Pfizer Sterile Filtration Skid Design

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Introduction

Purpose: Evaluate filtration skid designs to address process inefficiencies, economics, and environmental impacts.

Pfizer currently reports several inefficiencies with sterile product filtration and has requested an evaluation of current designs. Currently, several options exist: many reusable stainless-steel designs and single-use plastic designs. Each design has two filter steps and requires a filter integrity testing procedure. Some current issues include poor connections on both disposable and reusable designs, slow filter times, and varying filter cartridge sizes.

Skid Evaluation Constraints

- Compatible with batch processing
- Economic and environmental comparison of reusable vs. disposable designs
- Simple operability
- Strong connections to ensure product sterility
- HAZOP Analysis of Process

Fluid Dynamics

A flow rate of 20 L/min was used as a basis for these calculations

Variable	Est. Range
Shear Rate	2000 – 4000 1/s
Reynold's Number	15 – 20
Pressure Drop	0.5 – 1.5 bar
Pump Duty	196 W

Analysis of differential pressure against flow rate for Sartorius T-Style Maxicap filter cartridge. Comparing manufacturer's data to calculated process parameters.

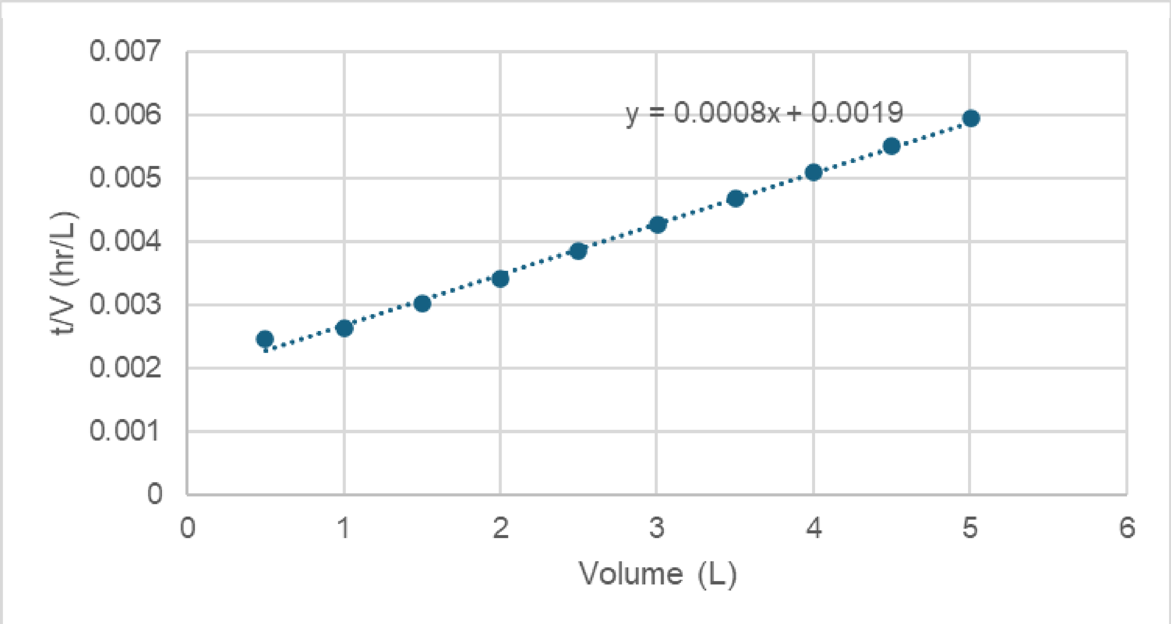


Figure 1. Batch filtration was modeled using filtrate volume and time to predict batch times.

Sterile Connections

Five types of sterile connections were evaluated for this process. Connector Requirements:

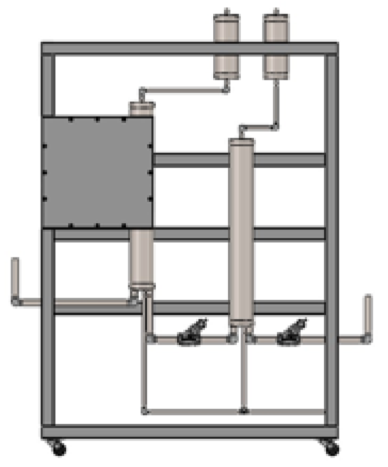
- 20 L/min flow rate
- 75 psi max operating pressure
- Minimal pressure drop and shear
- Must handle steam and/or chemical sterilization.

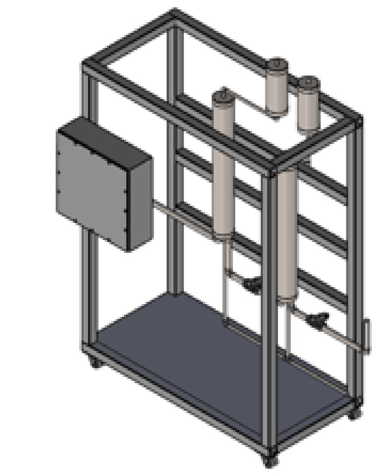
We propose using CPC AsepticQuick STC connectors for the filtration skid design. They address leakage concerns associated with earlier models and offer partial reusability. The stainless-steel part remains attached during sterilization, while a new connector is used for each batch, ensuring sterility and efficiency.

The Watson-Marlow Quantum Bioprocessing Pump meets the specified fluid dynamics parameters, accommodates sterile connections, and can be sterilized with the skid. This pump can be mounted directly on the skid frame before the first filter assembly.

Recommendation

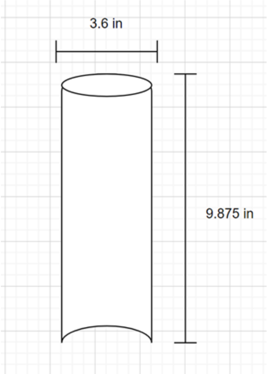
Our recommendation is to enhance the reusable skid design by integrating differential pressure sensors across filters, incorporating filter inserts for adaptability, and designing a flexible skid frame for future process adjustments. The design allows for the potential addition of a peristaltic pump, pending further research on its efficacy. A 6" vertical offset between filter cartridges optimizes fluid flow.



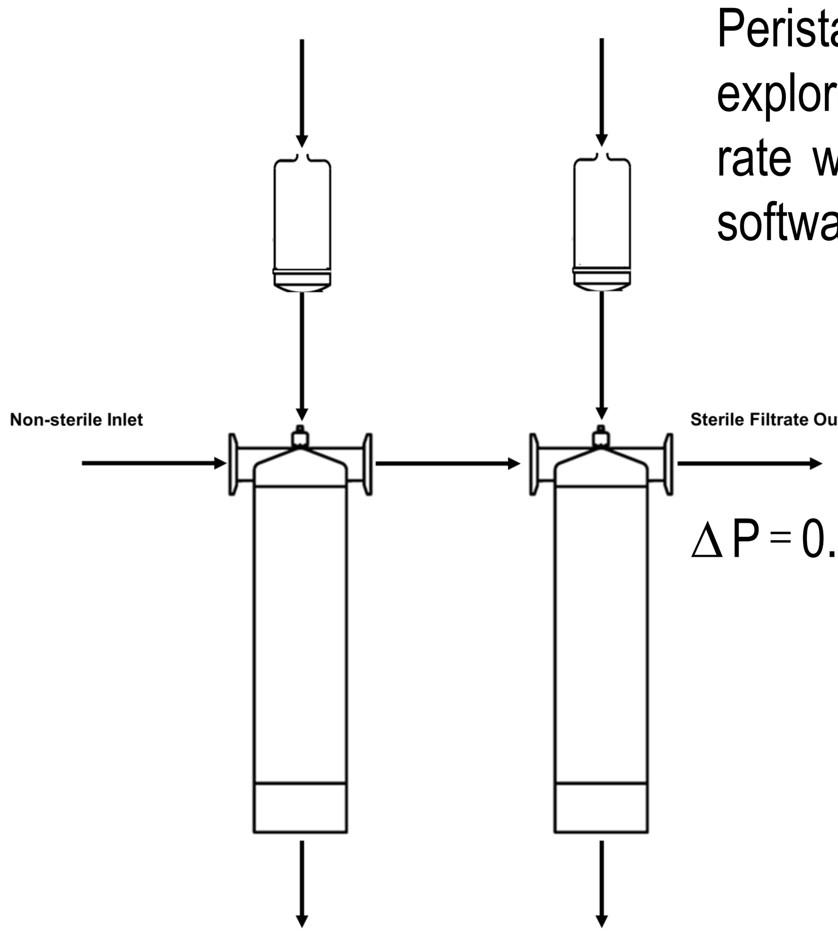


This design addresses the necessity for filter skids to accommodate varying filter cartridge sizes (15"-30") by designing the casings for a 30" filter, ensuring adaptability to future process requirements.

Polycarbonate inserts were designed to secure shorter cartridges, reducing internal casing volume and focusing fluid flow around the cartridges for enhanced filtration efficiency.

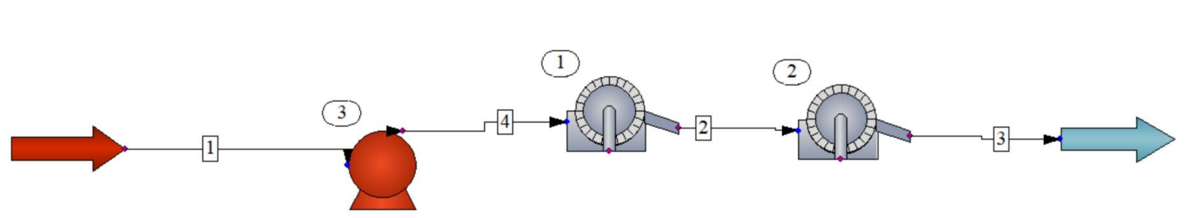


Process Flow Diagram



Peristaltic pumps were explored at low shear rate with CHEMCHAD software.

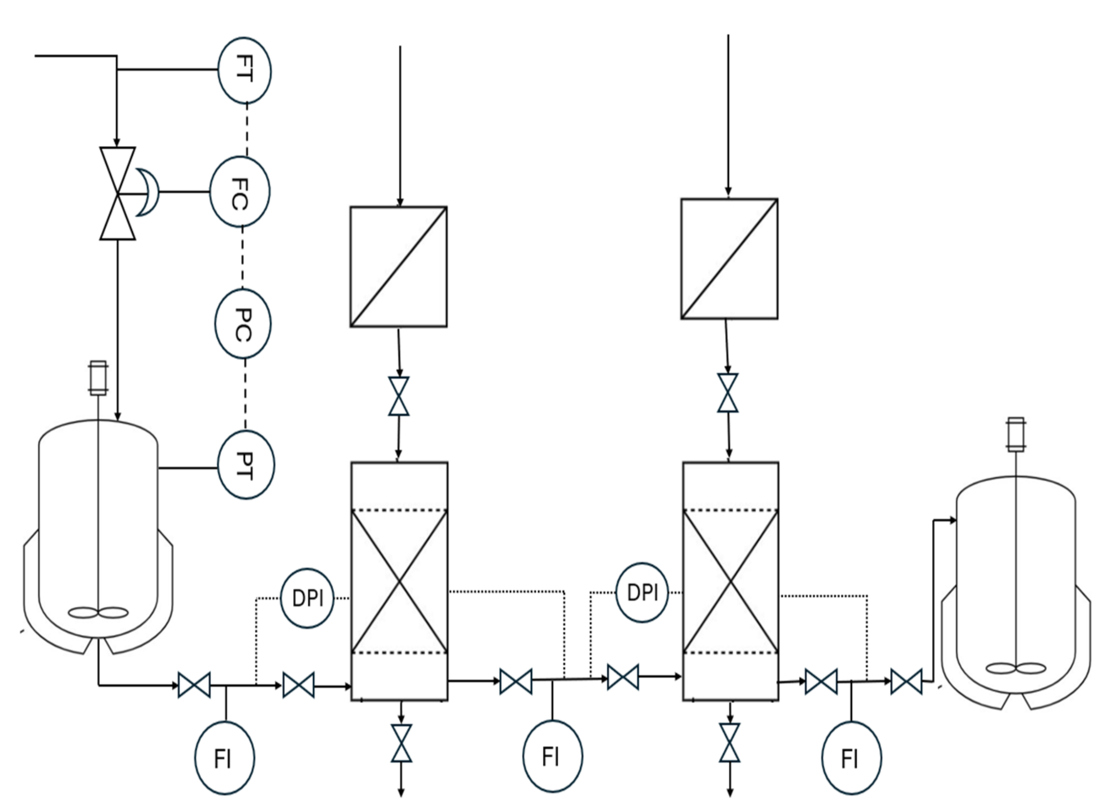
$\Delta P = 0.70$ Bar.



Process Control Scheme

Control System Features

- Maintain Fluid Velocity
- Adjustable PharmAir Inlet
- Differential Pressure System
- Feedback Control for Pressure Variations



Economics and Environmental

An estimation of 80 batches/year was used for economic calculations over a 20-year lifespan with an interest rate of 12%. The net present values of both disposable and reusable skid designs were compared. With these parameters, a breakeven point between the skid was estimated at less than one year.

Type	NPV (M USD)	Initial Investment	Annual Cost
Reusable	-2.05	$120,000	$292,000
Disposable	-3.07	$0	$460,000

The environmental impact of the incineration of the disposable skids was also analyzed. For the estimated number of batches annually, incineration would produce nearly 9 tons of CO_2 annually. Over the lifespan of this process, this results in nearly 180 tons of carbon emissions.

Process Safety/HAZOP

Process Unit: Filter Unit			**Reference Drawing**: Process Flow Diagram	
Process Parameter	**Guide Word**	**Possible Causes**	**Consequences**	**Safeguards**
Flow	Higher	Control valve failure	Exceed shear rate, overflow, overpressure	Flow control valve
	Lower	Connection blockage Connection leak	Extra time to process, leaks	Low flow alarm Maintenance and procedural schedule
	No	Closed valve Pipe blockage Filter blockage	Extra time to process, sterility breach	No flow alarm Maintenance and procedural schedule
Pressure	Higher	Closed valve Pipe blockage	Pressurization increases the risk of filter failure and contamination	Pressure Control loop High pressure alarm
	Lower	Pipe blockage Reverse flow	Sterility breach	Integrated loop system