PATsmart™ FlowVPX® Single-Use & Stainless Steel Flow Cells Comparability Study

Technical Note

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Introduction

The PATsmart™ FlowVPX® System is an innovative, in-line UV-Vis spectroscopy system that utilizes variable pathlength technology to determine sample concentration. The Slope Spectroscopy® method offers a unique application of the Beer-Lambert Law by generating a linear slope from the acquired absorbance data over multiple pathlengths.[1] The system features a stepper motor capable of adjusting the pathlength in 1-micron intervals, which can increase the linear range exponentially compared to traditional UV-Vis systems. The FlowVPX System uses a Flow Cell that integrates directly into the process tubing, enabling real-time concentration measurements and making it well-suited for applications like UF/DF, chromatography, mixing, and fill-finish.

The Flow Cell is the only component of the system that contacts the process material. It is available in various sizes for lab-scale, pilot-scale, and production-scale fluid processes. Furthermore, the FlowVPX instrument can be equipped with either a Stainless Steel Flow Cell or a Single-Use Flow Cell.[2,3]

The following study was performed by Sanofi to assess the accuracy of the Single-Use Flow Cell and confirm its ability to support real-time, high concentration measurements. The experiment tested concentrations representative of those typically measured in a continuous UF/DF process, where the product is concentrated and buffer-exchanged to reach targets for drug substance formulation.

This publication demonstrates that coupling the FlowVPX Single-Use Flow Cell provides accurate, real-time concentration measurement while addressing sterilization needs in downstream commercial manufacturing. The SoloVPE® System, Repligen's at-line UV-Vis variable pathlength system, was used to assess the accuracy of the FlowVPX measurements.

FlowVPX Single-Use Flow Cells

The Single-Use Flow Cell supports stringent bioprocesses, such as drug manufacturing, by eliminating cleaning and maintenance, thereby reducing operational downtime and lowering the potential for cross-contamination.[4] The Flow Cell body is made of polyphenylsulfone (PPSU) and fitted with AseptiQuik connectors for contamination-free connections. The Flow Cell can be x-ray irradiated to achieve a sterility assurance level of 10^{-6} inside the flow path.[5] The irradiation process has no impact on the performance of the Flow Cell.[6]

Materials & Methods

- FlowVPX System
- SoloVPE System
- 3 mm Stainless Steel Flow Cell (OC2002-2)
- 3 mm Single-Use Flow Cell (OC2008)
- Watson-Marlow 120U Variable-Speed Pump System
- Masterflex pump tubing (size #16)
- Monoclonal antibody (mAb) sample
- Histidine buffer

The study was performed by creating a recirculation loop with the FlowVPX System installed after the Watson-Marlow pump. Repligen recommends placing the FlowVPX instrument between the feed vessel and the pump to avoid effects of pulses generated by the pump; however, no such effects were observed in this study due to the low pump speed of 60 rpm.

The mAb sample began at a concentration of approximately 200 mg/mL. Concentration was monitored by the FlowVPX System until it stabilized. The flow was then stopped, and the

sample was diluted with histidine buffer and mixed via stir bar. The flow was then restarted and the new concentration was measured after stabilizing again. This was repeated for a total of 7 concentration levels.

Two separate experiments were conducted; the first used one FlowVPX System with a 3 mm Stainless Steel Flow Cell (SSFC), and the second used two FlowVPX Systems, each with a 3 mm Single-Use Flow Cell (SUFC). The setups are illustrated in Figure 1.

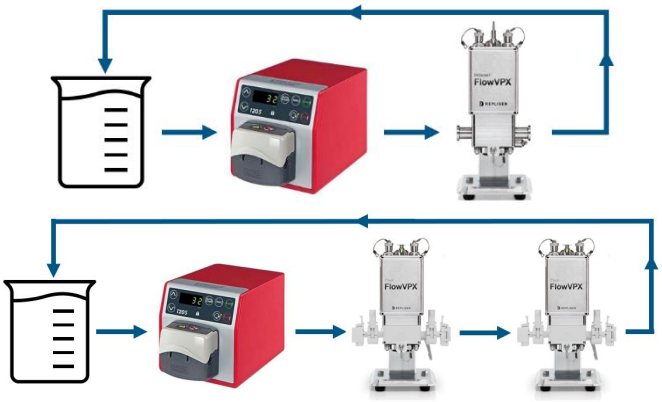

Figure 1. Flow Cell Comparability Study Setup with SSFC (top) and SUFC (bottom).

In both runs, percent error was calculated relative to the SoloVPE average measurement:

$$\%Error = \frac{|FlowVPX - SoloVPE|}{SoloVPE} \times 100\%$$

In the second run, percent difference between the Flow Cells was also calculated to assess variability between units:

$$\%Difference = 2 \times \frac{|SUFC\#1 - SUFC\#2|}{SUFC\#1 + SUFC\#2} \times 100\%$$

Results

Stainless Steel Flow Cell

The FlowVPX System using a Stainless Steel Flow Cell measured concentrations within 1.00% of the at-line SoloVPE readings for all but one dilution level. Results are listed in Table 1 and plotted in Figure 2. Relative standard deviation across all measurements was less than 2.0% at each concentration level.

Single-Use Flow Cells

The two FlowVPX Systems equipped with Single-Use Flow Cells demonstrated good agreement with the SoloVPE readings at all concentrations, yielding errors less than 3.00% for all concentration levels. Measurements from both FlowVPX Systems demonstrated low variability, differing by less than 2.00% at all levels and less than 1.00% at most levels. Table 2 shows the concentration measurements with corresponding percent differences and percent errors; results are plotted in Figure 2. Relative standard deviation was typically less than 1.0% for each Flow Cell.

Table 1. Stainless Steel Flow Cell concentration measurement

Expected Concentration (mg/mL)	SSFC Average (mg/mL)	SoloVPE Average (mg/mL)	% Error	SSFC %RSD
200	201.6	203.2	0.78%	0.6%
159	159.4	160.0	0.40%	1.0%
130	130.5	129.8	0.54%	1.0%
98	96.94	97.77	0.85%	0.9%
63	61.88	64.32	3.79%	1.5%
24	25.18	25.03	0.58%	1.5%
15	15.34	15.30	0.25%	0.8%

Table 2. Single-Use Flow Cell concentration measurements

Expected Concentration (mg/mL)	SUFC #1 Average (mg/mL)	SUFC #2 Average (mg/mL)	SUFC % Difference	SoloVPE (mg/mL)	SUFC #1 % Error	SUFC #2 % Error	SUFC #1 %RSD	SUFC #2 %RSD
200	207.1	208.9	0.88%	207.6	0.23%	0.65%	0.5%	0.6%
159	164.8	165.5	0.43%	161.1	2.30%	2.74%	0.6%	0.8%
130	132.6	130.6	1.53%	130.7	1.44%	0.10%	0.4%	1.1%
98	95.37	96.52	1.19%	95.12	0.27%	1.47%	0.4%	0.4%
63	59.18	58.75	0.72%	58.48	1.18%	0.45%	0.4%	0.2%
24	21.10	21.06	0.16%	21.12	0.09%	0.24%	0.2%	0.1%
15	12.95	12.96	0.10%	12.93	0.13%	0.23%	0.2%	0.1%

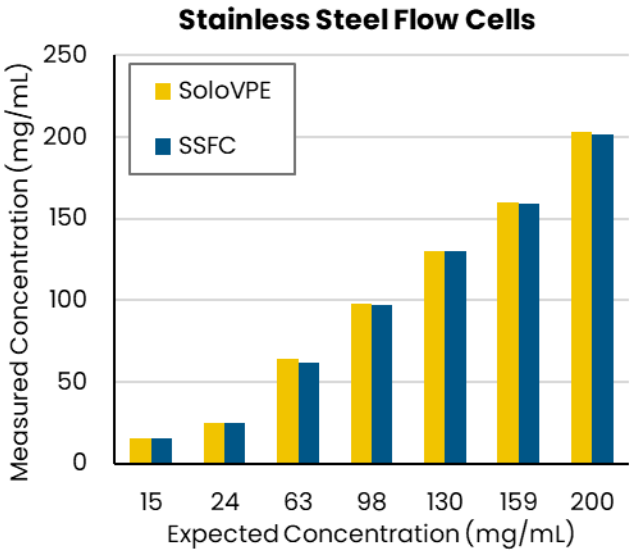

Figure 2. Concentration Data for Stainless Steel Flow Cells

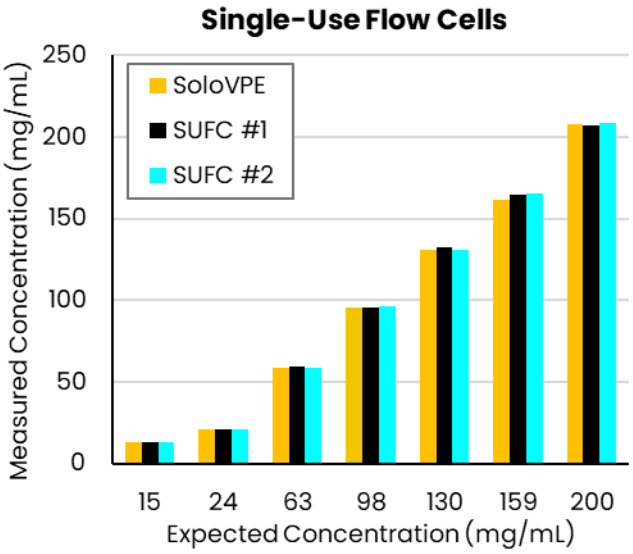

Figure 3. Concentration Data for Single-Use Flow Cells

Conclusion

This study demonstrated that FlowVPX Single-Use Flow Cells exhibit concentration measurement performance that is comparable to that of the Stainless Steel Flow Cells across a wide range of mAb concentrations representative of typical downstream UF/DF operations. Measurements using both types of Flow Cells showed strong agreement with the at-line SoloVPE System, confirming the accuracy and reliability of the FlowVPX System for real-time concentration monitoring.

The close alignment between Single-Use and Stainless Steel Flow Cell performance indicates that the materials of construction do not adversely affect measurement accuracy or repeatability. With proper method development, users can expect robust analytical performance using whichever Flow Cell is best suited to their operational needs.

References

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