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Blending of Viscous Solutions With the Flexsafe® Pro Mixer 5 L | 10 L | 20 L

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Abstract

Mixing is a critical step in bioprocessing operations, playing a vital role in ensuring the quality and consistency of biopharmaceutical products. Reliable technologies and consumables are necessary to achieve efficient blending across different unit operations, which can involve diverse volumes and liquid types.

This application note explores the capabilities of the single-use mixing solution, the Flexsafe® Pro Mixer, by testing its performance across different volumes and liquid viscosities.

Introduction

In biopharmaceutical manufacturing, mixing liquids with different viscosities is a critical step. Proper mixing ensures uniform distribution of components, which is essential for the consistency and quality of the final product. Different viscosities can significantly impact the mixing efficiency and time required to achieve homogeneity. For instance, higher-viscosity solutions may require more energy and time to mix thoroughly compared to lower-viscosity solutions. Bioprocessing applications can encounter a wide range of viscosities, typically from 1 cP (similar to water) to over 1,000 cP (similar to glycerol or highly concentrated protein solutions).[1,2] Therefore, evaluating the performance of mixing systems with solutions of varying viscosities is crucial to ensure they can handle a wide range of bioprocessing applications.

This application note summarizes the performance evaluation of the Flexsafe® Pro Mixer across different bag sizes (5, 10, and 20 L) and various solutions, including NaCl in water and PEG solutions of varying viscosities (25 cP, 75 cP, 1,200 cP).

Materials

Reagents

- Deionized water
- Sodium chloride solution 1 M (NaCl)
- Viscous polyethylene glycol (PEG) solution
- Conductimeter calibration solution

Consumables

- Flexsafe® Pro Mixer bags (5, 10, and 20 L)

Equipment

- Flexsafe® Pro Mixer Base unit (FMD300002)
- Flexsafe® Pro Mixer Bag Holder 5 L (FXC301595), 10 L (FXC301596) and 20 L (FXC301598)
- Conductometers
- Conductivity sensors

Methods

Viscous solutions were prepared to achieve target viscosities of approximately 25 cP, 75 cP, and 1,200 cP. The quantities of PEG and water were adjusted as necessary to reach the desired viscosity levels. Table 1 outlines the specific quantities used for each solution.

Table 1: *Quantities to Prepare PEG Solutions at Various Viscosities*

Solutions	Quantity of PEG8000 per kg	Quantity of Water per kg
PEG 25 cP	0.24	0.76
PEG 75 cP	0.32	0.68
PEG 1200 cP	0.65	0.35

The Flexsafe® Pro Mixer bag was installed into the system and filled with the test solution (water or PEG solution) to the nominal volume. The mixer was started at a low speed and gradually increased to the target speed (Table 2) avoiding splashing, foaming, or vortex formation.

Table 2: *Impeller Speed for Different Volumes and Viscosities*

	Impeller Speed [rpm]			
Volume [L]	In 1 cP Water	In 25 cP PEG	In 75 cP PEG	In 1,200 cP PEG
5	100	150	300	–
10	120	170	350	
20	150	200	450	750

Conductivity sensors were calibrated using standard solutions, such as a 0.01 M KCl solution, to ensure accurate measurements. Sensors were positioned in the bottom corners of the bag, with an additional sensor placed at the top surface for tests involving the 1,200 cP solution.

The mixing process was monitored using video cameras to ensure proper operation. NaCl solution was added through one of the top lines, with volumes of 2 mL for 5 L bags, 4 mL for 10 L bags, and 8 mL for 20 L bags.

Three trials were conducted for each condition, except for the 20 L trial with PEG solution at 1,200 cP, which was performed once. Blending time was determined when both conductivity values fell between 95 and 105% of the final conductivity value and remained within these boundaries for at least 1 minute.

Results

A total of 27 trials were conducted across three sizes using water at 1 cP, PEG at 25 cP, and PEG at 75 cP. A single trial was performed for the 20 L bag at 1,200 cP. Examples of results from various trials are illustrated in Figures 1 – 4, and all results are summarized in Table 3.

Figure 1: *Blending of NaCl in Deionized Water (1 cP) at 100 rpm in 5 L Flexsafe® Pro Mixer Bags*

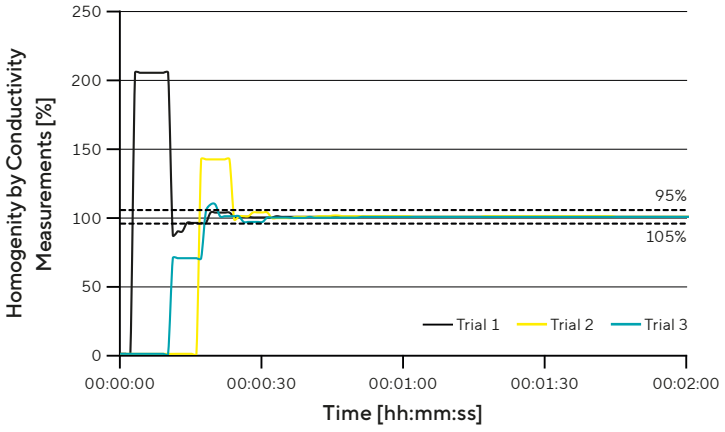


Figure 2: *Blending of NaCl in PEG (25 cP) at 170 rpm in 10 L Flexsafe® Pro Mixer Bags*

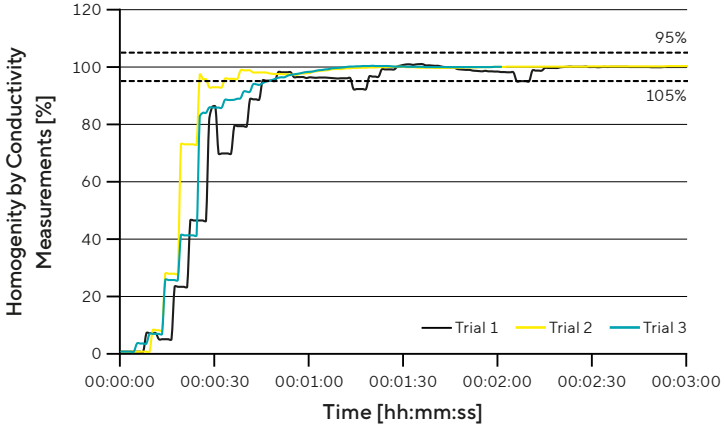


Figure 3: *Blending of NaCl in PEG (75 cP) at 450 rpm in 20 L Flexsafe® Pro Mixer Bags*

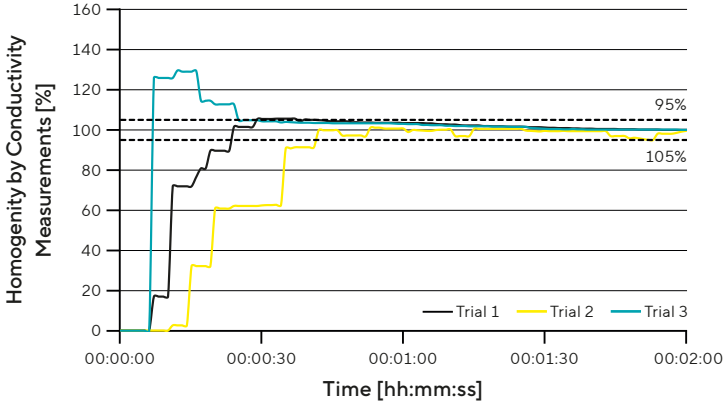
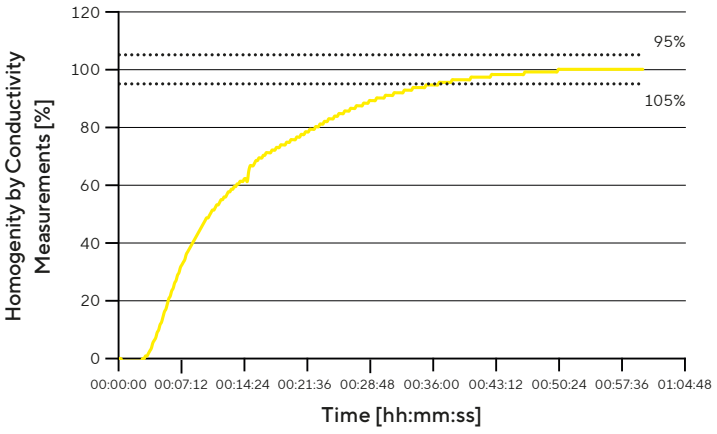


Figure 4: *Blending of NaCl in PEG (1200 cP) at 750 rpm in 20 L Flexsafe® Pro Mixer Bags*



The average t95% for all tested conditions was less than 1 minute, demonstrating efficient mixing performance across all bag sizes and solution types up to 75 cP. The t95% for the 20 L at maximum speed and with PEG solution at 1,200 cP was around 37 minutes. Under these conditions, the system reached a maximum speed of 420 rpm.

Table 3: *Summary of Blending Time at Different Volumes, Speeds, and Viscosities*

Volume [L]	Solution	Speed [rpm]	Time to 95% Conductivity (average) [hh:mm:ss]
5	NaCl in DI water 1 cP	100	00:00:20
5	NaCl in PEG 25 cP	150	00:00:43
5	NaCl in PEG 75 cP	300	00:00:34
10	NaCl in DI water 1 cP	120	00:00:36
10	NaCl in PEG 25 cP	170	00:00:53
10	NaCl in PEG 75 cP	350	00:00:25
20	NaCl in DI water 1 cP	150	00:00:35
20	NaCl in PEG 25 cP	200	00:00:40
20	NaCl in PEG 75 cP	450	00:00:43
20	NaCl in PEG 1,200 cP	420	00:36:40

Discussion

These results demonstrate the Flexsafe® Pro Mixer's ability to homogenize viscous solutions of up to 75 cP in less than one minute at speeds without visible vortex, foaming, or splashing. The viscosity of a monoclonal antibody (mAb) solution during final formulation is in the range of 1 – 100 cP, depending on the concentration.[1-5] Therefore, the Flexsafe® Pro Mixer is an powerful tool for mixing viscous solutions in excipient or drug substance formulation stages.

This study also evaluated the Flexsafe® Pro Mixer's ability to mix a highly viscous solution at 1,200 cP in a 20 L bag. The 20 L test represents a worst-case condition, as the distance between the impeller and the bag ends is the greatest in this configuration. A homogeneity of 95% was achieved in 37 minutes in the corners of the bag where fluid velocity is the lowest. Thanks to its high torque, the Flexsafe® Pro Mixer efficiently mixes highly viscous solutions within acceptable timescales.

Conclusion

The Flexsafe® Pro Mixer is a unique single-use technology platform suitable for all mixing applications from buffer and media preparations, downstream process intermediates to final formulation in 5 to 3,000 L volumes. Its ergonomic design enables intuitive, modular, and agile use to achieve fast installation and mixing operations.

This application note demonstrates the efficiency of the Flexsafe® Pro Mixer in performing liquid-liquid mixing and blending at different viscosities, even in worst-case conditions such as very high viscosity, quickly and easily.

References

1. Wang, W. (2005). Protein aggregation and its inhibition in biopharmaceutics. International Journal of Pharmaceutics, 289(1 – 2), 1 – 30.

2. Hamrang, Z. et al. (2014). Quantifying the effects of buffer additives on protein aggregation kinetics using light scattering. Biophysical Journal, 106(2), 374 – 383.

3. Loo, L. T., & Wong, R. L. (2017). Formulation of monoclonal antibody therapeutics: Influence of pH and buffers. Journal of Pharmaceutical Sciences, 106(6), 1536 – 1545.

4. Morishima, Y. et al. (2012). Viscosity of monoclonal antibody solutions as a function of concentration: Effect of buffer species and excipients. Journal of Pharmaceutical Sciences, 101(1), 204 – 213.

5. Shire, S. J. et al. (2004). Challenges in the development of high protein concentration formulations. Journal of Pharmaceutical Sciences, 93(6), 1390 – 1402.

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