

# KrosFlo® Systems

## User Guide

For use with:

- KrosFlo® KTF Tangential Flow Filtration (TFF) System
- KrosFlo® KPS Tangential Flow Filtration (TFF) System
- KrosFlo® TFDF® Tangential Flow Depth Filtration (TFDF) System



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## Abbreviations

Amp	Ampere
C	Celsius
CF	Concentration factor
cm	Centimeter
DV	Diafiltration volume
EU	Europe
F	Fahrenheit
ft	Feet
HMI	Human machine interface
Kg	Kilograms
TFDF	Tangential Depth Filtration System
Lbs	Pounds
LCD	Liquid-crystal display
lpm	Liters per minute
M	Meter
mA	Milliampere, or milliamp
MBT	Module bag tubing
NWP	Normalized Water Permeability
PLC	Programmable logic controller
Psi	Pounds per square inch
rpm	Revolutions per minute
SAS	Standard alert symbol
TFF	Tangential Flow Filtration
TMP	Transmembrane pressure
VAC	Volts AC power

## 1. Introduction

KrosFlo® Systems from Repligen provide ready-to-use, flexible flow path solutions for commercial-scale microfiltration and ultrafiltration process operations. The systems include one or two magnetically driven centrifugal pump heads, custom ProConnex® Flow Paths, flow meters, peristaltic pumps, Spectrum® Hollow Fiber Filters, KrosFlo® TFDF® Filters and optional connections for a weight scale for additional process monitoring.







Other components of the system include the retentate flow meters, permeate flow meter, pressure sensors, Repligen control panel controlled by an Allen-Bradley PLC, using an iFIX-based HMI program to initiate actions, flexible tube flow path, and a Repligen stainless steel frame/cart that serve as the system support structure.

## 2. Safety precautions

### 2.1 Signal words

The signal word and color distinguish the severity level of a hazard. Signal word definitions and colors are listed in [Table 1](#).











**Table 1. Signal words, definitions and colors**

	Description
	<b>Safety Alert Symbol (SAS)</b> - used when a hazard to personnel is present. The SAS is omitted when the hazard is related to property/equipment damage only.
	A <b>DANGER</b> notification indicates an imminently hazardous situation which, if not avoided, <b>will</b> result in death or serious injury.
	A <b>WARNING</b> notification indicates a potentially hazardous situation which, if not avoided, <b>could</b> result in death or serious injury.
	A <b>CAUTION</b> notification indicates a potentially hazardous situation which, if not avoided, <b>may</b> result in minor or moderate injury.
	A <b>CAUTION</b> notification without the Safety Alert Symbol  indicates a potentially hazardous situation which, if not avoided, <b>may</b> result in property/equipment damage.

### 2.2 Safety symbol icons

The typical safety symbol icons - hazard, prohibition, and mandatory action - used on Repligen systems are listed in [Table 2](#). The icons are pictograms that communicate hazards quickly and across language barriers.

Table 2. Safety symbol icons

 <p>Electrical Hazard</p>	 <p>Heavy Object</p>	 <p>Heat Hazard</p>
 <p>Radiation Hazard</p>	 <p>Crush Hazard</p>	 <p>Pinch Hazard</p>
 <p>Inhalation Hazard</p>	 <p>Authorized and Qualified Personnel Only</p>	 <p>Read the Manual</p>
 <p>Noise Level Hazard</p>		

### 3. Safety guidelines

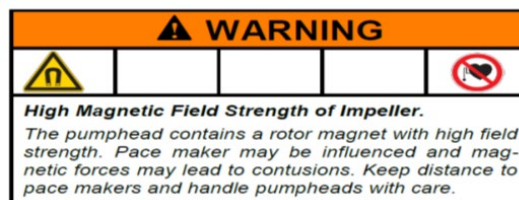
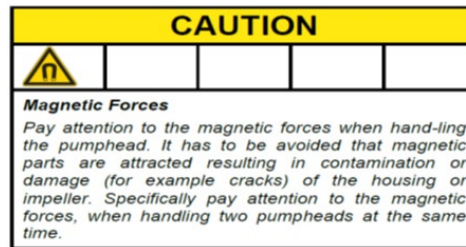
To ensure safe operation:

1. Do not operate the system without first reading this manual.
2. Read the following caution and warning statements:



**WARNING** – To avoid risk of electric shock, this equipment must only be connected to a supply main with protective earth. No modification of this equipment is allowed.

Figure 1. Caution and warning examples



**WARNING** – Do not plug the system in during Electrical Connections procedure until instructed.



**WARNING** – Do not plug in the system during Mechanical Assembly.



**WARNING** – System must be turned off when replacing fuses to prevent electrical hazard. Any electrical work beyond the electrical connections procedure and fuse replacement should be performed by trained personnel only.



**WARNING** – Peristaltic pumps must be turned off when replacing either tubing or pump heads to prevent crushing/pinching hazard.



**WARNING** – Due to a noise level of 80 decibels or greater, ear protection is required when the System pumps are operated at a speed of greater than (>) 6000 RPM.



## 4. System specifications

**Table 3. KrosFlo® Systems specifications**

Weight	300 lb. (approximately) 135 Kg	500 lb. (approximately) 225 Kg	
Dimensions (L x W x H)	32 x 24 x 52.5 inches 81 x 61 x 133 cm	47 x 24 x 80 inches 120 x 61 x 203 cm (with extension)	
Power requirements	200-240 VAC 1ph 10A (EU)	200-240 VAC 1ph 15A	
Outputs	Pumps: P-01 100 - 9000 RPM P-02 0.1 - 650 RPM P-03 0.1 - 650 RPM	Display: 15" LCD touchscreen	
Environmental	Electrical cabinet and HMI – IP66	Operating temperature: 0 - 40° C 32 - 104° F	
Chemical resistance	Frame and electrical cabinet: Stainless Steel-304	Casters: Stainless Steel-304 and Polyurethane	ProConnex® Flow path components: Polypropylene, polycarbonate, Polysulfone, and C-Flex®/ Pharmapure® materials

## 5. Major components

The major components used in KrosFlo® Systems are:

- **Retentate (recirculating) Pump (P-01)** - Levitronix LPM-600.3 - 10 low-shear centrifugal pump
- **Product pump (P-02)** - MasterFlex® 77420-10 I/P peristaltic pump
- **Buffer Pump (P-03)** - MasterFlex® 77420-10 I/P peristaltic pump
- **Retentate flowmeter** - Sonotec® FS04.210 C0.55/230 V2.0
- **Permeate flowmeter** - Levitronix LFS-06SU / LFS-10SU
- **Reactor scale input** - 4 - 20 mA
- **Pressure sensors** - Repligen disposable pressure transducers
- **Controller** - Allen-Bradley PLC (Programmable Logic Controller)
- **HMI** - Allen-Bradley Integrated Panel Display Computer (Human-Machine Interface)
- **ProConnex® Flow Path** - Designed flexible tube flow path from Repligen
- **Support structure** - Stainless steel filter stand and lab cart from Repligen

## 6. Instructions for use

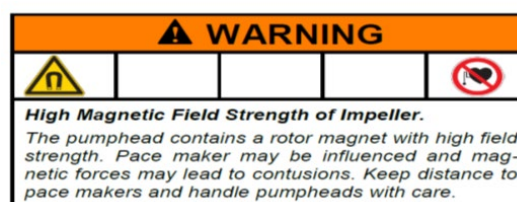
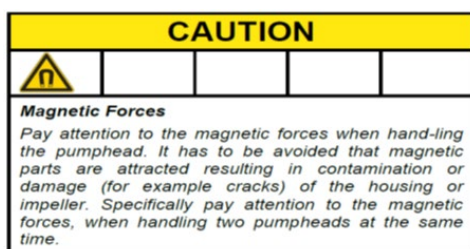
### 6.1 Installation and mechanical assembly

KrosFlo® Systems have a small footprint and require only a small clean area (approx. 3 m x 3 m/10 ft. x 10 ft.) for assembly. No tools are needed for system assembly, though some basic hand tools such as screw gun, pliers, and screwdrivers are needed to uncrate the system.

Some of the major components listed above are mounted on the cart. The other components can be removed from boxes and installed on the cart for use in the process.



**WARNING** – Do not plug in the system during Mechanical Assembly.



Follow these high-level steps to install and assemble the system:

1. Uncrate the system and remove all packaging material from the system components.
2. Locate and attach the proper filter brackets to the frame. The filter stand extension is attached to the cart frame by attaching it to the filter post. Be sure to place a black rubber gasket between the extension and frame post. Secure the extension with the provided metal clamp and hand tighten, or with a wrench.
3. Place the Product Pump (**P-02**) on the lower cart frame. Connect the power and control cables.
4. Place the Buffer Pump (**P-03**) on the cart frame. Connect the power and control cables.
5. The Recirculating Pump (**P-01**) will come already mounted. Consult the layout diagram provided in the documentation package.
6. Install and connect scale (**WE-01**), or scale interface cable. If the tanks are more than one, accordingly connect the scales as WE-02, WE-03 etc.
7. Route and connect all cables. Cables are marked based on their destination. All cables should be routed to minimize kinking and obstructions.
8. Once the filter stand is assembled and pump motor is mounted, ready the pump head and flow path/MBT assembly items. Make sure all necessary components to complete the process line are available and ready (reactor, tubing, welding equipment, etc.). Please note that the process assembly should be designed to minimize hold-up volume.
9. To prepare the pump head and flow path/MBT assembly:
  - a. Carefully support the MBT/filter/pump head assembly and hold at an angle such that the pump head discharge lines up with the green color band at the pump support on the end of the motor drive.
  - b. Install the pump head into the pump motor drive making sure to disengage/pull out the locking pin to fully seat the pump head.
  - c. Rotate the pump discharge port and filter assembly to the vertical position and towards the red color band on the pump drive. The locking pin will click into place when the pump head is properly oriented in the pump drive.
  - d. Locate the filter in the 2 filter clamps on the frame post, making sure the clamps attach to the filter on the clear section of the housing (not on end fittings). Inspect the filter and pump before tightening clamps in place; there should be no strain placed upon any of the filter, pressure sensor or pump connections.

10. With filter and pump securely in place, install the permeate tubing, making sure there is no bending or kinking of the permeate tubing. Run extra tubing to the permeate vessel. Make sure permeate pressure sensor (**PE-03**) is located between filter housing permeate port and any valves prior to permeate collection.
11. Locate the clamp-on retentate flowmeter (**FL-01**) on the filter stand. Install the retentate tubing in the flowmeter and close the flowmeter clamp. Make sure there is 10 - 15 cm (4" - 6") of straight run tubing on each side of the meter. The return tubing may need auxiliary support to prevent kinking. Clamp the meter onto tubing. Note flow direction arrow on meter should point in up direction.

## 6.2 Electrical installation

All electrical connections are made with plugs and sockets located on the rear side of the control panel.

Power requirements for system  
200 - 240 VAC, 10/15 Amp Service, single phase.



**WARNING** – Do not plug in the system during Electrical Assembly until instructed.

To complete the system electrical connections:

1. Connect **P-01**, **P-02**, and **P-03** connectors to panel.
2. Connect flow meter **FL-01**, **FL-02** connectors to the flow meters.
3. Connect three pressure sensor cables (**PE-01 feed**, **PE-02 retentate**, **PE-03 permeate**) to the flow patch pressure sensors.
4. Connect **Main Panel power cord** to suitable electrical outlet (200 - 240VAC, 10/15 Amp Service).
5. Make sure that the **Emergency Stop (E-Stop)** button is pulled to **OUT** (inactive) position.
6. Turn on the Main Power by rotating the handle on the front of the control cabinet; this starts the computer, and the control software loads automatically.
7. Press **Reset** button (Blue) on Control Panel.

## 6.3 Ferrite Bead installation

Polysulfone pressure sensors/transmitters are included as part of the sterile disposable ProConnex® Flow Path (Module Bag Tubing (MBT)) that is shipped with your KrosFlo® KTF System.

**Figure 2. Polysulfone pressure sensors example**



A ferrite bead (P/N 3000541) is provided for each flow path pressure sensor to protect it against possible electromagnetic interference (EMI). We recommend that you install the supplied ferrite bead on each flow path pressure sensor cable to provide EMI protection for the pressure sensor.

**Figure 3. Installed flow path pressure sensor ferrite bead**

To install the supplied flow path pressure sensor ferrite bead:

1. Locate the ferrite bead as close as possible to the flow path pressure sensor while ensuring there is enough cable to wrap around the ferrite bead.
2. Open the ferrite bead.



3. Seat the flow path pressure sensor cable in the bead.



4. Wrap the cable around the bead.



5. Snap the bead closed.



## 7. KrosFlo® System operation

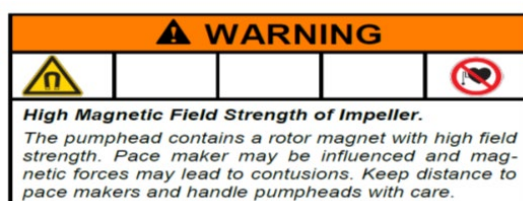
### 7.1 System overview

KrosFlo® Operating Systems are an iFIX-based program installed on a touchscreen HMI PC. The program consists of six primary screens – Main (Operational), Settings, Chart (Process Trending), Alarm Setup, Alarm, and Report. Screen navigation is performed using the buttons on the bottom of each screen. Simply touch the button to go to the desired screen.

To end a session, navigate to the Settings Screen. Touch the Exit iFIX button located at lower right of screen, then close the iFIX program before turning off computer.

The HMI screen will go into screen saver mode while the system is operating or while program is open, just as a typical PC during times of inactivity. This will not affect operation and touching the screen will display the present active screen.

### 7.2 Getting started



KrosFlo® Systems are ready to run after all Mechanical and Electrical Installation steps have been completed.

To run KrosFlo® Systems:

1. Pull the **E-Stop** button (located on front of Control Panel) to the **OUT** position.
2. Turn the front-panel **power switch** to **ON** position.
3. Press the **BLUE** reset button on control panel.

Once the computer is booted up, use the touchscreen to navigate to the **TFF icon** on the screen. Double click on the TFF icon to enter the KrosFlo® Operating System. The control system will open to the Introductory screen, which contains the system part number and Installed Software Rev information. Touch this screen anywhere to navigate to the Main screen.

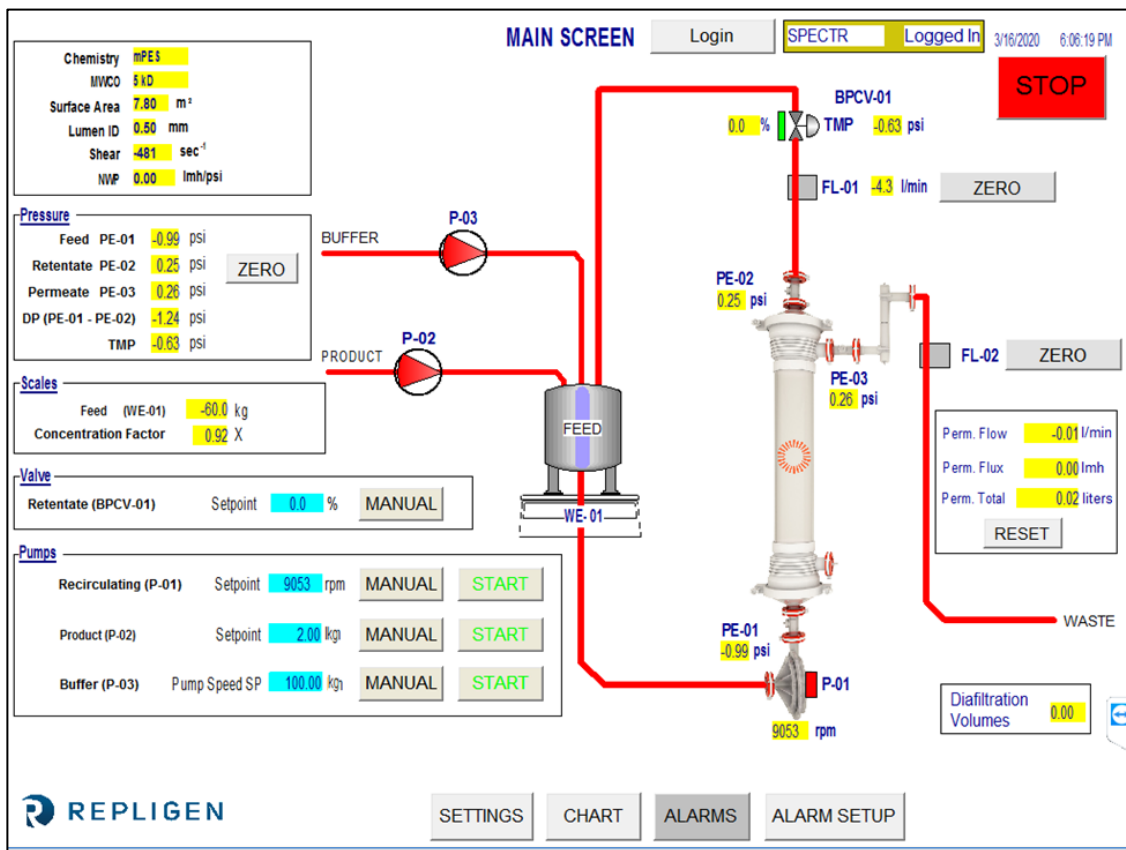
At startup, KrosFlo® Systems will display all alarms as being active; they should be cleared before operating the KrosFlo® System. From the Main screen, navigate to the Alarms screen. Once at the Alarms screen, touch the **Reset Alarm** button on the touchscreen then touch the **Ack Alarms** button. All Alarms will be cleared.

**NOTE:** The **BLUE** Reset button on the control panel enclosure is pressed to reset the Master Control Relay at startup, power outage, or E-Stop only. All other alarm conditions are reset from the Alarms screen on PC/HMI.

Be sure to exit iFix, and shutdown Windows before shutting down the KrosFlo® System.

## 7.3 Main screen

Figure 4. Main screen example



The Main screen displays the KrosFlo® Systems operational flow path. The system operation and control features can be observed on the Main screen. Process data (flow, pressure, volume) is displayed on screen in real time. Process data OUTPUTS are displayed in the **YELLOW** highlighted boxes. Setpoint input data is displayed in the **BLUE** highlighted boxes.

Auto and Manual modes of operation for the Recirculating and Product Pumps are selected here. The system can operate independently (outside of an automated process sequence), allowing the user greater flexibility in performing trials to optimize filter performance prior to entering a run.

Setpoint data is entered by touching a **BLUE** input box. Type in the new Setpoint data and press ENTER (= Equal Sign) button on the pop-up keyboard. The ENTER (= Equal) button **MUST** be pressed after data entry or the new Setpoint value will not be stored.

**Table 4. Input parameters for Main screen**

Parameter	Range	Units
<b>VALVE BPCV-01:</b>		
Manual Mode	0 - 100	%
Auto Mode	0 - 30	psi
<b>Pumps:</b>		
P-01 Manual Mode	0 - 9000	rpm
P-01 Auto Mode	0 - 10/45/85	lpm
P-02 Manual Mode	0 - 650	rpm
P-02 Auto Mode	0 - 20	lpm
P-03 Manual Mode	0 - 650	rpm
P-03 Auto Mode	0 - 20	lpm
P-01, P-02 and P-03 may change depending on the system design, pump models and identification tags used.		

#### 7.4 Automatic (Process) Mode

KrosFlo® Systems are designed with an automated Process Sequence that controls a product concentration step followed by a diafiltration (wash) step and then a final concentration step. The process mode includes an option for use of Fed Batch mode.

The **CONCENTRATION** steps allow the system to run at a constant Transmembrane Pressure (TMP) and recirculation flow (P-01 LPM) while concentrating the initial product sample volume to a predetermined volume reduction. The volume reduction, or Concentration Factor (CF) is determined by the user.

**DIAFILTRATION** sets the system to run at a constant Transmembrane Pressure (TMP) and recirculation flow rate (P-01 LPM) while washing the concentrated sample product volume (diafiltering) with buffer. The amount of wash (Diafiltration Volume, or DV) is determined by the user. **DV Setpoint** is used as the end point of the diafiltration sequence. This number signifies the number of diafiltration volumes that will be processed.

**FED BATCH CONCENTRATION** allows the initial concentration step to include additional volume from a vessel external to the primary recirculation vessel being used. The calculations for process estimate the remaining volume based on the permeate flow and scale reading for the main vessel. When the main vessel weight reduces below the **Level Setpoint During Concentration** setpoint for the time defined by the **Sample Feed Pump Stop Delay** setpoint, the KrosFlo® System will assume the feed vessel is empty and switch its volume calculation to monitoring only the scale.

The **FINAL CONCENTRATION** step takes place once the diavolume setpoint has been reached for the diafiltration step. The concentration factor is set on the process Settings screen and can be observed from the Main screen.

The process steps are accessed on the Settings screen (see [Section 7.6](#)). A **Reset Windup** button is available on the Settings Screen to reset PID control parameters after the system has been stopped. This feature allows for a smoother restart of the system at auto process parameters. When the **Reset Windup** button is not pressed, the control loop will start at the pump speeds previously arrived at output.

## 7.5 Manual Mode

KrosFlo® Systems can run in a manual mode which will operate the Back Pressure Control Valve (% Closed), Permeate Pump (RPM), Feed Pump (RPM) and Recirculation Pump (RPM) at constant settings with no process control.

The Manual mode button must be selected for each device (Pumps and Back Pressure Control Valve) and appropriate setpoints selected. Setpoints are entered in the **BLUE** boxes. Once started, KrosFlo® Systems will maintain setpoint control, however in Manual mode, it will use a constant pump speed (RPM) or valve setting (% closed), and NOT a process variable control. Once started, KrosFlo® Systems will maintain setpoint control during operation. Setpoints may be changed during TFF process operations.

## 7.6 Settings screen

The Settings screen provides the settings for the **Filter Model**. Selecting a filter model will populate the **Fiber Count**, **Lumen ID**, and **Surface Area**. These parameters are used for the calculation of shear and flux. In the event a filter is not listed, the Fiber Count and Lumen ID must be entered in the **BLUE** boxes shown in the Filter Model box to ensure correct shear rate data.

**Figure 5. Settings screen (Fed Batch disabled)**

The screenshot displays the 'SETTINGS' interface for a KrosFlo system. At the top, it shows the user 'SPECTR' is logged in on 3/16/2020 at 6:07:25 PM. The interface is divided into several sections:

- Process Setpoints:** Includes fields for Starting Volume (-60.0 liters), System Holdup Volume (5.0 liters), DV Setpoint (2.0 DV), TMP Setpoint (2.9 psi), Recirc Flow Setpoint (20.00 l/min), Permeate Flow (0 - 20 lpm), Initial Concentration Setpoint (5.0 X), Final Concentration Setpoint (10.0 X), Feed Temperature (20.0 C), and Sample Feed Pump Stop Delay (10 Sec). A 'Use CF' toggle is present. A red 'STOP' button is on the right.
- Filter Model:** A list of filter models is shown on the left. The selected model is X04-E005-05-N. Parameters for this model include Fiber Count (12000), Lumen ID (0.50 mm), MWCO (5ND), Chemistry (mPES), Effective Length (41.5 cm), Surface Area (7.80 m<sup>2</sup>), and Surface Area Entry (78000.00 cm<sup>2</sup>).
- PID Setup:** Contains three pump tuning sections: Recirc Pump (P-01), Product Pump (P-03), and Buffer Pump (P-03). Each has P, I, and D setpoints. A 'Back Pressure Valve (BPCV-01)' is set to 500% Closed. A 'RESET WINDUP' button is available with a warning: 'To RESET control loop windup, Press Below. Assume needed control loops are in MANUAL, before pressing.' A 'RESET PID TO FACTORY SETTINGS' button is also present.
- System Controls:** Includes a 'START PROCESS' button, a 'Re-Open Keypad' button, and a 'Tubing Selection' button.
- Footer:** Features the REPLIGEN logo and navigation buttons for MAIN, CHART, ALARMS, and REPORT.

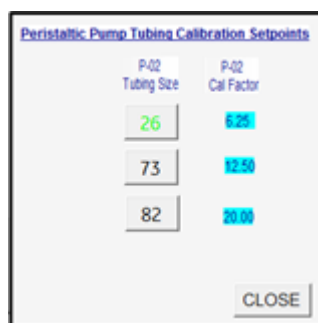
The Settings screen also allows PID loop tuning of pump response for all pumps. The pump response to startup and setpoint change can be tailored using PID tuning. Setpoint Data is entered as described before: navigate to the appropriate Blue box and touch the setpoint box, type in data, and press ENTER (= equal sign) button on the pop-up keyboard. All setpoint data should be entered prior to operation. Press **RESET PID TO FACTORY SETTINGS** to return all pumps to their default PID tuning values.

Press the **Use Weight/Use CF** toggle button to specify whether the Initial and Final Concentration setpoints are based on the specified weight (Kg) or concentration factor.



Press the **0 - 20 lpm/0 -8 lpm** toggle button to specify the range of the Permeate flow meter. Press **Tubing Selection** to select the size of the tubing to be used with the KTF/KPS/TFDF® peristaltic pump (Product Pump (P-02)). You may also enter a calibration factor for the selected tubing on this popup screen.

**Figure 6. Tubing Selection popup screen**



Press the **Fed Batch Enabled** / **Fed Batch Disabled** toggle button to enable or disable fed batch processing.

With Fed Batch disabled, you may press the **Starting Vol = Enter Above** / **Starting Vol. = Use Scale** toggle button to specify whether the Starting Volume (that is, the volume in the feed tank at the start of the concentration process) is entered as a setpoint or is based on the weight of the tank (WE-01).

With Fed Batch enabled, the **Level Setpoint During Concentration** and **Sample Feed Pump Stop Delay** setpoints are available for configuration.

The process setpoints that may be configured from the Settings screen are defined as follows:

- **Starting Volume** - the volume in the feed tank at the start of the concentration process. This setting will be used to calculate the Concentration Factor, over time based on the remaining volume after the start of the process.
- **System Holdup Volume** - used to compensate for the volume of liquid that is in the flow path during the concentration process.
- **Level Setpoint During Concentration** - the level that the system will maintain in the feed vessel while in fed batch concentration mode.
- **Initial Concentration Setpoint** - setpoint for the start of the Initial Concentration Sequence, if run.
- **Final Concentration Setpoint** - setpoint for the end of the Final Concentration Sequence.
- **Sample Feed Pump Stop Delay** - the amount of time that the sample pump will run after the weight on the feed tank drops below the setpoint volume.
- **DV Setpoint** - end point of the diafiltration sequence. This number signifies the number of diafiltration volumes that will be processed.
- **TMP Setpoint** - Constant Transmembrane Pressure setting for TFF processes.
- **Recirc Flow Setpoint** - controls the speed of the recirculation pump (P-01).
- **Feed Temp** - used in calculating Normalized Water Permeability (NWP). A description of NWP can be found in Section [12.5](#) at the end of this manual.

[Table 5](#) lists the ranges of values for all input parameters on the Settings screen.

**Table 5. Input parameters for Settings screen**

Parameter	Range	Units
<b>Process Setpoints:</b>		
Starting Volume	0 - 1600	liters
System Holdup Volume	0 - 100	liters
Level Setpoint During Concentration	0-600	liters
Initial Concentration Setpoint	0 - 600/0 - 100	kg/X
Final Concentration Setpoint	0 - 600/0 - 100	kg/X
Sample Feed Pump Stop Delay	0 - 300	seconds
DV Setpoint	0 - 100	DV
TMP Setpoint	0 - 30	psi
Recirc Flow Setpoint	0 - 85	lpm
Feed Temp	0 - 100	° C
Batch ID	Up to 20	characters

**NOTE:** Values shown in the “Range” column are examples and may vary depending on the system and process.

Parameter	Range	Units
<b>Filter Model:</b>		
Filter Model Number	Up to 13	characters
Fiber Count	0 - 50,000	fibers
Lumen ID	0 - 100	lumen
MWCO	Up to 10	characters
Chemistry	Up to 10	characters
Effective Length	Up to 5	characters
Surface Area Entry	Up to 200,000	cm <sup>2</sup>
Qty of Modules	Up to 1	characters

PID setup	Range	Units
<b>Recirculation Pump (P-01):</b>		
Recirculation Pump (P-01) <b>P</b>	0 - 1000	4
Recirculation Pump (P-01) <b>I</b>	0 - 1000	4
Recirculation Pump (P-01) <b>D</b>	0 - 1000	1
<b>Product Pump (P-02):</b>		
Product Pump (P-02) <b>P</b>	0 - 1000	4
Product Pump (P-02) <b>I</b>	0 - 1000	4
Product Pump (P-02) <b>D</b>	0 - 1000	1
<b>Buffer Pump (P-03):</b>		
Buffer Pump (P-03) <b>P</b>	0 - 1000	9
Buffer Pump (P-03) <b>I</b>	0 - 1000	5
Buffer Pump (P-03) <b>D</b>	0 - 1000	1

Press the **Exit iFix** button located on the lower right corner of the Settings screen to exit the program.

## 7.7 Alarm Setup screen

Figure 7. Alarm Setup screen example

**ALARM SETUP** Login SPECTR Logged In 3/16/2020 6:14:22 PM

**ALARM SETPOINTS:**

**FEED**

- Low Feed Pressure (PE-01) 28.99 psi Disabled
- High Feed Pressure (PE-01) 0.14 psi Disabled
- Feed High Press. Shutdown (PE-01) 1.45 psi Disabled
- Feed High Pressure Duration 5 sec.

**RETENTATE**

- Low Retentate Pressure (PE-02) 1.45 psi Disabled
- High Retentate Pressure (PE-02) 1.45 psi Disabled

**PERMEATE**

- Low Permeate Pressure (PE-03) 28.99 psi Disabled
- High Permeate Pressure (PE-03) 0.14 psi Disabled
- High Permeate Volume (FL-02) 9.0 liters Disabled
- Low Permeate Flow (FL-02) 3.00 l/min Disabled
- High Permeate Flow (FL-02) 2.50 l/min Disabled

**RECIRCULATION**

- Low Recirc Flow (FL-01) 22.00 l/min Disabled
- High Recirc Flow (FL-01) 21.00 l/min Disabled
- High Feed Tank Level (WE-01) 0.000 kg Disabled
- High Shear 1000.00 sec<sup>-1</sup> Disabled
- Low Shear 1095.00 sec<sup>-1</sup> Disabled

REPLIGEN MAIN SETTINGS CHART ALARMS

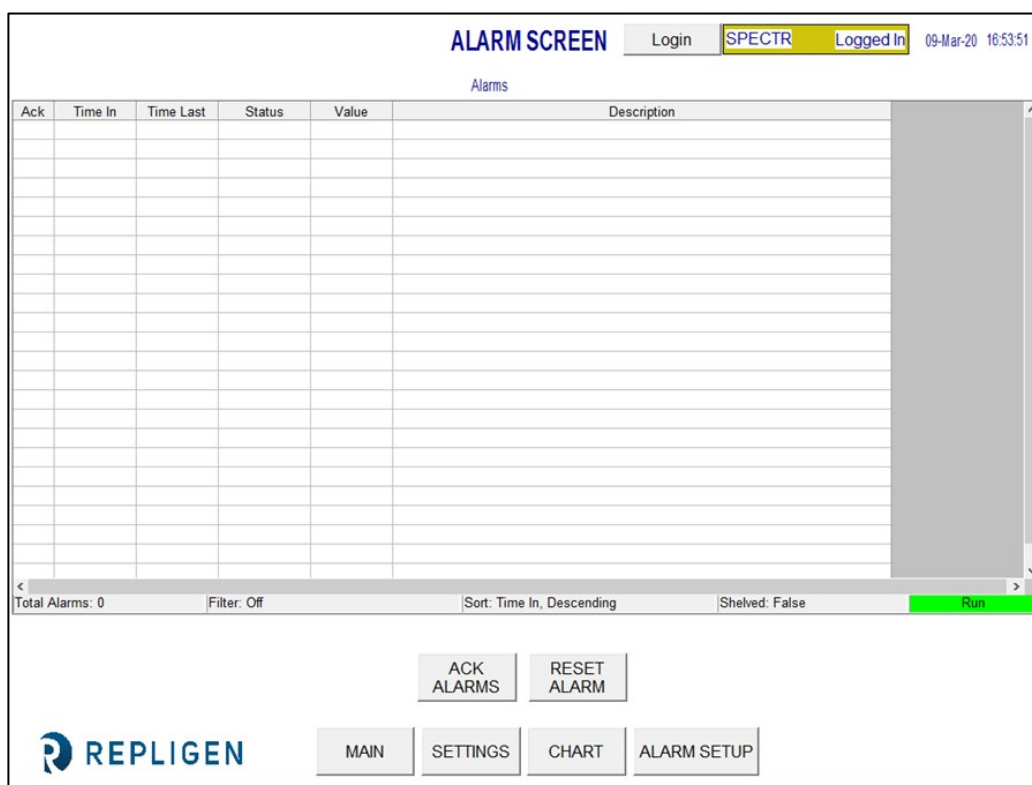
The Alarm Setup screen contains 16 process alarm conditions to help protect the process from unfavorable process conditions. 15 of the Alarms have the option of being Enabled or Disabled. The one alarm condition which cannot be disabled is Feed High Pressure duration because it describes how long an overpressure condition can exist without setting the shutdown alarm.

Table 6. Alarm Setup screen setpoint range

Alarm setpoints	Range	Units
Low Feed Pressure (PE-01)	0 - 30	psi
High Feed Pressure (PE-01)	0 - 30	psi
Feed High Pressure Shutdown (PE-01)	0 - 30	psi
Feed High Pressure Duration	300	seconds
Low Retentate Pressure (PE-02)	0 - 30	psi
High Retentate Pressure (PE-02)	0 - 30	psi
Low Permeate Pressure (PE-03)	0 - 30	psi
High Permeate Pressure (PE-03)	0 - 30	psi
High Permeate Volume (FL-02)	0 - 10000	l
Low Permeate Flow (FL-02)	0 - 20.0	lpm
High Permeate Flow (FL-02)	0 - 20.0	lpm
Low Recirc Flow (FL-01)	0 - 85	lpm
High Recirc Flow (FL-01)	0 - 85	lpm
High Feed Tank Level (FL-01)	0 - 200	kg
High Shear	0 - 12000	sec <sup>-1</sup>
Low Shear	0 - 12000	sec <sup>-1</sup>

## 7.8 Alarm screen

Figure 8. Alarms screen example



This Alarms screen is for viewing, acknowledging, clearing, and resetting all Alarms. A list of all Alarms, Alarm Range, and Tag (sensor or device responsible for Alarm Setpoint) is provided in [Table 7](#).

**Note:** For the initial start-up (plugging in system to power), or in the event of power outage or Emergency Stop, press the Blue Reset button on the control panel enclosure to reset alarms. All other alarm conditions are reset from the Alarms screen.

The **Ack Alarm** button will acknowledge the alarm and clear it from the screen if the alarm is not currently active.

The **RESET ALARM** button will silence the alarm and reset the flashing ALARM button once the system is operating in the normal range.

Alarms can be enabled or disabled manually using the **ALARM SETUP** screen. To disable or prevent an alarm, select the Disabled button. 'Disabled' should be displayed for alarm to be disabled. Likewise, 'Enabled' will be displayed if the alarm is enabled.

High alarms will trigger when process value rises to SP or above; Low alarms will trigger when process value falls to SP or below. The system is equipped with a short delay to avoid Low Alarms during start-up conditions. Alarms have two categories, Warning Alarms and Shutdown Alarms.

### 7.8.1 Warning alarms

Flashing Button and Beeper will sound when Alarm setpoint is reached. The system will continue to run during Alarm conditions and indicate active alarm. Alarms can be acknowledged and cleared when Alarm Conditions are satisfied (i.e. – system operation restored within Alarm boundaries).  
Shutdown alarms

The system will shut down when a Shutdown setpoint is reached. The only shutdown alarm is Feed High Pressure Shutdown (PE-01).

Select the Chart button on the Main screen to display a chart for closer monitoring of all pressure and TMP values. The Chart screen is set up to display the parameters listed in [Table 7](#).

### 7.9 Chart screen

Figure 9. Chart screen example



Table 7. Chart screen parameters

Tag#	Range	Units
FL-01	Feed Flow Rate	lpm
FL-02	Permeate Flow Rate	lpm
PE-01	Feed Pressure	psi
PE-02	Retentate Pressure	psi
PE-03	Permeate Pressure	psi
P-01	Recirc Pump Setpoint	rpm
TMP	Calculated TMP	psi
Shear Rate	Shear Rate	sec <sup>-1</sup>

Data can be viewed on the chart in real time or reviewed from a previous time period. Some features of the chart may be customized using the chart menu. The chart menu can be accessed by placing cursor on the chart and using left double-click.

## 8. Operation

### 8.1 Running TFF/TFDF® processes

**Note:** Enter all TFF/TFDF® parameters on the Settings screen and select all Alarm Settings on the Alarm Setup screen prior to starting a sequence. The system must be fully assembled, tanks and components in place, and ready to operate.

KrosFlo® Systems are designed to run controlled TFF (Tangential Flow Filtration) and TFDF® (Tangential Flow Depth Filtration) processes with minimal operator input. Process parameters for Retentate flow rate and Permeate Flow are entered on the Sequences screen. The Feed Vessel Volume and Permeate Volume setpoints are also entered on Sequences Screen. The Filter Model is selected from the installed database on the Settings Screen.

After input of all Setup data, navigate to the Main Screen to initiate a Process run. The preferred start-up technique is to start the TFF1 process with Pump P-01, in Manual Mode at setpoints below parameters of the selected Auto Mode.

Once started, run the system in Manual Mode for a few minutes to completely flood the MBT and ensure air has been displaced. Once this is complete, stop the system and run the automated sequences from the Sequences Screen.

Once in Auto Mode, KrosFlo® Systems will maintain setpoint control during operation. Setpoints can be changed while running during Auto operation.

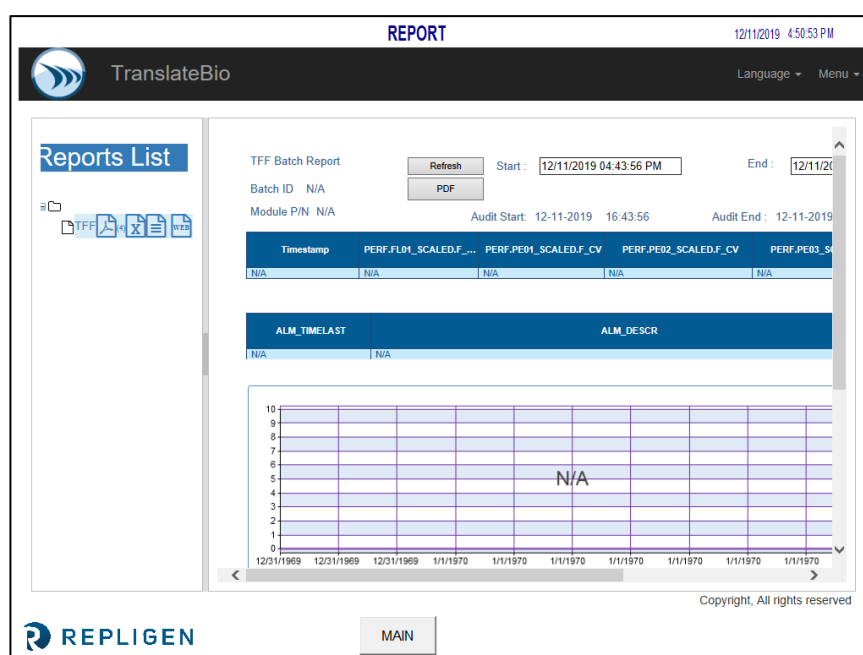
The TFF/TFDF® process supports use of a Fed Batch process. Press the **Fed Batch Enabled** button on the Settings screen to enable/disable the Fed Batch process.

Press **STOP** on the Settings or Main screens to stop the running process.

## 9. Generating reports

Click **REPORT** on the Settings screen to access the **Report** screen.

Figure 10. Report screen example



KrosFlo® Systems continually log collected data. Reports may be generated from this logged data as follows:

1. Click on the “WEB” icon under the ‘Reports List’. This will open the graphic shown above.
2. Enter the start time for the report in the **Start** field.
3. Enter the end time for the report in the **End** field.
4. Click **Refresh** to show the logged data collected over the specified time range displayed on the screen.
5. Click **PDF** to generate a portable document format (.PDF) of the report. This file will be opened when the report generation is done.
6. Click **MAIN** to return to the Main screen.

Select **Batch Report** and enter a general time frame to display Batch details for that time period.

Select **Time Report** and enter a general time frame to display system details for that time period.

## 10. Safety

A Production Stop button is located on the control panel enclosure. Pressing the Production Stop button will stop all operation immediately and prevent all components from operation. System operation can be restored by pulling the Production Stop out, pressing the Blue reset button, and then navigating to Alarms screen to Acknowledge and Reset the Production Stop Alarm. The desired sequence will have to be started/Restarted by the operator.

## 11. Maintenance

The robust design of KrosFlo® Systems are intended for use with process equipment. As such, lab or plant cleanliness and care are all that is needed to ensure quality operation when used in the systems intended manner. The frame, cabinet, and pumps can be cleaned by manual wipe-down using mild cleaning agents and/or warm water and a damp cloth or lab wipes. The HMI/Touchscreen should be cleaned with computer screen cleaner and computer screen wipes. Cleaning products are readily available from supply houses and the user must make sure the selected agent(s) are acceptable with their facility and compliant with system materials of construction as specified in [Section 3](#). OEM manuals for major components are included in the documentation package for reference.

An Electrical Schematic and Installation List of all major components (Process and Control Panel items) is also provided should any service be required.



**WARNING** – System must be turned off when replacing fuses to prevent electrical hazard. Any electrical work beyond the Electrical Installation and fuse replacement should be performed by trained personnel.



**WARNING** – Peristaltic pumps must be turned off when replacing either tubing or pump heads to prevent crushing/pinching hazard.

## 12. Appendix

**Table 8. System fuses**

Tag#	Description	Fuse type/size
FU-1 (120 VAC Model)	Main Power 120 VAC	Buss AGC-20 20A
FU-1 (220 VAC Model)	Main Power 220/240 VAC	Buss AGC-10 10A
FU-2	Empty	None
FU-2A	P-03	Buss AGC-5 5A
FU-2B	Empty	None
FU-3	PS-2 Input Supply 120-240 VAC	Buss AGC-5 5A
FU-4	PLC Input Supply 120-240 VAC	Buss AGC-2 2A
FU-5	PS-1 Input Supply 120-240 VAC	Buss AGC-5 5A
FU-6	PS-3 Input Supply 120-240 VAC	Buss AGC-10 10A
FU-13	BPCV-01, BPCV-02	Buss AGC-1 1A
FU-17	PS-1 Output 24VDC	Buss AGC-5 5A

**Table 9. Installed major components and identification tags**

Tag#	Item	Manufacturing/model
<b>System:</b>		
P-01	Recirculating Pump Motor Recirculating Pump Head	Levitronix LPM-600.3-10 Levitronix DCP-600
P-02	Product Pump Motor Product Pump Head	MasterFlex® 77420-10 I/P peristaltic pump MasterFlex®
P-03	Product Pump Motor Product Pump Head	MasterFlex® 77420-10 I/P peristaltic pump MasterFlex®
FL-01	Retentate flowmeter	Sonotec® FS04.210 CO.55/230 V2.0
FL-02	Permeate flowmeter/Flow converter	Levitronix LFC-1C-PC
PE-01/02/03	Pressure sensors	Repligen ACPM-799-01N
<b>Panel:</b>		
HMI	HMI/computer	Allen-Bradley 6181P15C2MWX1AC Integrated Panel Display Computer
PLC	PLC	Allen-Bradley 1766-L32BWA MicroLogix 1400
PE-01 to PE-03	Signal conditioner PE-01/PE-02/PE-03	Allen-Bradley 931S-B1C6D-DC
MCR-100	Master control relay Ethernet switch	Allen-Bradley 700-HF34Z24-4 N-Tron 104TX
PS-1	Power supply 48 VDC	Traco Power TSP600-148
PS-2	Power supply 24 VDC	MEAN WELL SDR-240-24
PS-3	Power supply 12 VDC	MEAN WELL MDR-20-12
PC-1	Pump Controller	Levitronix LPC 600.2-01

The spare parts listed in [Table 10](#) are recommended to prevent any downtime of the system should a minor failure occur.



Table 10. Recommended spare parts

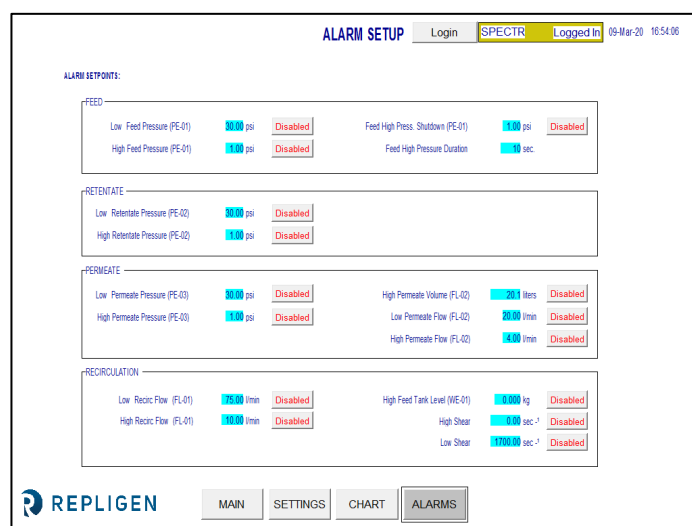
Item	Description	Quantity
1	FU-1, Main power 220VAC	AGC-10 10A
2	FU-2, Spare	
3	FU-2A, Pump P-03	AGC-5 5A
4	FU-2B, Spare	
5	FU-3, PS-2 Input supply 220VAC	AGC-5 5A
6	FU-4, PLC Input supply 220VAC	AGC-2 2A
7	FU-5, PS-1 Input supply 220VAC	AGC-5 5A
8	FU-6, PS-3 Input supply 220VAC	AGC-10 10A
9	FU-13, BPCV-01	AGC-1 1A
10	FU-17, PS-1 Output 24VDC	AGC-5 5A
11	Repligen Fittings Kit	1
12	1 ½" Tri-clamp	2
13	1 ½" Tri-clamp gasket	5
14	1" Tri-clamp gasket	5
15	Permeate tubing	5 m
16	Retentate tubing	5 m

## 12.1 Accessing the Scale Settings screen

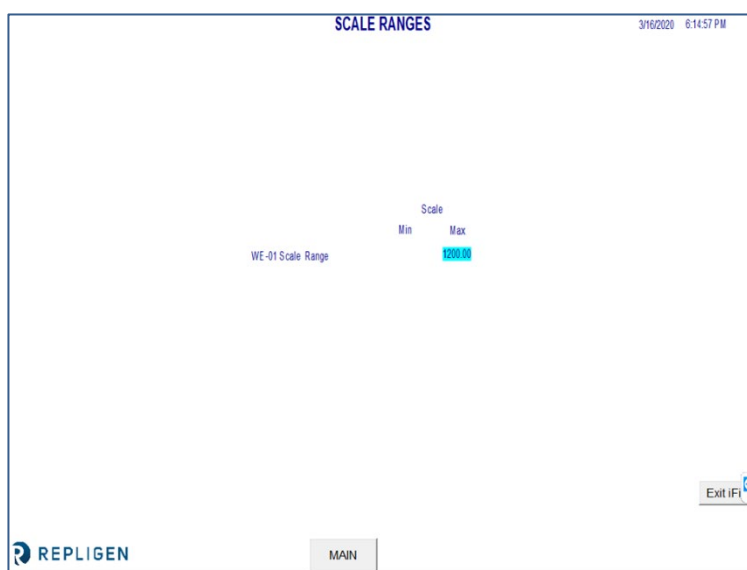
The Scale Settings screen is a “hidden” screen that enables you to configure the maximum weight value for the scale (**WE-01**) connected to the KrosFlo® System.

To access the Scale Settings screen and configure the maximum weight value for the scale (**WE-01**):

1. Tap the lower right corner on the Alarm Setup screen.



The Scale Settings screen appears.



1. Touch the **BLUE** field to configure the Maximum Value (0 to XXXX Kg) for **the WE-01 Scale Range** setpoint.
2. Touch the **Main** button to return the Main Screen.

## 12.2 Normalized Water Permeability

### NWP(Initial)

Initial Clean Membrane Water Permeability is defined to be the clean DI water filtrate flux rate over a given range of transmembrane pressure (typical 5-15 PSIG for UF membranes or 2-5 PSIG for MF membranes) for a given membrane area were the flow is normalized based upon temperature and is expressed as LMH / PSIG @ 20C. This information is used to determine productivity / impact to productivity as well as effectiveness of cleaning solution if membrane is going to be re-used.

### NWP (Post Cleaning)

Membrane Recovery is defined to be the percent ratio of the initial DI water NWP (normalized water permeability) after cleaning in relationship to the primary NWP initial which was measured before the membrane contacted any process fluid.

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