Biopharmaceutical-Manufacturing Processes Without Risk Of Contamination

Pharmaceutical and biotech applications require the highest level of operational purity, containment and cleanability. One growing manufacturing trend in these markets is the increased adoption of single-use pump technologies. Recognizing the benefits of single-use manufacturing, Quattroflow™ has equipped its quaternary (four-piston) diaphragm single-use pumps with a product-wetted plastic pump chamber that can be replaced as a complete unit. The simple disposal of the pump chamber saves time and money because it eliminates the need for expensive and time-consuming cleaning, sterilization and complex cleaning validation of the pump chamber.

The implementation of Quattroflow single-use pumps also creates a quicker production process, as well as one that delivers the required levels of product purity and sterility with no corresponding harm to the product and no chance for costly cross-batch or cross-product contamination. Single-use pumps reduce downtime between two batches and are quick and easy to change, as well. In the biotech and pharmaceutical development process, the Quattroflow single-use pumps allow manufacturers to meet the strict speed-to-market requirements that allow maximization of patent windows.

Particle Generation Compared

While Quattroflow single-use pumps check all the boxes for efficient, reliable and cost-effective biopharmaceutical manufacturing, many developers frequently choose to use peristaltic (hose) pumps in their biopharmaceutical-production processes. However, there is a major drawback in the operation of peristaltic pumps: the particle generation that is caused by the pump's design and operation. The working principle of peristaltic pumps causes permanent mechanical stress of the hose material, which can cause that material to shed or spall and be a substantial source of particles entering the fluid stream. These abrasive particles can contaminate the pumped liquid and the pharmaceutical end-product and ultimately represent a potential risk for the process and for the health of the patient.

Recently, Quattroflow commissioned a third-party test with a hypothesis that the gentle working principle of the Quattroflow quaternary pump minimizes component stress and, thus, the generation of particles. The test featured a comparison between a Quattroflow QF150SU model pump and a peristaltic pump that was using pharma-grade pumping hose. Both pumps performed an eight-hour continuous recirculation of a liquid through a 12µm filter at approximately 100 L/hr (26.4 gph).

After the test was completed, an examination of the filter membranes showed that 2 Mio particles with sizes between 6.1 and 12.7 µm were generated during the operation of the peristaltic pump. Conversely, no identifiable particles were generated during the operation of the Quattroflow pump.

In the end, the third-party test results show that Quattroflow pumps help minimize particle generation and subsequent contamination of the product and are suitable for securing the handling of expensive and/or sensitive liquids in biopharmaceutical-manufacturing operations.

More Potential Peristaltic Risks

Besides the danger of particle generation and product contamination, peristaltic pumps also have additional operational limitations, which can be a disadvantage and risk for biopharmaceutical production:

- **Pulsation.** Due to their operational design, peristaltic pumps create a pulsing flow, which can adversely affect the pumping process.
- **Tube failure.** High mechanical stress can result in tube rupture, which can lead to a catastrophic failure, product loss, downtime and costly maintenance.
- **Flow-rate consistency.** With an increase in operating time, mechanical stress can changes hose geometries and can lead to inconsistent product flow.
- **Pump technology change.** The limited flow and pressure capabilities of peristaltic pumps means that changing pump technologies as the processes move from development to cGMP can create scaleup issues.
- **Particle generation outside the hose.** Spallation release may also occur outside the hose. This may compromise the fluid path and also contaminate the external clean-room environment.

The disadvantages inherent in peristaltic-pump operation ultimately mean potential threats to the quality of the process and the final product. Spallation, performance loss and rupture are also described in scientific literature (see Bahal and Romansky, "Spalling and sorption of tubing for peristaltic pumps" in *Pharmaceutical Development and Technology*, 7(3), 317-323 (2002)).

The chart below shows where peristaltic pumps fall operationally short in bio-pharmaceutical applications when compared to Quattroflow Single-Use Quaternary Diaphragm Pump technology:

Pump Technology	Particle Generation	Product Contamination	Pulsation	Flow Rate Consistency	Self priming	Gamma irradiation
Peristaltic Pump	YES	YES	YES	NO	YES	Depends on tubing material
Quaternary Diaphragm	MINIMAL	NO	MINIMAL	HIGH	YES	YES

Quattroflow Advantages At-A-Glance
The single-use models of the Quattroflow Quaternary Pumps with the 4-piston-diaphragm technology and pump chambers made of plastic are available in four sizes, covering a performance range from 1 to 5,000 L/hr (0.26 to 1,321 gph).

Features and Benefits:
- No particle generation
- Low pulsation
- Superior containment
- Consistent flow rate
- High turn-up/down ratio
- Variable and wide performance range
- Minimal component wear
- Minimal maintenance/downtime
- Quiet operation
- Low heat input
- Proof against dry-running
- Self-priming
- Optional injection-molded PE diaphragms

Single-use technologies have created improved production opportunities in biopharmaceutical production processes and the right pump technology can make a significant contribution to enhanced operational efficiencies and product safety. Quattroflow pumps help minimize product

particle contamination and are ideally suitable for optimizing the handling of expensive and/or sensitive liquids.