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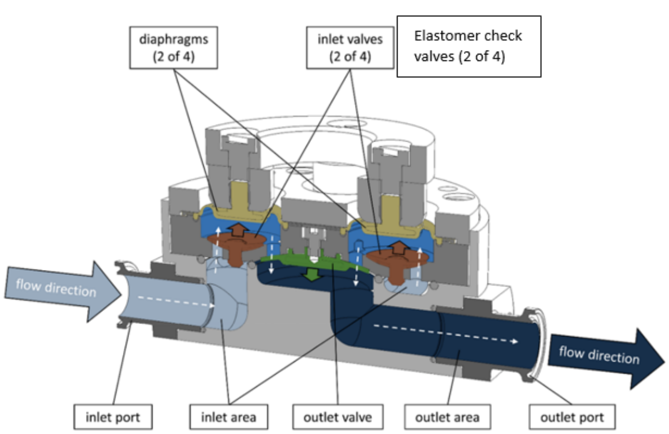
Using back pressure to prevent pump push-through flow in single use bioprocessing systems

CASE STUDY: HOW AN EQUILIBAR® SINGLE-USE BACK PRESSURE REGULATOR PREVENTS PUSH-THROUGH FLOW IN PSG BIOTECH QUATTROFLOW® SINGLE-USE DIAPHRAGM PUMP

Background

Positive displacement pumps such as diaphragm pumps are an industry standard for reliable and efficient transfer of aqueous solutions and biologics. They are used in single-use and multi-use biopharma manufacturing, including tangential flow filtration (TFF), Chromatography, centrifuge feed and more. In applications where the feed tank or single-use bag is placed below or at level with the diaphragm pump, the pump creates a suction lift to prime the fluid into the pump. The diaphragm action in conjunction with the elastomer inlet check valves feeds the fluid gracefully from lower pressure at the inlet to higher pressure on the outlet.

With clean room space being increasingly valuable in today's CDMO (Contract Development Manufacturing Organization) facilities, some feed fluids may be stored at elevated heights from the main floor to save floorspace for production needs. Buffers, for instance, are often stored on a level above the pump that feeds fluids to a chromatography skid or filtration skid. The geodetic height of these buffers above the suction port on the diaphragm pump creates hydraulic pressure, often referred to as "elevation pressure," or Net Positive Suction Head (NPSH). This positive pressure aids in system priming, however it also pushes the check valves open so fluid flows through the diaphragm pump chamber. The diaphragm pump cannot stop the flow in this pressure scenario and may result in flow rates above optimum bioprocess values. This push-through flow phenomenon occurs in positive displacement pumps in multi-use and single-use systems with elevated inlet pressures.



The sectional drawing to the left shows a PSG Biotech Quattroflow® QF1200SU pump chamber illustrating a flow path through a diaphragm pump with diaphragms and check valves. When high inlet pressure occurs, fluid pushes the check valves open.

Figure 1. Exemplary sectional drawing of a QF1200SU pump chamber

The Challenge

When NPSH creates a pressure at the inlet side of the pump chamber above the outlet pressure, uncontrolled flow passes through the diaphragm pump. This presents issues when the pump must control flow but the "push-through" flow is higher than the desired flow. The pump is unable to control flow below the rate of the push-through rate, thereby decreasing the practical control range of the pump. Push-through flow can lead to product waste or inaccurate buffer dilution and decreased yield.

Solution Evaluation

Engineers at Equilibar and PSG Biotech tested a single-use specific solution to this push-through behavior by placing a sensitive back pressure regulator (BPR) at the outlet of a positive displacement (PD) pump to prevent unwanted flow. By adding a BPR downstream of the pump to increase outlet pressure above the elevation pressure, the full control window of the pump can be realized independent of NPSH. In this study, an Equilibar® SDO6 single-use BPR was placed downstream of a PSG Biotech Quattroflow® single-use QF1200SU diaphragm pump.

The *PSG Biotech Quattroflow® QF1200SU pump* features quaternary (four-piston) diaphragm technology that enables gentle pumping. Each stroke of the four diaphragms is generated by an eccentric shaft, which is connected to the electric motor. This method of operation allows the Quattroflow pump to convey shear-sensitive aqueous solutions and biologic products with minimal impact. The practical control range of the Quattroflow pump has a very high turndown ratio under normal process conditions.

Figure 5: QF1200 Single-Use pump with an integrated drive unit

The Equilibar® SDO is a dome loaded single use back pressure regulator with pilot operation. Air is fed into the regulator's top (dome) area to provide the process pressure setpoint. The gas pressure in the dome is set by a secondary pressure reducing regulator (PRR) called a pilot regulator. The pilot air presses down on a supple diaphragm covering and sealing the parallel orifices in the body of the BPR. As fluids flow through the unit, the BPR holds the process pressure equal to the pilot setpoint. When the upstream process pressure exceeds the setpoint pressure, the diaphragm gradually lifts off the orifices to release pressure instantaneously and with extreme precision.

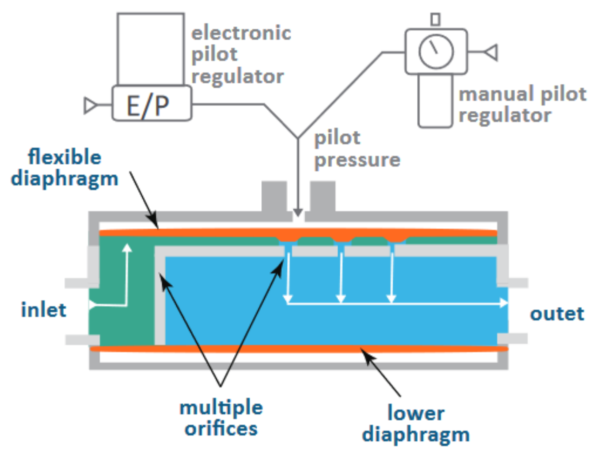


Figure 2: Simplified Cross-section view of Equilibar SDO

Experimental Set-Up

In this test, water was delivered from an overhead pressurized tank to simulate different elevation conditions; each foot of elevation is simulated by increasing suction pressure by ~0.43 psig / 0,03 barg. The QF1200 delivered water from the tank through the SDO BPR straight to the drain for simplicity. While there was a flow meter and pressure sensor downstream, there was no other process downstream of the BPR to reduce the push-through flow, so this setup represents an extreme case of push-through where little to no system restriction is present. A more typical system would have a downstream process (chromatography column, TFF, etc.) after the BPR adding resistance, thereby reducing push-through. See the schematic below for details of the system setup.

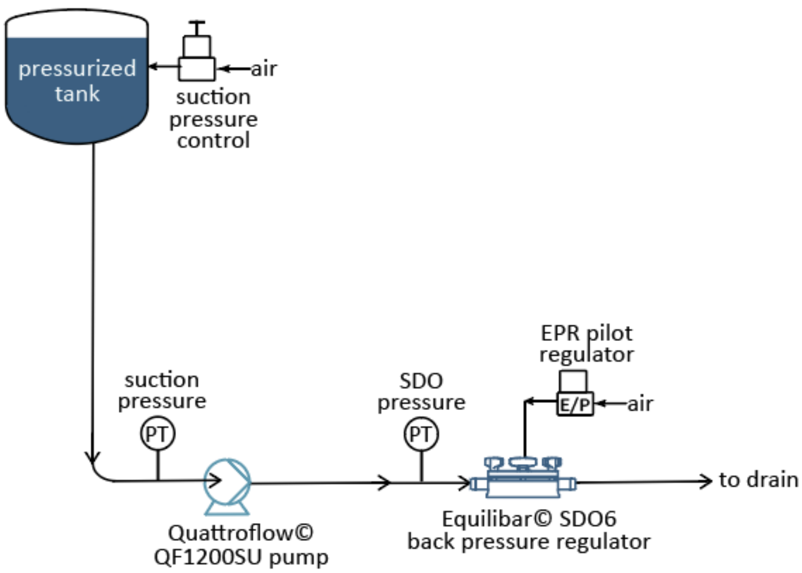


Figure 3: Experimental Schematic

The ***suction pressure*** was measured at the inlet of the QF1200 pump and ***back pressure*** was measured at the inlet of the Equilibar SDO. An electronic pilot pressure regulator (EPR) was used to control the setpoint pressure on the Equilibar SDO6NZA3 BPR.

The process was tested with the QF1200 pump off and with the pump set at a very low flow rate (100 ml/min). These flow rates were tested with a suction pressure setting of 3 psig / 0,2 barg (representing 7ft / 2m elevation) and 15 psig / 1 barg (representing 34.5 ft / 10,5m elevation).

Figure 4: Equilibar Single Use BPR with EPR to control setpoint

The lower elevation might simulate a single-use bag or small stainless steel tank mounted at the top of a TFF or chromatography skid. The higher elevation might simulate a buffer tank placed on a floor above the production system, which is a common setup in large manufacturing facilities.

Specifics of the test setup include:

- Water was used as the test fluid
- Pump RPM was used to reach the desired flow rate. No ramp was applied when RPM was set, creating a step change in flow rate
- Equilibar SDO6 BPR was set up in open loop setpoint control via electronic pilot pressure regulator
- Data was collected and graphed every ms via LabVIEW DAQ; No data filtering was applied

A note about push-through flow and system resistance

Fluid systems are characterized by a system resistance curve determined by resistance (pressure loss) from the pipes, valves, sensors, and installations along the fluid path. As flow through the system increases, the dP in the system increases and can be represented in a system resistance curve like the one below.

The graph below shows two example system curves, **Sys 1** and **Sys 2**, that represent a variation in system restriction to demonstrate how NPSH affects push-through flow with different process restrictions. The lower the system resistance, the higher is the resulting push-through flow rate at same positive inlet pressure (NPSH). A pump cannot control flow at a rate below the push-through flow.

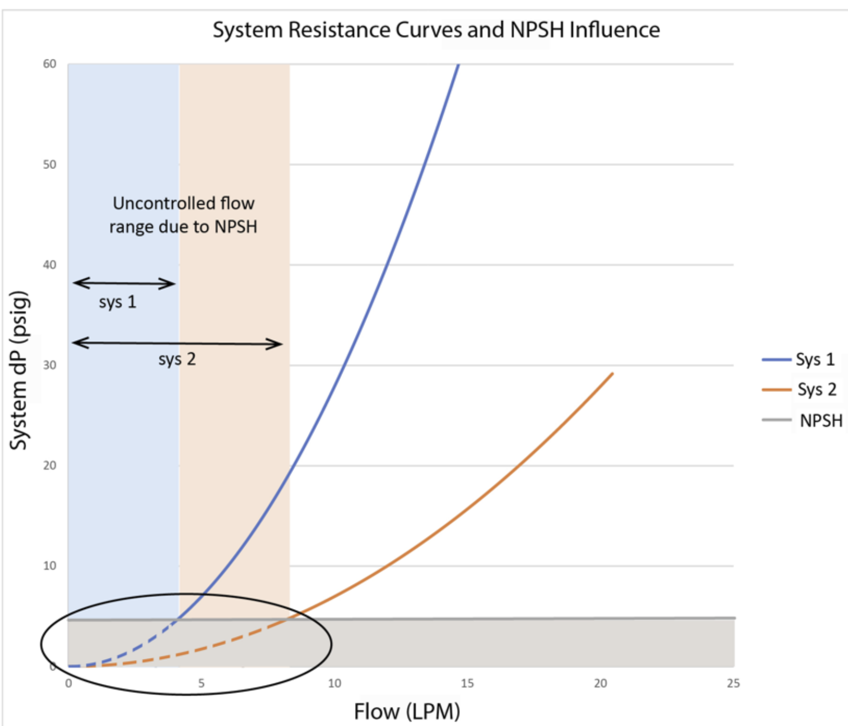


Figure 6: Two example system resistance curves for various system restrictions. See expanded view on next page.

The intersection of the resistance curve with the NPSH / suction pressure line estimates the push-through flow rate, which can be significant for low restriction systems. This, in turn, can impact certain applications like chromatography where flow precision is key.

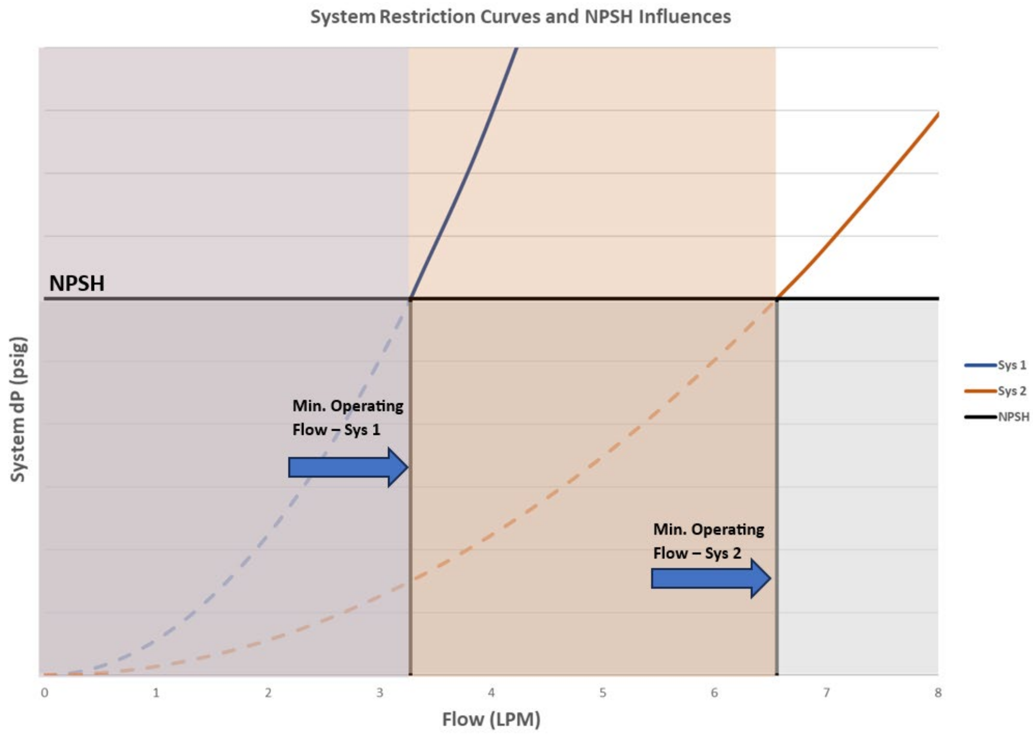


Figure 7: Minimum flow operating point for 2 systems resulting from NPSH

By adding back pressure to the outlet of the pump, the system resistance curve is effectively adjusted up the y axis by the BPR's pressure setpoint (see graph at right). Setting the SDO valve inlet pressure to a value greater than the suction pressure (NPSH) eliminates push-through flow in the system, allowing the pump to make use of its entire range of control.

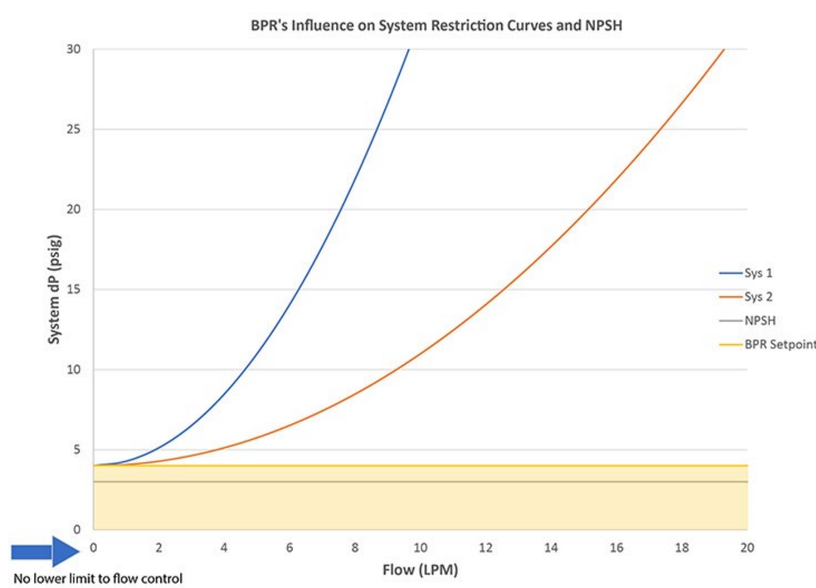


Figure 8: The SDO's correction of system curves to allow the full flow range to be controlled

Results

PUMP-OFF CONDITION

The first two tests were run with the QF1200 pump off to determine innate push-through rates. Push-through flow was measured at 3 psig / 0,2 barg suction pressure (elevation pressure) and 15 psig / 1 barg suction pressure both with and without applying back pressure. LabVIEW data is graphed for all the flow and pressure conditions. The left axis shows pressure, and the right axis shows flow rate.

A **3-psig / 0,2 barg suction pressure** is equivalent to 7 feet / 2,1 m of elevation from the pump inlet for water-like fluids. The results graphed below show that with no back pressure, the push-through flow (grey line/right axis) was 2.8 LPM. Flow decreased to zero when back pressure was applied and reached 3.2 psig / 0,22 barg (blue line/left axis), slightly above the suction pressure. Suction pressure (orange line/left axis) remained stable. See graph below.

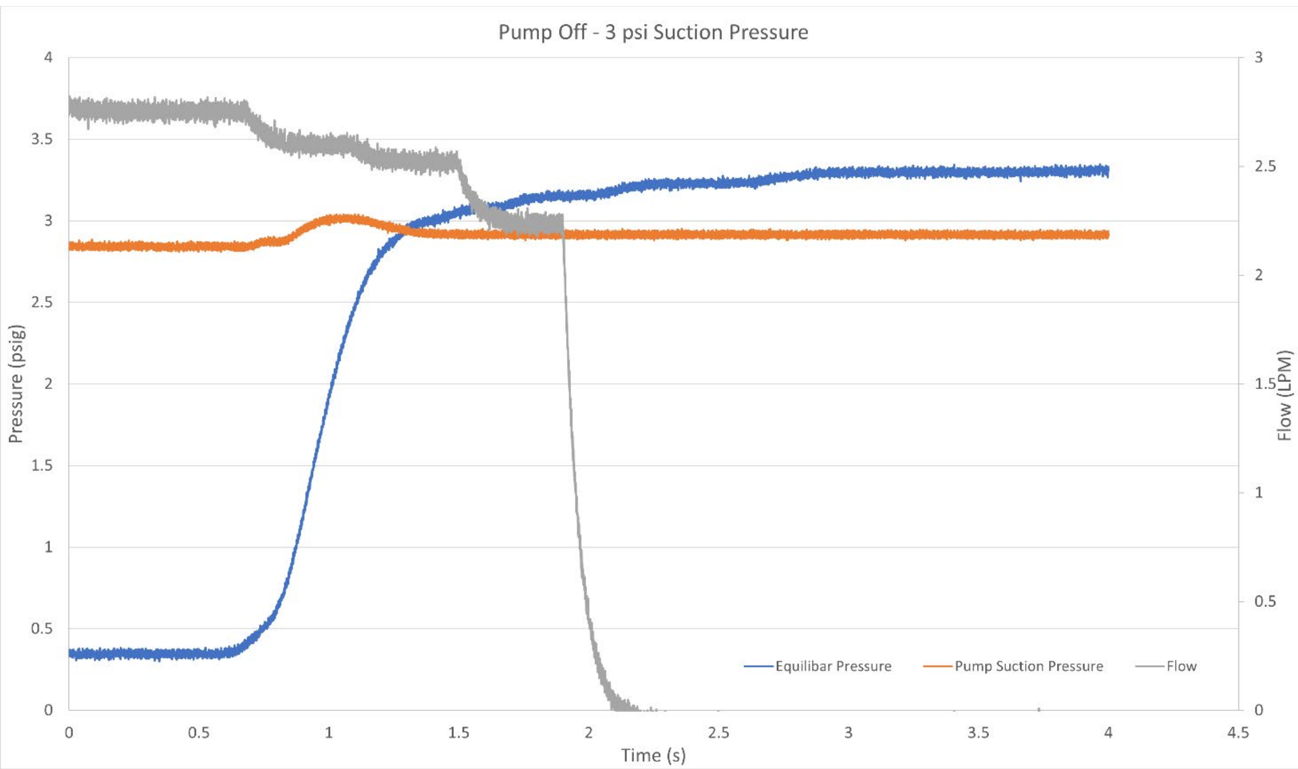


Figure 9: The Equilibar SDO BPR eliminates push-through flow when set slightly above suction pressure.

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In the second setup, the air blanket in the pressurized tank was increased to produce a **suction pressure of 15 psig / 1 barg**, representing a 34.6-foot / 10,5 m elevation from the pump outlet to the top of the water.

At 15 psig / 1 barg suction pressure (blue line), the push-through flow reached 14 LPM (grey line) and was again eliminated when the back pressure reached about 16.3 psig / 1,1 barg (orange line), slightly above the suction pressure.

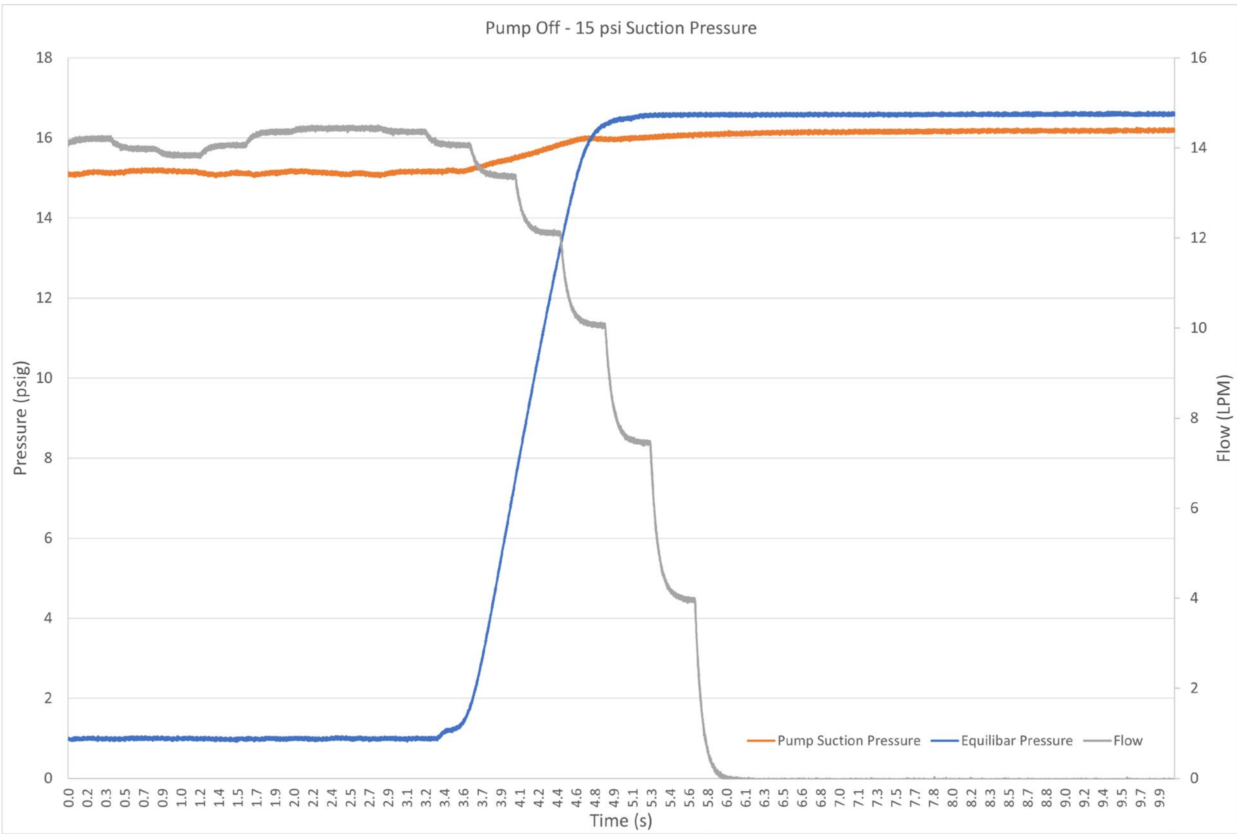

Figure 10: 1 bar NPSH being corrected by the SDO valve

LOW-FLOW CONDITION

With the suction pressure still set at 15 psig / 1 barg (orange line), the pump speed was set to 9RPM to reach the 100 ml/min target low flow rate. The flow rate is shown with the grey line and right axis in the graph below.

(Technical note: In general, Quattroflow recommends priming and venting the pump chamber at higher flow rates before the pump is used at very low flow rates to achieve a stable flow rate with low pulsation.)

A smaller flow meter was used for this condition to capture the low flow rates, so without the SDO BPR engaged, the excess pass-through flow was above the limit of the flow meter scale (4 LPM) and for this reason the data above 4 LPM are not shown on the graph.

Pilot pressure was initiated to the SDO BPR at the 2.2 sec mark (blue line starts to increase) and by the 4.8 sec mark, the flow had reached the target of 100 ml/min (grey line). The back pressure was held above 16 psig / 1,1 barg to eliminate the push-through flow.

Note: It is important to see that the pump generates a flow of 100 mL/min (6 LPH) at 9 RPM, because this is the absolute minimum specification of the Quattroflow QF1200 pump. So beyond preventing the push-through flow, the Equilibar BPR enables the pump to achieve a stable flow rate with low pulsation at the lowest point of the pump flow curve. Using this combination, the complete high turn down capability (1:200) of the QF1200 pump can be reached.

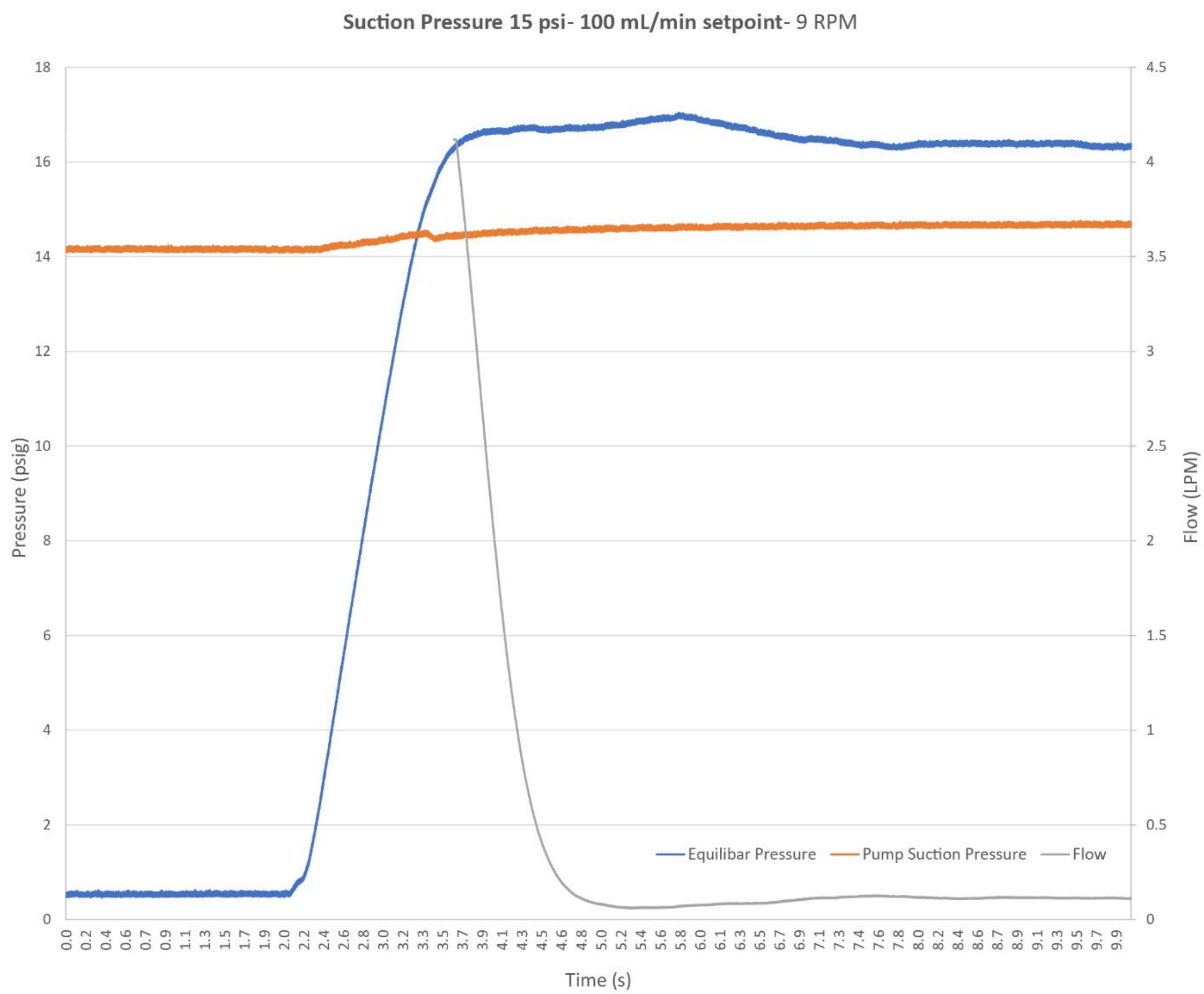

Figure 11: Demonstrating 100 mL/min flow with a 1 bar suction pressure

When the suction pressure was reduced to 3 psig / 0,2 barg, there was a similar response. The excess push-through flow was eliminated, and the 100 ml/min flow rate was reached at about 2 sec after the Equilibar SDO pilot pressure was set.

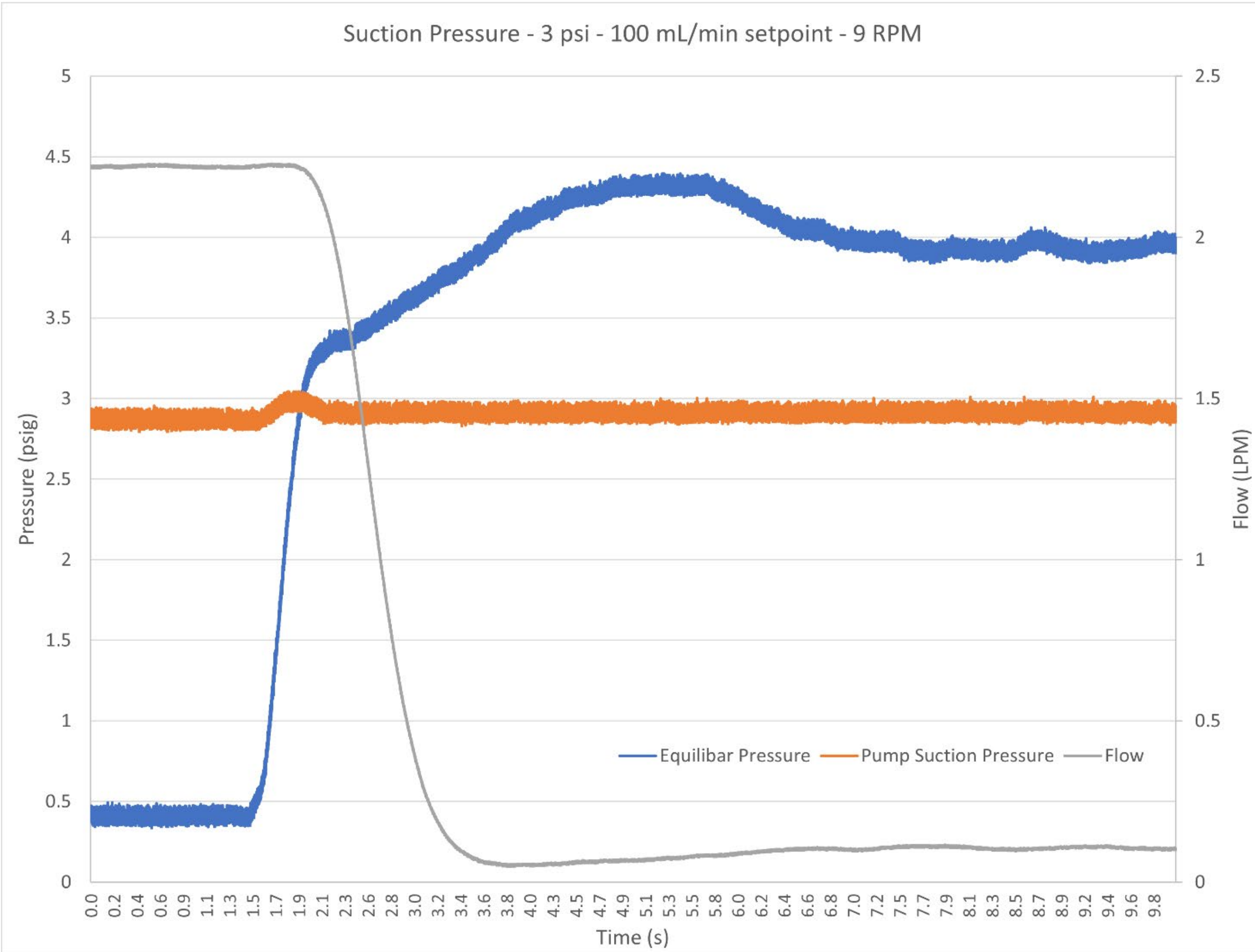

Figure 12: Graph showing how extremely low flow rate of 100 ml/min from the QF1200 is reached by engaging an Equilibar SDO back pressure regulator to eliminate push-through flow

Equilibar Contribution to System Resistance

One thing to consider is the restriction added by the Equilibar SDO valve on a system's resistance curve. Since each resistance curve will be unique to the system design, analysis will need to be done on a case-by-case basis. Fortunately, Equilibar's valve design offers industry leading valve turndown, so for a given line size the Equilibar's contribution to the system restriction curve will be minimal due to its capacity (valve Cv).

If the system pressure (e.g. working pressure point of the filter + pressure losses of the system) is above the setpoint of the Equilibar BPR, the valve acts like any other part in the fluid path. The fluid is pumped through the valve and every working pressure point which is required can be achieved. Quattroflow Single-Use pumps are specified for pressures up to 4 barg that cover most of the typical biotech applications. The BPR creates just a small pressure loss based on the flow rate.

Discussion

The advantage of having a responsive and accurate single-use back pressure regulator downstream of the Quattroflow QF1200 Single-Use positive displacement pump is clear from this data. By eliminating the push-through flow due to elevation pressure in the process, the pump can realize its true potential and, in many cases, increase its stable operating range at low RPMs. With stable back pressure, the pump can reach its highest and lowest delivery rates because pass-through flow is not adding to or interfering with the pump's optimal operating conditions. The pump's accuracy is also improved, resulting in precision pH and conductivity for the process.

Another advantage to using the *Equilibar SDO* BPR is that the setpoint can be changed as needed. As the fluid is delivered from the tank above, the level decreases, thereby decreasing the suction pressure. The Equilibar pilot setpoint can adjust to a new setpoint based on input from the suction pressure so that it maintains a slightly increased back pressure just enough to keep the pump at peak performance. Alternatively, the Equilibar SDO can have a simple manual pilot setpoint that is set at the highest expected suction pressure in the process and maintain zero pass-through flow for the duration of the delivery.

Diaphragm pumps are an industry standard technology used in single and multi-use bioprocessing. With the aid of Equilibar's back pressure technology, both single and multi-use systems can benefit from this approach to preventing varying suction pressures and for realizing the full flow range of delivery pumps. In addition to pass-through flow prevention, the Equilibar technology has a demonstrated pulsation dampening benefits both *upstream* and *downstream* of the valve, which stabilizes the system even further. Follow the links for further information on these benefits.

Contact Equilibar

Equilibar is a provider of unique and innovative fluid control solutions based near Asheville North Carolina. Our dome-loaded, multiple-orifice technology is used in a wide array of processes including biopharmaceutical, catalysis, fuel cells, supercritical and other industrial applications. The Equilibar Single Use Division was formed in 2021 to focus on delivering products tailored for single-use and multi-use biopharma customers. *www.equilibar.com* Follow us on *LinkedIn*

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