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A study of the peristaltic life and pumping performance of three TPE tubing products to assess their suitability for continuous bioprocessing

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Executive summary

Drug manufacturers are increasingly adopting continuous bioprocessing to manufacture biologics as efficiently as possible. This is being driven by a need to reduce production costs and prices of pharmaceutical products. Furthermore, the FDA has stated its support for the implementation of continuous bioprocessing. A key consequence of continuous bioprocessing is that single-use components and assemblies must maintain integrity for process cycle times of up to 90 days.

For peristaltic pump tubing, there is added complexity because of the loads placed on the tubing by the pump and the resultant dynamic wear on the tubing. A peristaltic tube must deliver confidence that it will not fail within the process cycle time and that it will deliver consistent flow rate over this time.

In view of this, Watson-Marlow Fluid Technology Group (WMFTG), fluid path solutions provider of peristaltic pumps and single-use components, outlines the results of a study which makes comparisons between the peristaltic life and pumping performance of PureWeld® XL TPE tubing and two leading industry alternatives.

Focus and outcome of this study

The study reveals noteworthy results that affirm the need for drug manufacturers to consider the peristaltic life of all tubing products used in continuous bioprocessing. This paper details that samples of WMFTG PureWeld XL tubing tubing were compared to two leading industry alternative SEBS TPE products to assess pumping performance over time and peristaltic life.

Three tubing materials were selected, PureWeld® XL, Competitor A and Competitor C. Tubing size 6.4 mm bore by 2.4 mm wall was used in each test. For each test conducted there were five samples of each material. The testing was carried out on three Watson-Marlow 530Du drives fitted with 520R2 pumpheads. The flow rate delivered by the pump system was automatically recorded every six seconds. The testing was conducted at room temperature and the pumps were run in the counter-clockwise direction at 220 rpm and a back pressure of 2 bar.

Introduction

With the increasing integration of robust single-use technologies into cGMP bioprocess, there is a greater value placed on tubing and tubing assemblies within critical fluid path.

Add to this the increasing adoption of continuous bioprocessing, and the resultant process cycle times of up to 90 days, it is essential that the peristaltic tubing used delivers long pumping life. The increasing burden of materials validation within the bioprocessing industry has driven a desire to rationalise inventory and reduce the number of fluid contact materials. To meet this need, it is advantageous for the tubing used in the bioprocess assembly to deliver high performance in terms of peristaltic life.

There is growing acceptance of SEBS TPE materials due to their compatibility with sterile welding and sealing technologies, performance and levels of purity which meet the expectations of the industry and regulators. In addition, the worldwide shortage of silicone raw materials has brought an additional focus to the implementation of TPEs.

PureWeld® XL in addition to BioPure Products and puresu® single-use assemblies are manufactured in ISO 14644-1 Class 7 cleanrooms

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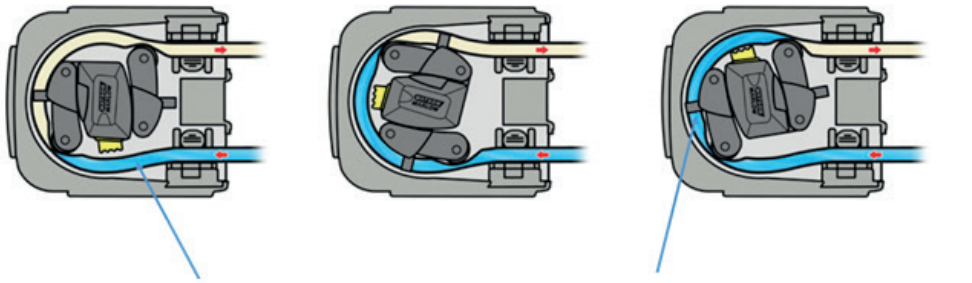
The peristaltic pump principle

Nothing but the pump tube touches the fluid, eliminating the risk of the pump contaminating the fluid, or the fluid contaminating the pump. Rollers compress the tube as they rotate, creating a vacuum which draws fluid through the tube. This fluid is trapped by the pumphead roller and then expelled by the next roller pass. As the rollers rotate, a vacuum is formed in the tube, pulling in more fluid, for the next roller pass. Figure 1 shows this principle diagrammatically.

Figure 1 The peristaltic principle



The complete closure of the tube when is it occluded (squeezed) between the roller and the track, gives the pump its positive displacement action, preventing backflow and eliminating the need for check-valves when the pump is not running.

Test conditions

Comparative pumping life testing is conducted under mildly accelerated conditions to allow the collection of sufficient data in a reasonable time frame. This requires testing at full pump speed, running the pump continuously at elevated discharge pressure. Clearly this is not fully representative of the conditions in a typical bioprocessing application. The expected peristaltic life of a given tubing material will be based on the number of roller passes (occlusions) and this can be used to indicate the expected life in a typical application.

Discharge pressure also has an influence on pumping life and a tube operating at 1 bar discharge pressure would be expected to deliver greater pumping life than a tube operating at 2 bar discharge pressure.

Outline of study

To explore the relative performance of PureWeld® XL, as compared to two leading weldable TPE tubing products; the following properties were assessed:

- pumping performance against elevated discharge pressures
- peristaltic life
- flow stability

Watson-Marlow is always seeking to improve its testing capabilities and with the addition of the Automated Test Equipment (ATE) it is possible to continually monitor flow and pressure to give greater understanding of how the tubing performs during use. Manual measurements only give a snapshot of performance at the time of measurement and are influenced by the operator. The ATE gives consistent, operator independent, results and any changes to flow or pressure are recorded instantaneously.

Experimental method

Test articles

Three tubing materials were selected, PureWeld® XL, Competitor A and Competitor C. Tubing size 6.4 mm bore by 2.4 mm wall was used in each test. For each test conducted there were 5 samples of each material.

Test equipment

The testing was carried out on three Watson-Marlow 530Du drives fitted with 520R2 pumpheads.

An IFM (SM 6000) flow meter and a Balluff pressure sensor were used to measure flow and pressure respectively. The data was recorded using LabVIEW software, and a data point was recorded every 6 seconds. A damped analogue pressure regulator on the discharge was used to create pressure.

Test method

The 15 test articles were randomly assigned to one of the three pumps to eliminate any differences resulting from the pump setup. The rotors were measured to ensure they were within specification before each test run. The testing was conducted at room temperature and the pumps were run in the counter-clockwise direction at 220 rpm and a back pressure of 2 bar (RMS).

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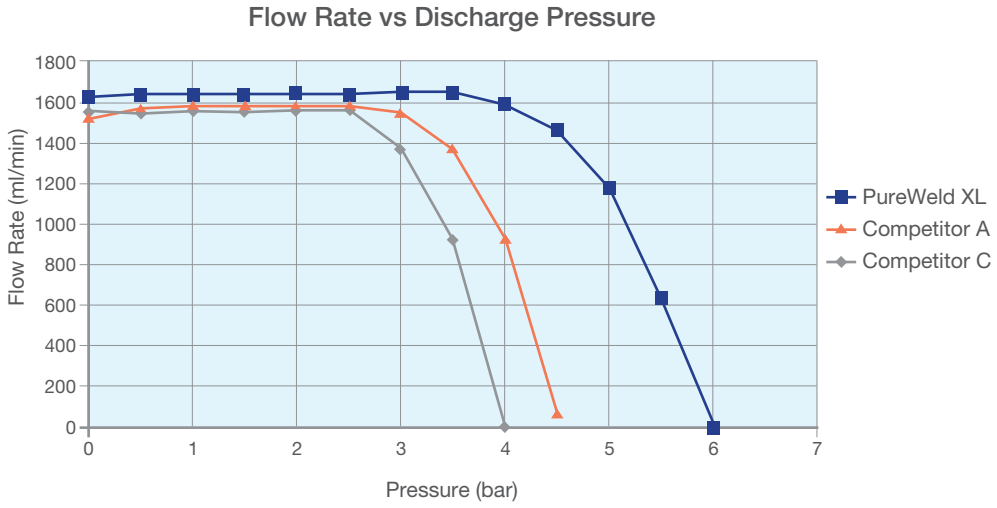
Test results and discussion

Pressure

The peristaltic performance of test articles of PureWeld XL against increasing discharge pressure was compared with test articles of Competitor A and Competitor C. As the back pressure of the system was increased the flow output was measured. There was no drop in flow with PureWeld XL until the back pressure reached 4 bar, and a reasonable flow was still achieved at 5 bar. Competitor C was only able to maintain consistent flow output to 2.5 bar and Competitor A maintained consistent flow to 3 bar. The results are shown graphically in Fig. 2

Figure 2 – Flow rates vs discharge pressure for 6.4 x 2.4 mm tube at 220 rpm on a 530Du pump



Life

The peristaltic life of each tube was assessed by running until catastrophic failure or until the tube was unable to produce a flow. Each result is an average of five repeats. The results are summarised in Table 1.

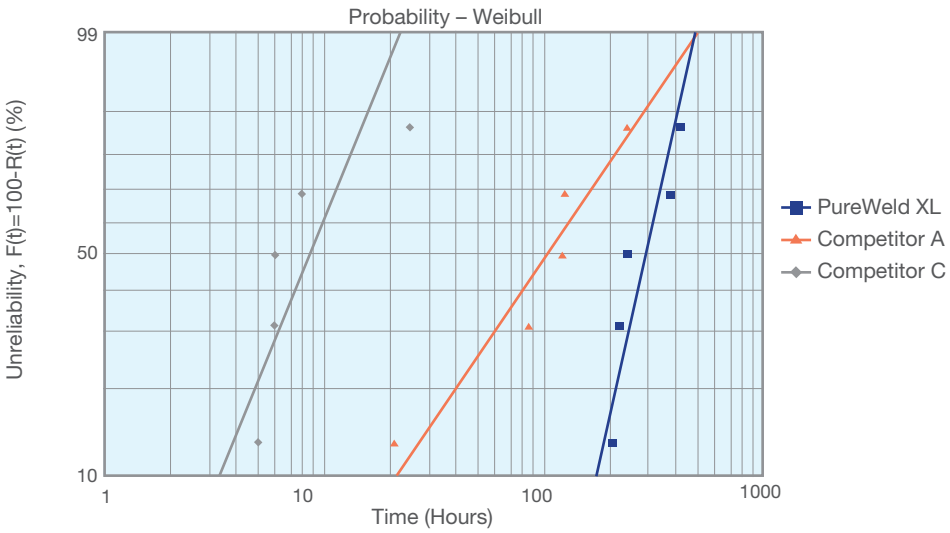
Table 1 – Peristaltic life (hours) running at 220 rpm with 2 bar discharge pressure

Tubing	Mean pumping life (hours)
PureWeld XL	293
Competitor A	119
Competitor C	10

In common with all elastomeric materials, TPEs demonstrate a range of time to failure and the average life data does not take into consideration this range of values. When conducting a risk assessment of single-use peristaltic tubing, an improved way of expressing life would be the level of confidence that a minimum life is achieved.

A useful statistical method for calculating this level of confidence is the Weibull analysis. The Weibull analysis probability plot for the test data is as shown in Figure 3. The unreliability (the inverse of reliability) is plotted on the y-axis and the pumping life (Log scale) is plotted on the x-axis. The gradient of the line gives information about the spread, a steep line represents a small spread of results. The angle of the line representing PureWeld XL is the steepest and therefore shows the smallest spread of results. The orange line representing competitor A has the shallowest angle and therefore shows the largest range of results. The 10% unreliability (90% confidence) line runs along the x axis, demonstrating 90% confidence in achieving a minimum of 180 hours pumping life with PureWeld® XL at 2 bar discharge pressure and maximum pump speed.

Figure 3 – Weibull probability analysis



The Weibull analysis can also be used to calculate the minimum achievable life for a given confidence limit. The minimum tubing life with 90% and 99% confidence for each tubing material is shown in Table 2.

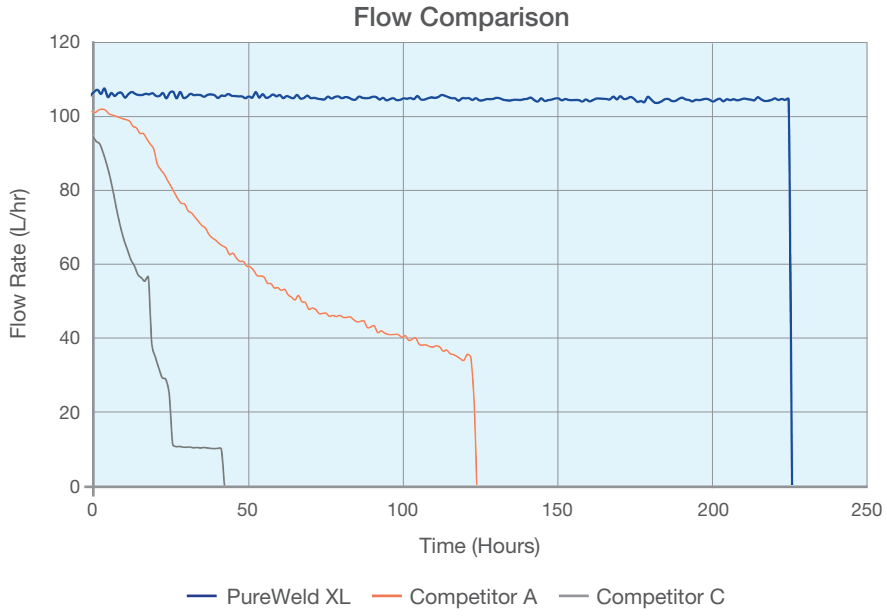
Table 2 – Weibull probability of failure analysis of PureWeld XL and competitors tubes

Tubing	Minimum pumping life (hrs, 90% confidence)	Minimum pumping life (hrs, 99% confidence)
PureWeld XL	173	90
Competitor A	21	2.95
Competitor C	3.5	1

Flow stability

When selecting tubing for use in a peristaltic pump, it is not only pumping life that is important, but also flow stability. Figure 4 shows the relative flow stability of the three tubing materials. PureWeld XL has a stable flow over the duration of its life, there is no reduction in flow over the pumping life of the tube. Competitor A and Competitor C show a reduction in flow, described as flow drop, from the start of the test. Both materials are unable to maintain the initial flow for more than a few hours. The drop in flow is typically caused by a phenomenon known as back streaming. This can result from two major mechanisms; damage to the tube bore resulting in channels which allow the discharge pressure to force fluid past the pump rotor, or wear on the outer surface of the tubing which thins the wall and results in incomplete occlusion of the tube. This back streaming introduces a great degree of shear into the process. The implication of this is that it can result in damage to live cells.

Figure 4 – Flow comparison over pump life of PureWeld XL and competitor tubes



Conclusion

The growth of continuous bioprocessing has driven the need for drug manufacturers to pay close attention to the functional life of single-use components. Flexible tubing suitable for continuous bioprocessing must demonstrate confidence that it will deliver long peristaltic life under typical process conditions. The level of control required by continuous processes also means that the tubing should deliver a consistent flow rate over the duration of the production cycle to maximise product yields and minimise the damage to live cells. This paper demonstrates that all TPE tubing is not the same and that a decision on which material to choose should take into account the supplier's data on tube life and flow stability. The data also demonstrates that PureWeld XL stands up to the technical challenges presented by continuous bioprocessing by delivering extended peristaltic life and unmatched flow stability.

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