KrosFlo® FS-15 RPM™ System

User Guide

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Abbreviations

ABV	Automatic Backpressure Valve
AC	Alternating current
C	Concentration (mode)
CF	Concentration factor
CFC	Constant Feed Concentration (mode)
D	Diafiltration (mode)
DV	Diafiltration volume
LPM	Liters per Minute
PPE	Personal Protective Equipment
RPM	Real-time Process Management
TFF	Tangential Flow Filtration
TMP	Transmembrane Pressure
VPT	Variable Pathlength Technology

1. Introduction

This user guide provides detailed instructions for the setup and operation of the KrosFlo® FS-15 RPM™ Tangential Flow Filtration (TFF) System. Included are descriptions of potential modes of operation (Chapter 7) and basic concepts of TFF (Chapter 13). For further information, please contact your Repligen representative.

The KrosFlo FS-15 RPM System integrates the functionality of the FS-15 tangential flow filtration (TFF) system and the CTech™ FlowVPX® in-line spectrophotometer, which provides real-time concentration monitoring and control. The TFF system is designed for flat sheet membrane and hollow fiber, single-use applications. The system includes a cassette filter holder, with optional hollow fiber stands that may be added. The system's capabilities are integrated by the KrosFlo® RPM™ Software, which can execute complicated TFF processes through user-specified end points.

2. About this document

This manual uses several different phrases. Each phrase should draw the following level of attention:

Table 1. Explanation of user attention phrases

Phrase	Description
WARNING!	Warns users that serious physical injury can result if warning precautions are not heeded.
PRECAUTION	Cautions users of potential physical injury or equipment damage if the information is not heeded.
IMPORTANT	Indicates information necessary for proper instrument operation.
Note:	Points out useful information.

3. Safety precautions

Table 2. Safety precautions

Symbol	Description
Danger 	High voltages exist and are accessible. Use extreme caution when servicing internal components. Remove power from the pump before any cleaning operation is started.
Warning 	To avoid electrical shock, the power cord protective grounding conductor must be connected to the ground. Not for operation in wet locations as defined by EN61010-1.
Warning 	**Pressure**: Do not allow pressure to exceed 65 PSI
Warning 	**Moving parts**: Pumps contain moving parts. Keep fingers away from pumps and pinch valves during operation. Stop pump before loading or unloading tubing.
Warning 	**Electric shock**: Remove power from the pump before attempting any maintenance.
Warning 	**Tubing**: Tubing breakage may result in fluid being sprayed from pump. Use appropriate measures to protect operator and equipment.
Warning 	**Lubricant**: Do not contaminate the lubricant in the container, on the shaft or on the seal with foreign material. Failure to observe this precaution may result in damage to the seal and premature failure of the seal.
Warning 	Wear standard laboratory PPE.
Warning 	Do not freeze.
Warning 	**UV radiation hazard:** Protect eyes and skin from exposure.
Warning 	**Moving parts:** Automated Backpressure Valve (ABV) contains moving parts. Keep fingers away from ABV during operation.
Warning 	**Hot Surface:** Do not touch.
Caution 	To prevent cracking the Panduit cable organizer, put only one cable in each slot.

4. System Specifications

The tables below outline the performance specifications, electrical requirements, physical attributes, environmental considerations, and compliance information of the major system components. Tubing specifications can be found in section 8.

Table 3. Performance Specifications

Specification	Value
FS-15 TFF System	
Main Pump	Quattroflow® QF150SU Diaphragm Pump
Flow Rate	0.018–3.0 LPM
Flow Rate Accuracy	±0.1%
Operating Pressure	0–4 Bar (0–58 PSI)
Speed regulation	Line: ±0.1% F.S. Load: ±0.1% F.S. Drift: ±0.1% F.S.
Recommended Process Volume	140 mL–15 L
Flat Sheet Membrane Filtration Area	0.1–0.3 m^2
Number of Pressure Sensors Supported	3
Pressure Sensor Range	-9.99 to +75 PSI
Number of Scales Supported	2
Scale Capacity	20 kg (44 lbs) 60 kg (130 lbs) available upon request
Number of Auxiliary Pumps Supported	2
Auxiliary Pump Model	KrosFlo KR Jr
Auxiliary Pump Flow Rate	0.36–380 ml/min
FlowVPX System	
Qualification Slope Range	0.10 to 46 AU/mm using NIST-Traceable Slope Standards
Qualification Slope Repeatability	±2%
Maximum Pathlength	5.000 mm
Minimum Pathlength Step	0.001 mm
Spectroscopic Engine	Agilent Cary 60 Spectrophotometer
Spectrophotometer Wavelength Range	190–1100 nm
KONDUiT Conductivity, Temperature, and UV Monitor	
Conductivity Range	0.1 to 100 mS/cm
Conductivity Accuracy	0.1 to 2 mS/cm: ± 0.1 mS/cm 2 to 50 mS/cm: ±5% of reading 50 to 100 mS/cm: ±5% of reading (typical)
Temperature Range	0–70°C
Temperature Accuracy	Better than ±0.2°C (typically better than ±0.1°C)
UV Sensor Output signal	4–20 mA sourcing with 400 Ω maximum at 24 VDC; scaled to 0–2 AU with repeatability of 1% of full scale (0.02 AU)
UV Sensor Typical Response Time	1 second

UV Sensor Maximum Zero Shift	<2% of full scale (<0.040 AU)
UV Sensor Long-term Output Drift	<5% per month of full scale (<0.100 AU)

Table 4. Electrical Input Specifications

Specification	Value
FS-15 TFF System	
Input Power	250 W
Supply voltage limits	115–230 V_{rms} at 50/60 Hz (Universal Input)
Current, Maximum	2.2 A at 115 V_{rms} / 1.1 A at 230 V_{rms}
FlowVPX System	
Supply voltage limits	100–230 VAC @ 50–60 Hz
Current, Maximum	0.6 A
Cary 60 Spectrophotometer	
Voltage	100–240 VAC
Input Frequency	47–63 Hz
KR Jr Auxiliary Pumps	
Voltage	24 VDC
Current, Maximum	1.3 A
KONDUiT Conductivity, Temperature, and UV Monitor	
Voltage	24 VDC
Current	0.625 A

Table 5. Physical Specifications

Specification	Value
FS-15 Main Pump	
Dimensions *(L × W × H)*	292 x 267 x 432 mm (11.5 x 10.5 x 17.0 in)
Weight	11.5 kg (25.2 lbs)
FlowVPX Instrument	
Dimensions *(L × W × H)*	102 x 121 x 229 mm (4.0 x 4.8 x 9.0 in)
Weight	4.3 kg (with stainless steel 3 mm Flow Cell) 4.2 kg (with stainless steel 10 mm Flow Cell)
Delivery Fiber Optic Cable Length	3 m (optional 6 m fiber available upon request)
Cary 60 Spectrophotometer	
Dimensions	559 x 483 x 203 mm (22.0 x 19.0 x 8.0 in)
Weight	18.1 kg
KONDUiT Conductivity, Temperature, and UV Monitor	
Dimensions (L × W × H)	197 x 121 x 114 mm (7.75 x 4.75 x 4.5 in)

Weight	1.6 kg
Housing Materials	Powder-coated aluminum, urethane

Table 6. Environmental Specifications

Specification	Value
FS-15 TFF System	
Enclosure Rating	IP33
Operating Temperature	4 to 40°C (39 to 104°F)
Storage Temperature	-25 to 65°C (-13 to 149°F)
Humidity (non-condensing)	10%–85%
Altitude	Less than 2000 m
Pollution Degree	Pollution Degree 2
FlowVPX System	
Enclosure Rating	IP65
Operating Temperature	0°C to 48°C (32°F to 118°F)
Operating Humidity (non-condensing)	15% to 80%
Storage Temperature	-34°C to 66°C (-29°F to 150°F)
Storage Humidity (non-condensing)	0% to 95%
Pollution Degree	Pollution Degree 2
KONDUiT Conductivity, Temperature, and UV Monitor	
Operating Temperature	2°C to 50°C (35°F to 122°F)
Storage Temperature	-25°C to 65°C (-13°F to 149°F)

Table 7. Compliance Summary

Specification	Value
FS-15 TFF System	
ETL	UL 61010-1, CAN/CSA C22.2 No. 61010-1
CE	Low Voltage Directive 2014/35/EU Electromagnetic Compatibility Directive 2014/30/EU
RoHS	RoHS Directive 2011/65/EU
FlowVPX System (including Agilent Cary 60)	
ETL	UL 61010-1, CAN/CSA C22.2 No. 61010-1
CE	EN61010-1 (EU Low Voltage Directive) EN61326 (EU EMC Directive)
RoHS	Directive 2011/65/EU
KONDUiT Conductivity, Temperature, and UV Monitor	

ETL	Conforms to ANSI/UL Std 61010-1 Certified to CAN/CSA Std C22.2 No. 61010-1 This product has been tested to the requirements of CAN/CSA-C22.2 No. 61010-1 second edition, including Amendment 1, or a later version of the same standard incorporating the same level of testing requirements.
CE	EN61010-1: (EU Low Voltage Directive) EN61326: (EU EMC Directive)

4.1 Computer

A computer tablet is provided to control the FS-15 RPM System.

Table 8. Computer Specifications: Included Tablet

Specification	Value
Model	Microsoft® Surface Pro®
Dimensions	292 x 201 x 8.5 mm (11.5" x 7.9" x 0.33")

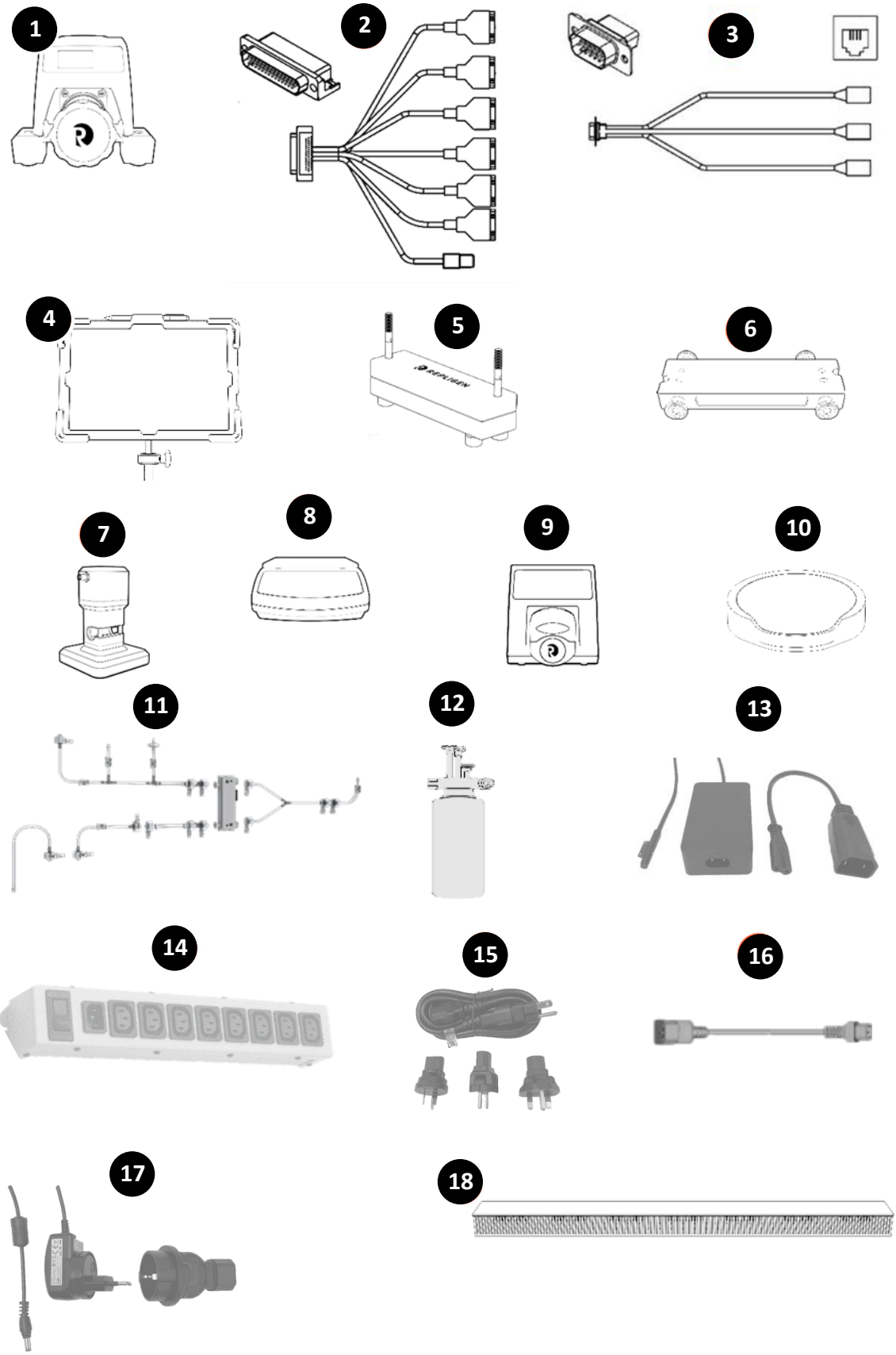
5. System Configuration and Major Components

See the following page for illustrations of the system components.

Table 9. System Parts List

#	Item	Quantity
TFF System Components		
1	Base pump with QF150SU EZ head	1
2	Component communication cable, 31 pin (octopus cable 1 of 2) – 7 outlet	1
3	Pressure sensor communication cable, 18 pin (octopus cable 2 of 2) – 3 outlet	1
4	Microsoft Surface Pro tablet with KrosFlo RPM Software and mount	1
5	TangenX® SIUS PD 2-bolt cassette clamp	1
6	Filter plate insert	1
7	Automatic Backpressure Control Valve (ABV) with vacuum base	1
8	Schuler scale, 20 kg capacity	2
9	KR Jr pump drive, 300 RPM	1
10	Magnetic stirrer and stirring bar	1
11	ProConnex® Single-use Flow Path (kit of 5 tubing sets). Includes three integrated, ½" TC pressure transducers.	1 Set
12	1 L, flat bottom, 4-ported reservoir	1
13	Tablet power block with Microsoft connector and C7 jumper cable	2
14	Power strip, universal, C14 inlet, sheet F outlets	1
15	Power cord for power strip	1
16	Power cord universal jumpers (multiple lengths)	7
17	Stir plate power cable and jumper cable adaptor (CEE7)	1
18	Panduit cable organizer	1
VPT System Components		
FlowVPX Head		
19	FlowVPX Head	1
Flow Cell Assembly		
20	Flow Cell (Choice of Stainless Steel or Single-Use and 3 mm or 10 mm Flow Path Diameter)	1
	Detector to Cell and Cell to Head Gasket Kit (set of 8 each)	1
FlowVPX Detector		
21	FlowVPX Detector Module	1
Standard Mount Assembly		
22	FlowVPX Standard Mount	1
	Standard Mount Clamp	1
	Standard Mount Clamp Handle	1
	Standard Mount Clamp Screws [M6]	2
VPT System Suitability Test Tools		

23	FlowVPX System Suitability Adapter (XSA)	1
	FlowVPX XSA Fibrette	2
VPT Quick Check Tools		
24	Detector Validation Adapter (DVA)	1
	Transmission Tool (Cary 60)	1
	Shortened Fused Silica Sample Vessel, 13 mm ID 16 mm OD 15 mm Tall	1
	Sample Vessel Holder, Large	1
Cables *(left to right, top to bottom)*		
25	FlowVPX Extender Power Cable	1
	FlowVPX Power Supply Cable	1
	FlowVPX Power and I/O Splitter Cable	1
	FlowVPX USB Cable	1
	FlowVPX I/O External Cable	1
Cary 60 and Accessories *(left to right, top to bottom)*		
26	Agilent Cary 60 Spectrophotometer	1
	Cary 60 USB Cable	1
	Detector Cable	1
	Delivery Fiber	1
	Cary 60 Power Supply and Cable	1
Miscellaneous *(left to right)*		
27	FC Connector Nut	1
	FX Connector Nut	1
	Acorn Nut (set of 8)	1
	12 in-lbs Torque Driver (10 mm hex socket)	1
	40 in-lbs Torque Driver (10 mm)	1
	4 mm Ball End Driver	1
	5 mm Ball End Driver	1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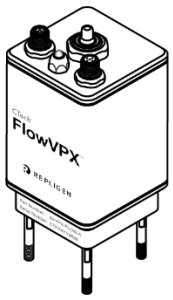

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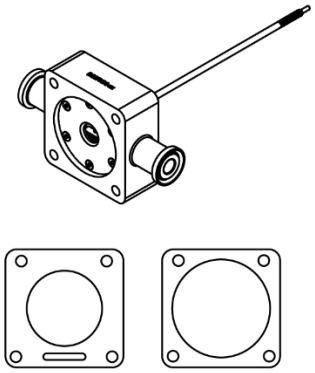

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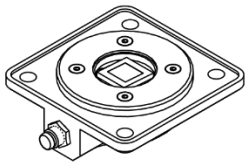

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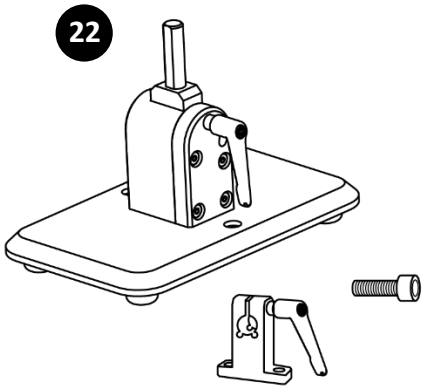

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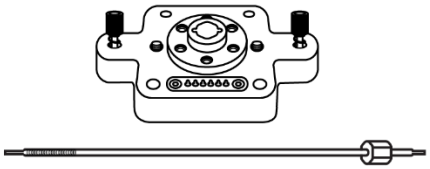

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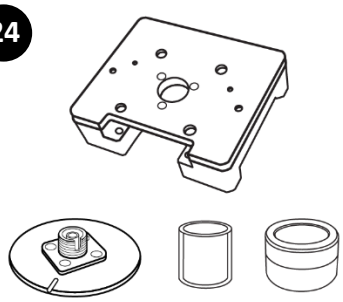

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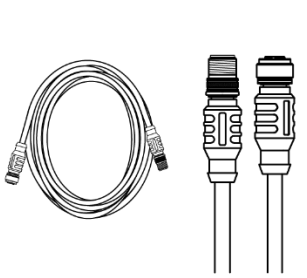

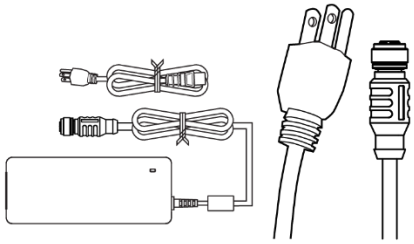

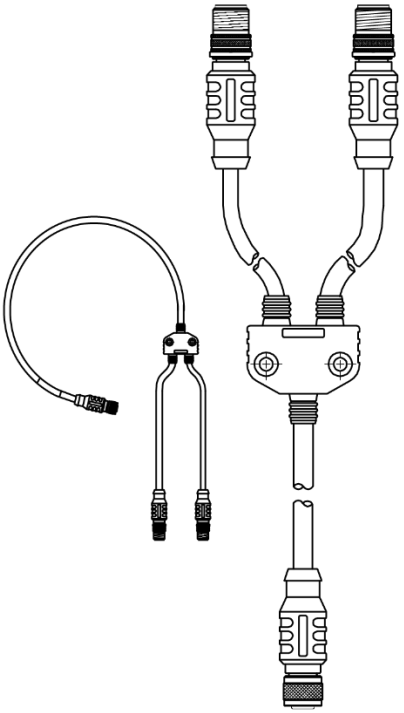

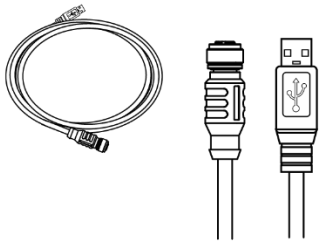

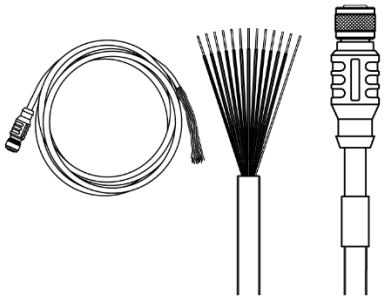

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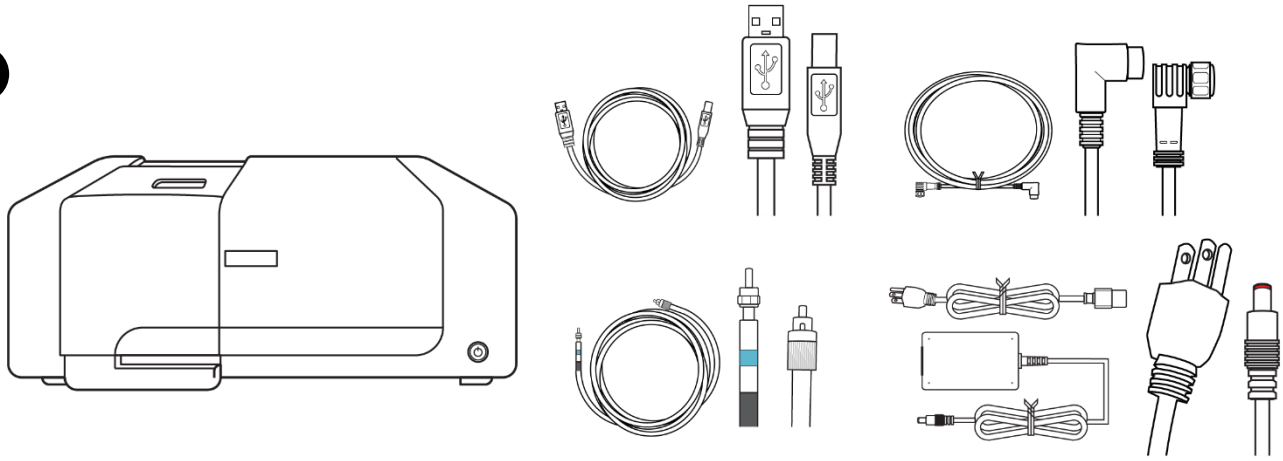

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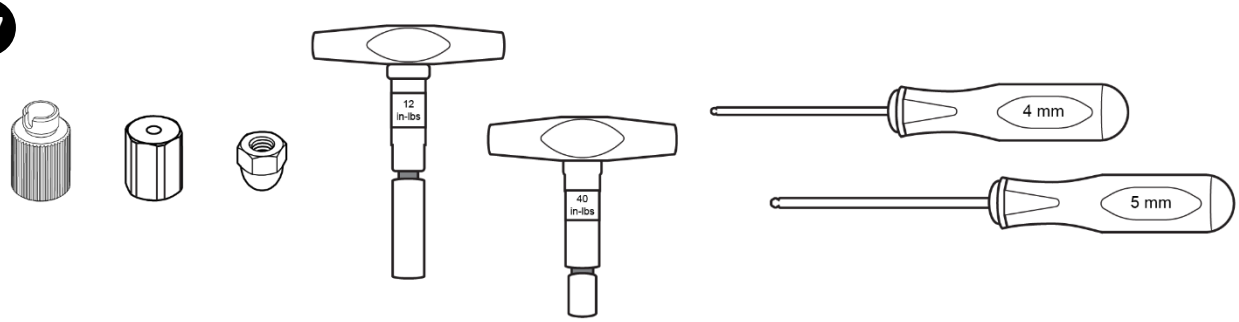


6. Materials of Construction

Table 10. Materials of Construction

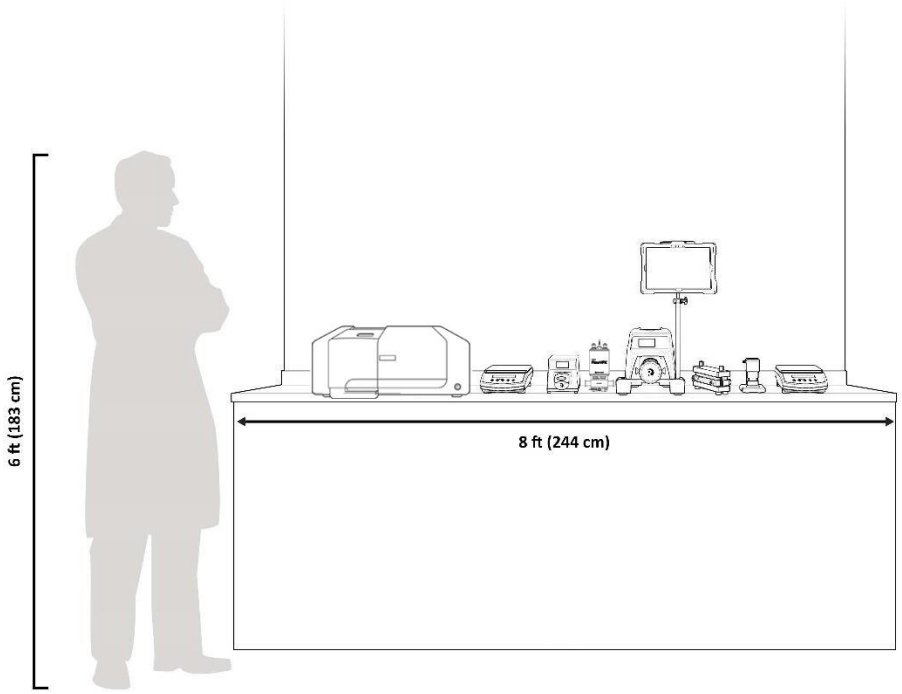
Contact Surface Material	
KR2i TFF System Process Contact Surfaces	
Tubing / Reservoir Closures	C-Flex® / Pharmapure®
Reservoirs	Polypropylene
Disposable Pressure Transducers	Polysulfone
Plastic Fittings	Polypropylene / Polysulfone
FlowVPX System Process Contact Surfaces	
Flow Path	316L Stainless Steel
Diaphragm Seal	EPDM
Detector Window	UV-Grade Fused Silica
Adhesive	Medical-Grade Epoxy
Single-Use Flow Cell	Polycarbonate, USP Class VI, animal-derived component free (ADCF)
	Platinum-cured silicone, USP Class VI, ADCF
Cary 60	N/A
KR2i TFF System Non-Process Contact Surfaces	
KR2i System	316 Stainless Steel
	Hard Coat Anodized Aluminum
	Polysulfone
	Polypropylene
	Polyphenylene Sulfide
	Polyester
	Nylon
FlowVPX System Non-Process Contact Surfaces	
FlowVPX System	316/316L Stainless Steel
	Stainless Steel Fiber Optic Connector
	Polyetheretherketone (PEEK)
	Polyphenylsulfone (PPSU)
	Medical-Grade Epoxy
	Gold-Plated Electrical Contacts
Single-Use Flow Cell	Glass-filled nylon
	Viton sealant
	Torlon PAI
	Hydrophobic polyethersulfone with PTFE, USP Class VI
Cary 60	Refer to Agilent documentation for more information.

7. Setup and Operation

7.1 Basic Setup

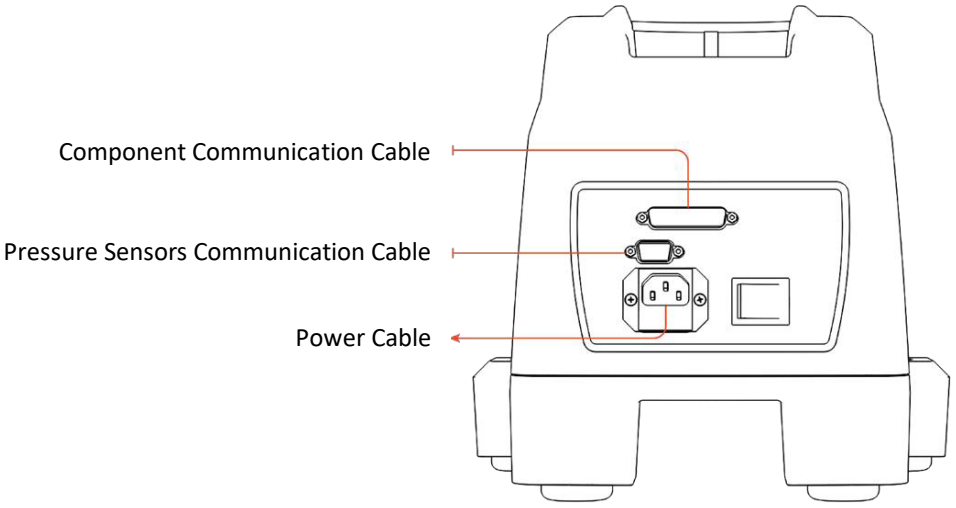
Note: *See sections 7.2 through 7.7 for example configurations.*

Figure 1. System space requirements



1. Mount the FS-15 main pump on a flat, horizontal surface with the pump head attached (see chapter 8 for pump head installation details).
2. Connect both Octopus Cables to the back of the main pump.
3. Connect up to three pressure transducers to the Pressure Transducer Octopus Cable ports, depending on the application.
4. Connect an Automatic Backpressure Valve (ABV) to the Auxiliary Component Octopus Cable labeled "Valve" (see section 8.3 for ABV Setup details).
5. Connect the FlowVPX to process tubing in between the feed reservoir and the FS-15 main pump. (See Chapter 10 for FlowVPX setup details.)
6. Connect power cable to the TFF system.
7. Follow guidelines and diagrams in sections 7.2 through 7.7 to determine which Auxiliary Components are required to operate specific process modes for manual, semi-automated, and automated processes.
8. If using auxiliary components, see Chapter 8 for setup details.
    a. After connecting auxiliary components, power on the TFF system first before powering on auxiliary components.
9. Connect TFF flow path to TFF system.
10. Set low and high pressure alarms and interlocks as required by the process conditions.
11. Enter concentration and diafiltration set-points into the TFF system's Process Mode settings to start application.

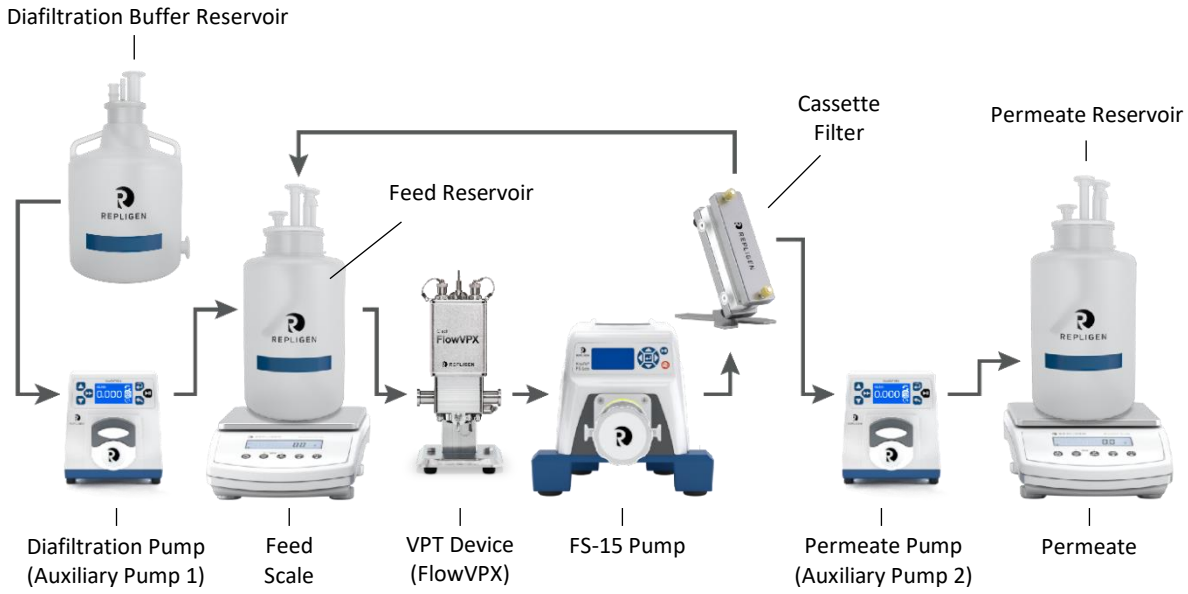
Figure 2. FS-15 Main Pump Electrical Connections



Note: *Valves, cables, and the computer are intentionally left out of the diagrams below for visual clarity.*

7.2 Manual Mode Setup

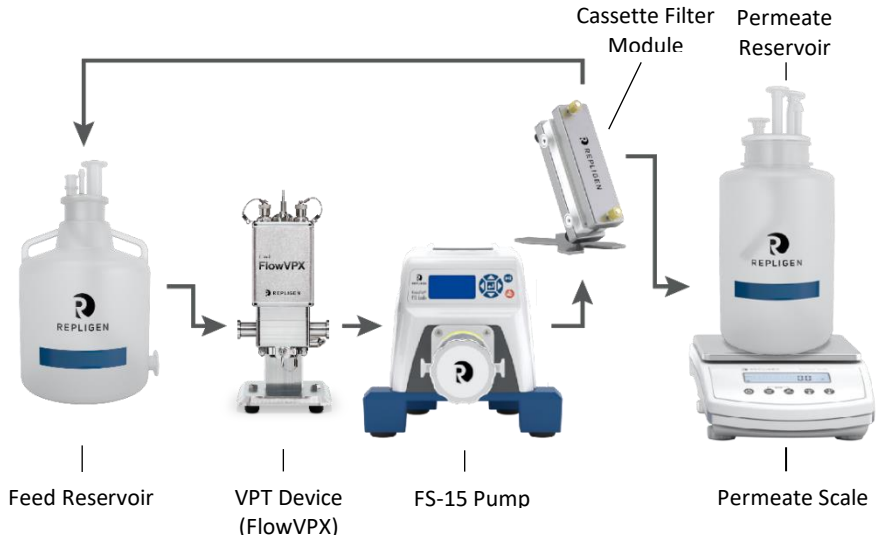
Figure 3. Manual Mode setup configuration



1. Any combination of Auxiliary Components is possible in Manual Mode—the only required component is the TFF system pump itself. The diagram above is a full setup with all Auxiliary Components.
2. Auxiliary Scales
    a. Connect up to two scales to the Auxiliary Component Cable's "Feed Scale" and/or "Permeate Scale" ports.

7.3 Concentration Mode (C Mode) Setup

Figure 4. Concentration Mode (C Mode) setup configuration.

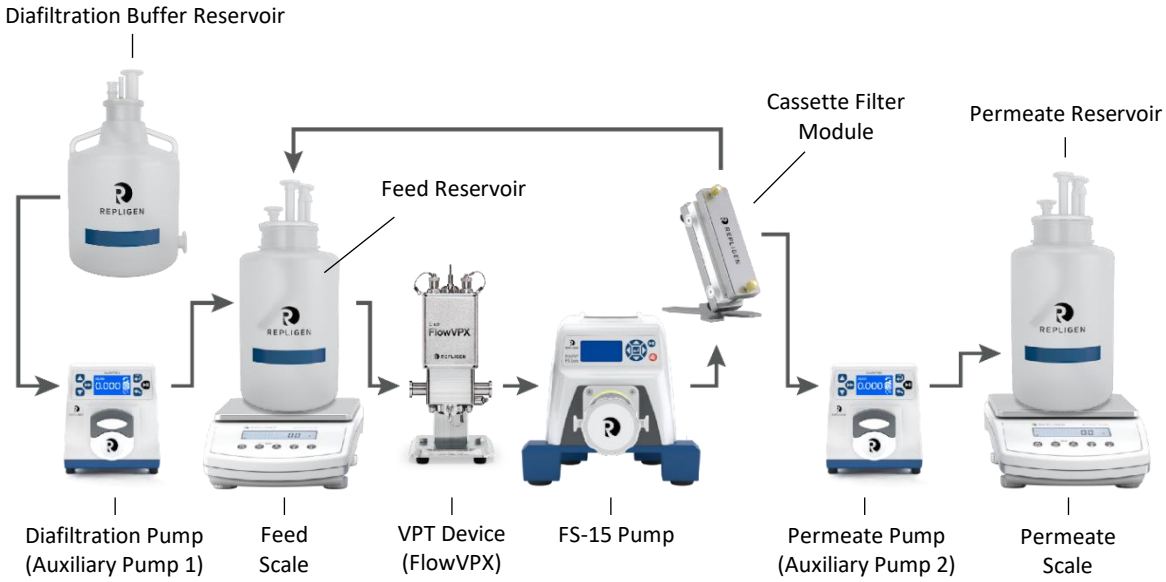


1. Auxiliary Scales
    a. Connect scale to the Auxiliary Component Cable's "Permeate Scale".

7.4 C/D and C/D/C Mode Setup

Note: *Permeate Pump is optional and shown in the diagram as an example for applications that require permeate control.*

Figure 5. C/D and C/D/C Mode setup configuration



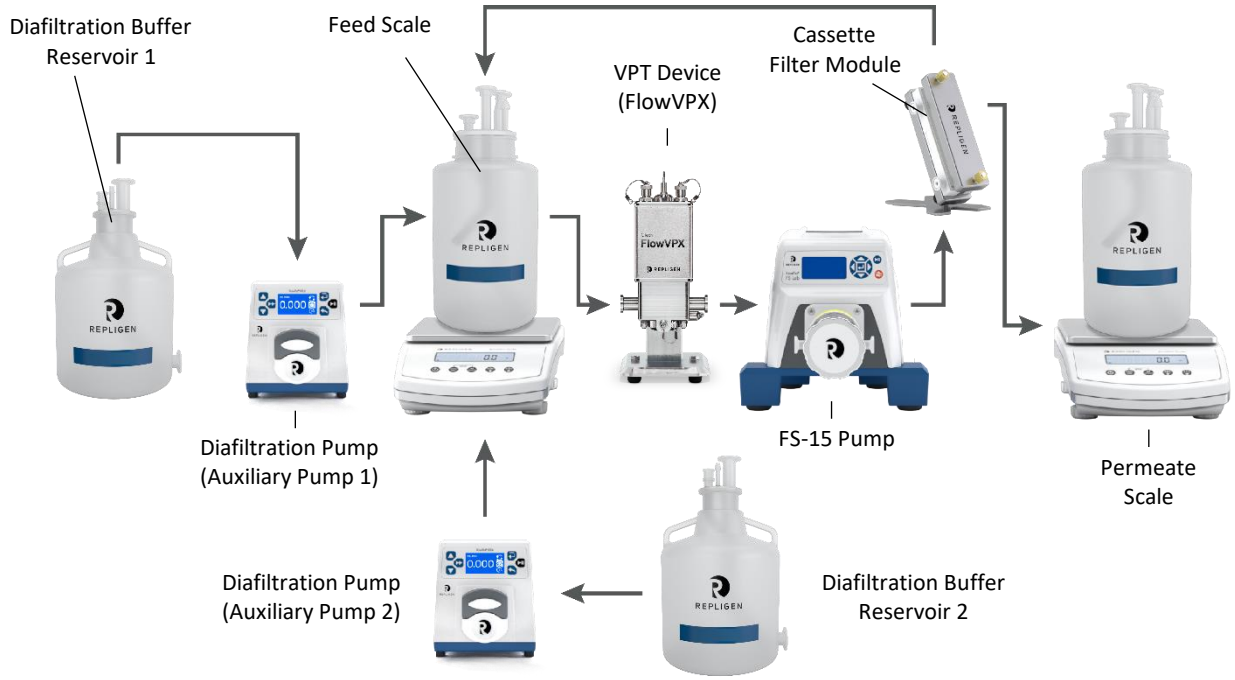
1. Auxiliary Pumps
    a. Connect auxiliary pump to the Auxiliary Component Cable's "Auxiliary Pump 1" port and second auxiliary pump to the Auxiliary Component Cable's "Auxiliary Pump 2" port.

b. Connect Auxiliary pump power cables(s).

2. Auxiliary Scales
   a. Connect first scale to the Auxiliary Component Cable's "Feed Scale" port and second scale to the Auxiliary Component Cable's "Permeate Scale" port.

7.5 C/D/D/C Mode Setup

Figure 6. C/D/D/C Mode setup configuration

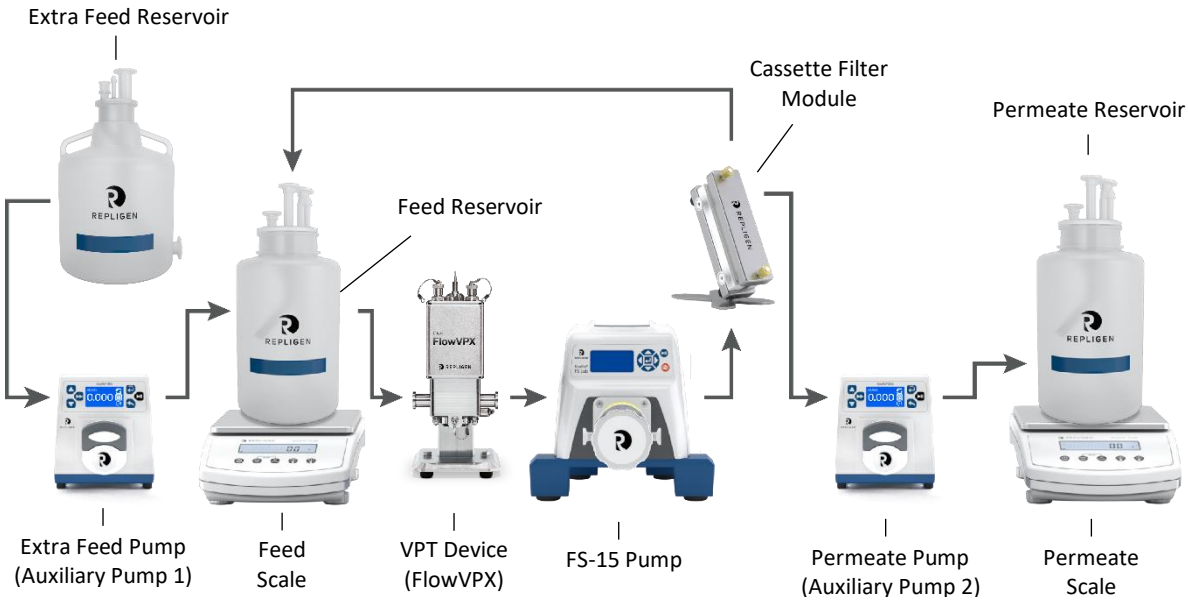


1. Auxiliary Pumps
   a. Connect first auxiliary pump to the Auxiliary Component Cable's "Auxiliary Pump 1" port and second auxiliary pump to the Auxiliary Component Cable's "Auxiliary Pump 2" port.
   b. Connect auxiliary power cables.
   c. Auxiliary Pump 1 will function as Diafiltration Pump 1, and the Auxiliary Pump 2 will function as Diafiltration Pump 2.
2. Auxiliary Scales
   a. Connect first scale to the Auxiliary Component Cable's "Feed Scale" port and second scale to the Auxiliary Component Cable's "Permeate Scale" port.

7.6 CFC Mode Setup

Note: *Permeate Pump is optional and shown in the diagram as an example for applications that require permeate control.*

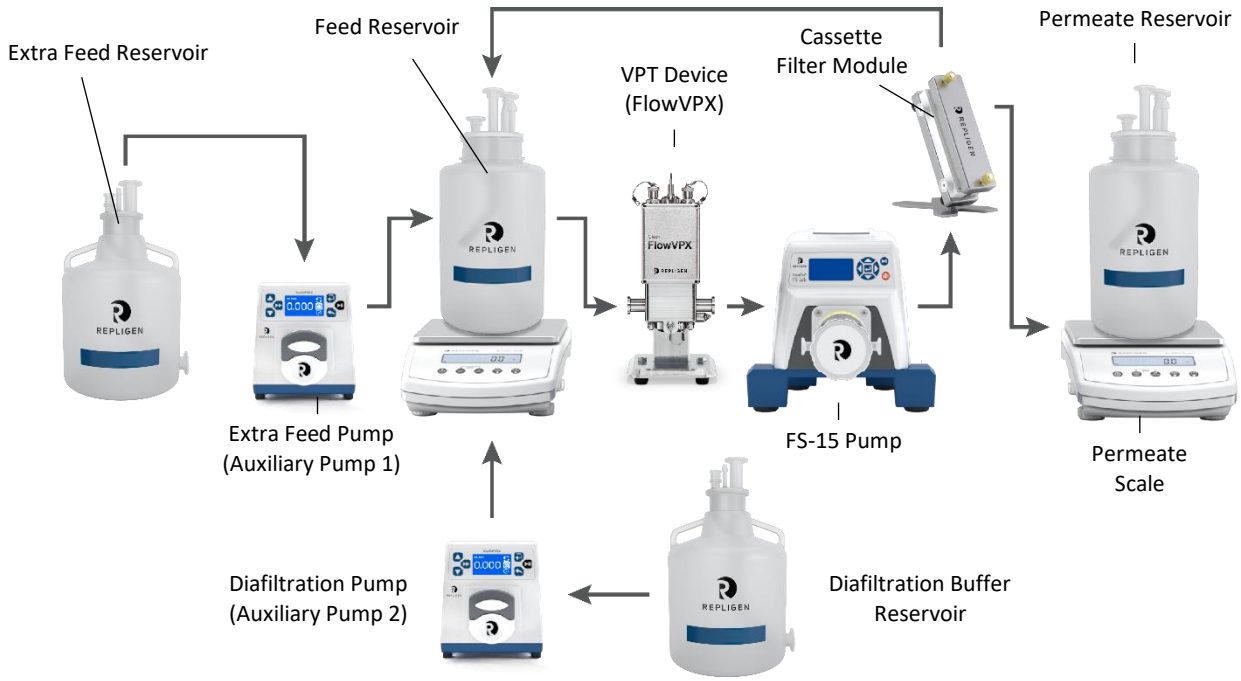
Figure 7. CFC Mode setup configuration



1. Auxiliary Scales
    a. Connect first scale to the Auxiliary Component Cable's "Feed Scale" port and second scale to the Auxiliary Component Cable's "Permeate Scale" port.

7.7 CFC/D/C Mode Setup

Figure 8. CFC/D/C Mode setup configuration

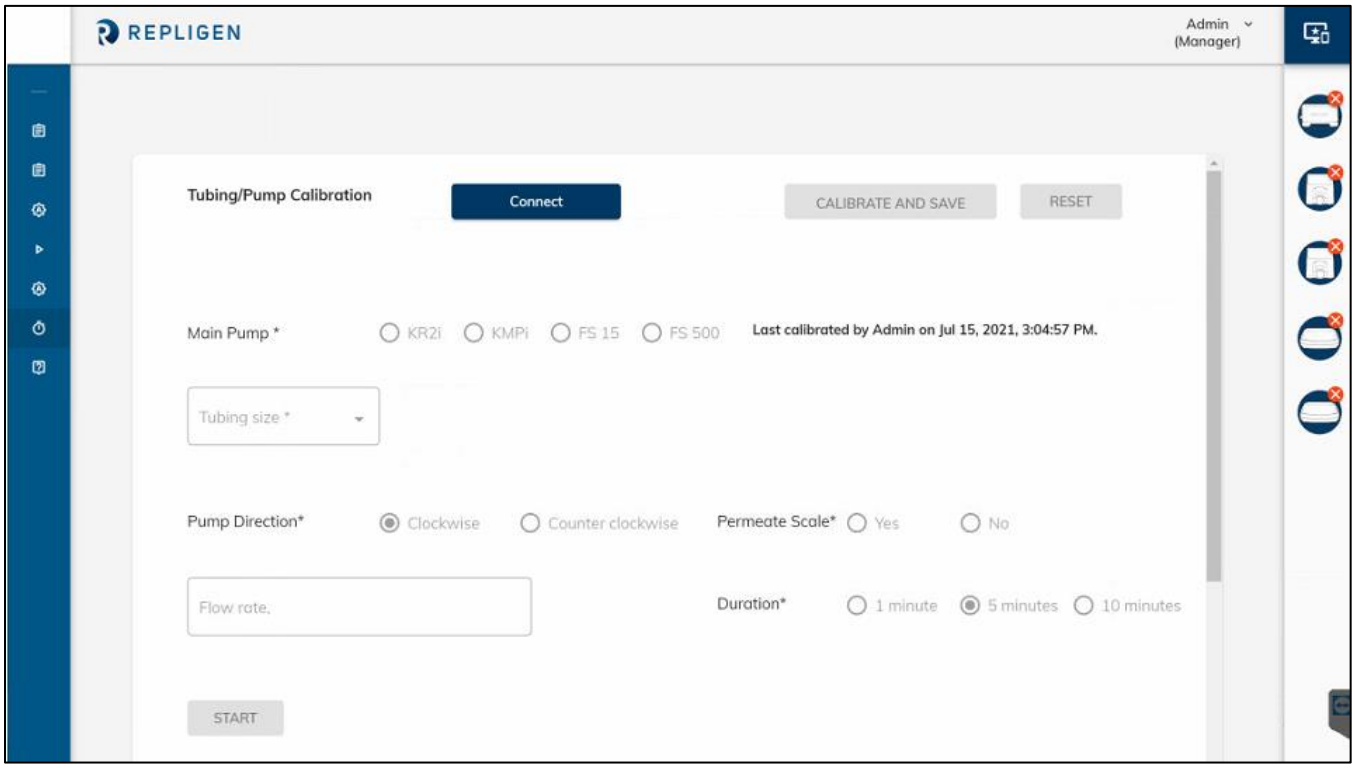


7.8 Calibration Using KrosFlo RPM Software

The main pump and pressure sensors can be calibrated through RPM software interface. In the left navigation menu, click on Calibration followed by either Tubing/Pump or Pressure.

7.8.1 Pump Calibration

Figure 9. Tubing/Pump Calibration page



1. Open the Tubing/Pump Calibration page in the RPM software (Figure 9).
2. Select the Main Pump (FS-15) and enter the tubing size.
3. Enter a flow rate. A minimum of 100 mL/min is recommended for accurate results.
4. Select Permeate Scale: Yes and Duration: 5 minutes.
5. Ensure tubing is properly connected to the FS-15 main pump and sufficient water is available to pump for the full duration.
6. Place an empty beaker on the Permeate scale to catch the water and help measure the final weight at the end of calibration.
7. Click START. Wait for the pump to finish.
8. When the pump is finished, click CALIBRATE AND SAVE to apply the calibrated settings.

Note: *The weight reading on the Permeate Scale will be higher than the data displayed in the RPM software. This is because about 1 mL of permeate flows through the system before calibration measurements begin.*

7.8.2 Pressure Sensor Calibration

Note: *Pressure sensor calibration requires an additional tool to independently maintain and measure pressure. Pressure sensor calibration should only be performed by a Repligen representative during system qualification and maintenance services.*

1. Connect a hand pump manifold with calibrated pressure gauge in line with the Feed pressure sensor.
2. Ensure the pressure sensor reads 0 psi when the pressure gauge reads 0 psi. If not, tare the pressure sensor.
3. Pump positive pressure into the manifold and compare the gauge reading to the pressure measured by the FS-15 system.

4. If the readings differ by more than the allowed tolerance, proceed with steps 5 through 12. If the readings are within the tolerance, skip to step 13.
5. Open the Pressure Calibration page in the RPM software. Select the appropriate sensor: Feed Pressure, Retentate Pressure, or Permeate Pressure.
6. Use the hand pump to set the pressure to 15 psi.
7. In the Calibration Pressure field, enter the pressure value displayed on the pressure gauge and then press CALIBRATE AND SAVE.
8. Increase the pressure to 45 psi.
9. In the Calibration Pressure field, enter the pressure value displayed on the pressure gauge and then press CALIBRATE AND SAVE.
10. Increase the pressure to 60 psi.
11. In the Calibration Pressure field, enter the pressure value displayed on the pressure gauge and then press CALIBRATE AND SAVE.
12. Set the pressure to 15 psi again, followed by 45 psi, and lastly 60 psi. Confirm that the gauge reading and the FS-15 system reading are within the allowed tolerance. If not, repeat this process starting from step 6. If the calibration process fails a second time, contact Repligen support.
13. Repeat this entire process for all three pressure sensors.

8. Auxiliary Component Setup and Operation

8.1 Auxiliary Scales

The TFF systems interface with digital load cell auxiliary scales. These scales are dynamic instruments suitable for various TFF processes. For detailed information on the scales, refer to the scale manufacturer's user manual.

8.1.1 Installation

1. Carefully unpack scale from shipping carton.
2. Place scale on a level surface and adjust the level legs so that all four legs are touching the surface and leveling bubble is within the circle.
3. Connect the serial connector on the octopus cable to either the Feed Scale or Permeate Scale.
4. The scale will boot up to display the weight screen.

For further information on scale functionality, including calibration, please refer to the manufacturer's manual.

8.2 Auxiliary Pumps

The KR Jr peristaltic pump has both internal and external control modes, enabling it as an auxiliary pump for the FS-15 TFF system.

8.2.1 Installation

Up to two auxiliary pumps can be connected to the TFF system's Auxiliary Component Octopus Cable. After connecting the auxiliary pumps to TFF system and the TFF system has been powered on, the Auxiliary Pumps can then be powered on and used in internal or external modes depending on the TFF process. To control the auxiliary pump via the TFF system , ensure that the auxiliary pump is in remote control mode by following these steps:

1. Enter the Settings Menu (wrench icon)
2. Enter Global Options Menu (paper with lines icon)
3. Enter Remote Control Menu (25-pin connector over box that alternately shows V and mA)
4. Enter Voltage Input Menu (voltmeter icon), then use the Up or Down arrows to highlight the “I” icon and press Enter to activate it.
5. Remote Control On (“I” icon)

Note: *The controls below are only accessible when the auxiliary pumps are in Internal control mode. When in External control mode, the auxiliary pumps are controlled by input from the TFF system.*

Table 11. KR Jr Tubing Specifications

	L/S Precision pump tubing			
	L/S 13	L/S 14	L/S 16	L/S 25
Silicone tubing P/N	ACTU-E13-25N	ACTU-E14-25N	ACTU-E16-25N	N/A
Pharmapure tubing P/N	ACTU-P13-25N	ACTU-P14-25N	ACTU-P16-25N	ACTU-925-25N
Inside diameter (nominal)	0.8 mm (0.03”)	1.6 mm (0.06”)	3.1 mm (0.12”)	4.8 mm (0.19”)
Hose barb size	1.6 mm (1/16”)	1.6 mm (1/16”)	3.2 mm (⅛”)	4.8 mm (3/16”)
Flow rate range (mL/min)	0.005 – 12	0.014 – 42	0.05 – 150	0.11 – 330
Maximum pressure	2.7 bar (40 psig)	2.4 bar (35 psig)	2.7 bar (40 psig)	2.4 bar (35 psig)

8.2.2 Auxiliary Pump Settings

In order for the TFF system to control the Auxiliary Pumps properly, enter the Auxiliary Pump type and the tubing size in the RPM software. For further information on Auxiliary Pump functionality, including operation outside of remote control mode, please refer to the manufacturer's manual.

8.3 Automatic Backpressure Valve

The KrosFlo® Automatic Backpressure Valve (ABV) controls a wide variety of pressure set-points during tangential flow filtration processes when used in conjunction with the TFF System. The valve is designed to pinch flexible tubing to maintain the user-set pressure. One ABV may be connected to the system.

Figure 10. Automatic Backpressure Valve

8.3.1 ABV Installation

1. Plug in the valve serial port to the serial connector labeled "Valve" on the Octopus Cable. The valve is powered through the octopus connector.
2. Place the tubing through the plunger mechanism by lifting up on the body of the valve and fitting the tubing between the metal bar and the white plastic plunger. The body of the valve can then be turned 180° to close the tubing opening by using the longer stainless steel rods or let the tubing opening remain accessible with the shorter rods.

8.3.2 ABV Settings

Auto Mode Menu

a. **Mode:** Can be set to Auto or Manual-- if set to Manual, settings will switch to Manual Mode Menu (see below)
b. **Set-point:** The pressure value the Valve will attempt to reach and maintain
c. **Tubing Size:** Used to determine pinch distance
d. **Control:** Set whether Valve is controlling Feed, Permeate, Retentate, or TMP pressure
e. **Start Position:** The initial Start position before adjusting pinch distance:
    - Open: no pinching
    - Half: 50% closed based on tubing size
    - Closed: 100% closed based on tubing size
    - Custom: user defined

Manual Mode Menu

a. **Mode:** Can be set to Manual or Auto-- if set to Auto, settings will switch to Auto Mode Menu (see above)
b. **% Closed:** % of opening closed by pinch
c. **Tubing Size:** Used to determine pinch distance

8.4 KONDUiT

The KONDUiT unit integrates Conductivity, Temperature, and UV monitoring and automation functionalities into the TFF System. There are two combination Conductivity and Temperature inputs (Cond/Temp), two UV and I/O inputs, one communication port, and one power supply port.

8.4.1 System Configuration

Single-use Conductivity/Temperature Flow Path Components
Combination Conductivity and Temperature in-line flow path sensors; made of Polysulfone and in assorted hose barb sizes.

Optional: UV Photometer
Available in either 260 nm or 280 nm models; consists of 2 fiber optic cables, 2 optical couplers to connect to flow cell, and power supply.

Note: *UV Photometer cannot be remotely tared; to tare UV Photometer, press "TARE" button on Photometer body.*

Optional: Single-use UV Flow Path Components
UV in-line flow path sensors; made of Polysulfone and in assorted hose barb sizes.

8.4.2 Basic Setup

Note: *Prior to assembling KONDUiT, ensure that TFF System has been properly set up (see Section 7).*

1. Connect KONDUiT Communication Cable to Auxiliary Octopus Cable.
2. Connect KONDUiT Power Cable to KONDUiT Power Port.
    - On back of KONDUiT, green power light on the On/Off button indicates if KONDUiT is receiving power.

Figure 11. KONDUiT Ports and Power Indicator Light

Figure 12. Front and back of KONDUiT

3. Assemble TFF flow path and place Cond/Temp and/or UV in-line sensors at the appropriate position in the flow path; see sensor descriptions below for details.

Conductivity Sensor
The sensors can be placed in either the permeate line or the recirculation line when used for the Diafiltration end point control.

Note: *Conductivity sensors need to be filled with the initial starting buffer prior to starting the automated sequence. When the sensor is placed on the permeate line, this buffer should be the same as that of the process material. This will avoid early shutdown in auto mode.*

When a conductivity set-point is entered, the system will stop the sequence when the value is reached. The system will only track in the linear range either positive or negative from the starting conductivity.

UV Sensor
For UV alarms, the sensors are usually placed on the permeate line to detect sample breakthrough.

Note: *Fill UV in-line sensor with buffer and press the physical "Tare" button on UV box prior to starting the sequence. For UV Diafiltration control on the permeate line, the molecule of interest should be detected in the cell prior to starting the automated sequence.*

Note: *Fiber optic cables are very fragile. Do not place heavy weight on top of fiber optic cables or fold fiber optic cables.*

4. Connect all sensors to the corresponding ports.
5. After making all connections, wait at least one minute for KONDUiT to establish connection with the TFF System.
6. KONDUiT can be placed behind the TFF system. No physical buttons or interfaces are necessary on the base unit. The UV photometer has a tare button that needs to be accessible. Cables can be placed in the cable boxes provided with the system.

8.4.3 Maintenance

Periodically clean KONDUiT base with damp cloth and/or mild detergent. Do not immerse or use excessive fluid. Inspect connectors to make sure they are not damaged and they are securely fastened.

9. Pump Head Replacement

The FS-15 pump head must be replaced periodically depending on the user's application and requirements. Follow the steps below to remove the old pump head and install a new one.

1. Rotate the knob on the end of the main pump counterclockwise to loosen the pressure plate.

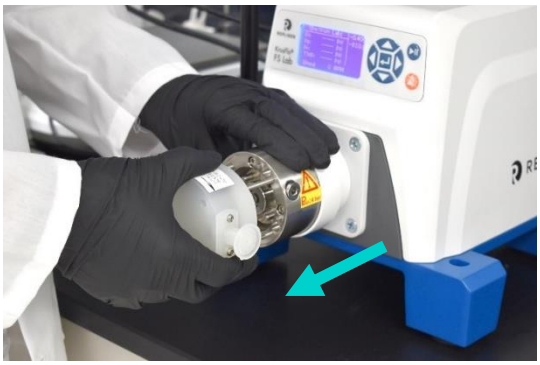
Figure 13. Loosen the pressure plate by rotating counterclockwise.

2. Pull the pressure plate straight off.

Figure 14. Remove the pressure plate.

3. Slide the pump head along the guide pins and pull it off the pump head mount.

Figure 15. Slide the pump head off.



4. Discard the pump head.

5. Take the new pump head and align the guide pins with the appropriate holes. Slide the pump head along the pins and push it firmly against the pump head mount.

Figure 16. Attach the new pump head.

6. Align the pressure plate, then push the plate against the pump head. Rotate the knob clockwise to secure the plate.

Figure 17. Tighten the pressure plate back onto the pump head.

10. FlowVPX Instrument Setup

Figure 18. CTech FlowVPX instrument

10.1 Installation and Basic Setup

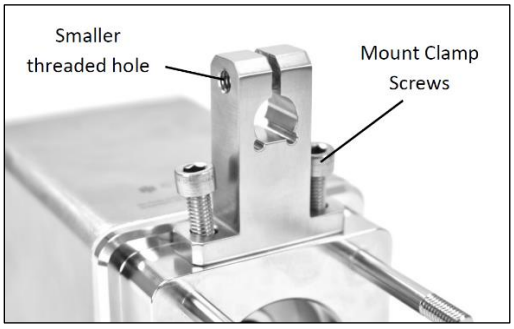
10.1.1 Connecting the FlowVPX Head to the FlowVPX Standard Mount

1. Turn the FlowVPX Head on its face (logo side down) so that the two mounting holes are facing up (see Figure 19).

Figure 19. FlowVPX Head, logo side down

2. Place the Standard Mount Clamp on the FlowVPX Head and align the holes. Ensure that the smaller threaded hole is facing left (Figure 20).

Figure 20. Standard Mount Clamp on FlowVPX Head



3. Insert the mount clamp screws. Tighten with the provided 5 mm ball end driver (Figure 21).

Figure 21. 5 mm Ball End Driver

4. Install the Clamp Handle from the right side of the Standard Mount Clamp (Figure 22).

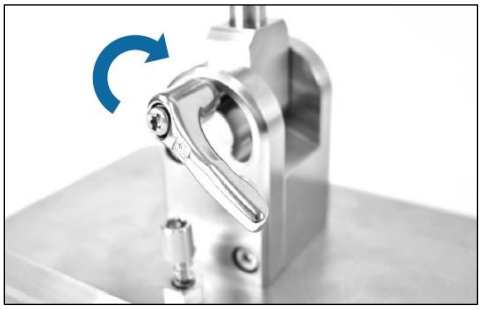
Figure 22. Clamp Handle installation

5. Turn until the threaded post on the Clamp Handle starts to appear at the other end (see Figure 23). Do not fully tighten.

Figure 23. Rotate Clamp Handle

6. Ensure the mounting post on the Standard Mount is fully vertical. Tighten the Mounting Post Clamp Handle, if not already tightened (Figure 24).

Figure 24. Tighten Mounting Post Clamp Handle

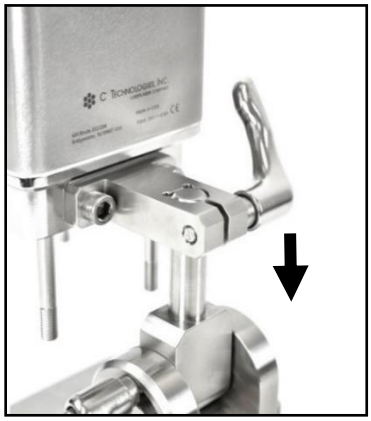


7. Pick up the FlowVPX Head and align the hole in the clamp with the mounting post. Ensure the flattened location on the post aligns with the flattened area on the clamp (Figure 25).

Figure 25. Install FlowVPX Head on mounting post

8. Carefully lower the FlowVPX Head so that the clamp slides over the post on the mounting plate (Figure 26).

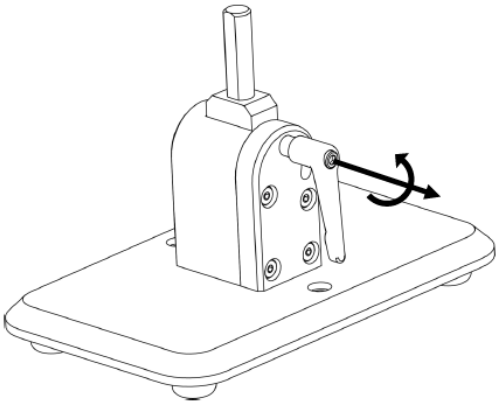
Figure 26. Lower FlowVPX Head on mounting post



9. Turn and tighten the Standard Mount Clamp Handle to secure the FlowVPX Head onto the mounting post (Figure 27).

Note: *The clamp handles can change orientation by pulling out and rotating. This allows them to be repositioned without obstruction.*

Figure 27. Tighten Standard Mount Clamp Handle (Left) and Repositioning the Clamp Handle (Right)



10.1.2 Connecting the FlowVPX Instrument to the Cary 60 Spectrophotometer and Computer

1. Pass the Detector Cable (EC0196) and the Delivery Fiber (SMA/hex-nut end) through the open accessory port at the back of the Cary 60 spectrophotometer into the sample compartment (Figure 28).

Figure 28. Accessory port in back of Cary 60 spectrophotometer

2. Connect the black, right-angle plug of the Detector Cable into the wall of the Cary 60 sample compartment (Figure 29).

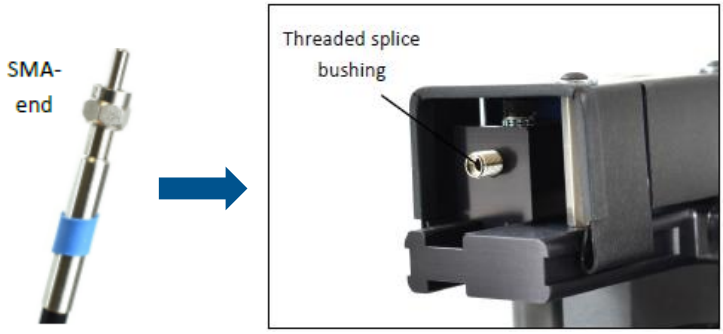
Figure 29. Detector Cable in sample compartment

3. Connect the Cary 60 power cable (supplied with the Cary 60) to the back of the Cary 60. Then connect the plug to an approved outlet (Figure 30).
4. Connect the Cary 60 USB cable, (supplied with the Cary 60) to the back panel of the Cary 60. Connect the other end to a USB port on the computer (Figure 30).

Figure 30. Cary 60 power cable and USB cable, back panel

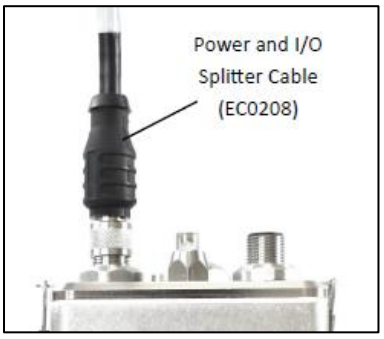
5. Connect the SMA end of the Delivery Fiber to the threaded splice bushing at the back of the Fiber Optic Coupler (Figure 31). Use the hex nut to securely tighten the connection.

Figure 31. Fiber Optic Coupler threaded splice bushing



6. Connect the FlowVPX Power and I/O Splitter Cable (EC0208) to the top of the FlowVPX Head (Figure 32). Connect the FlowVPX Power Cable (EC0205) to one leg of the Splitter Cable (Figure 33). The Power Cable uses a location-specific power adapter to plug into a standard wall outlet.

Figure 32. Connect Power and I/O Splitter Cable (EC0208) to FlowVPX Head



7. To utilize the FlowVPX I/O connections, connect the I/O External Cable (EC0214) to the Power and I/O Splitter Cable (Figure 33).

Figure 33. FlowVPX I/O cable connections

WARNING: *Explosion hazard for hazardous locations. Do not connect or disconnect any cabling while energized.*

8. If using I/O connections, connect the I/O External Cable (EC0214) to the DAQ device. Pin assignments are given in Table 12.

Table 12. I/O External Cable Pin Assignments

Pin No.	Wire Color	Function	Pin No.	Wire Color	Function
1	White	NC*/+24 VDC	7	Blue	Digital Out 0
2	Brown	NC*/0 VDC**	8	Red	Digital Out 1
3	Green	DIO Common	9	Orange	Digital Out 2
4	Yellow	Digital In 0	10	Tan	Analog Ground
5	Gray	Digital In 1	11	Black	Analog Out 1
6	Pink	Digital In 2	12	Violet	Analog Out 2
			-	Bare	Ground

**With Power Supply (EC0205) and Power/IO Splitter (EC0208).*
***User provided power (24 VDC, 120 W), direct connection to the FlowVPX Head.*

Note: *If providing a 24 VDC power source, connect the I/O External Cable (EC0214) directly to the Power and I/O labeled connector on the top of the FlowVPX Head.*

Figure 34. USB Cable (EC0207) to FlowVPX Head

9. Connect the USB cable (EC0207) to the USB communications connector on top of the FlowVPX® Head (Figure 34).
10. Connect the FlowVPX USB cable (EC0207) to a USB port on the computer (Figure 35). Make sure the computer is turned on.

Figure 35. FlowVPX USB cable (EC0207) to computer

11. Plug the FlowVPX location-specific power cable into an approved outlet.

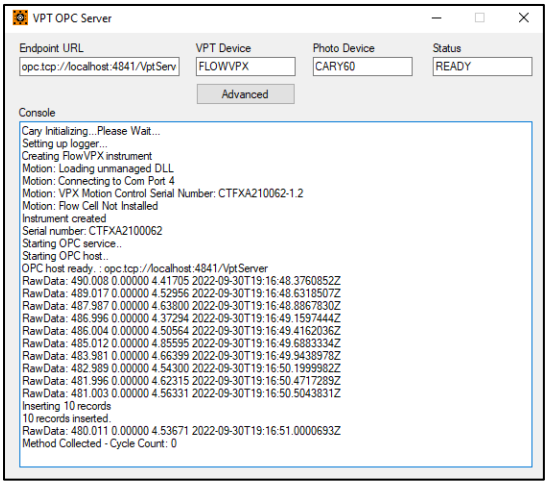
10.2 Loading and Unloading the Flow Cell

10.2.1 Loading the Flow Cell

1. Open VPT OPC Server from the desktop and allow the program to run diagnostics.

Figure 36. VPT OPC Server desktop icon

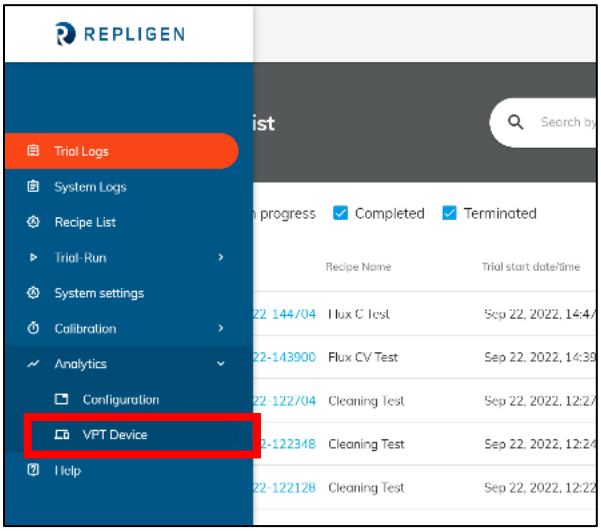
Figure 37. VPT OPC Server



2. Once diagnostics have been completed, open KrosFlo RPM Software and login using proper credentials.

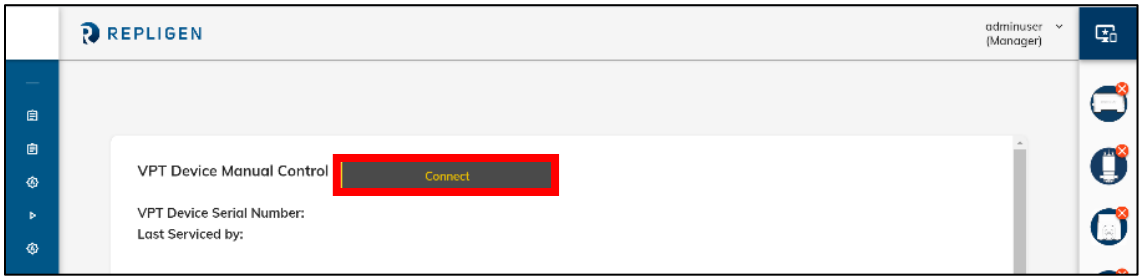
3. Within the software, navigate to the blue-ribbon menu and open the Analytics drop-down menu. Click VPT Device.

Figure 38. Analytics menu within navigation bar



4. Click Connect to establish communication between KrosFlo RPM and the VPT Device.

Figure 39. Connect VPT device to software

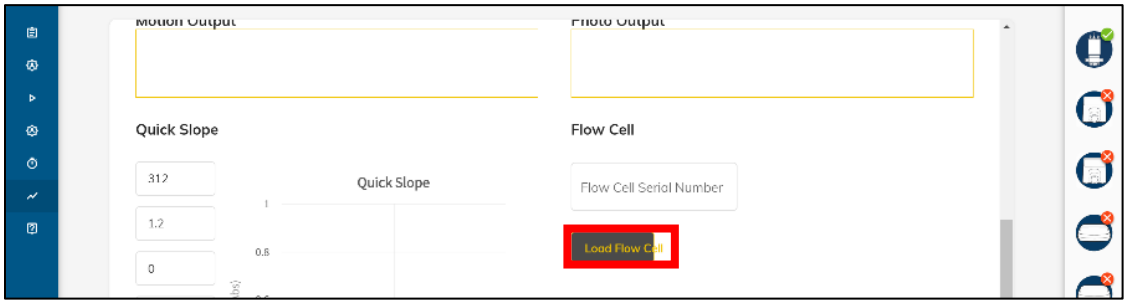


5. After clicking Connect, ensure that the serial number from the VPT device matches the serial number found by KrosFlo RPM Software (Figure 40).

Figure 40. VPT Device Serial Number

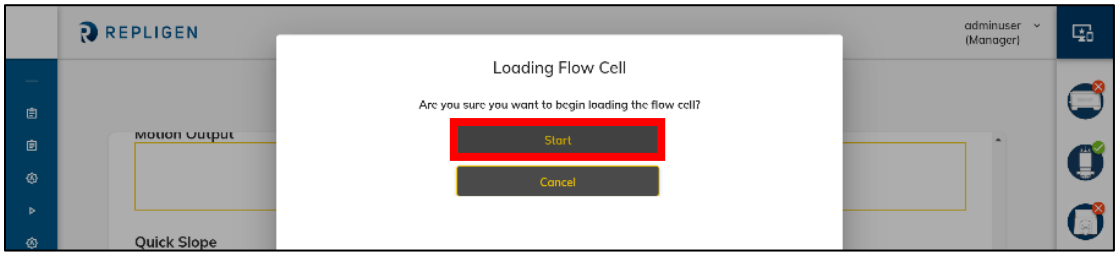
6. Scroll to Flow Cell and click Load Flow Cell.

Figure 41. Load Flow Cell button



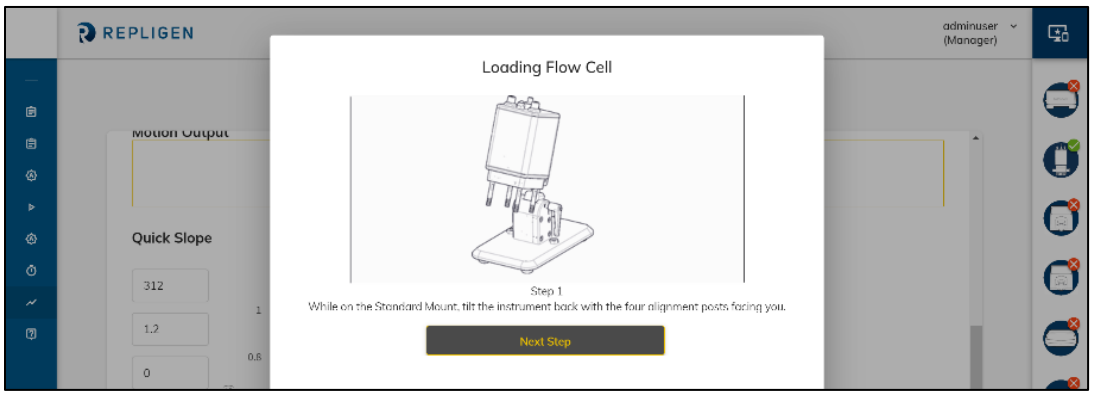
7. Click Start when the Loading Flow Cell pop-up window appears.

Figure 42. Loading Flow Cell Start button



8. Follow the on-screen instructions and animations to load a flow cell.

Figure 43. Loading Flow Cell instructions

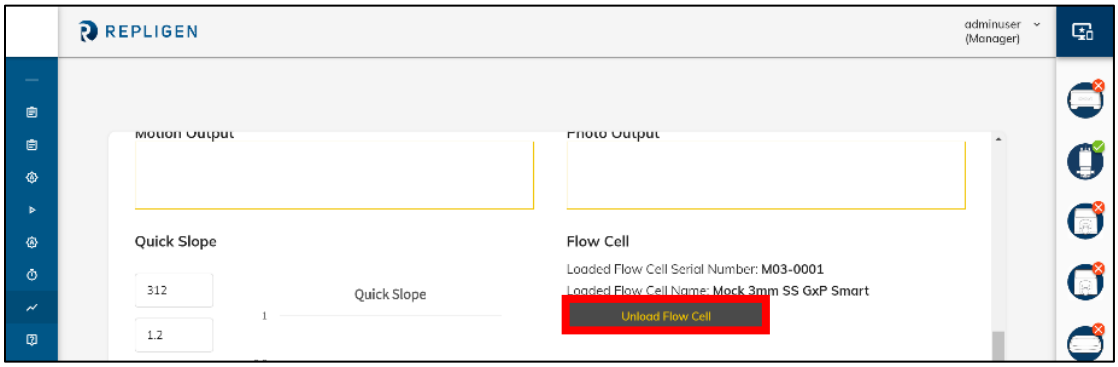


9. Upon completing the loading of the flow cell, the pop-up window will automatically close and return to the previous VPT Device menu. The serial number and flow cell name will automatically populate under the Loaded Flow Cell Serial Number and Loaded Flow Cell Name fields, respectively. A new option to Unload Flow Cell will also appear.

10.2.2 Unloading the Flow Cell

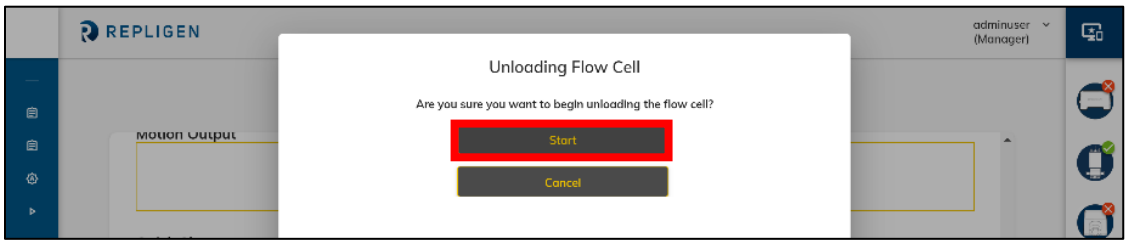
1. To unload the flow cell, click Unload Flow Cell from the VPT Device Menu.

Figure 44. Unload Flow Cell button



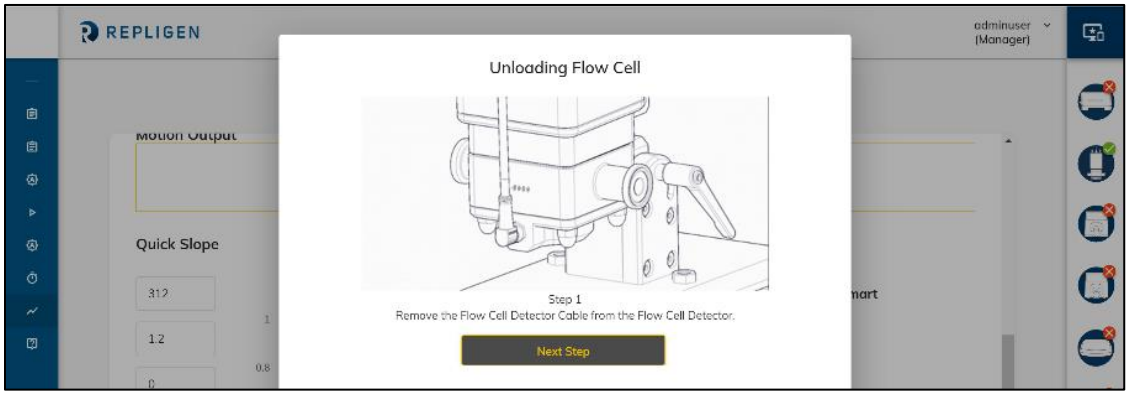
2. Click Start when the Unloading Flow Cell pop-up appears.

Figure 45. Unloading Flow Cell Start button



3. Follow the on-screen instructions and animations to unload a flow cell.

Figure 46. Unloading Flow Cell instructions



4. Upon completion of unloading the flow cell, the pop-up window will automatically close and return to the previous VPT Device menu. The serial number and flow cell name will be removed automatically.

11. Software

The KrosFlo FS-15 RPM System is controlled using software that can be installed either on the provided tablet or on a computer provided by the customer. The provided tablet is fully unlocked to the end user.

The system requires internet access for the setup process and for subsequent software and firmware updates. Internet access is not required during routine operation.

11.1 VPT OPC Server

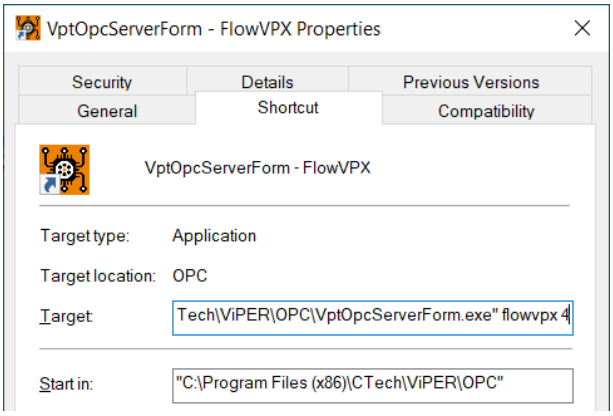
During TFF operation, VPT Devices operate through the RPM software and FS-15 firmware. The VPT OPC Server application must also be running in order to operate the VPT device during TFF operation.

Figure 47. VPT OPC Server desktop icon

To streamline VPT OPC Server startup for operation of the RPM System, follow these steps. Steps 1–4 only need to be performed once.

1. Navigate to C:\Program Files (x86)\CTech\ViPER\OPC
2. Right-click on **VptOpcServerForm.exe** and choose Send to > Desktop.
3. On the computer desktop, right-click the new shortcut and select Properties.
4. In the Target field, add “flowvpx #” where “#” represents the COM port number of the FlowVPX connection (Figure 48).

Figure 48. VPT OPC Server Application Properties—Example



5. Before starting RPM, double-click the shortcut to launch VPT OPC Server. The application should then connect to the Cary 60 and initialize the device. It is recommended to wait for VPT OPC Server to indicate “READY” before launching the RPM software.

VPT devices require CTech™ ViPER® ANLYTX software for system maintenance procedures. Please contact Repligen Customer Service to ensure the correct firmware and software are installed prior to operation.

12. Tubing

12.1 Tubing Guidelines

The KrosFlo FS-15 System is designed to accommodate high-pressure applications up to pressures of 4 bar (58 PSI) with use of the specified ProConnex flow paths. To ensure safe operation, it is important to adhere to the following guidelines:

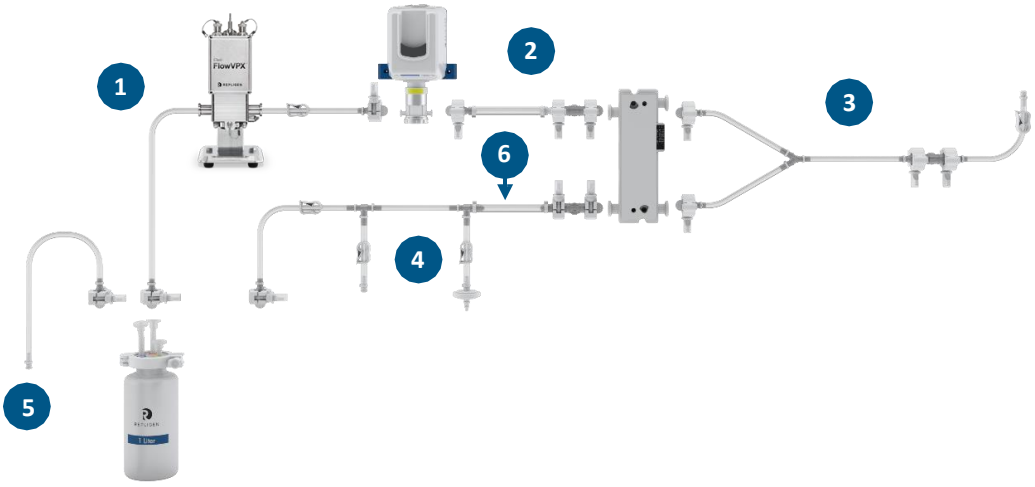
- Install only tube sets designed for high-pressure applications.
- Remove all end caps and/or terminal plugs prior to making connections.
- To minimize unintended air ingress or fluid leakage, securely fasten each connection, being sure to fully seat gaskets.
- Verify the flow path is correctly oriented through the base pump, as indicated by the directional arrow on the pump head.
- To optimize dip-tube configurations, connect each tube set to the designated port. The ports are color coded for clarity.
- ProConnex® tube sets are designed and intended for single use only. Repeat use is at the discretion of the end user.
- For custom ProConnex Flow Path configurations, contact your local Repligen representative.

12.2 Tubing Installation

The following diagram depicts the standard flow path (STUBEGN16315N) for the KrosFlo FS-15 System for illustrative purposes (Figure 49). Each FS System standard flow path contains five (5) sets of tubing engineered for high pressure applications up to 4 bar (58 psi). The five sets of tubing correspond to specific installation locations and should always be installed as recommended in this set-up guide.

For guidance on flow path construction with the FlowVPX device integrated, please contact your Repligen analytical representative.

Figure 49. FS-15 tube set



#	Description
1	Feed tube set
2	Reinforced feed tube set
3	Permeate tube set
4	Retentate tube set
5	Auxiliary tube set
6	Recommended location of ABV

12.3 Feed Tube Set

This tube set connects the reservoir vessel to the base pump.

1. Connect one end of the feed tube set to the base pump inlet and secure with a clamp and gasket.

2. Connect the other end of the feed tube to the outlet port on the reservoir vessel cap (blue connection) and secure with a clamp and gasket.

12.4 Reinforced Feed Tube Set

This tube set is one of two reinforced flow path sections required for high-pressure operation. Repligen recommends that the pressure transducers be located nearest the cassette filter holder for the most accurate representation of cassette pressure profile.

1. Connect the tubing (pressure transducer end) to the cassette Filter Plate Insert (FPI) inlet and secure it with a clamp and gasket.
2. Connect the remaining end to the base pump outlet and secure with clamp and gasket.

12.5 Permeate Tube Set

The permeate tube set connects to the two permeate ports from the filter plate insert and is designed with an open terminal end to allow the end user to adapt it to their application.

1. Connect the two manifold ends to the corresponding permeate ports of the FPI and secure with a clamp and gasket.
2. Direct the open end of the permeate tubing to the waste stream collection vessel, drain, or outlet.

12.6 Retentate Tube Set

The retentate tube set contains the retentate pressure transducer, auxiliary port, and air inlet port for air integrity testing of membranes. This tube set also contains a section of reinforced tubing critical for proper Automatic Backpressure Valve (ABV) placement and operation.

1. Lay the retentate tube set on the lab bench in front of the system, being careful to align the auxiliary port and air inlet port facing outward toward operator. This recommended orientation allows easier access to these ports, but other orientations may be used, as needed.
2. Connect the tubing end containing the inline pressure transducer to the retentate outlet of the FPI and secure with a clamp and gasket.
3. Secure the remaining end of the retentate tube set to the corresponding inlet port of the reservoir vessel cap (orange connection) with a clamp and gasket.
4. Install the reinforced tubing into the ABV. Secure the ABV to the countertop in a position that allows the reinforced retentate tubing section to be inserted into the ABV without pinching or excessive bending.

12.7 Auxiliary Tube Set

The auxiliary tube set is provided for use with an auxiliary pump to transfer process fluids (additional feed, buffer, water, etc.) from an external source to the reservoir vessel. The tubing is designed with one open terminal end to allow end user-specified adaptation.

1. Connect the sanitary fitting to the corresponding buffer port of the reservoir vessel cap (yellow connection) with clamp and gasket.

13. Basic Concepts of Tangential Flow Filtration (TFF)

13.1 Introduction

Filter membranes differentiate components based on size: components larger than the membrane pore are held back by the membrane, while smaller components pass through the membrane structure along with the permeate. Repligen's hollow fiber TFF modules are designed for pressure-driven applications, though there are other methods for driving the separation process.

Tangential Flow Filtration is an efficient way to separate streams that would quickly become plugged if processed by dead-end filtration techniques. Most of the process fluid flows along the membrane surface, rather than passing through the membrane structure. Fluid is pumped at a relatively high velocity parallel to the membrane surface.

Except for water treatment applications, only a small percentage of the tangential flow along the membrane surface ends up as permeate. In most cell and particle separations, only 1–5% of the inlet flow to the membrane device becomes permeate. The remaining 95–99% exits the membrane device as retentate. The retentate is recirculated back to the process reservoir and the module inlet so that another 1–5% can be removed as permeate. This recirculation process continues in rapid succession, generating a significant and continuous permeation rate.

Continuous filtration flow may result in a buildup of retained material on the membrane's inner surface, which can accumulate into a cake layer instead of being carried away by the sweeping action of the recirculation fluid. This cake layer becomes a membrane barrier, reducing the functional size of the membrane pore and affecting module performance.

Caking is influenced by several fluid variables, including degree of solvation, concentration and nature of the solids and solutes, fluid temperature, the solution's velocity along the membrane, and TMP. Controlling this phenomenon by ensuring adequate fluid velocity at the liquid-membrane wall interface will maximize flux, solute passage, and optimize process parameters. Fluid velocity is controlled by the pumping rate. Pumping rate depends on the filter module and shear rate considerations. Typically, a shear rate of 12000 s^{-1} is used for filtration applications and up to 4000 s^{-1} is used for perfusion applications. However, certain applications work well at reduced rates while others may require rates that are significantly higher. These are the considerations that the user usually investigates during Research and Development prior to moving to Pilot phase for their applications.

13.2 Concentration

Concentration is the reduction of the initial sample volume to a lower sample volume. For example, if the process volume is 10 L and needs to be concentrated to 10X, then the final sample volume will be 1 L. The opposite would be a dilution, where the initial sample volume is increased to the final sample volume through the addition of buffer or other medium.

The in-line variable pathlength technology (VPT) spectrophotometer monitors concentration directly in the flow path using absorbance spectroscopy. The VPT device uses the Beer-Lambert law, $A = \varepsilon c l$, to measure the absorbance *A* at various pathlengths *l*, and then calculate concentration *c* based on the given extinction coefficient ε. The concentration value is communicated to the TFF system in real time during the process, allowing the system to recognize when the sample has reached the desired concentration.

13.3 Diafiltration

Diafiltration is the washing of cells, cell debris, virus, precipitates, proteins, and other materials. This is often done as an efficient method of buffer exchange, for instance. Diafiltration is measured in terms of how many washes the process volume has undergone. If the process volume is 10 L and needs to be washed 5 times, then 50 L of diafiltration buffer must wash through the process volume.

The TFF system's Diafiltration function relies upon feedback from both the Feed and Permeate Scales and the VPT instrument to monitor concentration. The TFF system will add buffer to maintain the concentration as measured by the VPT instrument. Once the desired weight is reached on the Permeate Scale—which would indicate that the desired number of Diafiltration Volumes have washed through the process volume—the TFF system will know that the process volume has been washed the correct number of times.

14. Troubleshooting

Table 13. Troubleshooting

Symptom	Diagnosis	Remedy
Hardware does not connect to software	Connection cable may be loose or system did not recognize connections properly.	• Ensure all connections to the Component Communication Cable are secure. • Toggle the USB connection to the PC/tablet and the FS-15 main pump power switch.
Pressure Sensor readings are wrong (either -9.9 psi or >35 psi when no pressure is on them)	Pressure sensor octopus cable not functioning or pressure sensor broken	• Check that the sensors are properly tared. • Check sensor calibration. • Replace pressure sensor and/or octopus cable.
Scale not reading properly	Refer to manufacturer's scale manual.	Refer to manufacturer's scale manual.
Main Pump or Aux Pump not working correctly	Refer to pump manufacturer's manual, troubleshooting section.	Refer to pump manufacturer's manual, troubleshooting section.
Process ending early or late in the DV or CF auto modes	Input for the holdup volumes is wrong	Enter the correct feed holdup and permeate holdup volumes, and select if they are empty or full when starting the process.
Process ending early when using the Conductivity or UV sensors (fixed pathlength sensors for auto modes)	Sensor not full of proper liquid	Conductivity sensor should be filled with same buffer that sample is in when starting the process. UV sensor should be zeroed with the same buffer sample is in.
Concentration reading not consistent with off-line measurements	Process fluid not homogenic	Ensure concentration vessel is properly mixed; recommendation is using a magnetic mixer or stir bar in the feed tank when possible.

For further Technical Assistance, please contact Repligen at analytics-support@repligen.com or (908) 707-1009.

15. Index

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