



Celsius-Pak Holdup Volume with High Viscosity Solution

By Matthew Olsen



Sartorius Stedim Biotech is the world leader in controlled Freeze-Thaw technology

Executive Summary

As high concentration protein solutions become more common in the biotech industry their processing becomes more important. One challenging aspect of working with high concentration protein solutions is the high viscosity which can occur due to this concentration.

The holdup volume of a 16.6 L Celsius-Pak and standard tubing set was examined using a 70% sorbitol solution to represent a challenging high viscosity solution for filling and draining. The viscosity of this solution is about 110 cPs at 25°C whereas pure water has a viscosity of 0.89 cP at 25°C. This high viscosity is intended to provide conditions sufficient to mimic the difficulty in draining often encountered with high concentration protein solutions. The holdup volume of the 16.6 L Celsius-Pak was found to be 20 mL or less. This represents less than 0.1% of the nominal fill volume. For a minimally filled pak this same volume would represent only 0.3% of the fill volume. Similar holdup volumes were observed when using either a peristaltic pump or gravity draining procedure.

Introduction

High concentration formulations represent a potentially challenging processing condition for single use systems. A high viscosity sorbitol solution was used to simulate the viscosity of a high concentration protein solution to determine the potential holdup volume of such high viscosity solutions in a 16.6 L Celsius-Pak.

Experimental Setup

The draining experiments for this study were setup using a laboratory scale (Sartorius Stedim Biotech LC34000 P) for measurement of tare and fill weights as well as residual weights of material remaining in the Celsius-Pak. The scale has a stated accuracy of 0.1 g which allows for accurate measurement of small changes in holdup volume.

The sorbitol solution was made from a 70% solution of sorbitol diluted with deionized water to produce a final solution viscosity of 110 cP which would represent a worst case scenario of viscosity for a protein solution. The combined solution had a final density of 1.29 g/mL.

The solution was filled from a reservoir into the Celsius-Pak and then drained back to the reservoir using either a peristaltic pump or gravity draining methodology. Three runs were performed with the peristaltic pump while only one was performed using gravity draining.

In each experiment, the holdup volume was calculated based upon mass remaining in the Celsius-Pak after completion of draining. This number was calculated by taring the weight of the empty Celsius-Pak and frame on the scale prior to filling.

The Celsius-Paks used in all experiments were MPC quick disconnect type (Sartorius Stedim Biotech P/N-DB0016-1). All Celsius-Paks use 3/8" ID Pt-cured Silicone tubing for both inlet and outlet. This tubing was used in conjunction with a Watson-Marlow 520UN/R2 peristaltic pump running at 200 rpm.

Results & Discussion

The first set of experiments performed for this study involved draining with the peristaltic pump. The results of this set of experiments are shown in Table 1 below. The average holdup volume was 13 mL which agrees well with previous results obtained using deionized water.

Draining time was not specifically measured, however, no difference was found in behavior of this high viscosity solution to pumping of water with the same equipment. The pump was run at a flowrate of ~2 L/min during both filling and draining which results in a fill or drain time of just over 8 minutes when used with water.

Table 1: Peristaltic Pump Draining Results

Run Number	Fill Mass (g)	Holdup (g)	Holdup (mL)
1	21386.0	19.5	15.2
2	21497.5	9.5	7.4
3	21558.0	21.1	16.4
Average			13

One run was performed using gravity to drain the high viscosity solution back into the reservoir. This technique was found to be equally successful in achieving full draining of the Celsius-Pak although there is a clear process time disadvantage for the procedure. The full process time for gravity draining is just over 1 hour depending upon the exact setup (height of Celsius-Pak and draining reservoir). The results of this experiment are offered below in Table 2.

Table 2: Gravity Draining Results

Run Number	Fill Mass (g)	Holdup (g)	Holdup (mL)
4	21372.0	11.2	8.7

The overall holdup volume in the system was found to be less than 0.1% of nominal volume for either draining method. In the case of filling an entire Celsius FT100 system with product solution this would result in losses of only 100 mL out of 100 L.

The high viscosity solutions used in this testing are meant to provide a proxy for the viscosity experienced in high concentration protein formulations. While the viscosity is matched in this system it is possible that some high viscosity solutions may induce greater holdup volumes in the Celsius-Pak due to different surface properties of the solutions such as surface tension or other parameters.

Conclusions

The Celsius-Pak allows for a holdup volume of the tested high viscosity solution of less than 0.1% of the nominal fill volume. Previous experimentation with deionized water has revealed substantially similar results. Most pharmaceutically relevant product solutions would also be expected to result in similar values as their solution properties would fall between these two values.

Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen, Germany

Phone +49.551.308.0
Fax +49.551.308.3289
www.sartorius-stedim.com

USA +1.800.3687178
UK +44.1372.737100
France +33.442.845600
Italy +39.055.634041
Spain +34.91.3586102
Japan +81.3.37405407

Specifications subject to change
without notice. Printed and copyrighted
by Sartorius Stedim Biotech GmbH
W/sart-000 - G
Publication No.: SL-1061-e07121
Order No.: 85032-534-43