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# Flexsafe<sup>®</sup> Pro Mixer

The Fast, Flexible and Intelligent Solution for Liquid-Liquid Mixing Applications and Blending of Viscous Solutions

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## Abstract

Flexsafe<sup>®</sup> Pro Mixer is a unique single-use technology suitable for all mixing applications from buffer and media preparations, downstream steps to final formulation. The Flexsafe<sup>®</sup> Pro Mixer's ergonomic design enables intuitive, modular and agile use to achieve fast installation and mixing operations. Additionally, the Flexsafe<sup>®</sup> film offers high standard quality attributes such as biocompatibility, integrity and robust supply chain.

This application study presents liquid-liquid mixing performance as well as blending performance at different fluid viscosities of the Flexsafe<sup>®</sup> Pro Mixer from 50 L to 1,000 L.

Solution viscosity can influence mixing performance. Most biopharmaceutical fluid's viscosity do not exceed 25cP. In this note, Flexsafe<sup>®</sup> Pro Mixer has been tested at 1cP, 25cP and 75cP as a worse-case scenario.

The performance of the single-use mixing system is assessed using conductivity measurements. Flexsafe<sup>®</sup> Pro Mixer is able to mix liquid-liquid and blend viscous solution's in less than 1 minute, whatever the conditions tested.

**Find out more:** [www.sartorius.com/flexsafe-pro-mixer](http://www.sartorius.com/flexsafe-pro-mixer)

## Introduction

The purpose of this application study is to assess liquid-liquid mixing performance and blending performance at different viscosities of the Flexsafe® Pro Mixer.

Solution viscosity can affect mixing as increasing viscosity of the solution limits turbulent flow. However, biopharmaceutical solutions usually stands at viscosity between 1cP and 20cP at maximum. For example, mAb formulations are in the range of 2cP to 10cP depending on the concentration. Also, at 20cP and above, a lot of bioprocessing steps, like ultrafiltration, become quite challenging. Nevertheless the Flexsafe® Pro Mixer has been tested at 25cP which corresponds to high-viscosity bulk and 75cP which constitutes a worst-case scenario.

Liquid-liquid mixing has been tested in Flexsafe® Pro Mixer at 50 L, 100 L, 200 L, 400 L, 650 L, and 1000 L volumes. Additional tests for higher-viscosity applications were performed at 50 L, 200 L, and 1,000 L. The 200 L system has been tested at different impeller speeds for each viscosity.

A total of 80 trials were run corresponding to 16 different conditions (volume, impeller speed and viscosity) that have been tested each 5 times to increase result accuracy.

Polyethylene glycol is used as the viscous solution and a small amount of concentrated sodium chloride is used as a tracer to determine the blend time. The performance of the single-use mixing system is assessed using conductivity measurements with 2 conductivity sensors positioned in 2 different locations. Blending time is obtained when the 2 conductivity signals stabilize within a +/-5% homogeneity range for at least 1 minute.



## Materials and Methods

### Materials

#### Consumable

- Standard Flexsafe® Pro Mixer bags (50 L, 100 L, 200 L, 400 L, 650 L, and 1,000 L)
- Deionized water (1 cP)
- Viscous polyethylene glycol (PEG) solution (25 cP & 75 cP)
- Sodium chloride solution (NaCl)
- Conductivity standard solution: 0.01 M KCl

#### Equipment

- Palletank® for Mixing
- Flexsafe® Pro Mixer drive unit
- 2 conductivity sensors
- Multichannel electrochemical meter
- MEMS-based viscometer

### Method

1. Prepare viscous solution at 25 cP and 75 cP. Examples of quantities to be added for the 200L are given in table 1. These quantities are approximate and can be adjusted to get required viscosity.

Table 1: Quantities of PEG 8000 required for the preparation of the 200L viscous solutions

Volume (L)	Viscosity (cP)	Water (kg)	PEG (kg)
200	25	152	48
	75	136	64

2. Install Flexsafe® Pro Mixer bag in the Palletank® for Mixing.
3. Fill up the mixing bag with the test fluid (DI water or PEG solution) to 100% of its nominal volume. Couple the drive unit to the Palletank®.
4. Calibrate the two conductivity sensors, using the 0.01 M KCl conductivity standard. Connect the conductivity sensors to the electrochemical meter. Install a blend time test fixture including the two conductivity sensors and a tracer addition tube at the top of the bag, through the canotier (figure 1).

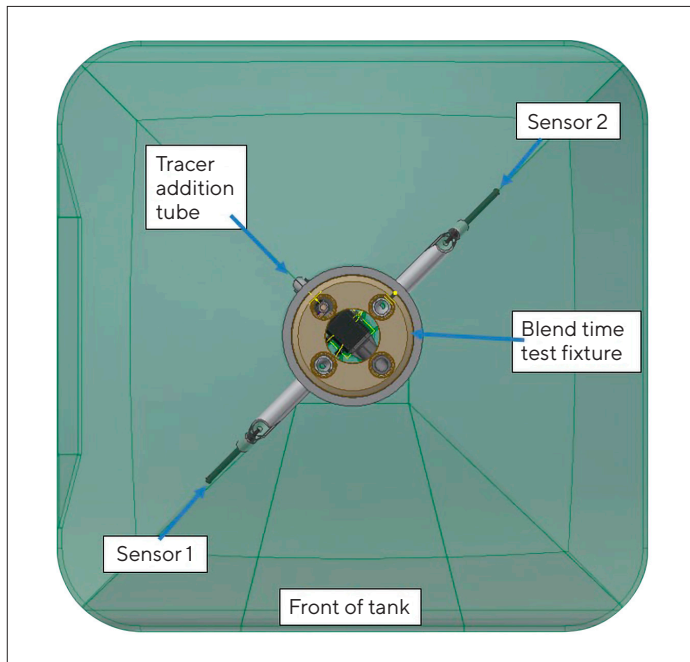


Figure 1: Sensors and tracer addition tube location

5. Check that the viscosity is within 5% of the desired viscosity just before the test.
6. Set impeller speed (table 2). Impeller speed values have been adjusted according to bag nominal volume to avoid high air bubbles level that could interfere with conductivity sensor readings. The 200L volume is tested at different speeds for each type of solution.

Table 2: Impeller speed values

Volume (L)	Impeller speeds (rpm)		
	in 1 cP water	in 25 cP PEG	in 75 cP PEG
50	200	200	200
100	325	/	/
200	150 & 450	150, 300, & 450	150, 450
400	525	/	/
650	650	/	/
1000	750	750	750

7. Start mixing. Wait at least 5 minutes before any material additions to ensure that the flow is fully-developed.
8. Add an amount of NaCl solution, as defined in table 3, through the tracer addition tube and record conductivity values until conductivity stabilizes on all channels.

Table 3: NaCl volume to be added per trial

Volume (L)	NaCl volume (mL)
50	18.8
100	37.7
200	75.3
400	150.7
650	244.8
1000	376.7

Note: The small amount of NaCl added to the bag has no significant effect on the viscosity of the solution and this is confirmed at step 10.

9. Perform 5 trials for each condition (bag volume, test solution and impeller speed).
10. Check that the viscosity is still within 5% of the desired viscosity after the test.
11. Determine blending time. It corresponds to the time when both conductivity values fall between 95% and 105% of the final conductivity value and stay between those boundaries for at least 1 minute.

# Results

80 trials were performed. The Flexsafe® Pro Mixer was able to achieve the different blending in few seconds for each condition (volume, impeller speed and viscosity).

Examples of curves obtained in different trials:

50L in 1cP Water at 200rpm

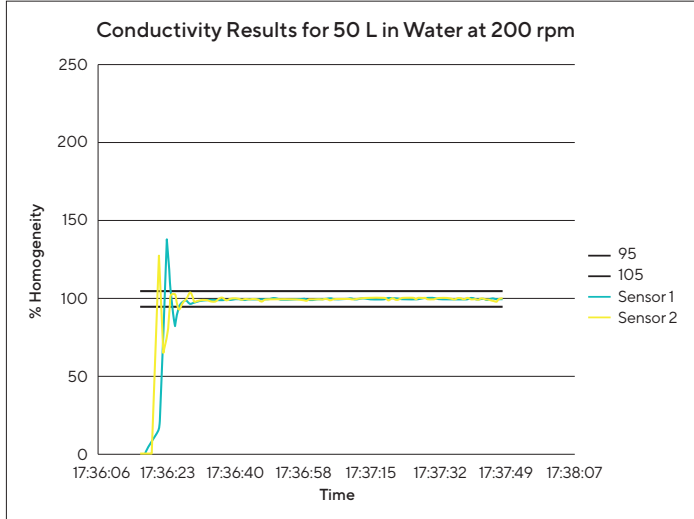


Figure 2: Curve obtained for 50L in 1cP Water at 200rpm

Blend time for this trial was obtained in 11 seconds.

200L in 25cP at 300rpm

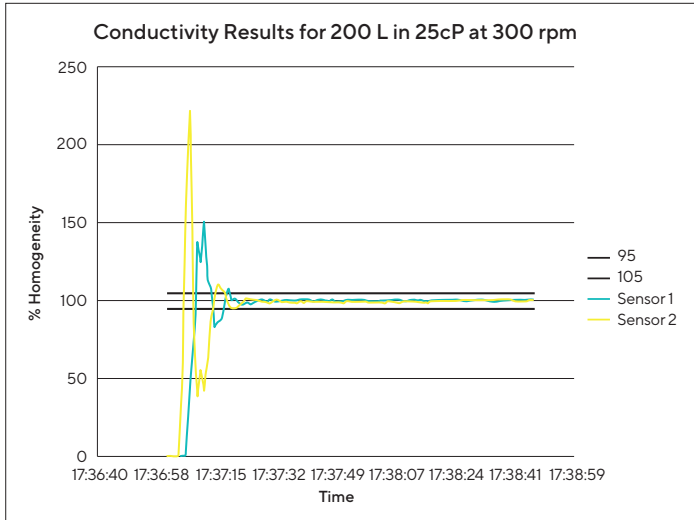


Figure 3: Curve obtained for 200L in 25cP solution at 300rpm

Blend time for this trial was obtained in 19 seconds.

1000L in 75cP at 750rpm

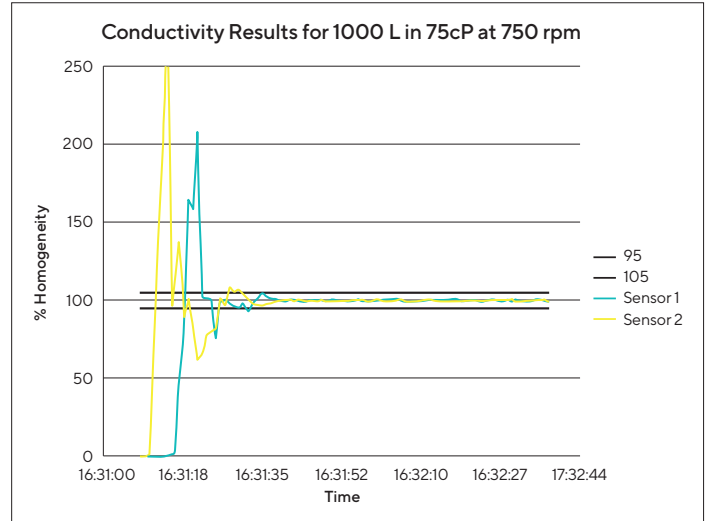


Figure 4: Curve obtained for 1000L in 75cP solution at 750rpm.

Blend time for this trial was obtained in 24 seconds.

## Summary of the Flexsafe® Pro Mixer Performance

Table 4: Blend time at different viscosity for each different volume and impeller speed tested

Volume (L)	Blend time		
	in 1 cP water	in 25 cP PEG	in 75 cP PEG
50			
100			
200			
400		< 1 minute	
650			
1000			

From 50 L to 1000 L, the Flexsafe® Pro Mixer shows excellent performance with very quick blending times for viscosity up to 75cP even at low impeller speeds.

Computational Fluid Dynamics analysis corroborate the excellent performance obtained during blending trials and shows high mixing efficiency throughout the entire bag volume. Indeed, the Flexsafe® Pro Mixer vortex allow a good fluid dispersion in the tank and CFD analysis showed the existence of ascending and descending flows without any stagnant areas as well as the formation of a recirculation loop above the impeller for an efficient mixing process. The data are available in a specific technical note.

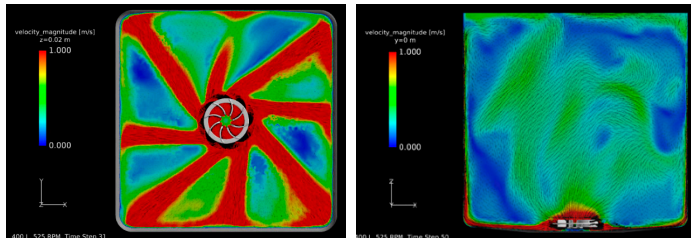


Figure 5: Top and side views extracted from CFD analysis

## 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 50 L, 100 L, 200 L, 400 L, 650 L and 1,000 L volumes.

This application note demonstrates the efficiency of the Flexsafe® Pro Mixer to perform liquid-liquid mixing and blending at different viscosity even in worse case conditions such as high viscosity, in a very quick and easy step.

The Flexsafe® Pro Mixer's ergonomic design enables intuitive, modular and agile use to achieve fast installation and mixing operations.




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