KrosFlo® KR2i/KMPi TFF Systems

User Guide

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Abbreviations

ABV	Automatic Backpressure Valve
Aux	Auxiliary
CF	Constant Feed
DV	Diafiltration Volume
FS	Flat Sheet
HF	Hollow Fiber
kg	kilogram
L	liter
LCD	Liquid-crystal display
LPM	Liter per minute
mL	milliliter
NWP	Normalized Water Permeability
Pf	Feed Pressure
PPE	Personal Protective Equipment
Pp	Permeate Pressure
Pr	Retentate Pressure
R&D	Research and Development
Temp	Temperature
TFF	Tangential Flow Filtration
TMP	Transmembrane Pressure
UV	Ultraviolet

1. Introduction

This User Guide provides detailed instructions for the set up and operation of the KrosFlo® KR2i and KMPi Tangential Flow Filtration (TFF) Systems and auxiliary components. Included are descriptions of potential modes of operation and basic concepts of tangential flow filtration. For questions and further information, please contact your Repligen representative.

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

Table 2. Safety Precautions

Symbol		Description
Caution		Risk of danger. Consult Operating Instructions for nature of hazard and corrective actions. Potentially hazardous situation which, if not avoided, may result in property/equipment damage
Caution		Risk of crushing. Keep fingers away from rotor while pump is in operation. Stop pump before loading or unloading tubing
Caution		Hot surface. Do not touch
Caution		Risk of electric shock, consult Operating Instructions for nature of hazard and corrective actions
Safety Alert Symbol		Hazard to personnel is present, the SAS is omitted when the hazard is related to property/equipment damage only
Danger		Imminently hazardous situation which, if not avoided, will result in death or serious injury
Warning		Pay attention to the magnetic forces when handling the magnetic levitating centrifugal pump head. Avoid other magnets or metal parts as contamination from physical damage or cracks may arise from the magnetic attraction. Specifically pay attention to the magnetic forces when handling two pump heads at the same time

Table 3. Instrument Safety Labels

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		Remove power from the pump before attempting any maintenance.
Warning		Tubing breakage may result in fluid being sprayed from pump. Use appropriate measures to protect operator and equipment Turn drive off before removing or installing tubes Fingers or loose clothing could get caught in drive mechanism
Caution		Power must be turned off before connecting the external remote-control cable to prevent damage to the drive 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 No foreign matter should be allowed under the gasket on the back of the front plate or under the heads of the screws. Failure to observe this precaution may result in leakage during washdown of the drive
Caution		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		UV Radiation Hazard. Protect Eyes & Skin from Exposure
Caution		Hot Surface: Do not touch.
Caution		Automated Backpressure Valve (ABV) contains moving parts. Keep fingers away from ABV during operation.
Warning		Wear standard laboratory PPE.

Environmental Protection

Waste electrical products should not be disposed of with household waste. Please recycle where facilities exist. Check with your local authority or retailer for recycling advice.

3. Product Description

The KrosFlo KR2i and KMPi TFF Systems enable full automation of both lab-scale (2 mL – 15 L) and large-scale (100 mL – 500 L) ultrafiltration/diafilitration (UF/DF) processes. The menu-driven KF Comm 2 Software monitors and controls runs.

4. Setup and Operation

Experienced user may opt to follow the instructions below to set up the system; however, Repligen strongly recommends that setup and basic training be performed by Repligen service personnel.

4.1 Basic Setup

1. Mount the TFF System on a flat, horizontal surface with no more than two pump heads attached (Section 6).
2. Connect both octopus cables to the back of the TFF System.
3. Connect up to three pressure transducers to the pressure transducer octopus cable ports as suitable for application.
4. Connect one (if using KR2i) or up to two (if using KMPi) Automatic Backpressure Valves (ABVs) to the Auxiliary Component Octopus Cable Valve 1 (Valve for KR2i) and/or Valve 2 (Section 7.3).
5. Connect power cable to the TFF System.
6. Follow guidelines to determine which auxiliary components are required to operate specific process modes for manual, semi-automated, and automated processes (Section 4.2). If using auxiliary pump(s), configure pump(s) before starting application (Section 7.2).
7. Connect ProConnex® Flow Paths to system.
8. Set low- and high-pressure alarms as required by the process conditions.
9. Input Concentration Factor/Diafiltration Volume (CF/DV) set points into the software to start application.

4.2 Process Mode Configurations

The KrosFlo TFF System can be configured to perform several functions described as process modes (Table 4). The KF Comm 2 Software controls all auxiliary components based on process mode and user-defined variables. All process modes are composed of sequences of concentration (reducing volume of process solution) and diafiltration (washing permeable molecules from the process solution) functions.

The level of automation and the data outputs provided may drive the decision to use a specific mode. Not all auxiliary components are required for all modes. Auxiliary components are connected to the software via the KR2i/KMPi pump using the provided auxiliary component (octopus) cable (Figure 31, Figure 32).

Refer to the KF Comm 2 Software User Guide for specific details regarding operation of the software.

Table 4. Process Mode Abbreviations

Abbreviation	Description
C	Concentration
CD	Concentration/Diafiltration
CDC	Concentration/Diafiltration/Concentration
CFC	Constant Feed Concentration
CDDC	Concentration/Diafiltration/Diafiltration/Concentration
CDCD	Concentration/Diafiltration/Concentration/Diafiltration
D	Diafiltration
N/A	Cleaning
Flux C	Flux concentration
Flux CV	Flux constant volume
N/A	Flushing
NWP	Normalized water permeability
N/A	Vacuum

Table 5. Process Mode Configurations

	Process Mode		C	C, CD, CDC, CFC	CFC/D/C, CDDC, CDCD
Capability	**Process Data**		Pressure	Pressure, flowrate, permeate weight, and feed weight	Pressure, flowrate, permeate weight, feed weight, conductivity, temperature, and UV
	Automation		+	++	++++
Component/Description			**Setup 1**	**Setup 2**	**Setup 3**
	KF Comm 2 Software	Controls system	●	●	●
	Base Pump	Recirculates feed through module and sends retentate back to feed vessel	●	●	●
	Feed Scale	Weighs volume in feed reservoir to monitor concentration and diafiltration functions		●	●
	Back pressure control valve	Controls TMP, permeate, pressure	●	●	●
	Permeate Scale	Weighs volume in permeate reservoir to monitor concentration and diafiltration functions	●	●	●
	Auxiliary pump 1	Replenishes feed reservoir volume during diafiltration or fed batch function		●	●
	Auxiliary pump 2	Controls permeate rate for MF applications or replenishes feed reservoir during second diafiltration function			●
	Konduit	Monitors conductivity, temperature, and UV; can signal the end of a process mode.			●
	Sensors (conductivity, UV, temperature)	Measure conductivity, UV, and temperature			●

Table 6. Auxiliary Component Cable Usage

Auxiliary Components	Octupus Cable Ports
Pumps	Aux pump 1 and Aux pump 2
Scales	Feed or permeate scale port
Konduit	UV/Aux and Conductivity/Temp ports

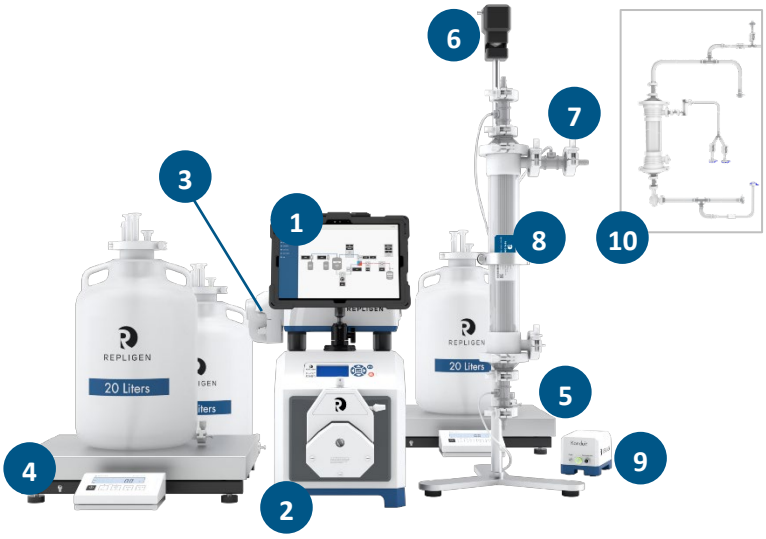
4.3 Process Modes

The KrosFlo KR2i and KMPi TFF Systems achieve an unparalleled combination of integration, configurability, and automation through modular, plug-and-play hardware. All components, either directly or indirectly, connect to the main peristaltic pump, which then communicates with the KF Comm 2 Software for control and monitoring. The systems utilize several user-defined set-points to run complex application processes with numerous built-in safety alarms and stops. A minimal number of components can be configured for simple applications such as concentration (C) or diafiltration (D). Additional plug-and-play components can be added for more complex processes such as those including multiple concentration and diafiltration steps.

Figure 1. KR2i Complete System

1. KF Comm 2 Software
2. Base pump
3. Auxiliary pump 1
4. Feed scale
5. Permeate scale
6. Automatic Back Pressure Valve (ABV)
7. Conductivity and/or UV sensor
8. Hollow fiber filter
9. Konduit
10. ProConnex flow path (example)

Figure 2. KMPi Complete System



1. KF Comm 2 Software
2. Base pump
3. Auxiliary pump 1
4. Feed scale
5. Permeate scale
6. Automatic Back Pressure Valve (ABV)
7. Conductivity and/or UV sensor
8. Hollow fiber filter
9. Konduit
10. ProConnex flow path (example)

4.3.1 Manual Mode

Manual mode is used to ensure the main pump and auxiliary components are operational and connected or to run the system without automation. From the software, users can start/stop the main pump and auxiliary pump(s), tare scales, calibrate pressure sensors, change tubing sizes, and start/stop manual valve control. Any or all components can be operated in manual mode. The only required components for manual mode are the system base pumps and the KF Comm 2 Software.

4.3.2 C Mode

C mode can be performed using the following components (numbers in parentheses refer to the legends in Figure 1 and Figure 2):

a. KF Comm 2 Software (1)
b. Base pump (2)
c. Feed scale (4)
d. Permeate scale (5)
e. Automatic Backpressure Valve (6)
f. Hollow fiber filter (8)
g. ProConnex flow path (10)

The feed scale (4) can be omitted if the starting feed volume is putt into the software. In C mode, the system will reduce the volume in the feed vessel based on the permeate weight chosen (Table 5, Setup 1).

Table 7. C Mode Example

Step	Volumes and Factor[1]
Concentration (C)	
Feed weight (kg)	32
Concentration factor (X)	2
Feed weight after concentration (kg)	16
Permeate weight after concentration (kg)	16

[1]For simplicity purposes, assumes zero hold-up volume.

4.3.3 D, C, CD, CDC, CFC Modes

D, C, CD, CDC, CFC modes utilize the following components (numbers in parentheses refer to the legends in Figure 1 and Figure 2):

a. KF Comm 2 Software (1)
b. Base pump (2)
c. Auxiliary pump (3)
d. Feed scale (4)
e. Permeate scale (5)
f. Automatic Backpressure Valve (6)
g. Hollow fiber filter (8)
h. ProConnex flow path (10)

The combination of concentration and diafiltration with or without constant feed is determined based on process requirements (Table 5, Setup 2).

Table 8. CDC Mode Example

Steps	Volumes and Factors[1]
Concentration 1 (C)	
Feed weight (kg)	20
Concentration factor 1 (X)	10
Feed weight after concentration 1 (kg)	2
Permeate weight after concentration 1 (kg)	18
Diafiltration (D)	
Diafiltration volumes (X)	7 (2 kg x 7 = 14 kg total)
Feed weight (kg)	2
Permeate weight after diafiltration (kg)	32
Concentration 2 (C)	
Concentration factor 2 (X)	2
Feed weight after concentration 2	1
Permeate weight after concentration 2 (kg)	33

[1]For simplicity purposes, assumes zero hold-up volume; permeate weights are cumulative.

Setting up CFC Mode

Constant feed concentration (CFC) is used only if the feed volume exceeds the capacity of the feed vessel. The concentration process is then performed in fed-batch mode. The extra feed volume can be pumped into the primary feed vessel using Auxiliary pump 1. The software adjusts the flow rate of the auxiliary pump to maintain the volume in the primary feed vessel. If also performing a diafiltration, the buffer would need to be pumped with Auxiliary pump 2 (not shown).

Figure 3. Feed Reservoir Port Orientation for Vacuum Draw (No Vent)

Alternatively, an additional feed vessel may be set up to draw a vacuum. To create a vacuum, on the primary feed reservoir, set up four ports (Figure 3) to draw excess feed into the primary reservoir from the additional feed vessel:

1. **Feed line to filter:** Connect tubing from this line through pump head to filter feed port.
2. **Retentate line from filter:** Connect tubing from filter retentate port to this line.
3. **Buffer (if performing diafiltration):** Connect through auxiliary pump 1 to diafiltration buffer reservoir.

4. **Vacuum feed:** Connect to additional feed reservoir.

Install a vent on both the additional feed reservoir and buffer reservoir, if performing diafiltration. Ensure that the diafiltration pump head is closed on the tubing between the diafiltration buffer and the feed reservoir. The vacuum feed line will pull the contents of the extra feed reservoir during the concentration function. When the concentration set point is reached the system will switch to diafiltration or concentration mode.

For constant feed (fed-batch) processes, line c should be used for both buffer addition AND constant feed. This is done with the addition of a branched Y- or T-fitting on line c. Line d should be used as a vent to avoid bottle collapse during concentration.

Table 9. CFC Mode Example

Step	Volumes and Factor[1]
Constant feed concentration (CFC)	
Feed weight in primary vessel (kg)	20
Additional feed weight in secondary vessel (kg)	15
Concentration factor (X)	10
Feed weight after Concentration (kg)	3.5
Permeate weight (kg)	31.5

[1]For simplicity purposes, assumes zero hold-up volume.

4.3.4 CFC/D/C, CDDC, CDCD modes

CFC/D/C, CDDC, CDCD modes utilize the following components (numbers in parentheses refer to the legend in Figure 1 and Figure 2):

a. KF Comm 2 Software (1)
b. Base pump (2)
c. Auxiliary pump X2 (3)
d. Feed scale (4)
e. Permeate scale (5)
f. Automatic Backpressure Valve (6)
g. Conductivity and/or UV sensor (7)
h. Hollow fiber filter (8)
i. Konduit (9)
j. ProConnex flow path (10)
k. Auxiliary pump 2 (not shown)

In modes requiring diafiltrations of two buffers, auxiliary pump 2 functions as diafiltration pump 2. Each buffer reservoir leads into the feed reservoir, via auxiliary pump 1 and auxiliary pump 2 (Table 5, Setup 3).

Table 10. CDDC Mode Example

Steps	Volumes and Factors
Concentration 1 (C)	
Feed weight (kg)	20
Concentration factor 1 (X)	10
Feed weight after Concentration 1 (kg)	2
Permeate weight after Concentration 1 (kg)	18
Diafiltration 1 (D)	
Diafiltration volumes (kg)	7 (2 kg x 7 = 14 kg total)
Feed weight after Diafiltration 1 (kg)	2
Permeate weight after Diafiltration 1 (kg)	32
Diafiltration 2 (D)	
Diafiltration volumes (kg)	8 (2 kg x 8 = 16 kg total)
Feed weight after Diafiltration 2 (kg)	2
Permeate weight after Diafiltration 2 (kg)	48
Concentration 2 (C)	
Concentration factor 2 (X)	2
Feed weight after Concentration 2 (kg)	1
Permeate weight after 2 (kg)	49

[1]For simplicity purposes, assumes zero hold-up volume; permeate weights are cumulative.

In addition to the processing modes, KrosFlo TFF Systems provide several modes used to set up and breakdown the system. Flushing, NWP (normalized water permeability), cleaning, and flux excursion modes are described in the KF Comm 2 User Guide.

5. Base Pumps

Base pumps are controlled through the KF Comm 2 Software. The LCD screen on the pump face contains arrows and an enter key that are disabled. The alarm acknowledgement button silences audio alarms. The Start/Pause button functions as an emergency stop. Using this emergency stop ends the process, which will not be recoverable.

5.1 Keypad

The following information is provided to familiarize the user with the information displayed on both the KR2i (not shown) and KMPi (Figure 4) pumps.

1. **Start/Pause** – **Emergency stop only (ends process)**
2. **Alarm Acknowledgement** – Silence alarm
3. **Directional Arrows** – Disabled
4. **Enter** – Disabled

Figure 4. KMPi Base Pump Keypad

5.2 Main Screen

The main screen display provides useful information to the end user.

- **Current Process Mode** –displays process mode in use
- **Pressure Readings** – The current values read by any connected pressure transducers.
  - Feed pressure (*Pf*)
  - Permeate pressure (*Pp*)
  - Retentate pressure (*Pr*)
  - Transmembrane pressure (TMP); Average of feed and retentate pressures minus permeate pressure:

$$\left((Pf + Pr) \div 2\right) - Pp$$

6. Pump Heads

The Easy-Load and High-Performance Pump Heads are designed to be used with the TFF System peristaltic pumps. The pump heads accept several tubing sizes for a wide range of flow rates, and the unique designs and automatic tubing retention allows for quick tubing changes.

6.1 KR2i Pump Head Specifications and Installation

Table 11. KR2i Pump Head Specifications

Part Number	Roller and Bearing Material	Number of Rollers	Tubing Material	MasterFlex® L/S® Tubing
ACR2-H3I-01R	Stainless Steel	3	Norprene, Pharmed, Tygon, Pharmapure[1]	L/S® 13, 14, 16, 25, 17, 18

Typical Flow, Pressure and Vacuum Data—3 Roller Pumps						
MasterFlex® L/S® Tubing	Flow Rate Discharge Pressure				Vacuum @ 600 rpm in (mm) Hg	Suction lift @ 600 rpm ft (m) H20
	@ 1 rpm mL/Rev	@ 600 rpm mL/min	Continuous psig (bar)	Intermittent psig (bar)		
L/S® 13	0.06	36	25 (1.7)	40 (2.7)	26 (660)	29 (8.8)
L/S® 14	0.22	130	25 (1.7)	40 (2.7)	26 (660)	29 (8.8)
L/S® 16	0.8	480	25 (1.7)	40 (2.7)	26 (660)	29 (8.8)
L/S® 25	1.7	1000	20 (1.4)	35 (2.4)	26 (660)	29 (8.8)
L/S® 17	2.8	1700	15 (1.0)	20 (1.4)	20 (510)	22 (6.7)
L/S® 18	3.8	2300	10 (0.7)	15 (1.0)	20 (510)	22 (6.7)

Part Number	Roller and Bearing Material	Number of Rollers	Tubing Material	MasterFlex® L/S® Tubing
ACR2-H4I-01N	Stainless Steel	3	Norprene, Pharmed, Tygon, Pharmapure[1]	L/S® 15, 24, 35, 26

[1]Silicone, C-Flex, and Viton values will be lower.

Typical Flow, Pressure and Vacuum Data—3 RollerPumps						
MasterFlex® L/S® Tubing	Flow Rate Discharge Pressure				Vacuum @ 600 rpm in (mm) Hg	Suction lift @ 600 rpm ft (m) H20
	@ 1 rpm mL/Rev	@ 600 rpm mL/min	Continuous psig (bar)	Intermittent psig (bar)		
L/S® 15	1.7	1000	25 (1.7)	30 (2.7)	26 (660)	29 (8.8)
L/S® 24	2.8	1700	25 (1.7)	30 (2.7)	26 (660)	29 (8.8)
L/S® 35	3.8	2300	20 (1.4)	25 (2.4)	26 (660)	29 (8.8)
L/S® 36	4.8	2900	15 (1.0)	20 (1.4)	24 (610)	27 (8.3)
Number of rollers:	3					
Maximum pump speed (rpm):	600					
Maximum torque load—Starting:	400 oz-in (29 kg-cm)					
Maximum torque load—Running:	Up to 180 oz-in (13 kg-cm)					
Housing materials:	Glass-filled polypropylene (PP), polyphenylene sulfide (PPS), nylon (PA)					
Roller materials:	Stainless steel (SS)					
Bearing materials:	Sealed stainless steel					
Rotor materials:	Stainless steel					
Chemical resistance:	Most substances, except strong acids or alkalis, organic solvents or hydrocarbons					
Temperature:	(for continuous duty operation)					
Operating:	32°F to 104°F (0°C to 40°C)					
Storage:	–49°F to 149°F (–45°C to 65°C)					
Humidity:	10% to 90% (non-condensing)					
Altitude:	2000 m or less					
Dimensions (W x H x D):	(Excluding shaft and cosmetic cover)					
Operating:	3.45" x 4.75" x 3.08" (8.8 cm x 12.1 cm x 7.8 cm)					
Open:	3.45" x 5.65" x 3.08" (8.8 cm x 14.4 cm x 7.8 cm)					
Weight:	1.1 lb (0.5 kg)					

[1]Silicone, C-Flex, and Viton values will be lower.

6.1.1 Installation

WARNING: *Stop the pump drive before installing or removing pump head from the drive.*

1. If mounting plate is not attached to the pump drive, attach it using the provided four Phillips head screws (Figure 5).
2. Orient the pump head with its back facing the drive and insert the tang on the pump head shaft into the shaft's slot on the drive. Align the bayonet features on the back of the pump head with the bayonet tabs on the front of the mounting plate (Figure 6). The pump head should be tilted about 30° counterclockwise from the intended installed orientation (Figure 7). Press pump head firmly against the drive and rotate clockwise until no more rotation is possible (Figure 8). The bayonet lock lever will automatically snap toward the back of the pump, locking it to the mounting plate. Remove the pump head from the drive by holding the bayonet lock lever forward while rotating the pump head as far as possible in the counterclockwise direction, then pull the pump head away from the drive to detach it. The actuator lever should be in the far-right position when removing the pump head (Figure 9).

Figure 5. Attaching Mounting Plate to Drive

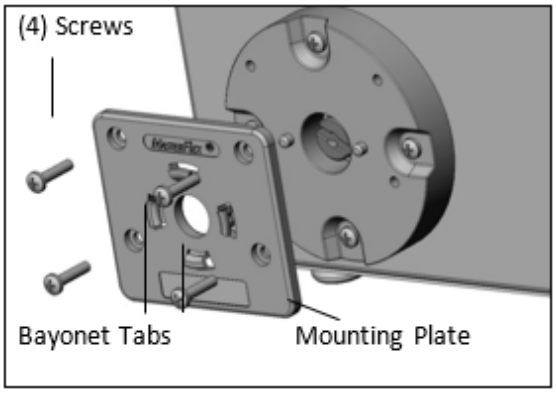


Figure 6. Back of Research II Pump Head

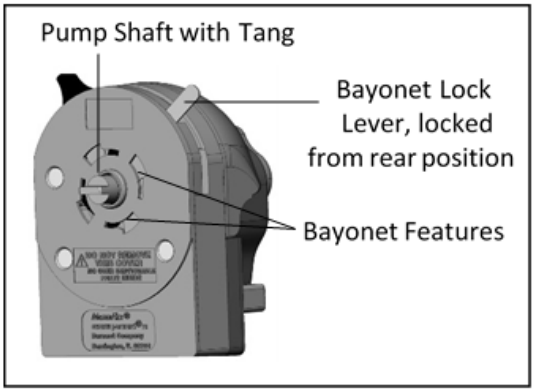


Figure 7. Position for Engaging Bayonet Feature for Horizontal Mounting

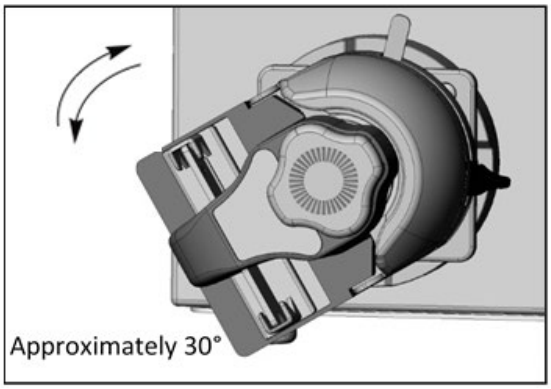


Figure 8. Bayonet Feature Locked in Horizontal Pump Orientation

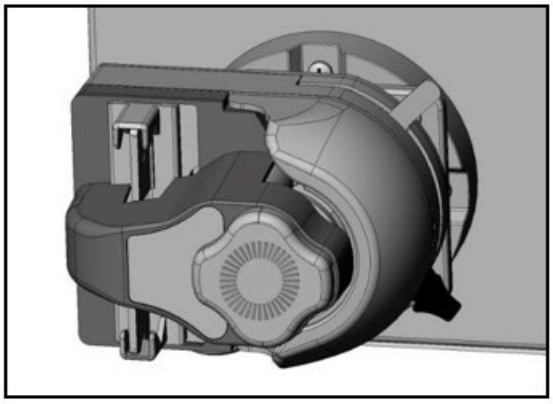


Figure 9. Pump Head in Fully Closed Position

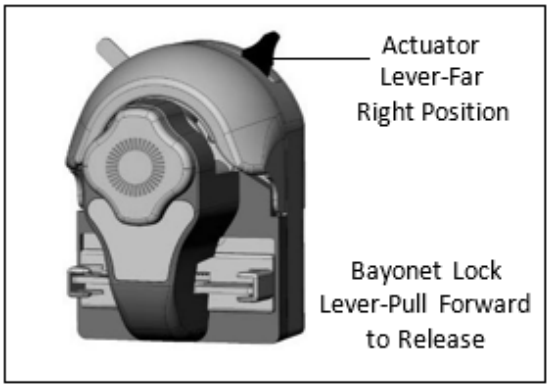
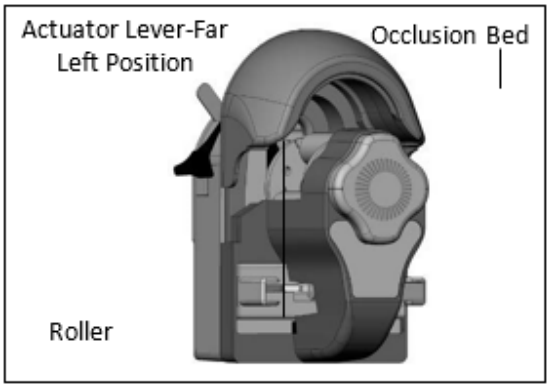


Figure 10. Pump Head in Fully Open Position



6.1.2 KR2i Tubing

WARNING: *Stop the pump drive before installing or removing pump head from the drive.*

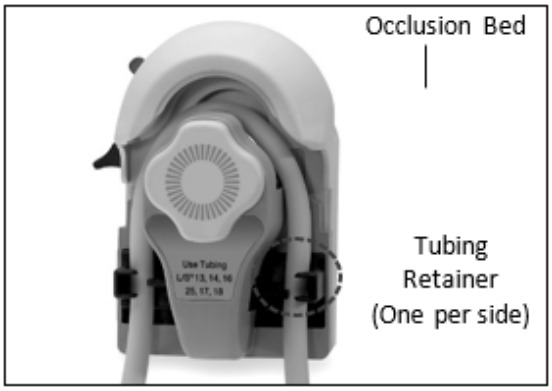
WARNING: *Stop the pump drive before installing or removing tubing from the pump head. To load tubing, open the pump head by moving the actuator lever counterclockwise.*

1. Insert a loop of tubing into one open tubing retainer, between the occlusion bed and the rollers, and into the other tubing retainer (Figure 11). Position the tubing so that it is firmly centered against the rollers. While holding the tubing ends, move the actuator lever back to the far clockwise (right) position (Figure 9). The pump head will automatically grip the tubing. Approximately 5 pounds of force must be applied to the actuator lever to fully close the pump head and place the lever in its locked position (far right position) or to fully open the pump head (far left position).
2. Before unloading tubing from the pump head, first turn off the drive. Open the pump head by moving the actuator lever counterclockwise (left, Figure 10). This will automatically open the tubing retainers, as well as lift the occlusion bed away from the tubing. Pull the tubing away from the pump head.

Note: *It is unnecessary to have an end of the tubing free to load or unload tubing from the pump head. A length of tubing may be loaded into the pump without disconnecting it from adjacent devices.*

Note: *When pump is not being used, store with actuator lever half-way between far left and far right positions.*

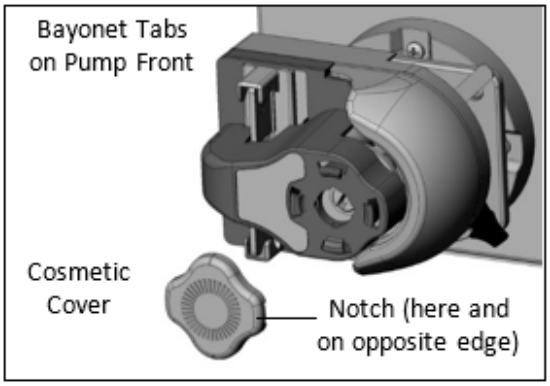
Figure 11. Tubing Path Through Pump Head During Loading



6.1.3 KR2i Multi-Channel

1. Two (2) KrosFlo Research II Pump Heads can be mounted in tandem. Once the mounting plate is attached to the pump drive, no additional mounting hardware is required.
2. Install the first pump head (Section 6.2.1).
3. To install a second pump head, the cosmetic cover must be removed from the first pump head. Grasp the cover by the notches and pull it off (Figure 12).
4. Align the second pump head to the first, as if the first pump head were the drive, and continue to follow pump head mounting instructions (Figure 13).

Figure 12. Removing Cosmetic Cover



Note: *The tubing on the inner pump head(s) can be changed without removing the outer pump head(s) from the drive.*

Figure 13. Engaging Bayonet of Second Pump Head to Bayonet Tabs on the First

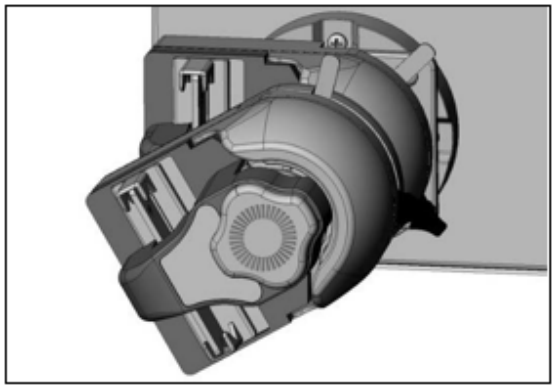
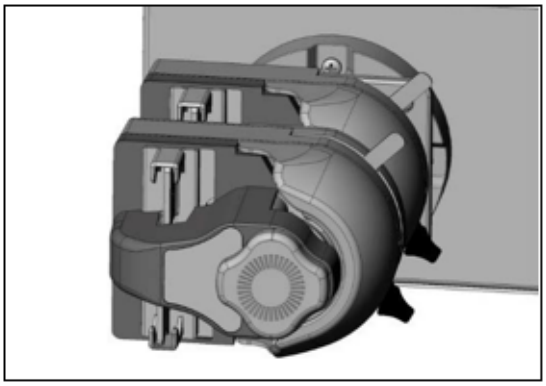


Figure 14. Drive With Both Pump Heads Locked in Position



CAUTION: *Be sure that bayonet features on back of each pump head are fully engaged with bayonet tabs on the mounting plate or adjacent pump head before operating pump drive. Bayonet lock lever will snap back when bayonet features engage completely.*

6.1.4 KR2i Maintenance

No lubrication is required for the KrosFlo Research II Pump Head. Only use a mild detergent solution or 70% isopropyl alcohol to clean the pump head. Do not immerse or use excessive fluid. Pump head requires no maintenance beyond cleaning. There are no user serviceable or replaceable parts inside.

6.2 KMPi Pump Head Specifications and Installation

Table 12. KMPi Pump Head (A) Specifications

Part Number	Roller and Bearing Material	Number of Rollers	Tubing Material	MasterFlex® I/P® Tubing
ACM3-H3S-01N	Stainless Steel	3	Norprene, Pharmed, Tygon, Pharmapure	I/P 26, 73, 82

Typical Flow, Pressure and Vacuum Data—3 Roller Pumps						
I/P Tubing	Flow Rate LPM			mL per revolution	Maximum System Pressure psi (bar)	
	100 rpm	540 rpm	1 - 650 rpm		Continuous	Intermittent
26	0.6	3.3	0.01 - 4.0	6.2	25 (1.7)	40 (2.7)
73	1.2	6.6	0.01 - 8.0	12.3		
82	2	10.8	0.02 - 13.0	20	10 (0.7)	20 (1.4)

	I/P 26, I/P 73	I/P 82
Maximum continuous discharge pressure:	25 psi (1.7 bar)	10 psi (0.7 bar)
Maximum intermittent discharge pressure:	40 psi (2.7 bar)	20 psi (1.4 bar)
Maximum vacuum:	660 mmHg (26 inHg)	610 mmHg (24 inHg)
Ma Maximum suction lift:	8.8 m (29 ft) H20	8.2 m (27 ft) H20
Occlusion:	Adjustable (with knob on top of Pump Head)	
Maximum pump speed:	650 rpm	
Normal torque load-Starting:	up to 13 kg-cm (180 oz-in)	
Normal torque load-Running:	up to 9 kg-cm (120 oz-in)	
Housing materials:	Polysulfone (PSF) or Polyphenylene sulfide (PPS), Polyester, Aluminum, Nylon	
Operating temperature:	0 to 40°C (32 to 104°F)	

Table 13. KMPi Pump Head (B) Specifications

Part Number	Roller and Bearing Material	Number of Rollers	MasterFlex® I/P Tubing
ACM3-PHP-01N	Stainless Steel	3	I/P 70, 88, 89

Typical Flow, Pressure and Vacuum Data—3 Roller Pumps						
I/P Tubing	Flow Rate		Discharge Pressure		Vacuum* @ 600 rpm in (mm) Hg	Suction lift* @ 600 rpm ft (m) H20
	@ 20 rpm L/min	@ 600 rpm mL/min	Continuous psig (bar)	Intermittent psig (bar)		
I/P 70	0.06	8	25 (1.7)	40 (2.7)	26 (660)	29 (8.8)
I/P 88	0.4	13	20 (1.4)	35 (2.4)	26 (660)	29 (8.8)
I/P 89	0.52	17	15 (1.0)	20 (1.4)	24 (610)	27 (8.3)
Occlusion:	Fixed					
Maximum pump speed (rpm):	650					
Nominal torque load-running:	up to 600 oz-in (43 kg-cm)					
Housing materials:	Stainless Steel (SS), polyester (PE) body and tubing bed, polypropylene (PP) knob					
Temperature:						
Operating:	32°F to 104°F (0°C to 40°C)					
Storage:	-40°F to 149°F (-40°C to 65°C)					
Humidity:	5% to 95% (non-condensing)					
Dimensions (W x H x D):						
Operating:	7.5" x 7.0" x 6.0" (191 mm x 178 mm x 152 mm)					
Open:	8.7" x 7.0" x 10.0" (221 mm x 178 mm x 254 mm)					
Weight:	6 lb (3.63 kg)					

6.2.1 Installation

Two types of pump heads are available for the KMPi: Easy-Load (Figure 15) and High-Performance (Figure 16).

Note: *A flat-blade screwdriver is required to complete installation.*

1. Check that tang boot has plastic dampening to prevent damage to the pump shaft.
2. Raise occlusion bed to expose mounting holes for top two short screws of Easy-Load Pump Head.
3. Aim back of pump head toward mounting plate to align pump shaft tang and five screwholes (for Easy-Load Pump Head) or four screw holes (for High-Performance Pump Head).

Note: *Inspect the tang boot after 1,000 hours of operation and replace if necessary.*

4. Insert mounting bolts into the mounting holes through the pump head and into the KMPi mounting plate. On High-Performance Pump Head, use round mounting holes for left side tubing entry and exit, or hexagonal mounting holes for top tubing entry and exit.
5. Secure pump head to mounting plate and KMPi by tightening mounting bolt screws with flat-blade screwdriver.

Figure 15. Components of the Easy-Load Pump Head

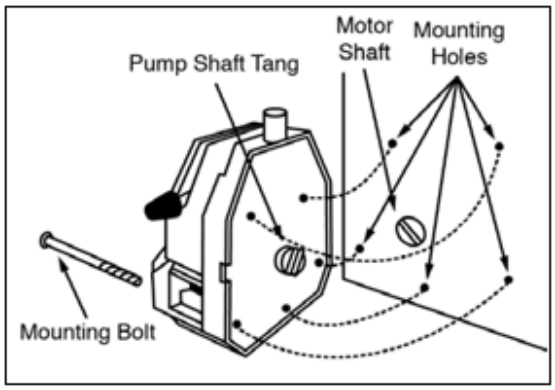
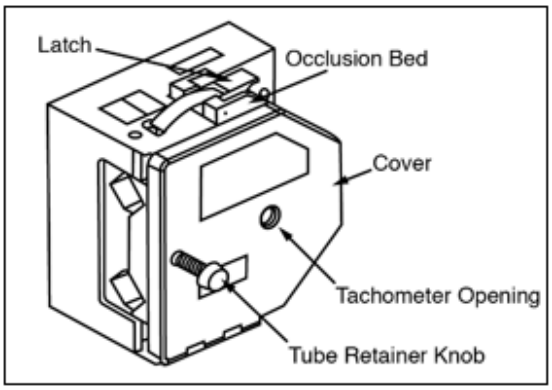


Figure 16. Components of the High-Performance Pump Head



6.2.2 KMPi Tubing

1. Ensure that KMPi is turned off
2. For Easy-Load Pump Head (Figure 17), move KMPi Easy-Load Pump Head lever to the left to open the pump occlusion bed. For High-Performance Pump Head (Figure 18), rotate tubing retainer knob counterclockwise to release retainer, then pull open the cover and lift latch to open occlusion bed.
3. Load the correct tubing into tubing retainers.
4. For Easy-Load Pump Head (Figure 19), move the lever to the right to close the occlusion bed. For High-Performance Pump Head, press occlusion bed against the tubing, snap the latch closed, close cover, and pull tubing snugly around rotor assembly. Finish by tightening tubing retainer by rotating tubing retainer knob clockwise to prevent tubing from moving and run the drive for at least one revolution to break-in tubing (Figure 20). Unlatch the bed from Slot 1 and then relatch using Slot 2.

Figure 17. Loading Tubing into Open Occlusion Bed of Easy-Load Pump Head

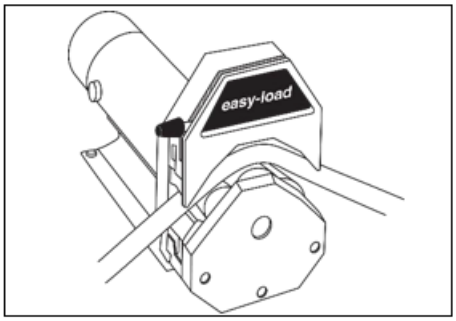


Figure 18. Loading Tubing into Open Occlusion Bed of High-Performance Pump Head

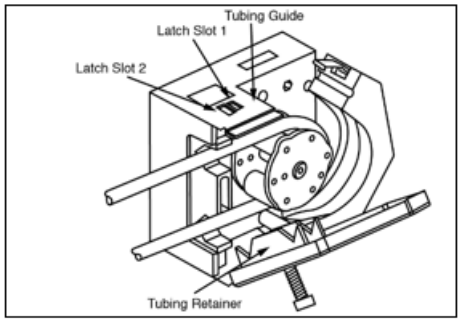


Figure 19. Closing Occlusion Bed of Easy-Load Pump Head

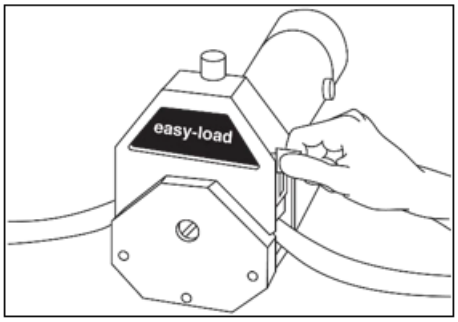
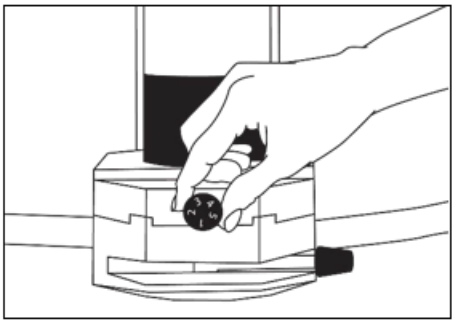


Figure 20. Occlusion Knob on Top of Easy-Load Pump Head



6.2.3 Occlusion Adjustment on KMPi Easy-Load Pump Head

Use knob on top of KMPi Easy-Load Pump Head to adjust occlusion to suit application (Figure 20). Occlusion usually does not need to be readjusted when changing tubing.

- **3** for nominal performance; recommended for most uses
- **4** or **5** for increased pressure/vacuum with reduced tubing life
- **1** or **2** for longer life with less pressure and vacuum

Note: *For optimum performance, turn occlusion knob to **1** after loading—then start drive and adjust knob until pump primes and fluid begins to flow.*

Note: *After operation for some time, the retainer teeth of the Pump Head may scratch or mark the surface of the tubing—this is expected and does not necessarily reduce the tubing quality or life.*

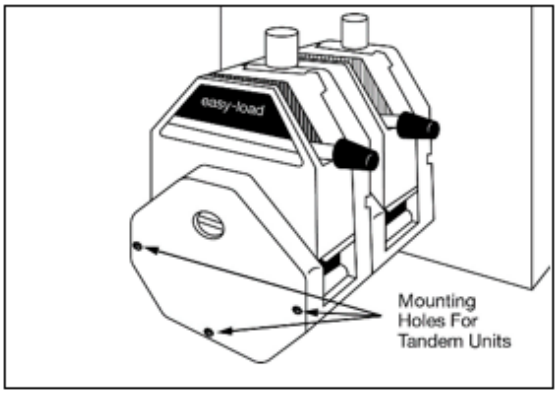
6.2.4 KMPi Multi-Channel

Note: *Do not overtighten screws or wing nuts.*

To mount two KMPi Easy-Load Pump Heads, use the additional mounting hardware that comes withthe purchase of a second set of KMPi Easy-Load Pump Heads. The High-Performance Pump Head is incompatible with Multi-Channel Mounting.

1. Aim the three mounting holes (Figure 21) and pump shaft tang on the back of the second Easy-Load Pump Head towards the front three mounting holes and exposed motor shaft on the front ofthe original Easy-Load Pump Head.
2. Insert threaded rods into three mounting holes through second and original Easy-load PumpHeads, then secure with wing nuts.

Figure 21. Easy-Load Pump Head Mounting Holes for Multi-Channel Mounting



6.2.5 KMPi Maintenance

Use mild detergent with water to clean the pump and rotor assembly for both Easy-Load and High-Performance Pump Heads. Do not immerse or use excessive fluid.

7. Auxiliary Component Setup and Operation

7.1 Auxiliary Scales

The TFF Systems interface with digital scales available in 20, 60, 200, and 600 kg versions. For detailed information on operating scales, refer to product-specific User Guide. Please contact Repligen for additional scale compatibility.

7.1.1 Installation

- Carefully unpack scale from shipping carton
- Place scale on a level surface and adjust the level legs so that all four legs are touching thesurface and leveling bubble is within the circle
- Connect serial adaptor to either Feed Scale or Permeate Scale on the KR2i/KMPi octopus cable.
- In most cases, the scale will boot directly into the weight screen. If not, press the ON/OFFbutton
- For further scale functionality including calibration please refer to the User Guide

7.2 Auxiliary Pumps

The KrosFlo Research 1 (KR1), KrosFlo Junior (KR Jr), and I/P Digital peristaltic pumps can be used with KrosFlo TFF Systems . The KR1 and the I/P auxiliary pumps can be fitted with up to two pump heads. Up to two auxiliary pumps can be connected to the TFF System's Auxiliary Component Octopus Cable.

Tubing compatibility and flow rate ranges are described in Figure 22.

Figure 22. Accessory Pump Tubing Compatibility

Tubing Compatibility

Tubing size	L/S 13	L/S 14	L/S 16	L/S 25	L/S 17	L/S 18	L/S 15	L/S 24	L/S 35	L/S 36
Tubing flow range	0.36 to 36 (mL/min)	1.3 to 130 (mL/min)	4.8 to 480 (mL/min)	10 to 1000 (mL/min)	17 to 1700 (mL/min)	23 to 2300 (mL/min)	10 to 1000 (11 to 1100) [1] (mL/min)	17 to 1700 (18 to 1800) [1] (mL/min)	23 to 2300 (26 to 2600) [1] (mL/min)	29 to 2900 (34 to 3400) [1] (mL/min)
KRJr (300 RPM)	✓	✓	✓	✓	Tubing not compatible	Tubing not compatible	Tubing not compatible	Tubing not compatible	Tubing not compatible	Tubing not compatible
KR1 (600 RPM)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[1] High Performance pump head required to achieve flow rate value in ( ). Requires part number ACR2-H4I-*01N* or *-01R*.

Tubing size	I/P 26	I/P 70	I/P 73	I/P 82	I/P 88	I/P 89
Tubing flow range	0.12 to 4 (LPM)	0.24 to 8 [1] (LPM)	0.2 to 8 (LPM)	0.4 to 13 (LPM)	0.4 to 17 [1] (LPM)	0.52 to 19 [1] (LPM)
I/P series (650RPM)	✓	✓	✓	✓	✓	✓

[1] High Performance pump head required, part number ACM3-PHP-01N.

7.2.1.1 KR1 Pump (600 RPM)

The KR1 remote control setting is found in the KF Comm 2 Software. Tubing sizes and flow rates are identical to KR2i (Table 11).

Note: *The KR1 pump head is unidirectional. Ensure tubing is placed appropriately.*

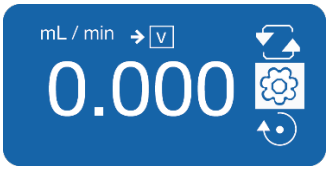
Figure 23. KR1 Pump

7.2.1.2 KR Jr Pump (300 RPM)

KR Jr pumps are shipped in remote-control mode. If a KR Jr is in remote control mode, a boxed V will be seen on the upper left-hand side of the main screen after startup (Figure 25). The pumps are operated with L/S tubing.

Figure 24. KR Jr Pump

Figure 25. KR Jr Remote Control Mode



If the KR Jr is not in remote control mode:

1. Enter **Settings Menu**
2. Enter **Global Options Menu**
3. Enter **Remote Control Menu**
4. Enter **Voltage Input Menu** **:**Use up or down arrows to highlight “I” icon and press ENTER
5. **Remote Control On**

Note: *The controls are only accessible when the auxiliary pumps are in Internal control mode. When in remote control mode, the auxiliary pumps are controlled by input from the KF Comm 2 Software. Traceability and data integrity are only maintained when the KF Comm 2 Software is used for all controls.*

7.2.1.3 KR1 Pump (600 RPM)

The KR1 remote control setting is found in the KF Comm 2 Software. Tubing sizes and flow rates are identical to KR2i (Table 11).

Note: *The KR1 pump head is unidirectional. Ensure tubing is placed appropriately.*

Figure 26. KR1 Pump

7.2.1.4 I/P Digital Peristaltic Pump (650 RPM – for KMPi only)

The I/P Digital Peristaltic Pump has both internal (Figure 28) and remote (Figure 27) capabilities but should be used in remote control.

1. Connect power cable to I/P Digital Peristaltic pump.
2. Connect adapter dongle to I/P Digital Peristaltic pump and desired Auxiliary Pump cord on KMPi's Auxiliary Component Octopus Cable.
3. Power on I/P Digital Peristaltic pump.
4. Select ENGLISH if prompted to select language and press ENTER.
5. Use up arrow to select CONTINUOUS MODE if prompted, and press ENTER.

Figure 27. Remote Control Mode

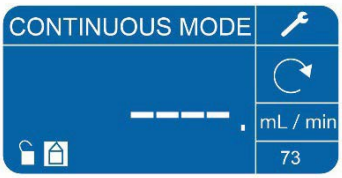


Figure 28. Internal Control Mode

If pump shows "---" after starting up (Figure 27), it is in remote control mode and is ready to use. If pump shows a flowrate after starting (Figure 28), it needs to be set to remote control mode.

1. Use arrow key to select wrench icon and press ENTER
2. Press down arrow to REMOTE CONTROL and press ENTER
3. Use arrow key to select VOLTAGE INPUT and press ENTER twice. Press up arrow, then ENTER. This will set MIN to 0.1 VDC.
4. Press the down arrow until EXIT appears on bottom left. Press left key to select EXIT and press ENTER.
5. Use arrow key to select START/STOP and press ENTER.
6. Select ON and press ENTER.
7. I/P Digital Peristaltic pump is now in remote control mode and ready to use.

7.2.2 Auxiliary Pump Settings

The KF Comm 2 Software will control the pumps once the pump type and tubing size are input. Refer to the KF Comm 2 Software User Guide.

7.3 Automatic Backpressure Valve

The KrosFlo Automatic Backpressure Valve (ABV) controls a 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 can be connected to the KR2i, while up to two can be connected to the KMPi. Refer to the KF Comm 2 Software User Guide for operation and tubing recommendations.

7.3.1 ABV Installation

Plug in the valve serial port to the serial connector labeled Valve on the Octopus Cable. For the KMPi choose Valve 1 if only using one valve. The valve is powered through the octopus connector.

Place the tubing through the plunger mechanism by lifting 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 beturned 180 deg to close the tubing opening by using the longer stainless steel rods or let the tubing opening remain accessible with the shorter rods.

7.3.2 ABV Settings

Depending on the style and number of valves that are connected, not all settings are accessible.

7.3.2.1 ABV Operation Settings

a. **ABV Type:** KR2i or KMPi
b. **Control based on ABV position:** TMP, Retentate pressure, Permeate pressure, Feed pressure
c. **Mode:** Select Auto.
d. **Valve start position:** Directs valve to control feed, permeate, retentate, or TMP pressure
    - Open: no pinching
    - Half: 50% closed based on tubing size
    - Closed: 100% closed based on tubing size
    - Custom: User-defined
e. Operating pressure: Input pressure.
f. ABV response: high, medium, low
g. Retentate tubing: Select size.

7.3.2.2 Manual Mode Menu

a. **ABV Type:** KR2i or KMPi
b. **Mode:** Select Manual
c. **Control:** TMP, Retentate pressure, Permeate pressure, Feed pressure
d. **Operating pressure:** Input pressure.
e. **Tubing Size:** Select size
f. **Position:** Directs valve to control feed, permeate, retentate, or TMP pressure
    - Open: no pinching
    - Half: 50% closed based on tubing size
    - Closed: 100% closed based on tubing size
    - Custom: User-defined

7.4 Connecting computer and accessories to TFF System

The KR2i (Figure 29) and KMPi (Figure 30) TFF Systems both have ports for a power cable, a pressure sensor cable, and an auxiliary component cable (octopus cable, Figure 31, Figure 32).

Figure 29. KrosFlo KR2i TFF System Cable Connections

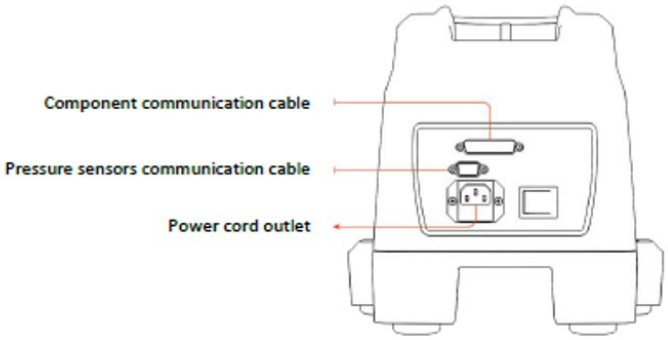


Figure 30. KrosFlo KMPi TFF System Cable Connections

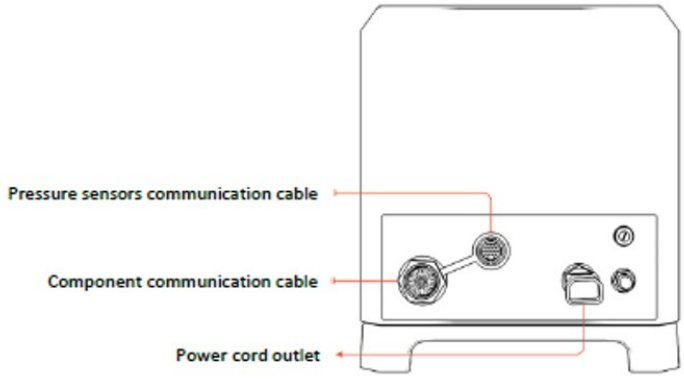


Figure 31. KR2i Auxiliary Component Cable

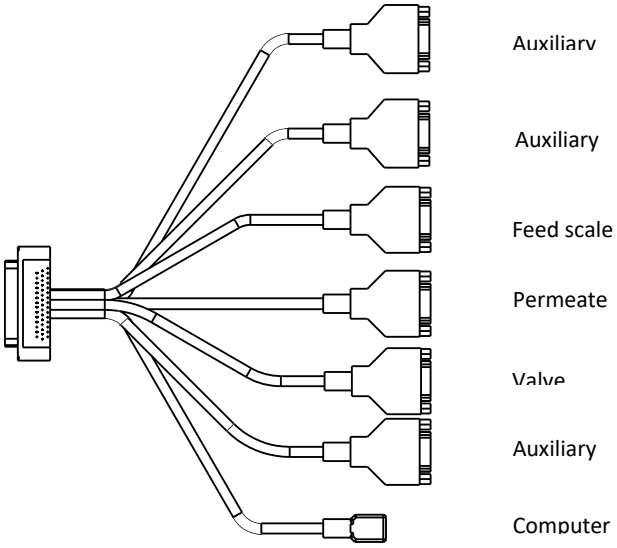
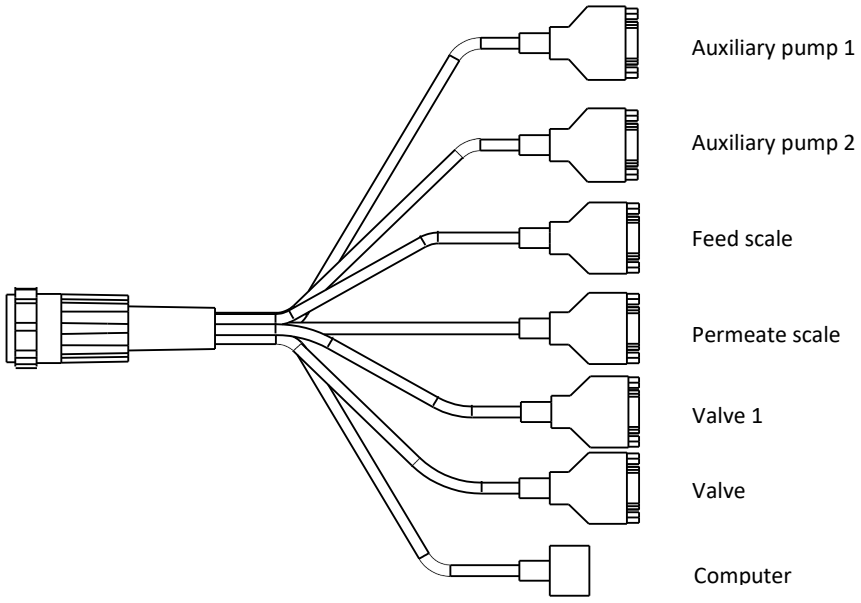


Figure 32. KMPi Auxiliary Component Cable



8. Software Setup

Provided is a basic overview of the KF Comm 2 (or 2C) software setup. For complete instructions, see the KF Comm 2 Software User Guide (IF.UG.022). The system is required to have internet access during setup and software and firmware updates, but not during routine operations.

Minimum system requirements:

- Windows 10
- 16 GB RAM recommended (8 GB RAM minimum)
- Intel® Core™ i5 processor (or equivalent/faster)

The computer must maintain a physical connection to the KrosFlo TFF System at all times.

8.1 Supported Software

Two versions of software are available:

- KF Comm 2
- KF Comm 2C (21 CFR Part 11 compliance-ready)

Ensure that a Super-Admin account has been created and the account holder has received an email from Repligen detailing account information. If email has not been received and needs to be resent, contact Repligen Customer Service (customerserviceus@repligen.com).

To start system:

1. Power on TFF System.
2. Power on computer.
3. Launch Device Manager on computer to monitor installation progress.
4. Connect USB cable from Auxiliary Component Octopus Cable to computer.
5. Device Manager will automatically refresh to indicate recognition of a hardware change.
6. Monitor the installation of the USB drivers through Device Manager.
    a. The TFF System connection will be read through multiple drivers in a sequence of three before it is completely installed.

b. The entire process may take ten minutes or more depending on computer.
c. After loading the KF Comm 2 Software Suite drivers, the computer will read the TFF System connection as a single virtual serial (COM) port. If a dialog box indicating the device driver was incorrectly installed appears, disconnect the USB cable, restart the system and the computer, and connect the USB cable to a different port. If the problem persists, update the driver software, manually select the KF Comm Software Suite installation folder and allow console to search through subfolders.

7. After software installation is complete, log in and activate license.
8. Create users.
9. Update the pump firmware.

9. Basic Concepts of Tangential Flow Filtration (TFF)

9.1 Introduction

Membranes use the principle of barrier separation, differentiating components based on size. Components larger than the membrane pore are retained by the membrane while smaller components pass through the membrane into the permeate. Although there are other methods for driving the separation process, Repligen hollow fiber module and flat sheet cassette TFF filters are designed for pressure-driven applications.

Tangential Flow Filtration is an efficient way to separate streams that would cause plugging if processed by dead-end filtration. During TFF, the process fluid flows at a defined velocity/flow rate tangentially across the membrane surface, generating a 'sweeping' force to prevent membrane fouling. The majority of the flow delivered to the device exits the filter as retentate, while a smaller portion flows through the membrane as permeate. The retentate is recirculated back to the process reservoir and then can reenter the filter inlet to continue the circulation. This recirculation process generates a continuous permeation rate.

The permeate flow results in an increased concentration of retained components at the membrane surface . This layer (often referred to as gel layer, wall concentration or cake layer) becomes an additional barrier, increasing resistance across the membrane that results in reduced permeation rate (permeate flux) and can sometimes affect molecule transmission across the membrane.

The wall concentration is influenced by fluid variables: degree of solvation, concentration and nature of the solids and solutes, and fluid temperature. Operating variables such as the recirculation flow velocity and TMP also are major contributors. Ensuring adequate fluid velocity at the liquid-membrane wall interface will maximize flux and solute passage.Fluid velocity is controlled by the pumping rate. Pumping rate depends on the surface area of the device and molecule shear sensitivity. Recommendations for these flow rates are available in the TFF device User Guides and can also be discussed with the Repligen Field Applications team. Process development experiments will always be recommended to optimize flow rates for your molecule.

9.2 Concentration

Concentration is the reduction of the initial sample volume to the desired final sample volume. If a process volume of 10L is concentrated 10X, then the final sample volume will be 1L. The retained molecule concentration will have increased 10X. Repligen hollow fiber and flat sheet TFF filters reduce the initial sample volume by passing and removing fluid across the membrane while retaining molecules larger than the membrane pore size. When using feed and permeate scales, this reduction is measured by weight and is communicated to the TFF System Software, which will determine when the desired concentration factor has been reached. If the weight stays constant on the feed scale while increasing on the permeate scale, the TFF System recognizes a Constant Feed (or fed-batch) concentration. Constant feed is used when the volume of the feed vessel is less than the starting process volume. Additional feed is pumped by 34 auxiliary pumps or pulled by vacuum into the primary feed vessel, until the volume is reduced enough to fit. Concentration then proceeds normally.

9.3 Diafiltration

Diafiltration is the addition of a desired exchange fluid (often buffer) to the feed material, replenishing the volume removed in the permeate. As small molecules such as salts and other low molecular weight species are removed through the permeate, they are replaced with the salts of the new solvent, resulting in buffer exchange. Diafiltration is measured based on initial process volume at the start of the diafiltration. When the permeate volume increases by the initial process volume, one diafiltration volume (DV) has been added to the initial feed.

The TFF System diafiltration function relies upon feedback from both the feed and permeate scales. The TFF System will add buffer to maintain the weight on the feed scale. When the permeate scale reaches the weight required to meet the desired DV, the system will end the diafiltration .

Determination of the number of diafiltration volumes to use is based on the percentage of exchange that is required for the application and the make-up of the feed. Theoretically, 6 DV are required to exchange 99.7% of the buffer salts, assuming 100% of the buffer components are permeable. TFF processes often use 5 - 7 DVs to reach an acceptable exchange.

10. Troubleshooting

Table 14. Troubleshooting Categories

Problem	Symptom	Diagnosis	Remedy
Pressure measurement	Incorrect Readings (ex: -9.9 psi, >35 psi with no applied pressure)	Transducer not tared	Tare transducer in KF Comm 2 Software
		Malfunctioning octopus cable or transducer	Replace broken component
		Disconnected transducer	Check/re-make connections of cable and transducers
		Transducer connected to incorrect octopus cable port.	Check/confirm labels on octopus cable (Feed, retentate and permeate)
Scale/Mass Measurement	Scale(s) fails to tare	Error code presented	Remove/protect from exposure to HVAC vents or excessive airflow
		Scale zero overweight error	Confirm scale pan is properly seated
			Remove all weight and power-cycle system
	Scale not reading properly		Refer to scale User Guide for error code definitions
Pump Problems	Base pump not delivering correct flow rate	Pump calibration is off	Recalibrate pump in KFCOMM2
		Tubing under/oversized	Select tubing size to keep operating flow rates in 20-80% of recommended range
	Tubing being damaged in pump head (cuts/damage/breakage)	Tubing misaligned in head	Ensure tubing is centered on rollers, restrained in tubing clamps (teeth) on each side of pump head, and slack is eliminated
		Tubing slipping in pump head	Adjust occlusion knob to tighten as needed

Problem	Symptom	Diagnosis	Remedy
	Auxiliary pumps suddenly run at high speed in CF or D modes	Operator accidental contact with scales or removal of weight from scales	Avoid contact with scales or manipulation of items on scales at all times during automated process runs.
	Auxiliary pump(s) losing connection	Loose/damaged cable	Reseat aux pump cable connections on pump and octopus cable ports. Inspect pins.
	Pump not working properly (other)	Contact your Repligen Account Manager, Technical Support Team or Customer Service for assistance. Refer to pump manufacturer's manual for additional troubleshooting	
Process Problems	Process ends unexpectedly (early or late) in auto mode	Incorrect holdup volume	Enter correct values for feed and permeate holdup volumes in recipe and trial settings.
		Incorrect Endpoints	Recalculate and re-enter endpoints in recipe. Confirm holdup volume is utilized in calculation, if needed.
		Operator accidental contact with scales	Avoid contact with scales or manipulation of items on scales at all times during process runs.
	Process with conductivity or UV endpoints ends unexpectedly	Conductivity/UV crossing target endpoint during startup	Flood conductivity sensor with starting buffer
			Zero UV flow cell with starting buffer
	Pressure spike during recipe execution	ABV closed unexpectedly or started process closed	Press Emergency Open button in software (Trial ends) and restart process
			Confirm appropriate circulation flow rate for filter size/MWCO.
		Tubing blockage	Review flow path and remove any pinches, kinks or undersized fittings.
KFCOMM2 Errors	Data Export Error	"Undefined" error message during export	Avoid use of special characters in Trial ID names
	Permeate flux data highly erratic	Data collection rate too fast	Increase 'Q Permeate Frequency' setting in trial settings
	KFCOMM2 errors (other)	Refer to KFCOMM2 User Guide for additional troubleshooting	
KFCOMM Errors	Support for KFCOMM (Excel spreadsheet/macro – based legacy version) is limited as the software has been discontinued. Please consider a software upgrade to KF Comm 2		

Problem	Symptom	Diagnosis	Remedy
Additional Technical Support	There are two technical teams devoted to supporting our customers in the field: • Repligen Field Applications Scientist (FAS) team is ready to support your TFF application and process needs and troubleshooting. • Repligen Field Service Engineers (FSE) are ready to support your TFF equipment needs and troubleshooting. Contact your Repligen account manager for referral.		

11. System Maintenance

The KrosFlo TFF System design is robust and intended for use with other process and lab equipment. The frame, cabinet, and pumps can be cleaned by wiping down surfaces with mild cleaning agents and/or warm water, a damp cloth or lab wipes. The display should be cleaned with computer screen cleaner and computer screen wipes.

All repairs of the system must be performed by a qualified Repligen service engineer. Opening of the system and attempted repair by the user or third party shall void the product warranty.

The KrosFlo TFF Lab System is manufactured in Marlborough, MA, USA.

12. General Information

12.1 Safety Guidelines

Table 15. Warning: Product Use Limitation

Symbol	Description
Caution 	Risk of danger. Consult Operating Instructions for nature of hazard and corrective actions This product is not designed for, nor intended for use in patient-connected applications; including, but not limited to, medical and dental use, and accordingly has not been submitted for FDA approval This product is not designed for, nor intended for use in hazardous duty areas as defined by ATEX or the NEC (National Electrical Code); including, but not limited to use with flammable liquids, consult the factory for products suitable for these types of application

12.2 System Specifications

12.2.1 KR2i

Table 16. System Pump Output

Description	Specifications
Speed	0.1 to 600 rpm
Torque output, Maximum	180 oz-in (13 kg•cm) 540 oz-in Starting
Speed regulation	Line ±0.1% FS Load ±0.1% FS Drift ±0.1% FS
Display	128 x 64 LCD w/ LED Backlight
Pressure Sensor Limits	-9.99 to 75 psi

Table 17. System Pump Input

Description	Specifications
Supply voltage limits	90 to 260 V_{RMS} @ 50/60 Hz (Universal Input)
Current, Maximum	2.2A @ 115 VRMS, or 1.1A @ 230 VRMS

Table 18. System Pump Construction

Description	Weight
Dimensions (L × W × H)	10.5 in × 8 in × 8 in (267 × 203 × 203 mm)
Weight	13 lb. (5.9 kg)
Enclosure Rating	IP33

Table 19. System Environment

Description	Specifications
Temperature, Operating	0° to 40°C (32° to 104°F)
Temperature, Storage	–25° to 65°C (–13° to 149°F)
Humidity (non-condensing)	10% to 90%
Altitude	Less than 2000 m
Pollution Degree	Pollution Degree 2

Table 20. Compliance

Descriptions	Specifications
For ETL Mark	UL 61010-1, CAN/CSA C22.2 No. 61010-1
For CE Mark	EN61010-1 (EU Low Voltage Directive) EN61326 (EU EMC Directive)
RoHS	Directive 2011/65/EU

12.2.2 KMPi

Table 21. KMPi System Pump Output

Description	Specifications
Speed	0.1 to 650 rpm
Torque output, Maximum	520 oz-in (37.4 kg•cm) 1560 oz-in Starting
Speed regulation	Line ±0.1% FS Load ±0.1% FS Drift ±0.1% F.S.
Display	128 x 64 LCD w/ LED Backlight
Voltage speed	0-10V DC @ 1 kΩ min
Current speed	0-10 mA @ 0-600Ω
Tach	100 to 6500 Hz, 50% duty cycle, 10 Hz/rpm
Motor running	N.O. & N.C. contact closure, 1A @ 28V DC

Table 22. System Pump Input

Description	Specifications
Supply voltage limits	90 to 260 Vrms @ 50/60 Hz (Universal Input)
Current, Maximum	4.5A @ 115 Vrms, or 2.6A @ 230 Vrms
START/STOP	CW/CCW
Voltage	0-10V DC @ 10 kΩ ±50V common mode range
Current	0-20 mA or 4-20 mA @ 250 Ω ±50V common mode range

Table 23. System Construction

Description	Weight
Dimensions (L × W × H)	17.5 in × 11 in × 13 in (445 × 280 × 330 mm)
Weight	40 lb (18 kg)
Enclosure Rating	NEMA 4X

Table 24. System Environment

Description	Specifications
Temperature, Operating	0° to 40°C (32° to 104°F)
Temperature, Storage	–25° to 65°C (–13° to 149°F)
Humidity (non-condensing)	10% to 100%
Altitude	Less than 2000 m
Pollution Degree	Pollution Degree 3
Noise Level	<70dBa @ 1 meter
Chemical resistance (stainless steel)	Exposed material is 316 stainless steel enclosure and hard coat anodized aluminum
Chemical resistance (powder-coated steel)	Exposed material is polyester coated steel enclosure steel and hard coat anodized aluminum

Table 25. Compliance

Descriptions	Specifications
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. 61010-1second edition, including Amendment 1, or a later version of the same standard incorporating the same level of testing requirements
For CE Mark	EN61010-1 (EU Low Voltage Directive) EN61326 (EU EMC Directive)

12.3 System Components

12.3.1 Pump Drive, Pump Head, and Integrated Pressure Monitor

The TFF System comes with the Digital Pressure Monitor integrated into the Pump Drive as one unit. The internal microprocessor runs both the Pump and Pressure monitor functions.

12.3.2 Mounting Hardware

The KMPi TFF System comes with the Easy-Load Pump Head that requires no extra hardware to mount. The KR2i TFF System comes with an attached mounting plate for the KR2i Easy-Load Pump Head.

12.3.3 Octopus Cables

The TFF System comes with two Octopus Cables—one with more pins for the Auxiliary Components, and one with fewer connections for use withg the Pressure Transducers. On the back of the TFF System are two Interface ports for the Octopus Cables.

12.4 System Parts List

12.4.1 KR2i

Table 26. KR2i SYR2-U50 Components

Component	Description	Ext Qty	Unit of Measure
SYR2-U10	KR2i Drive and stand	1	EA
ACPC-U10	0.625” BPCV and dongle	1	EA
ACBT-015-S1N	15 mL Conical bottom reservoir, 3 port	1	EA
ACBT-050-S1N	50 mL Conical bottom reservoir, 4 port	1	EA
ACBT-250-S1N	250 mL Conical bottom reservoir, 4 port	1	EA
ACBT-500-S1N	500 ml Conical bottom reservoir, 4 port	1	EA
ACPX-BHC-50	Bottle holder, conical, 15 – 50 mL	1	EA
ACPX-BHC-500	Bottle holder, conical, 250 – 500 mL	1	EA
ACR2-SKT	Starter kit, KR2i	1	EA
ACPX-CD	Microkros/Midikros luer accessory kit	1	EA
ACTU-P14-25N	Pharmapure tubing pack, #14	1	EA
ACTU-P16-25N	Pharmapure tubing pack, #16	1	EA
	KF Systems Surface Pro	1	EA
550-13723-001	KR2i Surface mount	1	EA
SCL-0020-SCLR	Schuler scale – 20 kg	2	EA
KFCOMM2KR2iKMPi	KF Comm 2 Software	1	EA

Table 27. KR2i Part Numbers

Description	Part Number
KR2i TFF System	SYR2-XXX (see software/scale specifc part numbers)
KF Comm 2 Software	SYR2-U30
KF Comm 2C Software	SYR2-U40
KF Comm 2 Software with 2 scales	SYR2-U50
KF Comm 2C Software with 2 scales	SYR2-U60

KF Comm Software is offered in two versions. Version 2C is 21CFR Part 11 compliance-capable, has an auditor role, and requires an e-signature for changes. Version 2 can be changed by the user. Part numbers for the KR2i System reflect the choice of software.

12.4.2 KMPi

Table 28. KMPi SYM3-U30 Components

Component	Description	Ext Qty	Unit of Measure
SYM3-U10	KMPi DRIVE with octopus cables	1	EA
ACM3-STND	KMPi Lab stand	1	EA

13. List of TangenX Cassette and Device Studies

1. TX1001-POQ-117-R Protein Binding Study
2. 10827-19-3528 SC Gamma Cassette & Tubing Assembly Extractables Assessment
3. TX1001-POQ-159-R SC Gamma Cassette Robustness Study
4. TX1001-POQ-125-R Membrane QC Testing Method Validation
5. TX1001-POQ-132-R Cassette QC Testing Method Validation
6. TX1001-POQ-164 SC Gamma Cassette Shelf Life Study
7. R-TANGENX-190902 Membrane Validation
8. PV-TANGENX-220910 Process Validation Report — SC Gamma Manufacturing (0.5 - 5 m^2)
9. PV-TANGENX-230710 Process Validation Report — SC Gamma Manufacturing (10 m^2)

14. References

1. Class VI Test per USP <88> Includes: Systemic Injection, Intracutaneous Injection, and 7-Day Muscle Implantation.
2. ANSI/AAMI/ISO 11137-1. 2006/(R) 2010 & A1:2013 Sterilization of health care products — Radiation — Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices.
3. ISO/IEC 17025, 2017, General requirements for the competence of testing and calibration laboratories.
4. USP 42, NF 37, 2019 <85> Bacterial Endotoxin Test, USP current revision, <161> Medical Devices — Bacterial Endotoxin and Pyrogen Tests.
5. BPOG - Best Practices Guide for Evaluating Leachables Risk from Polymeric Single Use Systems Used in Biopharmaceutical Manufacturing: 2017; Sexton, Aidan W., et.al.
6. Standardized Extractables Testing Protocol for Single-Use Systems in Biomanufacturing: 2014; Weibing Ding, Gary Madsen, Ekta Mahajan, Seamus O'Connor, Ken Wong.
7. EMA Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMA/410/01 rev.3).
8. ICH Topic Q3C (R4) Impurities: Guideline for Residual Solvents.

15. Index

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