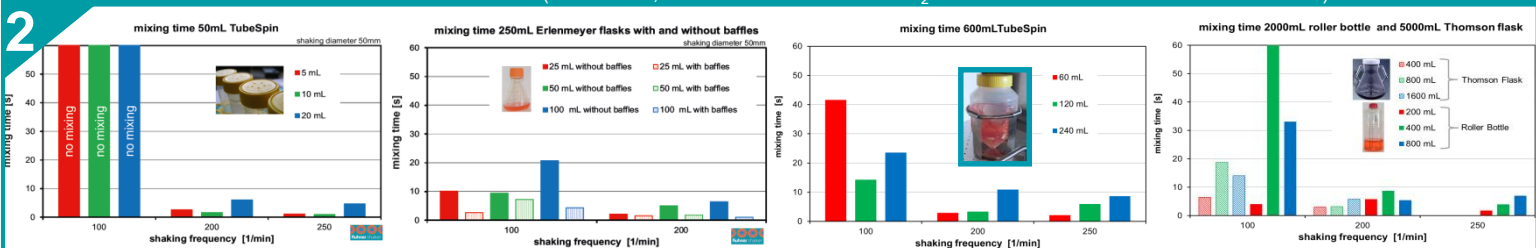
Small-batch therapeutic protein production requires predictable scale-up to meet bulk delivery timelines. Here, an orbital-shaken 2L-12L bioreactor is presented as an alternative to stirred and shaken vessels for batch production and scale-up. Orbital-shaken bioreactors offer a technically conservative approach which preserves mixing hydrodynamics and  $k_La$ 's from the µl stage to scales as large as 2,500L. Cultivation success at well plate, tube or flask scales easily translates to larger volumes.  $k_La$ 's, mixing times and some basic application data are shown here for the SB10, 2-12L orbitally shaken disposable bioreactor.

## SHAKING MACHINES AVAILABLE TO ROUTINELY SCALE FROM 50µL TO 2,500L



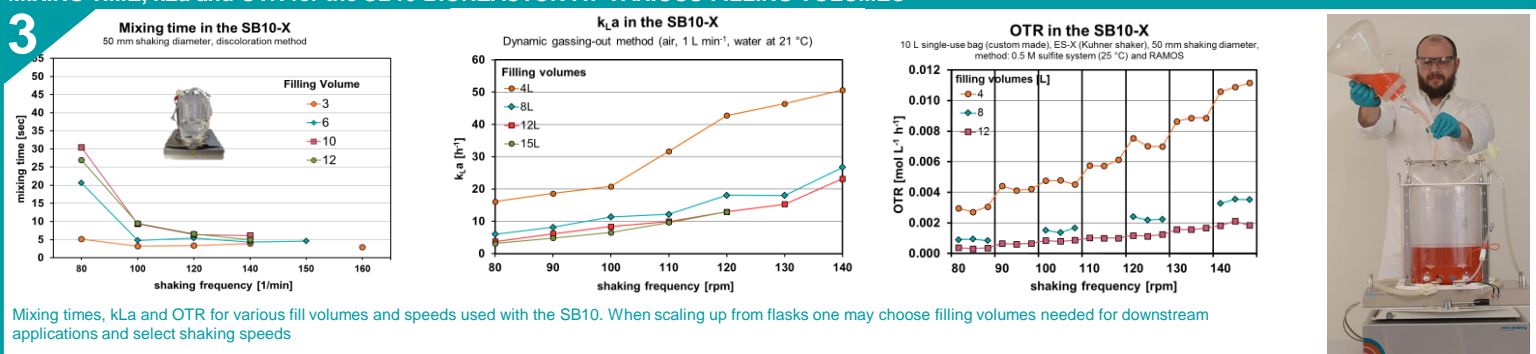
$CO_2$ -controlled shaker incubators like the Kühner ISF1-XC (A) handle cultures from 50µl to 5L. Well known mixing times (Panel 2),  $k_La$ 's and hydrodynamics are used to scale from well plates to larger vessels such as tubes or flasks. Large shaken disposable bioreactors have working volumes of 2L-12L (SB10 – B), 10L-50L (SB50 – C), 40L-200L (SB200 – D) and 200L-2500L (SB2500 – E). Shaken Single Use bioreactors preserve the hydrodynamics of smaller scale cultivations for a straight forward scale-up process - mixing times and  $k_La$ 's for these vessels are shown in Panels 3 and 4 respectively.

## MIXING TIME DATA FOR SMALL SCALE CULTURES (5ml – 2.5L, COMMONLY USED IN $CO_2$ -CONTROLLED SHAKER INCUBATORS)



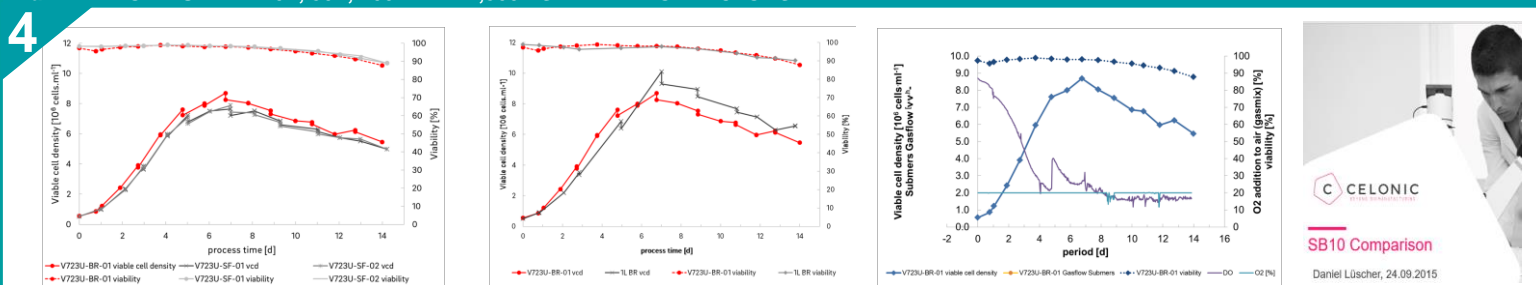
Mixing times for commonly used vessels: 50ml Tubespin®, 250ml Corning Flasks, 600ml Tubespin®, and 5L Thomson Optimum Growth® flasks. At smaller scales, mixing times of <10 seconds are accepted as sufficient. Though not reported here, mixing hydrodynamics are available for each of these scales and are conserved with the hydrodynamics of the larger scales shown below.

## MIXING TIME, $k_La$ and OTR for the SB10 BIOREACTOR AT VARIOUS FILLING VOLUMES



Mixing times,  $k_La$  and OTR for various fill volumes and speeds used with the SB10. When scaling up from flasks one may choose filling volumes needed for downstream applications and select shaking speeds

## $k_La$ DATA FOR KÜHNER 10L, 50L, 200L AND 2,500L SHAKEN BIOREACTORS



CHO-K1 Stable mAb expressing cell line from a fully established production process. Initial volume 6.5L, final volume 8.3L. 80-90rpm, headspace aeration at 0.5-0.75 slpm air with 5%  $CO_2$ , temp shift from 37C to 32C at day 5.

## Conclusions:

- Mixing time data is available for commonly used small scale shaker-incubator vessels.
- Small scale mixing time data may be used to select shaking speeds and fill volumes of larger shaken Single Use Bioreactors.
- $k_La$  data from the 10L, 50L, 200L and 2,500L supports their use for CHO and low-OTR microbial cell culture production processes.

