

XCell™ C24 Controller (v3)

User Guide

For use with:

- XCell ATF® 2 Device
- XCell ATF® 4 Device



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Abbreviations

AT	Actual time
ATF	Alternating tangential flow
A2B	ATF Device to Bioreactor connection
CT	Calculated time
cSP	Cycle Switch Pressure (The sum of sP2 + SO pressures where cycle change occurs)
DF	Driving force, Same as DP
DP	Driving pressure, same as DF
FC	Flow control
HFM	Hollow fiber module
HMI	Human machine interface
PA	Pump air chamber
PC	Pressure control
PL	Pump liquid chamber
PLC	Programmable logic controller
PRV	Pressure regulating valve
PV	Process value
SM	Screen module
SO	Switch offset. Pressure increment above sP2 pressure
SP	Set point
sP2	Sampled P2 pressure, during either the Exhaust (-sP2) or Pressure (+sP2) cycle
SIP	Steam in place
SUB	Single-use bioreactor
WFI	Water for Injection

1. Description of Process

XCell ATF® provides an efficient filtration technology for fractionating a mixture or suspension of cells, molecules or other particulates. Two possible process configurations are shown in [Figure 1](#) and [Figure 2](#). The filtration Device includes a filtration assembly that can accept either a hollow fiber module (HFM) or a screen module (SM) for fractionation of larger particles. The filter housing is positioned between a process vessel or a bioreactor at one end and a diaphragm pump at the other end. The process vessel serves as a container for the content to be filtered. The diaphragm pump provides the means for generating alternating tangential flow (ATF), back and forth, between the vessel and pump, through the hollow fibers or screen module. During this process, a rapid, low shear, tangential flow is generated. A filtrate/harvest pump, as shown in Fig. 1, is used for controlled removal of a filtered stream. Only a single connection is required between the XCell ATF® Device and the vessel. As shown in [Figure 1](#), this single connection (A2B) is through the head plate of the vessel, requiring a dip tube to penetrate the liquid in the vessel. The XCell ATF® Device can be connected to most process vessels. [Figure 2](#) and [Figure 3](#) illustrate two additional examples: Connection to a single use bioreactor (SUB) and a steam in place (SIP) connection. Such connections will be described in greater detail in this guide.

Figure 1. XCell ATF® 4 Device connected through a head plate

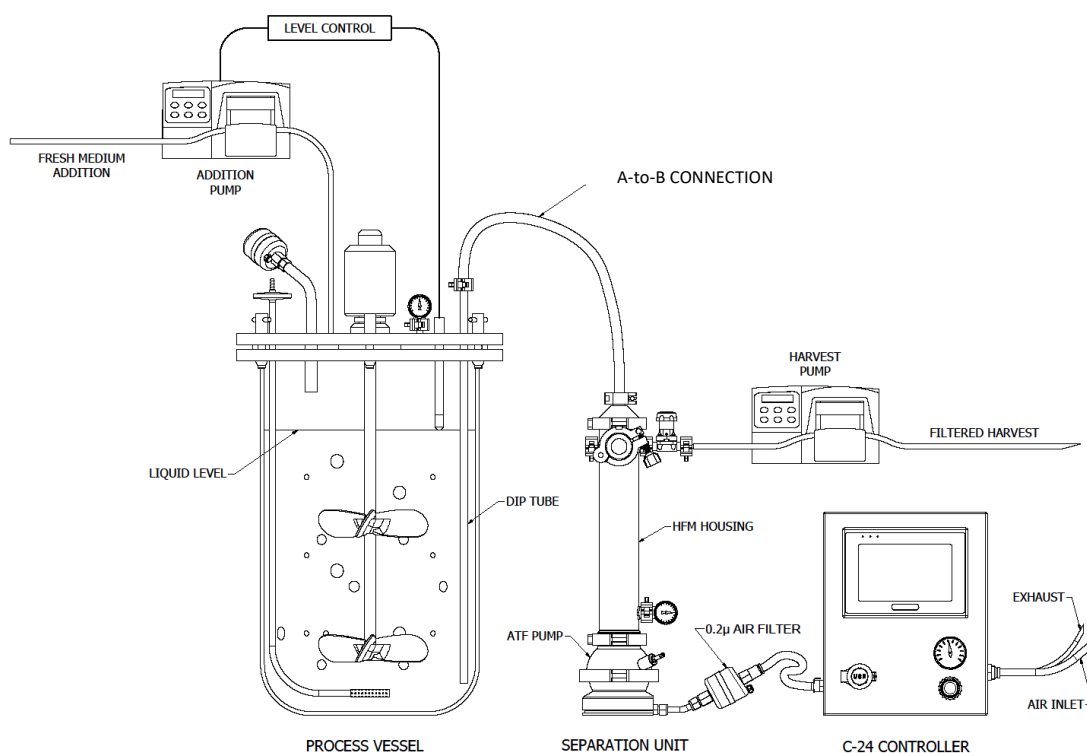


Figure 2. XCell ATF® 2 Device connected to a wave SUB

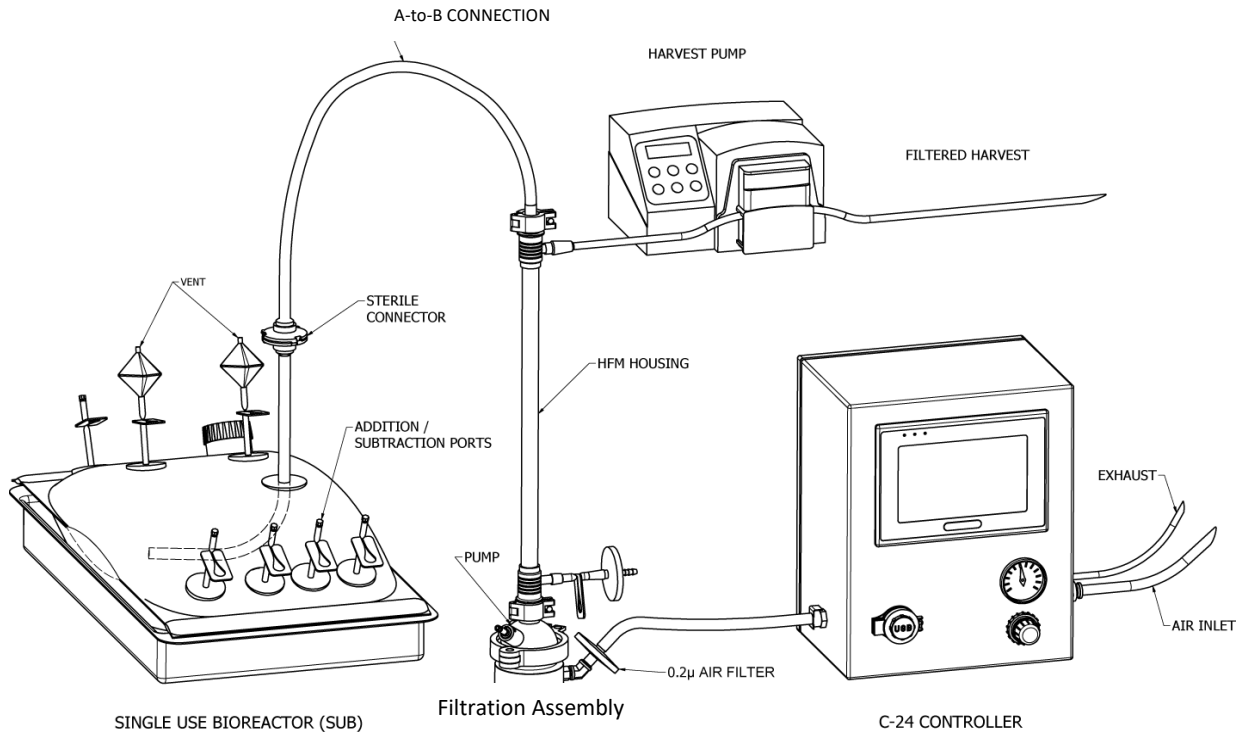
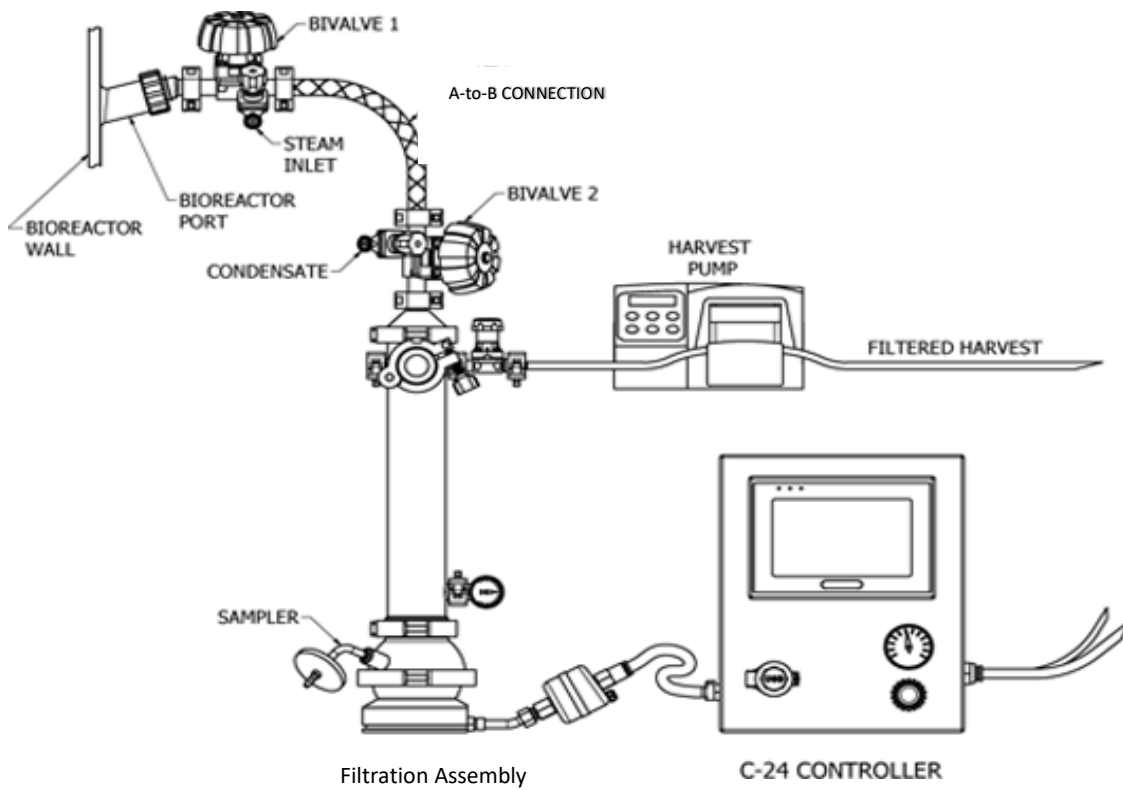


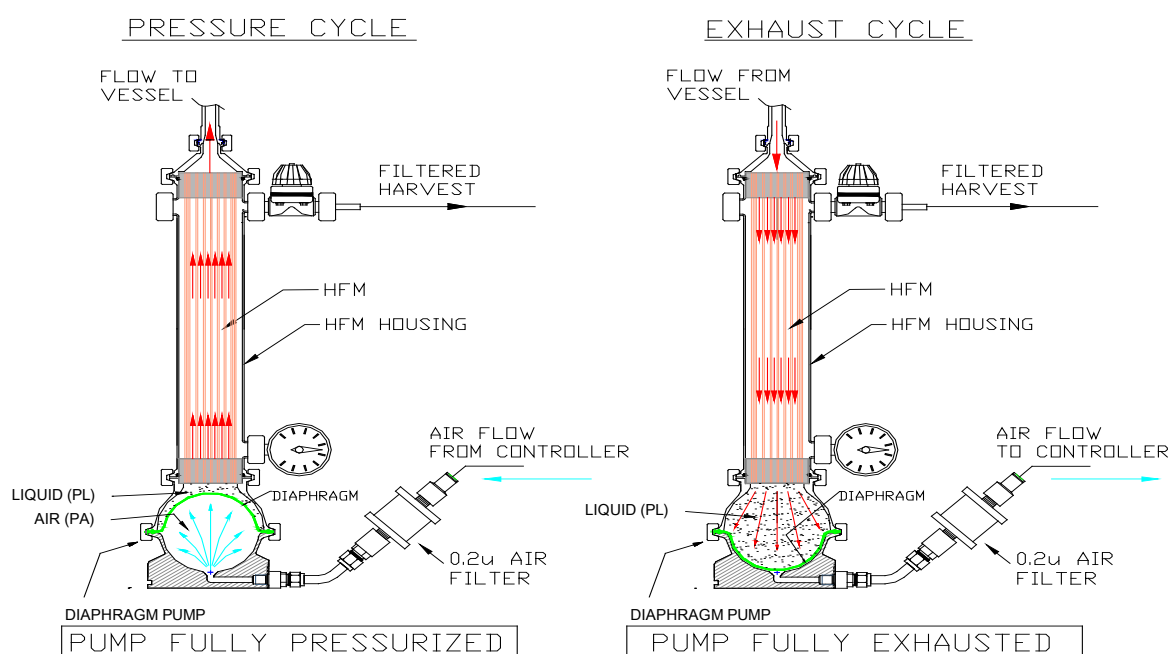
Figure 3. XCell ATF® 4 Device connected to a vessel with an SIP connection



2. Alternating Tangential Flow Filtration

The diaphragm pump is the heart of the ATF process. It generates alternating tangential flow (ATF) through the hollow fibers (or a screen module). ATF is a pulsating, reversible, flow of liquid, back and forth, between a process vessel and diaphragm pump, [Figure 4](#). The process consists of two cycles, the Pressure cycle (P-cycle) and the Exhaust cycle (E-cycle). The P-cycle occurs when air is fed into the ATF pump from the controller, thus moving the diaphragm up towards the *pump liquid-side* (PL) hemisphere and driving the liquid from the diaphragm pump through the HFM and into the process vessel. The E-cycle occurs when the controller introduces vacuum, thus pulling the diaphragm down towards the *pump airside* (PA) hemisphere, and liquid is pulled from the process vessel through the HFM, and back into the diaphragm pump. The diaphragm must travel between the two extremes for one complete cycle. The flow through the hollow fibers generates tangential flow in one direction in an alternating fashion. The two cycles are shown in [Figure 4](#).

Figure 4. ATF pressure and exhaust cycle



WARNING: When using any vessel or bioreactor, be sure to maintain an unrestricted vent or exhaust from the vessel. In the case of a diaphragm failure, air will penetrate the ATF pump, through the filter and into the vessel. A free exhaust from the vessel will minimize the build-up of pressure in the vessel.



WARNING: Note on the Exhaust Cycle: Vessels or bioreactors should not be pressurized unless otherwise specified by the manufacture should not be pressurized. Glass and single-use bags can explode if pressurized. Therefore, when using vessels that cannot be pressurized, both air pressure and vacuum services are required to operate the XCell ATF® Device.

3. Utility Requirements and Size

Prior to set up please ensure the required utilities for correct functioning of the XCell ATF® Device are available.

Table 1. Utilities

Utility	Requirement	Comments
Compressed Air (Gas)	Minimum 50 psi (3.4 bar) Maximum 90 psi (6.1 bar)	Filtered clean, oil free, moisture free gas. Recommended 50-60 psi inlet at point-of-use, which is regulated down to 35 psig at the XCell™ C24 Controller
Vacuum	Minimum -9 psig, Preferred -12.5 psig*	Vacuum supplied by a local pump capable of maintaining a minimum of 5L/min for XCell ATF® 2 and a minimum of 20 L/min for XCell ATF® 4.
Pollution degree	Pollution degree 2	This product is intended to be used in an environmental of pollution degree 2. Pollution degree 2 area is normally where only nonconductive pollution can be present. Temporary conductivity that is caused by condensation is to be expected.
Current	50/60Hz	
Frequency	0.6 Amp	
Supply Voltage	100-240V AC (+10%, -10%)	Main supply voltage with a fluctuation of +/- 10%.
Environmental Temperature, Humidity	Ambient Temperature (0-50 °C) Low Humidity (0-80% RH) Indoor (Dry)	Environmental specifications only apply to controller. Controller is designed to be used indoor (dry) and low humidity location.
Altitude	2000m	This product has been assessed for a maximum altitude of 2000m.

* (-28" or 724 mm. Hg)

Table 2. Dimensions

Component	Dimensions (inches) (H) X (W) X (D)			Comments
XCell™ C24 Controller (v3) Enclosure	13	10.5	8	Recommended space dimension with fittings and interconnections 14" (H) X 14.5" (W) X 10" (W).
XCell ATF® 2 Device	32	10	4	Height of the Device varies according to which hollow fibre cartridge is being used.
XCell ATF® 4 Device	~24	12	6	Height of the Device varies according to connections to the housing.

The XCell ATF® Device dimensions vary based on Device configuration. The controller dimensions are fixed.

4. XCell™ C24 Controller (v3)

The XCell™ C24 Controller (v3) replaces the XCell™ C24 Controller (v2.5) previously used with the XCell ATF® 2 Device and the XCell ATF® 4 Device. The XCell™ C24 Controller will be operating version 3 software.

4.1 Features of the XCell™ C24 Controller (v3)

- Intended for benchtop-use
- Control of XCell ATF® Device flow rates in both pressure and exhaust cycles
- Monitoring capabilities for air flow rate and cycle time
- Set-up and selection of operation parameters
- Display of real-time process data
- Ethernet capabilities for remote monitoring and data logging
- Alarm for error conditions
- Information on algorithm performance
- Simple recipes
- Two-point calibration for pressure
- Manual mode of operation
- Power failure restart option
- Ability to have software or firmware upgrades in the field by replacing memory modules
- Ability to operate an XCell ATF® 2 Device or XCell ATF® 4 Device with standard control parameters or any variations thereof with the same hardware and software.
- Programmed to also support XCell ATF® 2 and XCell ATF® 4 Microcarrier Devices

The XCell™ C24 Controller (v3) consists of the controller, a connection for compressed air supply, a connection for exhaust/vacuum service, a connecting air line between the controller and XCell ATF® Device diaphragm pump, and a 0.2 micron hydrophobic filter (F1) on the air line between the controller and ATF diaphragm pump (to ensure a physical barrier to prevent the back flow of liquid in case of diaphragm failure). The XCell™ C24 Controller (v3) will regulate the airflow rate and direction to establish the pressure and exhaust cycles of the XCell ATF® Device diaphragm pump.

See attached table for a list of updates with XCell™ C24 Controller (v3)



USAGE: If the controller is used in a manner not specified by the Repligen, the protection provided by the equipment may be impaired.

XCell™ C24 Controller Upgrade Summary: Version 2.5 to Version 3

4.2 The XCell™ C24 Controller (v3) external interfaces

Figure 5. Controller Interfaces

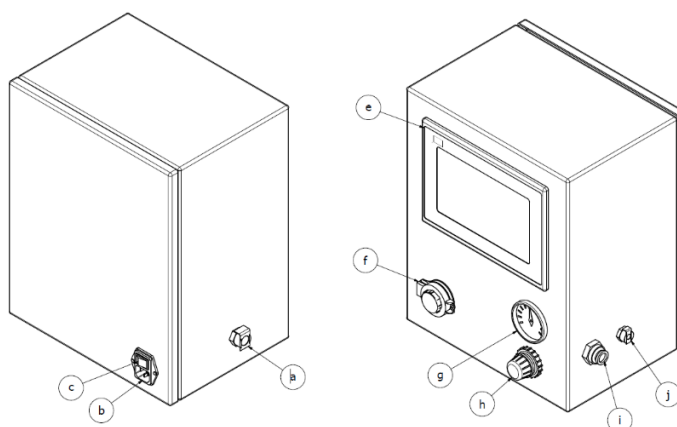


Table 3. Controller Labeled Interface Connections

Item	Description	Item	Description
a	Pump line for connection to the ATF Device diaphragm pump	f	Ethernet Port
b	120/220 (+10%/ -10%) power input	g	Second stage air pressure gauge
c	Power ON/OFF switch	h	Secondary air pressure regulator
d	(N/A)	i	Exhaust/vacuum line connection
e	Human Machine Interface (HMI) See Appendix 1 for description of HMI Screens.	j	Air inlet port

Utility requirements for the XCell™ C24 Controller are summarized in [Section 3](#). The following provide a more detailed description of the utility requirements refer to [Figure 5](#).

Air inlet (j) Recommended minimum air pressure requirement is ~50psi / 3.4bar.



WARNING: Do not exceed 90 psi / 6.1 bar on the Air inlet.

Exhaust/ vacuum line (i) - Whether the Exhaust outlet is left open to the atmosphere or connected to a vacuum line depends on the type of process vessel used. For a vessel that cannot be pressurized (e.g. glass vessels, SUBs, etc.) the vacuum line is connected to a vacuum source. For a vessel that is pressure rated, vessel pressure may be used to drive the Exhaust cycle, particularly at low XCell ATF® rates; but, if vessel pressure is limited, or at high ATF Device settings, a vacuum source supplement may be required.

In addition to vessel pressure, the hydrostatic pressure generated by the height difference between vessel liquid level and the XCell ATF® Device diaphragm pump level may assist or hamper the exhaust flow.

Pump line (a) - The line connects the XCell™ C24 Controller (v3) to the diaphragm pump. A hydrophobic 0.2µm filter in this line provides a physical and potentially sterile barrier to the back flow of liquid from the pump to the controller should a diaphragm rupture.



NOTE: Be sure to use a 0.2µm hydrophobic filter.

Air Pressure regulator (h) - Typical range of the regulator is 0-60psi/ 4.1bar. This is a second stage pressure regulator for down regulating house air pressure to a specified, user-required, pressure setting.

Typically, the secondary air pressure is regulated to 35psi/2.4bar. That value is selected because that pressure is recommended to drive the pressure control valve, PC valve, and it is generally the upper limit of the pressure required to achieve the entire range of flow rates.

Air Pressure Gauge (g) - Typical range of gauge is 0-60psi. It shows second stage Device pressure.

PLC (Programmable Logic Controller) - The XCell™ C24 Controller (v3) is controlled by Siemens 1215C DC/DC/DC PLC.

Human Machine Interface (HMI) is Siemens TP700 Comfort Panel.

4.3 The XCell™ C24 Controller (v3) ethernet set-up and connectivity

Ethernet Infrastructure

The communication link between the Windows environment and the XCell™ C24 Controller (v3) is based on Profinet®. Profinet® is an open Industrial Ethernet standard developed by the PROFIBUS Organization and is standard Ethernet (IEEE802.3). The Profinet® communication protocol sends and receives data using the open Ethernet TCP/IP standard at a bandwidth of 100 Mbit/s and functions identical to traditional industrial Ethernet in providing “real-time” channel for time-critical communications (i.e. process data).

Ethernet Configuration

The communications interface between the controller HMI and PLC is based on Profinet (Industrial Ethernet). The controller is factory set to the following IP settings:

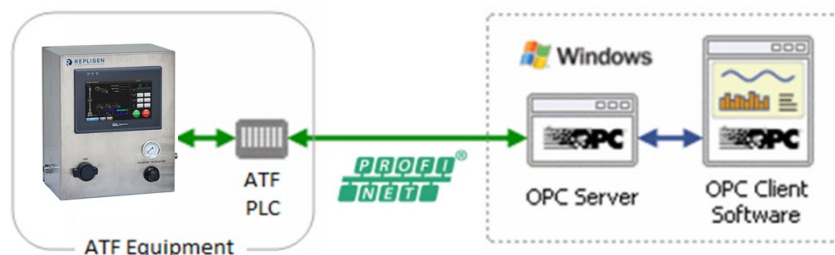
Table 4. IP Settings

	IP Address	Subnet Mask	Default Gateway
PLC	192.168.0.1	255.255.255.0	None
HMI	192.168.0.3	255.255.255.0	None

This factory default setting has the HMI and PLC on the same subnet allowing proper communications to take place. If ‘#####’ appears in input fields and the software version is not displayed on the administration screen, the HMI and PLC may not be properly connected, and the connection may need to be reset. See [Appendix 1](#) - Controller Admin section for instructions on how to set IP Addresses and connections.

ATF Operations- Remote Monitoring and Data Acquisition

The following diagram shows the network architecture for controlling the ATF Equipment from an OPC Server and OPC Client Software over Profinet®:



The OPC Client Software is any OPC capable program that will connect through the OPC Server to the ATF Equipment. The OPC Client Software will Control the ATF Equipment remotely and/or read the status of the ATF Equipment. Examples of OPC Client Software include Microsoft Excel, WinCC HMI by Siemens, and FTVIEW HMI by Rockwell Automation.

- The acronym "OPC" comes from "OLE (Object Linking and Embedding) for Process Control". Since OLE is based on the Windows COM (Component Object Model) standard, under the hood OPC is essentially COM. Over a network, OPC relies on DCOM (Distributed COM), which was not designed for real-time industrial applications and is often set aside in favor of OPC tunneling.
- OPC is implemented in Server/Client pairs. The OPC Server is a software application that bridges the communication of the PLC with the Windows environment and then with the OPC Client Software application. Some common OPC Server program suppliers include Delta Logic (OPC Server & Data Logger) and Siemens (WinCC Siemens).
- OPC also comprises several standards including OPC Data Access (OPC DA) and other standards for alarms & events, historical data, batch data and XML.

Proceed to [Appendix 1](#) for details of XCell™ C24 Controller (v3) screens.

Proceed to [Appendix 2](#) for data tables for Remote Data Logging via OPC.

5. Theory of Operation

5.1 Control Objectives

To ensure optimal results with the XCell ATF® Device, one should keep in mind the following two general rules:

1. The diaphragm must be in continuous motion between the Pressure cycle and the Exhaust cycle, *without dwelling during any part of the cycle*.
2. The stroke travel of the diaphragm must be between the fully Pressurized and the fully Exhausted extremes.

There should be no dwell time for the diaphragm at any point of its cycle. The continuous movement of the diaphragm ensures continuous tangential flow through the HFM or Microcarrier SM. The full displacement of the diaphragm ensures maximum mixing and minimizes "dead space" retention within the XCell ATF® Device.

5.2 Control Overview

As shown in [Figure 6](#) (and illustrated in [Figure 2](#)), when the pressure cycle starts, the pressure to the diaphragm pump rapidly increases (as measured by the P2 pressure sensor in the controller). At some critical pressure, the diaphragm begins to move, and the PA begins to expand. As the PA expands, P2 levels off and must be sustained to maintain the expansion of the PA. This critical P2 pressure is also known as the "Driving Pressure" or "Driving Force" (DP or DF).

Once the PA is fully inflated, the pressure within the pump chamber will begin to spike, e.g. the diaphragm stops moving and begins to stretch. The controller takes advantage of this spike by using

a cycle Switch Offset (SO) to indicate when to switch to the Exhaust cycle. Similar mechanism applies to the Exhaust cycle.

Principle of operation

The XCell ATF® Device, having a constant pump volume and a known flow rate (as determined by the user) allows the controller to calculate the pump cycle time according to the following relationship:

$$\text{Flow Rate} \left(\frac{\text{L}}{\text{min}} \right) = \text{Pump displacement volume (L)} \div \text{Cycle time (min)}$$

The default pump displacement volumes for v2.5 and v3 are:

XCell ATF® 2 Device	0.086L (no longer supplied)
XCell ATF® 2H Device	0.099 L(standard)
XCell ATF® 2MC Device	0.115L
XCell ATF® 4 Device	0.420 L
XCell ATF® 4MC Device	0.420 L



NOTE: The default displacement values coded into v3 are different from v2.0. The values of v3 are deemed to be more accurate. However, v3 allows the user to override the default displacement values should the user want to control based on v2.0 values.

The default pump displacement volumes for v2.0 are:

XCell ATF® 2 Device	0.086L (no longer supplied)
XCell ATF® 2H Device	0.120 L (standard)
XCell ATF® 2MC Device	n/a
XCell ATF® 4 Device	0.380 L
XCell ATF® 4MC Device	n/a

5.3 Control Functional Algorithms

To control the diaphragm movement within the pump housing, the XCell™ C24 Controller (v3) uses four (4) algorithms:

5.3.1 Start Algorithm

Default relationship is generated experimentally in the factory between orifice size and PC_SP pressure vs. Flow Rate. This relationship is programmed into the controller; therefore, selection of a Flow rate set point by a user is reciprocated by the controller with a pre-determined default Pressure Control set point (PC_SP) and Flow Control (FC) Orifice size needed to maintain that selected Flow rate. This Algorithm provides the controller with a starting point. Depending on the ATF setup with the bioreactor, the controller will take a few minutes to tune itself to the appropriate PC_SP and Orifice size. Furthermore, the start algorithm values are effective during the start of a run, when the cell culture viscosity is similar to water. As the culture grows and viscosity increases, the control algorithm will adjust PC_SP and Orifice size automatically to maintain Flow set point.

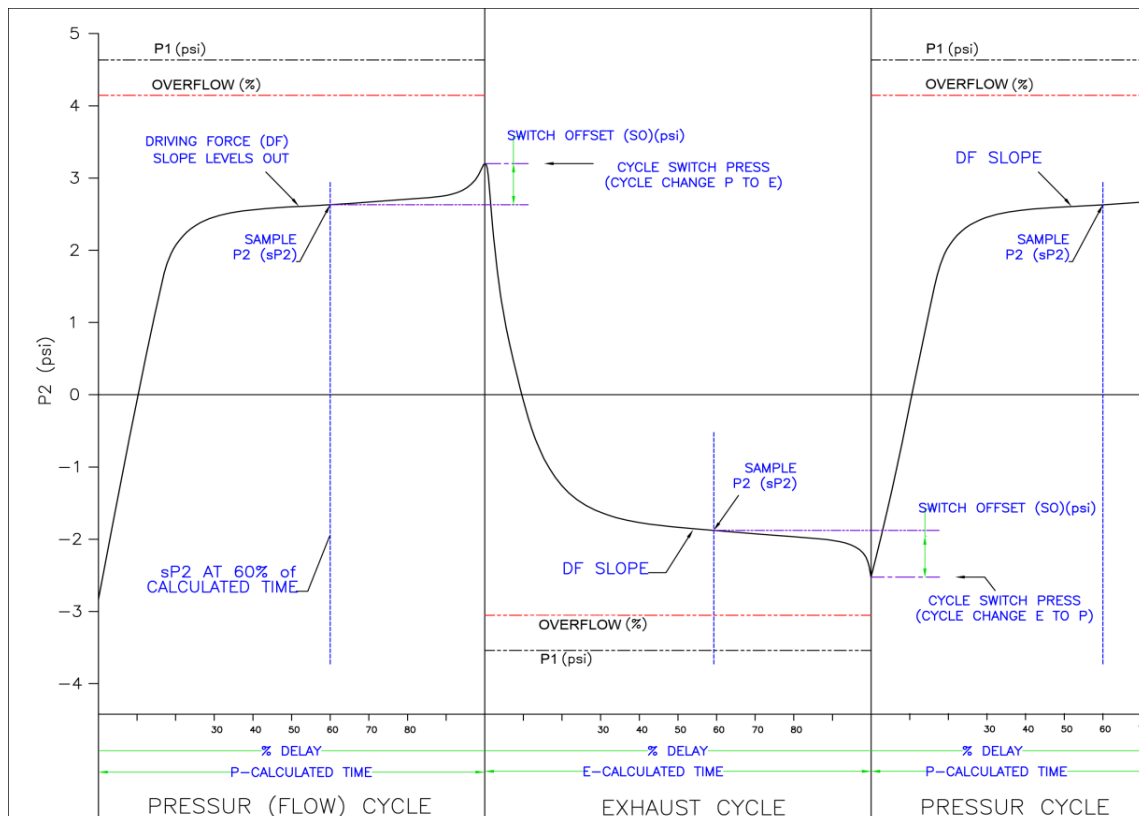
5.3.2 Switch Algorithms (Primary Method)

Switch Offset: This Algorithm is based on first detecting a steady state pressure phase or “Driving Force” during each pump cycle followed by addition of a Switch Offset, i.e. a pressure increment (or spike). A cycle change is executed when actual pump pressure (as determined by P2) is equal or greater than the sum of Driving Force pressure and Switch Offset pressure. Refer to Pump Parameters screen and [Figure 6](#).

5.3.3 Delay function

The Delay function is a user defined value, (entered in the Pump Parameters screen), which defines the point when the controller will sample P2, (sP2) and begin looking for the Switch Offset (SO) pressure spike. The Delay value is a Percentage (%) of the Calculated Cycle Time (CT).

Figure 6. Basis of ATF Device Cycle Control



5.3.4 Override timer (Backup Method 1)

Default “Overtime” is set for 120% of the Calculated-CT, so in the event that the Primary Method does not work, P2 will, nevertheless, cause a cycle switch to/from Pressure/Vacuum flow.

5.3.5 Overflow Switch (Backup Method 2)

A third condition which may trigger a cycle change is when the relationship of P2 relative to P1 ((P2/P1) x 100) is equal to or greater than the “Overflow” pressure.

The above conditions can occur when:

- Actual Flow is significantly greater than the Set Flow and the pump fully pressurizes or exhausts before sP2 is sampled. At high flows, P2 rapidly approaches P1, i.e., sP2 + SO become \geq than P1 pressure and Cycle Switch Pressure cannot be achieved.
- Improper Orifice size is selected by the controller or user. A larger than needed orifice may not produce a sufficient pressure drop across the orifice such that P2 and P1 pressures approach each other. This may occur particularly at low flows or extreme set ups where the pump is significantly above or below the process vessel liquid level.

In either of the above two cases Cycle Switch Pressure (CSP) cannot be reached and the controller will continue to Pressurize or Exhaust until the Override timer is reached; in which case, the controller will respond as though flow is too slow. More flow will be demanded, exacerbating the problem, with eventual result in an Alarm condition. This is corrected with the Overflow.

The Overflow, set by user (in Pump Parameters screen, Overflow (%), enables the controller to switch cycle whenever P2 pressure approaches P1 pressure, within a % of P1 pressure. This function can prevent the diaphragm from being over pressurized and prevent the cycle from going into Override timer (5.4.4).

For example: if CSP pressure is greater than P1 pressure, the Overflow will initiate an early cycle change, before calculated-CT is reached. The controller will cut demand with a lower PC_SP or smaller FC (Orifice).

5.4 Controller Start-up

5.4.1 Connect the Pneumatic services

- Air inlet - Connect the Pressurized air service. Pressure supply must be ~50psi.
 - Exhaust/vacuum line – Connect the Exhaust service which may be a vacuum pump supplied by Repligen or house vacuum if it is sufficient and dedicated for the XCell ATF® Device.
 - Pump line - Connect the controller to the ATF Device diaphragm pump. Ensure a hydrophobic 0.2micron filter is in line.
1. Press LOGIN- Enter Admin and 111111 for user and password (unless another ID is provided) Press OK on the Login pop-up screen. A successful login displays the MAIN Screen.
 2. Press the Menu button and go through each screen in the BASIC SETUP (ATF Select, Bioreactor Configuration, Controller Configuration, Flow Ranges, and Pump Parameters). Press Next or Previous to scroll through the Basic setup screens.
 3. In the ATF Select screen, select the XCell ATF® Device size,
 4. In the Bioreactor Configuration screen, no (0) value for both Bioreactor Pressure and Height Differential unless the configuration is atypical (i.e. connection to a pressurized bioreactor)
 5. In the Controller Configuration screen, select desired configuration
 - a. Auto Restart is a function that occurs following a power failure.
 - “ON” allows the controller to restart and continue running as it was prior to the power failure. Note, you must login again, but status is maintained.
 - “OFF” will stop XCell ATF® Device control after a power failure.
 - b. Control Mode
 - Auto” mode (recommended) – diaphragm movement is controlled based on the control algorithm and the P2 curve.
 - “Manual” mode – diaphragm movement is only based on cycle time as defined by the Flow setpoint.
 - c. Pressure Unit
 6. In the Flow Ranges screen, simply press the Default Settings button for Repligen recommended values. Refer to [Table 5](#) below.



NOTE: The PC_SP Min is -12.5psi, assuming the vacuum source is greater than this. The Auto Detect button offers the option of setting the PC_SP Min based on actual vacuum utilities. It is recommended that the auto detect function is used when setting up a controller for the first time, annually, or whenever a change to the vacuum source has occurred.

Table 5. Typical Flow Ranges

Field	Values				
User Set Point Range	ATF2	ATF2-H	ATF2-MC	ATF4	ATF4-MC
Max P-Flow SP (LPM)	1.5	1.5	3	8	10
Min P-Flow SP (LPM)	0.2	0.2	0.3	1.5	1.5
Max E-Flow SP (LPM)	1.5	1.5	3.0	8	10
Min E-Flow SP (LPM)	0.2	0.2	0.3	1.5	1.5
Max PC SP(psi)	25				
Min PC_SP(psi)	-12.5				

- In the Pump Parameters screen, simply press the Default Settings button for Repligen recommended values. Refer to [Table 6](#) below.



NOTE: The Initialization Pressure should be a negative value (typically -3.0 psi). This allows the diaphragm to start from a fully bottomed out position. Also confirm that the Default Pump Volume reflects the current connected ATF unit.

Table 6. Typical Pump Parameters

Field	Flow	Exhaust
Delay (%)	70	70
Switch Offset (psi)	0.5	-0.5
Overflow (%)	95	95
Overtime (%)	120	120
Initialization Pressure (psi)	-3.0 (-5.0 for ATFMC Devices)	
Pump Volume Override	(dependent on ATF Device size selected)	

- Return to the main screen and check the fields for agreement with entered values.
- The PC_SP values and Orifice settings are determined by the Start Algorithm.
- If this is the first time the XCell™ C24 controller will be used, or if calibration has not been done for a long period of time, a 2-point pressure calibration must be performed. Refer to [Section 9.5](#) for calibration procedure.
- Push START only when ATF is assembled, properly connected to the process vessel, and connected to the controller. See [Section 6](#) for ATF assembly and startup.

5.5 Process Guide

5.5.1 Selection of XCell ATF® Device flow rates

ATF flow rate:

Generally, the higher the ATF rate, the more efficient the backflush, thus longer filter performance. However, this must be balanced against the cell line requirements:

- i.e. Type of cell line used: fragile cell line or cultures inoculated at low cell concentration, may require a gentle start up using low ATF rates (XCell ATF® 2 = 0.3 to 0.6L/min or XCell ATF® 4 = 2.5 - 4L/min). As the cells begin to grow and adapt, gradually increase flow rate by increments of 0.1L/min using an XCell ATF® 2 Device and 0.5-1L/min using an XCell ATF® 4 Device.
- When a less shear sensitive cell line is used, one may begin at higher ATF rate (e.g. 0.7-0.9L/min using an XCell ATF® 2 Device or 5.0 – 8.0L/min using an XCell ATF® 4 Device).

XCell ATF® 2 is capable of flow rate maximum of 1.2LPM. But for scale-up considerations, XCell ATF® 2 rate should not exceed 0.9 LPM. Please refer to the Engineering Scale-up Guide from Repligen.

Harvest or Filtration rate:

Generally, the higher the filtration rate, the higher the required ATF flow rate. The maximum filtration rate depends on the size of the filter relative to the process conditions, while the minimum filtration rate depends on the requirements of the cell culture. General guidance for ATF flow rate during a Perfusion process is as follows:

$$\text{XCell ATF}^{\circledR} \text{ rate (L/min)} \approx 100 \text{ to } 250 \text{ times higher than Filtration rate (L/min)}$$

The above relationship is only a guide. Each cell line and culture conditions may have its unique requirements. For filtration application with rapid filtration rates, the ratio between ATF rate and filtrate rate may be substantially less.

Major changes in process parameters may be executed by an Engineer or Administrator from the main screen. These include Changes in flow rates, Pressure Control set points (PC_SP) and Flow Control (FC) Orifice selection.

Changes can be made directly, even while the ATF Device is cycling. (There is no need to push PAUSE as required in software v2.0.)

- Simply press on any white field to change that value
- A keypad will appear
- Enter the new value(s) into the keypad
- Press “Enter” to accept new value

Manually changing the PC_SP and FC (Orifice) values will impact the ATF flow rate immediately and should be done with expert knowledge of the XCell™ C24 Controller or contact a technical representative from Repligen. It is best practice to have the ATF filtration assembly on a scale to ensure that a full displacement is ultimately achieved when doing manual manipulations.

5.6 Use of Recipe function

The Recipe function can be useful for customizing ATF operating parameters for your cell culture environment.

1. If end-user ATF setup differs significantly from standard ATF setup conditions.
 - The XCell™ C24 Controller may take longer than normal to tune for end-user setup. An example of custom set-up is an XCell ATF® Device connected to a stainless steel bioreactor under head pressure. Here a custom recipe allows for quick start-up of ATF operation
2. During a process change whereby the cell culture changes dramatically within a short period.
 - If the consistency of the culture changes rapidly, there may be a lag while the Device adjusts to new process conditions. Invoking a preprogrammed Recipe allows quick adjustment to new process conditions.
3. Using ATF during middle or end of a run.
 - If the ATF is used for harvest operations, the cell culture viscosity may be significantly higher than water. A recipe defined for harvest conditions would immediately allow the ATF to have the proper flow rate and displacement volume.
4. During an ATF or controller swap-out.
 - For an ATF swap-out, the controller must be put on PAUSE, not STOPPED or else the PRV and Orifice values will be reset to starting algorithm default. Invoking Recipe setting for last known operating conditions minimizes deviation from settled process conditions.

6. Assembly and use of the XCell ATF® Device

6.1 Choosing a Spectrum® Hollow Fiber Module (HFM)

- XCell ATF® Device accommodates a variety of hollow fiber modules (HFM)
- Ultimately the appropriate filter will be determined by the application
 - i.e. Perfusion – Microfilter (0.2 µm or 0.5 µm)
 - i.e. Concentrated fed-batch – Ultrafilter (30 kDa or 50 kDa)
- Microfiltration filters are available in either Polysulfone (PS) or Polyethersulfone (PES), while Ultrafiltration filters are only available in PS

6.2 Installation and Usage Notes

- The XCell ATF® 2 Device is suggested for use with 2-10L bioreactors. The XCell ATF® 4 Device is suggested for use with 10-50L bioreactors. Ultimately, the ATF selected depends on the perfusion rate or total volume throughput in addition to other process conditions.
- The ATF to bioreactor connection (A2B) for a glass vessel is made via a dip tube connected through the head-plate of the vessel. The dip tube should be positioned to minimize bubbles entering the XCell ATF® Device path from the sparger.
- Arrange the ATF assembly and bioreactor such that the bioreactor headplate and the top of the ATF are level.
- Perfusion is typically started 2-3 days after inoculation when the cells are still in exponential growth phase and before nutrient limitation occurs.
- For XCell ATF® 2 Device, an ATF rate of 0.7 – 0.9 L/min is a good starting point for a process involving robust cell lines. More shear sensitive cell lines may respond better to lower rates ranging from 0.3 – 0.6 L/min. For ATF4, an ATF rate of 5.0 – 8.0 L/min is typical.
- Cell specific perfusion rate (CSPR) equals the perfusion rate divided by the cell density, and minimum CSPR will depend on the cell line and medium.
- Typical perfusion rates range from 1 - 3 vessel volumes per day (VVD), with most users starting 2-3 days after inoculation at an inoculation density of 0.5 – 1.0 e⁶ cells/ml. Final values depend on optimization for your specific process.
- Feed/harvest rates, i.e. perfusion rate, are currently controlled by separate peristaltic pump(s) connected to the feed/harvest lines.
- To keep the bioreactor volume constant, the volume inputs (i.e. feed, base addition) should be kept equal to the volume outputs (i.e. harvest, bleed). Strategies to achieve this include using weight-based controls, level probes, or equalizing pump rates (with caution).
- Variables that can affect ATF flow and filtration rates may include volume of culture for processing, cell density, viability, cell line properties, and shear sensitivity.

Please refer to Repligen Perfusion Development Guide and FAQ for further information on ATF process control and operation.

Figure 7. Connecting utilities to the controller

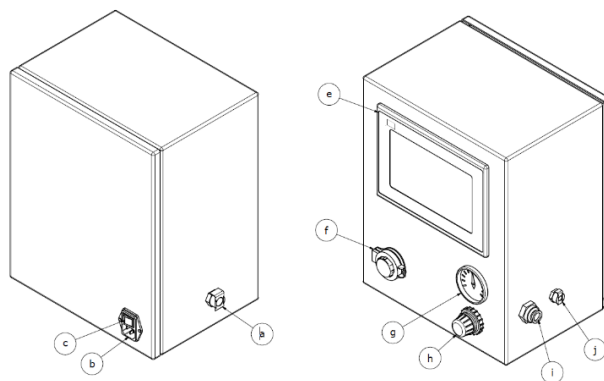


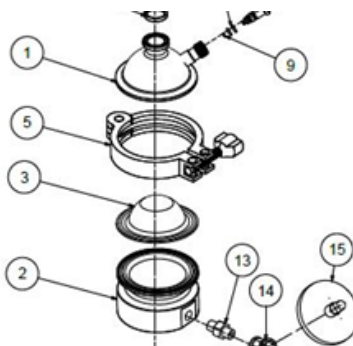
Table 7. Controller listed parts

Item	Description	Item	Description
a	Pump line for connection to the ATF Device diaphragm pump	g	Second stage air pressure gauge
b	120/220 V (+10%/ -10%) power input	h	Secondary air pressure regulator
c	Power ON/OFF switch	i	Exhaust/vacuum line connection
e	Human Machine Interface (HMI) See Appendix 1 for description of HMI Screens	j	Air inlet port
f	Ethernet Port		

- a. Connect vacuum service to the controller via the exhaust/vacuum line connection (i) using the green tubing provided by Repligen (vacuum source can be either a dedicated external vacuum pump or house vacuum with sufficient capacity)
- b. Connect air service to the controller via the air inlet port (j) using the red tubing provided by Repligen. Recommended minimum air pressure requirement is ~50psi / 3.4bar, not to exceed 90 psi.
- c. When the ATF unit is sterile and cooled to ambient temperature, it can be connected to the controller - connect the controller to the ATF diaphragm pump via the pump line (a) using the white tubing provided by Repligen. When the connection is made ensure that a hydrophobic 0.2micron filter is in line (this acts as a physical and potentially sterile barrier should the diaphragm rupture.)

6.3 Assembly of the XCell ATF® 2 Device

Figure 8. Installation of the silicon diaphragm in the XCell ATF® 2 Device pump housing

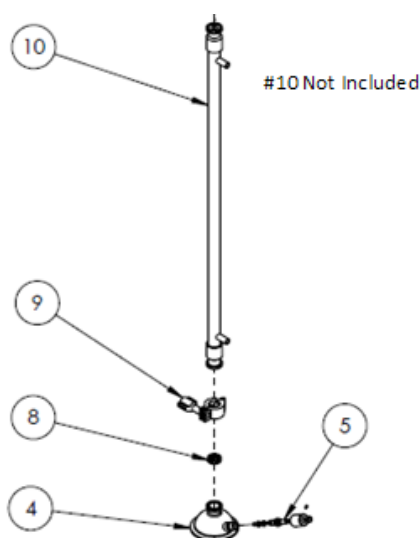


Important: The silicone diaphragm must be replaced after each run prior to sterilization

- a. Set the Pump Air-side (P_A) hemisphere (part #2) on a flat surface with the hemisphere facing up.

- b. Insert a new diaphragm (#3) into the sanitary groove of the PA hemisphere. The diaphragm, in the relaxed form, must be positioned with the dome pointed up, towards the PL hemisphere and HFM.
- c. Ensure the diaphragm's integrated gasket is uniformly seated in the sanitary groove of the pump hemisphere.
- d. Place the Pump Liquid-side (P_L) hemisphere (part #1) flange side down onto the diaphragm. Confirm that the diaphragm gasket is aligned with the sanitary groove on the Pump liquid-side (P_L) hemisphere.
- e. Squeeze the two pump hemispheres together. Ensure that the diaphragm is seated and aligned between the pump flanges with no spaces in between.
- f. Secure the pump hemispheres in place with the supplied tri-clamp (part #5)

Figure 9. XCell ATF® 2 Device diaphragm pump and HFM



6.3.1 Attach the Spectrum® Hollow Fiber module (HFM) to the ATF pump housing

- a. Place a sanitary gasket (part #8) into the sanitary groove on top of the Pump Liquid-side (P_L) hemisphere (part #4).
- b. Thoroughly wet the hollow fiber module (part #10) before proceeding (Microfiltration HFM require WFI; Ultrafiltration HFM require IPA or Ethanol, followed by WFI rinse). See Filter Prep and Autoclave Guide from Repligen for further details.
- c. Connect the HFM (#10) to the ATF pump housing by aligning it with the sanitary gasket on the top of the PL hemisphere (part #4).
- d. Secure the connection tightly with a 3/4" tri-clamp (part #9).

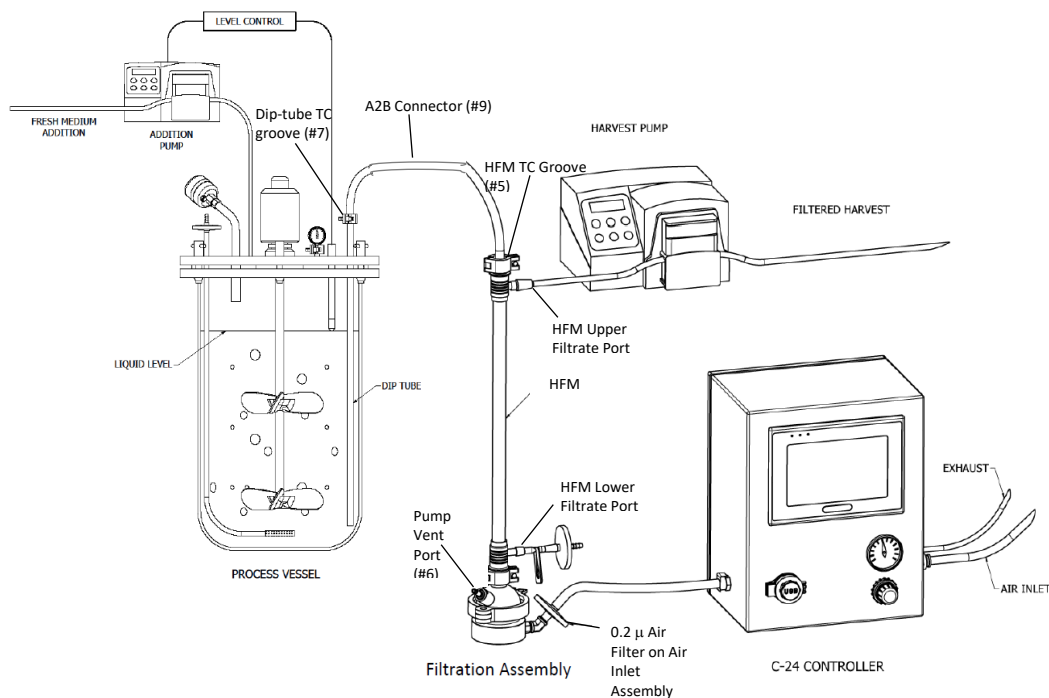
6.3.2 Preparing and sterilizing the XCell ATF® 2 Device-Bioreactor Assembly

Attach tubing and vent filters to assembly ports for autoclaving.

- a. Attach tubing and a 0.2 micron vent filter to the ventilation port on the Pump Liquid-side (pL) hemisphere (part #5). Leave the vent port valve open during autoclaving for proper steam penetration but must be closed during ATF use.
- b. Attach tubing and a 0.2 micron vent filter to the lower filtrate port on the HFM. Leave open during autoclaving but clamp off (i.e. with a C clamp) during ATF use.
- c. Attach the filtrate line (preferably weld-able pump tubing) and a 0.2 micron vent filter to the upper filtrate port on the HFM. Leave open during autoclaving.

6.3.3 Connecting the XCell ATF® 2 Device to the process vessel

Figure 10. XCell ATF® 2 Device bioreactor assembly



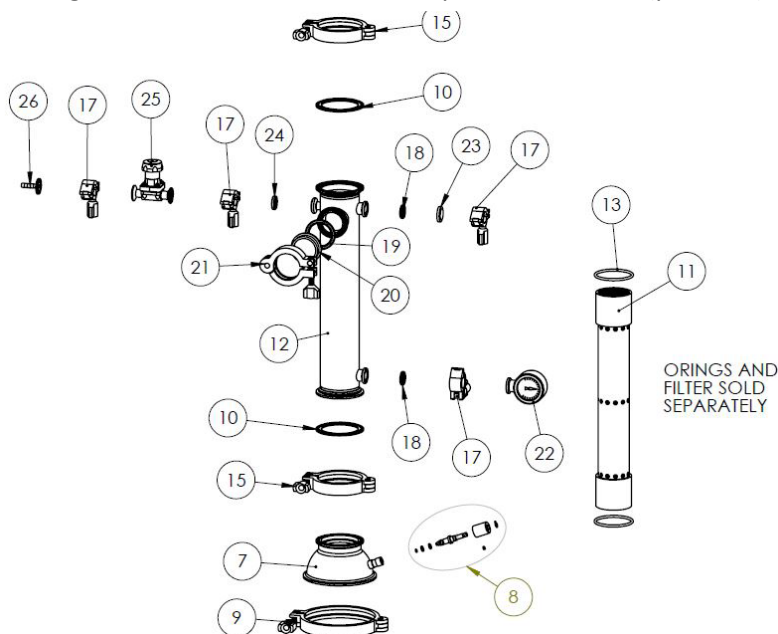
- The XCell ATF® 2 Device and process vessel are typically attached and autoclaved together as one unit.
- Choose a compatible headplate compression fitting for your bioreactor. Install the dip-tube through bioreactor headplate compression fitting. Position the dip-tube to minimize bubbles from sparger entering the dip-tube as this may affect device operation.
- Position the ATF Device proximal to bioreactor to prevent kinking of the A2B tubing.
- Place the sanitary end of the A2B connector (part #9) into the tri-clamp groove of the HFM (part #5) and secure with a 3/4" TC clamp.
- Place the other sanitary end of the A2B connector into the TC groove of the dip tube (part #7) on the process vessel and secure with a 3/4" TC clamp.
- The process vessel and XCell ATF® 2 Device filter assembly can alternatively be autoclaved separately, then attached after sterilization using single-use couplings (i.e. AseptiQuik (Colder) or Ready Mate (GE)), or other weld-able tubing, paying specific attention to maintain length and ID requirements (i.e. ≤14 inches length and 3/8" ID).

6.4 Autoclaving the XCell ATF® 2 Device with the process vessel (also see [Section 7 Sterilization](#))

If autoclaving the bioreactor with liquid (i.e. WFI or PBS), ensure that the liquid level is below the XCell ATF® dip-tube so that liquid is not pulled into the XCell ATF® during the autoclave cycle.

- Place the air inlet assembly, with attached air filter, on the XCell ATF® pump air inlet port (part #8).
- Ensure that the path between the ATF and the process vessel is open.
- Autoclave the entire setup (ATF filtration assembly with the Bioreactor) using a liquid cycle. (Liquid cycle is required for the slow temperature ramping, preventing damage to the filter).
- Following the autoclave cycle, allow the Device to cool slowly to ambient room temperature.

- e. Once at ambient room temperature, close off the PL hemisphere vent port (part #6) and clamp the tubing attached to the lower filtrate port on the HFM (part #12).



6.5 Assembly of the XCell ATF® 4 Device

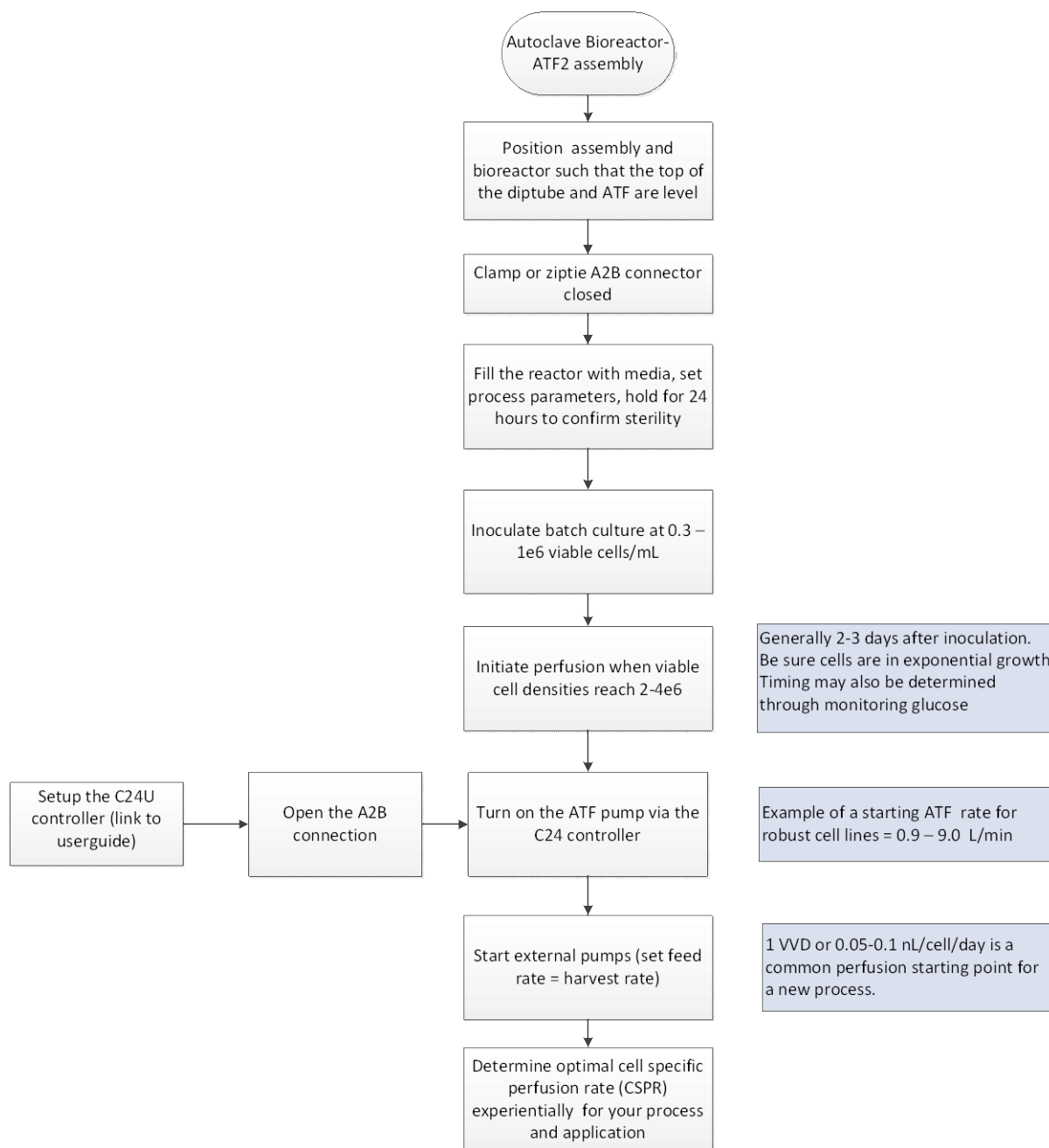
Assembly of the XCell ATF® 4 Device is similar to the XCell ATF® 2 Device, except for the assembly of the filter housing. The following steps describe the installation of the XCell ATF® 4 Device filter element into the stainless steel filter housing.

- a. Position the XCell ATF® 4 Device filter housing (part #12) upside-down, insert the HFM (part #11) into the housing. Note that the HFM is slightly longer than the filter housing.
- b. Place an “O” ring (part #13) evenly around the exposed end of the filter.
- c. Uniformly squeeze the “O” ring into the groove created by the filter and the housing.
- d. Place the sanitary gasket (part #10) atop the Pump Liquid-side hemisphere (part #7).
- e. Flip over the filter housing assembly and position concentrically atop the PL hemisphere. Push the filter housing down such that the filter slides into place and the filter housing connects with the PL hemisphere at the gasket.
- f. Secure the connection tightly with tri-clamp, (part #15).
- g. Place second “O” ring on the other exposed end of the HFM and push the “O” ring into the corresponding “O” ring groove created by the filter and the housing (part #13).
- h. Place a sanitary gasket on the exposed end.
- i. Top the exposed end of the HFM with the XCell ATF® Device Reducer segment (part #14 in Figure 8).
- j. Secure the connection tightly with tri-clamp (part #15).



NOTE: is recommended that after clamping both ends of the housing, each end is unclamped and inspected to confirm that the “O” rings are firmly and uniformly seated in their respective “O” ring grooves; if they are seated properly, re-clamp and continue with assembly. If not, make the necessary adjustments or re-do steps 1-10 above.

Figure 11. Representative Process Flow for ATF Start-up



6.5.1 Replacing the XCell ATF® Device mid run

It is possible to replace or exchange an in-process ATF filtration assembly with a fresh Device if it becomes necessary to do so. The exchange can be performed without compromising Device sterility. Some reasons for making such exchanges include: The need to replace a failed HFM with a new HFM, the need to replace an HFM with another having different properties, the need to replace due to mechanical failure, or the need to change the process from one set of requirements to another, etc.

The following summarizes the type of connections that may be used to exchange one XCell ATF® Device with another:

- SIP connection
- Use of Disposable Coupling: If using sterile single-use couplings, the setup must include a Y-connector with the common leg of the “Y” connected to the vessel and the other two legs being available for connection to two separate XCell ATF® Devices so that when one Device is inactivated from one of the legs, the second leg of the “Y” can be used for attachment of the secondary XCell ATF® Device.
- Use of a tube welder: A tube welder may be used to cut and replace the attached Device with a fresh, sterile ATF Device.
- Sterile procedure within a bio safety hood.
- The A2B connection tubing should be clamped at both ends of the severing point before uncoupling the XCell ATF® Device from the vessel.



WARNING: The ATF must first be stopped prior to an ATF change-out. Secure all tubing and filter connections with cable ties, especially the A2B connection when using sterile-coupling connectors.

6.6 Diaphragm installation

A new diaphragm must be used for each run. To properly install the diaphragm:

- a. Place Pump (PA) hemisphere with the wide opening facing up.
- b. Insert a new diaphragm into the sanitary groove, with the dome facing upwards.
- c. Ensure that the diaphragm integrated gasket is uniformly seated within the sanitary groove.
- d. Place the Pump PL hemisphere, flange side down, onto the diaphragm, again aligning the diaphragm gasket with the corresponding sanitary groove of the pump PL hemisphere.
- e. Squeeze the two pump hemispheres together. Ensure that the diaphragm is seated between the pump flanges securely with no spaces in between.
- f. Secure the pump hemispheres and diaphragm with the tri-clamp. It is recommended that a torque wrench (set to 25 in-lb) be used to prevent over-tightening.

Ensure that the diaphragm hemisphere, in the relaxed form, is positioned with the dome pointed towards PL hemisphere or HFM.



WARNING: The following procedures refer to steam sterilization. Steam is supplied at high pressure and at high temperature, in excess of 100°C. All parts of the ATF Device filtration assembly are rapidly heated and should only be handled by qualified personnel taking all proper safety precautions.

7. Sterilization

7.1 Sterilization of XCell ATF® Device by autoclaving

The XCell ATF® Device is sterilized by autoclave. Please refer the Filter Prep and Autoclave Guide from Repligen for further details. The ATF filtration assembly can be autoclaved with the process vessel while connected, or separately.

Autoclaving the ATF filtration assembly connected to the process vessel

- a. Connect the XCell ATF® Device to the process vessel using the standard A2B tubing, and the entire setup is autoclaved together. Refer to [Figure 1](#). The 0.2 micron air filter on the PA side of the pump housing is included in the setup.
- b. Ensure that the HFM has been wetted prior to assembly. Microfilters require WFI only, while Ultrafilters require alcohol followed by a WFI rinse.
- c. If autoclaving the bioreactor with liquid (i.e. WFI or PBS), ensure that the liquid level is below the dip tube, so that liquid is not pulled into the XCell ATF® Device during the autoclave cycle.
- d. Ensure that the pathway from vessel to XCell ATF® Device is open.
- e. Ensure that the harvest/filtrate line is open. Protect the Filtrate line with a 0.2 micron autoclavable filter with sufficient surface area to ensure the unrestricted flow of steam.
- f. The PL hemisphere vent port must be open during autoclaving, so make sure that this line is also equipped with a 0.2 micron autoclavable filter.

Both the filtrate and retentate ports should be vented using 0.2µm autoclavable filters. This will minimize formation of pressure gradients within the HFM during sterilization. This ensures free flow of steam into the unit and unobstructed pressure equilibration between all compartments. Make sure that the vessel has also been appropriately vented and prepared for autoclaving.

- a. Insert the entire setup (bioreactor with the ATF filtration assembly) into a sufficiently large autoclave.
- b. Autoclave using a liquid cycle, for 50-60 minutes. Liquid cycle is required for the slow temperature ramping, preventing damage to the filter
- c. Following the autoclave cycle, allow the set up to cool first inside the autoclave, ultimately to ambient room temperature.



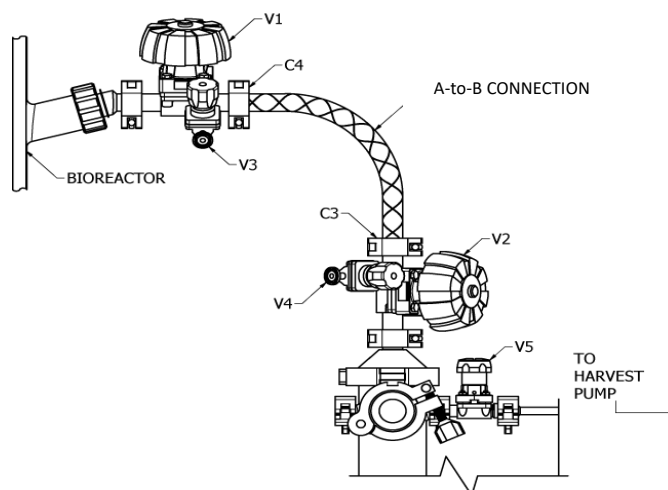
WARNING: Immediately out of the Autoclave, secure all sanitary clamps with an additional hand-tightening. Use gloves and caution since the autoclave and components may still be hot.

- d. Remember to close the PA hemisphere vent port, and a C clamp can also be used on the tubing for additional protection.

This procedure requires a steam source, ~25psi (1.7bar), for sterilization.

This procedure is relevant for XCell ATF® 4 Device and larger. This procedure may also be used for replacing an operational ATF Device during a run with a fresh sterile ATF Device. Unlike the fully assembled Device described above, this procedure requires a sterilisable connection between the XCell ATF® Device and the vessel as illustrated in [Figure 12](#).

Figure 12. A2B Connection



Autoclaving the ATF Filtration Assembly and steam connection to an SS bioreactor

- The proper fitting (i.e. ING1) must be installed into an available Ingold port on the stainless steel bioreactor.
- The first bivalve must be installed onto this Ingold fitting, configured such that V1 is proximal to the bioreactor. The stainless steel bioreactor is steam sterilized separately, with V1 closed. (Alternatively, V1 may be open, but with an end cap at C4. V3 is used as a steam outlet. V1 must then be closed after SIP.)
- A second bivalve is installed onto the ATF and configured such that V2 is proximal to the ATF reducer. The ATF filtration assembly is autoclaved separately with V4 closed, but V2 open with a 0.2µm hydrophobic vent filter attached at C3.
- After the ATF filtration assembly has cooled in the autoclave, V2 must be closed.
- A reinforced hose is used to connect between the SS bioreactor and the ATF.
- By opening V3 and V4, steam can pass through the connection.
- Steam and condensate line connection to either port V3 or V4 will depend on relative height between the two. The lower port is typically selected as the condensate port.
- After steaming, V3 and V4 are closed, and V1 and V2 are opened, resulting in a sterile connection between the bioreactor and ATF.

V1 and V2 must be opened immediately after steaming to prevent the formation of a vacuum inside the A2B line.

One may pre-assemble and sterilize a second XCell ATF® Device for rapid exchange with a deactivated filtration assembly. In this case, one may perform a rapid assembly exchange, requiring only A2B connection sterilization.

8. Stopping a Run

8.1 Disconnecting the XCell ATF® Device from the bioreactor

- Stop the filtrate peristaltic pump.
- Stop the XCell ATF® Device by pressing the STOP button.
- Disconnect the ATF to controller (A2C) line at the F1 air filter. (F1 air filter can be used more than once)
- Turn off the air and vacuum services to the controller.
- Disconnect the filtrate line from the harvest vessel, while maintaining sterility of the harvest vessel.
- Separate the XCell ATF® Device from the vessel by detaching the sanitary connection at the top of the dip-tube or the HFM.

- g. Remove the XCell ATF® Device to an appropriate work area (i.e. near a sink) for discarding content, disassembly, and cleaning.
- h. Drain remaining liquid in the filtrate side of the HFM housing through the lower filtrate line.
- i. Disconnect the HFM from the ATF Device pump and dispose of HFM (see section 8.2).
- j. Wash or rinse ATF stainless steel parts with appropriate cleaning solution (i.e. CIP solution or Tergazyme). Disinfect as necessary with appropriate disinfectant (i.e. diluted NaOH).

8.2 Decontaminating the HFM for Disposal

- a. Rinse the HFM two times with water to remove residual cells and debris.
- b. Decontaminate with either 0.5M NaOH or bleach



NOTE: 5.25% chlorine is equivalent to 52,500 parts per million (ppm). If household chlorine bleach is used, two working solutions are generally recommended: 5000 - 6000 ppm for initial decontamination of organic spill material, and 500 - 600 ppm for disinfection of cleaned surfaces.

- Exposure is typically 2 - 24 hours
- Wash the HFM three times with water to remove the decontamination solution.

8.3 Disconnecting controller

- a. Controller must stay connected to the power supply in order to function.
- b. Controller must be placed clear from the any other cord in the workstation/ bench top for safety.
- c. Filters and tubing must be connected away from the appliance inlet for power supply for operator safety in case of disconnecting device.
- d. Press ON to allow the controller to continue its previous status, following a power failure.
- e. On the switch adjacent to the power cord, Press OFF to allow the controller status to default to STOPPED status, following a power failure or in need for a disconnect
- f. Supply cord is detachable and must be kept clear behind the product to avoid operator from safety hazards.

9. Maintenance

9.1 Diaphragm

The silicon diaphragm is a consumable item and should be replaced for each run.

Diaphragm is made of silicone and should only be exposed to aqueous solutions.

9.2 Pump Air Filter (F1)

It is recommended that the XCell ATF® Device pump air filter (F1) be replaced after several runs, or as required. It is included in the Repligen Annual Service Kit, along with other replaceable parts.

The F1 air filter, as well as the C24 controller performance is subject to the quality of the air connected. Therefore, use clean filtered air to prolong F1 air filter and controller life.

9.3 O-Rings and Quick Connects

If the quick connectors (for A2C line and pressurized air line) on the XCell™ C24 controller become difficult to connect, the “O”- rings on the couplings may require lubrication. Use an appropriate lubricant such as silicone vacuum grease.

Use a small amount of the lubricant. Apply only to the O-rings and not inside the fitting.

The “O” rings within the PL hemisphere vent port should be replaced periodically, about once or twice per year, depending on use.

HFM Filter “O” rings (ATF4) - Use new “O” rings supplied with the filter only once.

Gaskets: Inspect sanitary gaskets after every use. Replace as needed.

9.4 Device Components

9.4.1 XCell™ C24 Controller maintenance

Failure of electrical components is difficult to predict; nevertheless, it is recommended that the controller be serviced periodically, with hardware replacement according to the following schedule:

1. Bi-annual maintenance
 - P2 verification or calibration
 - Complete Device visual inspection for damage or risk to the operator or surrounding personnel
2. Annual maintenance
 - Controller vacuum Device leak test
 - Verification that the pressure regulator is set to correct pressure
 - Inspection of air and vacuum connection to the controller
 - Inspection of pneumatic fittings
 - Inspection of the pneumatic tube from the controller to the ATF pump housing
 - Inspection of enclosure for damage, locks and hinge performance, external electrical connection, cables and pneumatic tubing
 - Inspection that all components inside of the enclosures are secured and intact
 - P2 verification / calibration
 - Inspection of touch screen alignment and performance
 - Flow test (low, middle, and high flow rate)
3. Every four years
 - Replacement of complete pneumatic manifolds, pneumatic tubing, and orifices
 - Annual maintenance routine

9.4.2 ATF Pump Housing Maintenance

1. Batch maintenance
 - Replacement of pump diaphragm
 - Replacement of hollow fiber module
 - Replacement of hollow fiber module O-rings
2. Annual maintenance
 - Replacement of all gaskets, diaphragms, O-rings, and seals
 - Inspection of pieces for damage, rust, cracks, anything out of the ordinary
 - Replacement of air filter between the ATF pump housing and the controller
 - Pressure hold test

Controller maintenance and service should be performed by a Repligen Service Representative or a trained/qualified technician. Repligen offers service contracts.

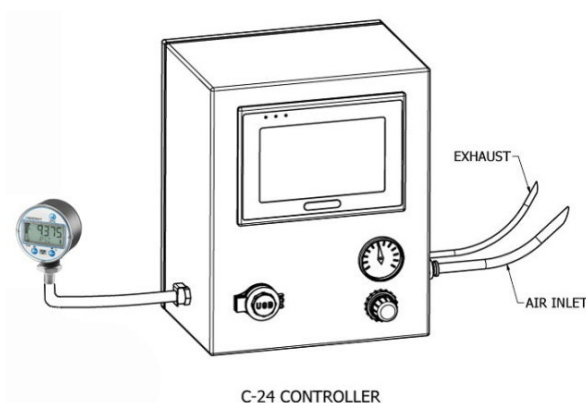
Air quality may vary from one source to the next. Humidity, filtration level, oil may be present in the air service. Treatment of the air prior to use is an obvious advantage; nevertheless, continuous use of the Device or storage in an uncontrolled area may introduce contaminants into the hardware of the controller.

9.5 Pressure Calibration

The XCell™ C24 Controller is calibrated at the factory prior to shipment. But it is recommended that the controller be checked for pressure calibration and re-calibrated if necessary, during installation. Regular calibrations are recommended during service and maintenance periods.

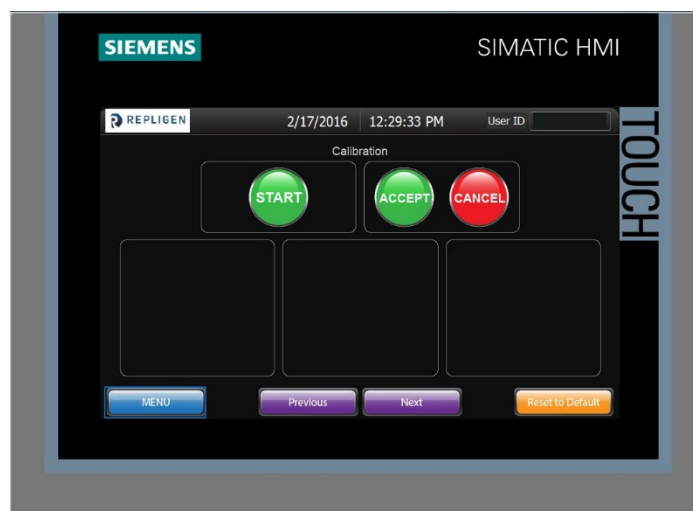
- Make sure pressure and vacuum are supplied to the XCell™ C24 Controller.
- Turn on the XCell™ C24 Controller.
- Connect a pre-calibrated electronic pressure gauge to the C24 air output line as shown below.

Figure 13. XCell™ C24 Controller pressure calibration

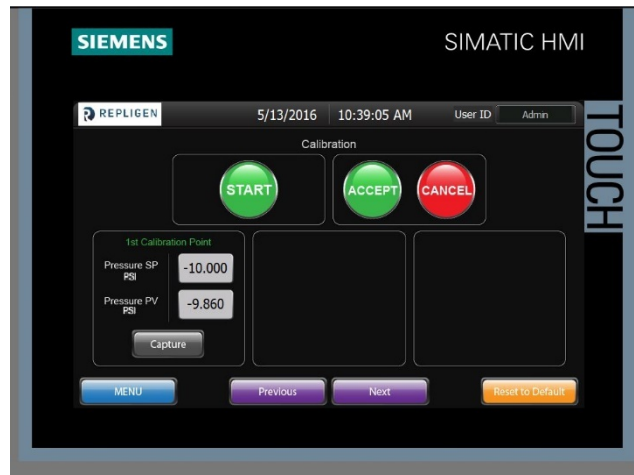


From the HMI,

- Access the Calibration screen in the Menu, under the Advanced Setup section.
- Press Start.



- Under 1st Calibration Point, enter Pressure SP i.e. -10.0 psi (-0.689 bar).



- b. Read pressure gauge.
- c. Input pressure gauge value into Pressure PV field. (Note: mmHg or inHg should be converted into PSI or bar units and remember to include the “-” sign.)
- d. Press Capture.
- e. Under 2nd Calibration Point, enter Pressure SP i.e. 25.0 psi (1.724 bar).



- f. Read pressure gauge.
- g. Input pressure gauge value into Pressure PV field.
- h. Press Capture.

Before pressing Accept, you can verify that the pressures are in fact calibrated, using the following verification procedure:

- i. Under Verification box, enter PC_SP (i.e. any value between -10.0 psi and 25.0 psi).



- j. If P1 and P2 are equivalent to PC_SP (within 0.1psi), pressure is calibrated.
- k. Press Accept.
- l. The pressure gauge reading and the “P1” and P2” fields should show similar values as that entered into “PC_SP”
 - If the values are close, but not within 0.1psi, Press “Accept” and repeat the calibration
 - If the values are way off, press the “Cancel” button and then run the calibration over again
 - If at any point things go wrong with entries, Press the “Reset to Default” button and start over

If multiple calibration attempts do not yield values within ≤ 0.2 psi, then trouble shoot for leaks or defects in pneumatic components.

- m. If you wish to cancel the calibration at any time, press Cancel.

10. Appendix 1–Human Machine Interface (HMI)

A Siemens TP700 Comfort Panel Human Machine Interface (HMI) provides the user with the following features:

- Pump Status including cycle rate, flow rate, pressure, controller status and cycles count.
- Set Up Parameters
- Ability to acknowledge and clear machine faults
- Process and sensor trending

Figure 14. HMI Graphic Screen Hierarchy

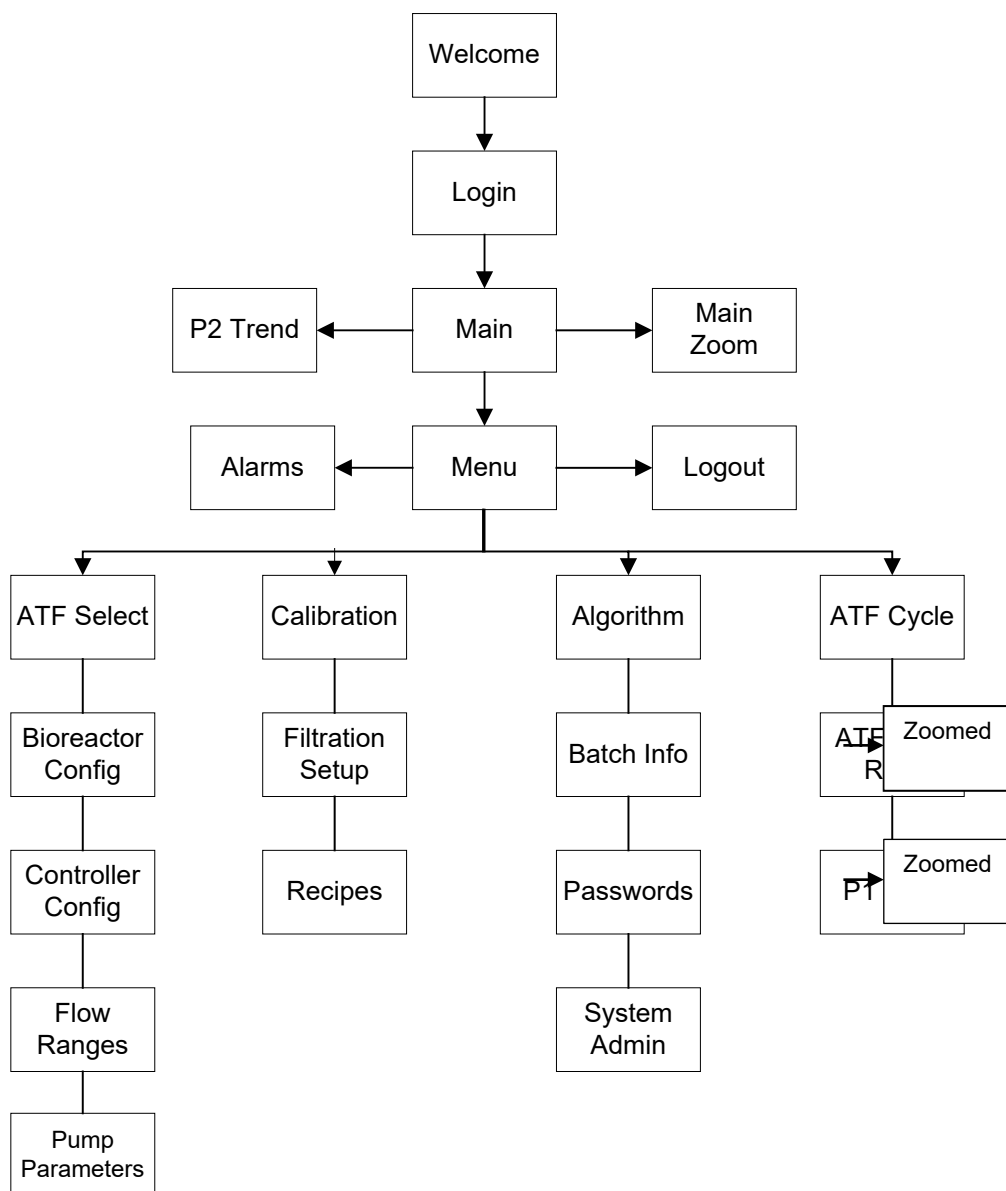


Figure 15. Welcome Screen

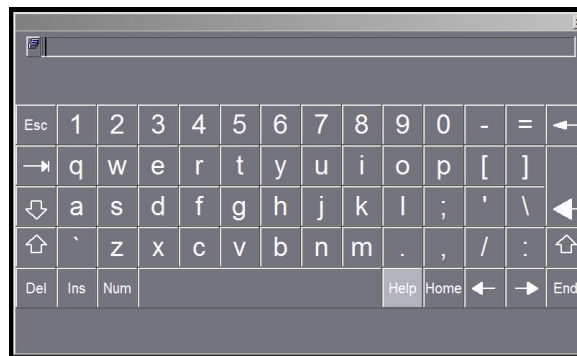


Upon Power up, the following Welcome screen displays.

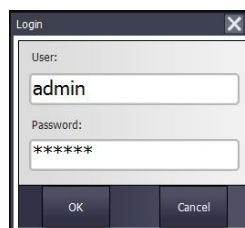
Click on LOG IN button to bring up the Login pop-up window.



Press in the white User or Password entry box to bring up the Alpha-Numeric Keypad

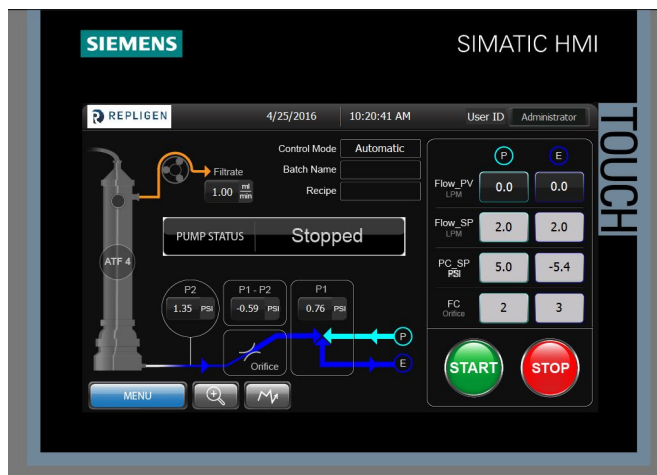


Enter "admin" and "111111" as shown
Press "OK" button



A successful login displays the MAIN Screen.

Figure 16. Main screen



From the Main screen, a user can:

- Monitor XCell ATF® Device Operating Parameters
- Start/Stop Device Pump
- Access other screens
- Monitor the XCell ATF® Device Cycle Trend
- Navigate to the Main Zoomed screen

Field	Description
Date/Time	Displays current Date and Time
User ID	Displays current User ID
Control Mode	Displays current Control Mode (Auto or Manual)
Batch Name	Displays current Batch Name
Recipe	Displays current Recipe
P-Flow_PV	When running, displays actual flow Rate of last pump Pressure cycle (LPM)
P-Flow_SP	Displays current (Pressure cycle) P-Flow Set Point (LPM)
E-Flow_PV	When running, displays actual flow Rate of last pump Exhaust cycle (LPM)
E-Flow_SP	Displays current Exhaust cycle E-Flow Set Point (LPM)
P-PC_SP	Displays current PLC Pressure Control Output for the Pressure cycle (0 to 30psi)
E-PC_SP	Displays current PLC Pressure Control Output for the Exhaust Cycle (-15 to 0 psi)
P-FC (Orifice)	P-Flow restrictor: provides primary (Rough) Flow Control between P1 and pump
E-FC (Orifice)	Exhaust flow restrictor: provides primary (Rough) Flow Control between pump and P1
P1	Represents the pressure before the restrictors. This is the actual measured value of the Pressure Control.
P2	Represents the pressure between the restrictors and the diaphragm, the “Pump” pressure (PSI) of the current Pressure/Exhaust cycle.
P1-P2	Represents the pressure drop caused by the Orifice restrictors.
Filtrate	Displays the filtration rate, defined by the user
Pump Status	Displays current C24 Controller Status which include: PUMP STOPPED PUMP PAUSED PUMP PRESSURIZING PUMP EXHAUSTING PUMP INITIALIZING PUMP WARNING PUMP ALARM

Buttons	Description
Start	Press to START the operation. A pop-up will allow selection of Current Settings or Recipe, then ENTER or CANCEL.
Stop	Press to STOP or PAUSE the operation. A popup will allow selection and confirmation or CANCEL.
Menu	Press to access all other screens
Zoom (icon)	Press to toggle between Main screen and a zoomed-in version of current Operating Parameters.
Trending (icon)	Press to toggle view the ATF Device Cycle Trend on the Main screen.
Filtrate	Press this field as a shortcut to the Filtration Setup screen.



NOTE: For the Main screen and all subsequent screens, all data fields with a dark background are for display only. The operator, based upon security levels, can change data fields with a light or yellow background.

Figure 17. Numeric Keypad

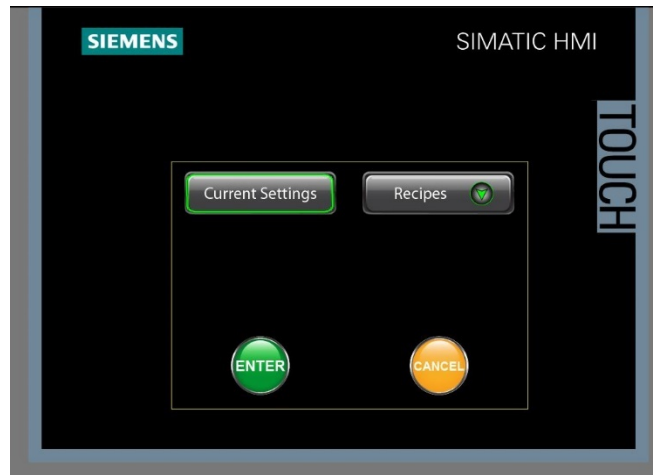


Many screens will include data fields which the user can enter/change new data values for the proper set up of the C24 Controller. Two different keypads will appear on the screen once a user selects a particular data field.

Figure 18. Alpha-Numeric Keypad



Figure 19. Start Select from Main Screen (Current Settings)



To begin running the ATF; press the START Button. The Start Select screen appears.

To accept the current settings, simply press “Enter” if the “Current Settings” button is highlighted. Highlighting this button is accomplished by pressing it. ATF Pump Status “Initializing” is displayed on the Main Screen until the Initialization pressure is reached, then Pressurizing and Exhausting.

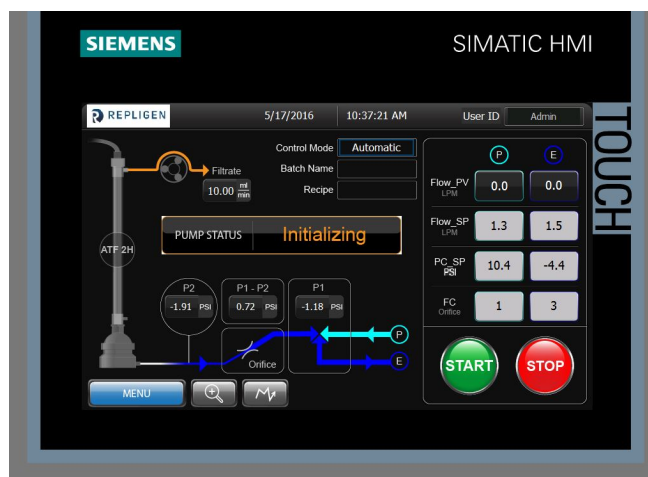
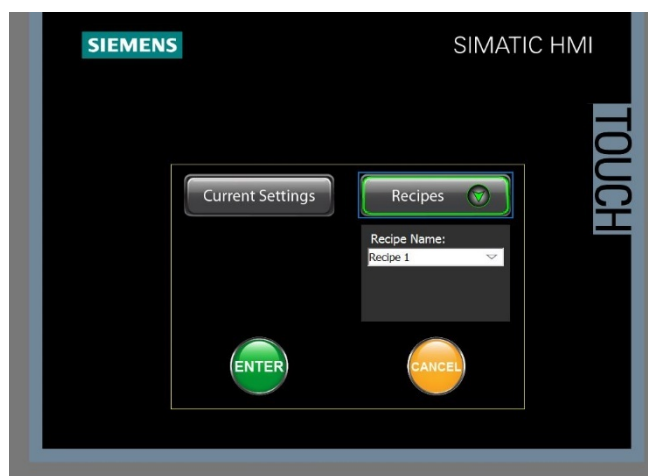


Figure 20. Start Select from Main Screen (Recipe Settings)



After pressing the START Button, a user defined recipe can be selected from the Recipes pull down button.

Upon selecting a recipe, the recipe values are downloaded into the Current Settings. Any parameter value can be entered directly into individual recipe parameters, so use care when selecting recipes that the parameters are appropriate for the ATF size and type when making selections.



NOTE: Recipes can be easily uploaded (on the recipe screen) when desired parameters have been attained through experimentation.

While running using recipe parameters, the recipe name is displayed on the Main Screen. Recipe name continues to be displayed even if parameters are manually adjusted.

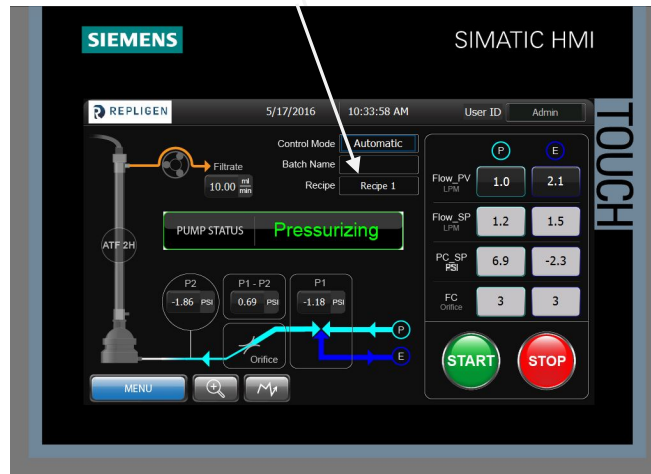
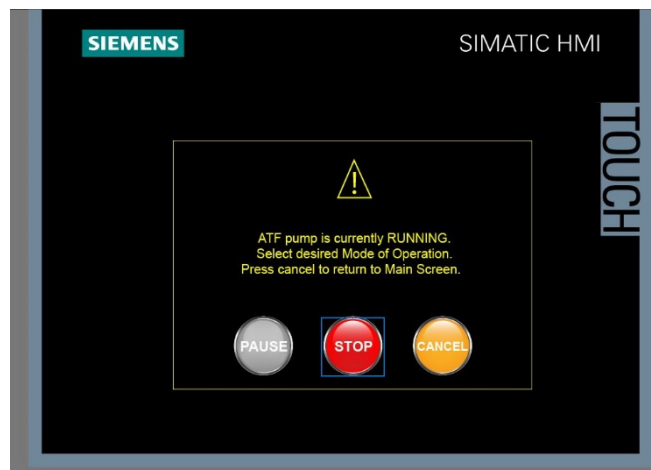


Figure 21. Stop Select from Main Screen



To stop or pause running the ATF; press the STOP Button. The Stop Select screen appears.

Both Pause and Stop options suspend ATF running (Pressurizing and Exhausting). The difference is pressing START from a paused state immediately restores the ATF running. Whereas pressing START from the Stopped state brings up the Start select screen to choose Current Settings or a recipe.

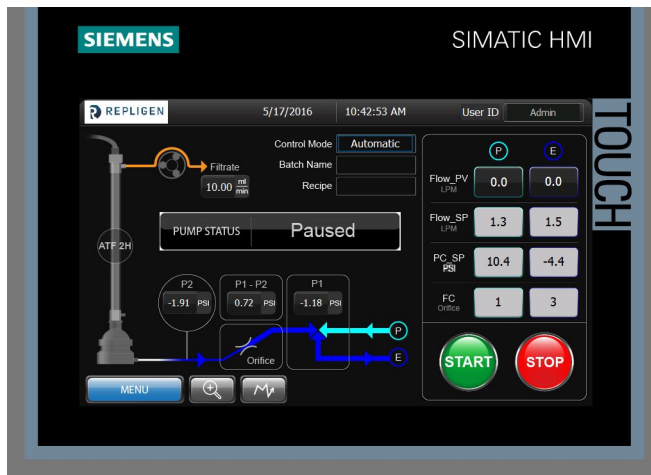
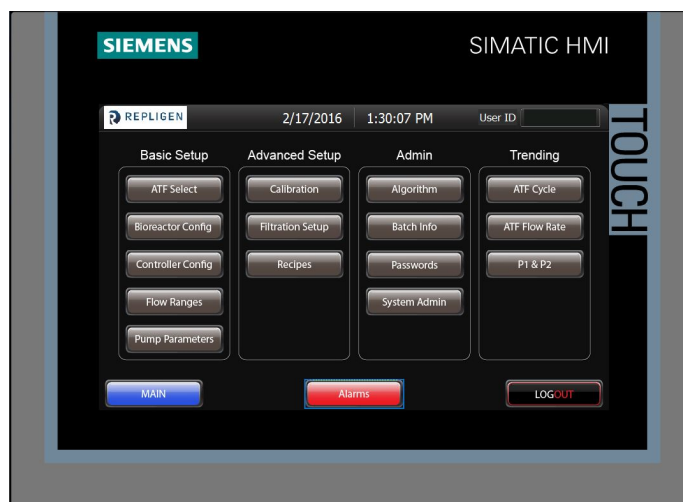


Figure 22. Zoomed-in version of Main Screen



Pressing the MENU button in the lower left-hand corner of the Main screen will display the Menu screen for navigation to all other C24 screens.

Figure 23. Menu screen

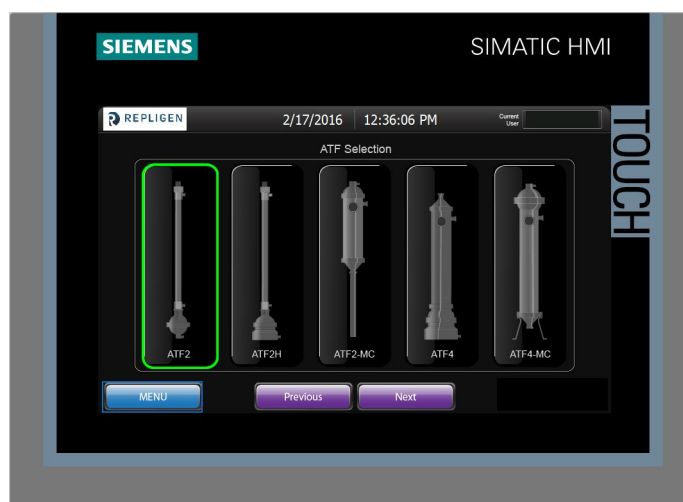


The Menu screen enables the user to navigate to any screen in the HMI, including the Main screen, Alarms screen, and Log-out screen. The Menu screen will also be accessible from any screen via the Menu button.

Buttons	Description
ATF Select	Navigates to ATF Select screen, where the ATF filtration assembly can be selected.
Bioreactor Config	Navigates to the Bioreactor Configuration screen, where the bioreactor pressure and height differential between the bioreactor and the ATF Device can be defined.
Controller Config	Navigates to the Controller Configuration screen, where the Auto Restart option, Control Mode, Date Format and Pressure Unit can be selected
Flow Ranges	Navigates to the Flow Ranges screen, where the P-Flow and E-flow ranges, as well as PC_SP range can be defined
Pump Parameters	Navigates to the Pump Parameters screen, where Delay, Switch Offset, Overflow, Overtime, Initialization Pressure, and Pump Volume Override can be defined.
Calibration	Navigates to the Calibration screen, where Pressure can be calibrated against an external pressure gauge.
Filtration Setup	Navigates to the Filtration Setup screen, where the Filter type and Filtrate rate can be defined, and ATF: Filtrate ratio, Flow per fiber and Flux calculations are displayed.
Recipes	Navigates to the Recipe screen, where simple Recipes can be defined, edited, or deleted
Algorithm	Navigates to the Algorithm Performance screen, where the counters for the switch algorithms are displayed.
Batch Info	Navigates to the Batch Info screen, where the Batch name can be defined, and Elapsed time and Cycle count are displayed.
Passwords	Navigates to the Passwords screen, where passwords can be defined based on level.
Device Admin	Navigates to the Device Admin screen, where the HMI and PLC version are displayed, and where HMI Settings and the Repligen Service screen can be accessed.
ATF Cycle	Navigates to the ATF Cycle Trend screen, where the real-time trends for P2, Delay, and Cycle are displayed.
ATF Flow Rate	Navigates to the ATF Flow Trend screen, where the real-time trends for P-Flow and E-Flow are displayed
P1 and P2	Navigates to the P1 and P2 Trend screen, where the real-time trends for P2, PC_SP, P1 and P1-P2 are displayed.
Alarms	Navigates to Alarms screen, where alarms are displayed, and horn can be acknowledged, and alarms cleared.
Logout	Press to logout and be directed to Welcome screen.
Main	Navigates to Main screen.

10.1.1 Basic Setup Screens

Figure 24. ATF Select



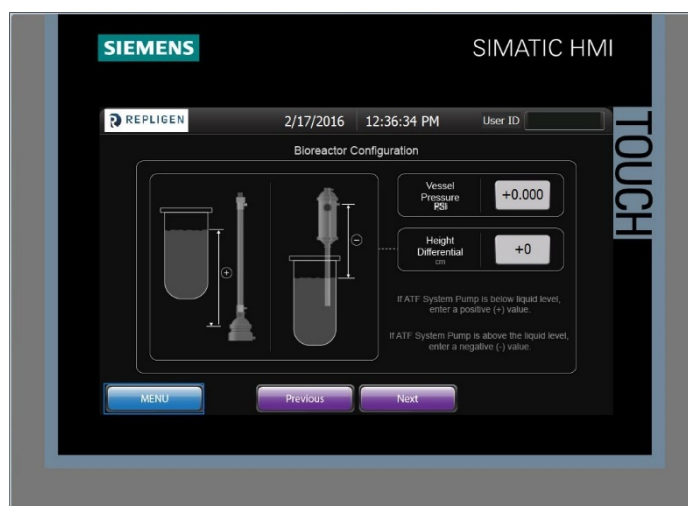
The ATF Select screen enables the user to select the type of XCell ATF® filtration assembly that will be connected to the C24 controller. The current selection will be highlighted. The selection will be updated on the ATF Device schematic on the Main screen.

Buttons	Description
XCell ATF® 2	Press to select XCell ATF® 2 Device.
XCell ATF® 2H	Press to select XCell ATF® 2H Device.
XCell ATF® 2-MC	Press to select XCell ATF® 2-MC Device for Microcarrier process.
XCell ATF® 4	Press to select XCell ATF® 4 Device.
XCell ATF® 4-MC	Press to select XCell ATF® 4-MC Device for Microcarrier process.
Menu	Press to access the Menu screen.
Previous	Navigates backwards to the previous screen within the Basic Setup screens loop.
Next	Navigates forward to the next screen within the Basic Setup screens loop.



NOTE: While the Device is running, be careful not to accidentally push another ATF selection on this screen.

Figure 25. Bioreactor configuration



10.2 Bioreactor Configuration

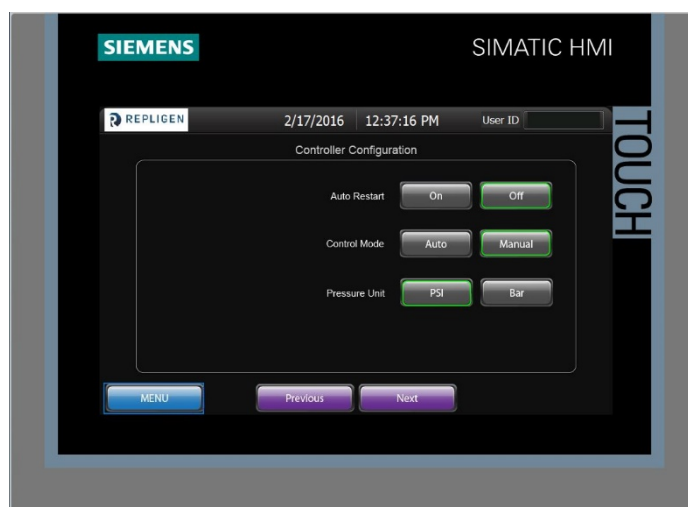
The Bioreactor Configuration screen enables the user to enter the vessel pressure (stainless steel bioreactors only) and height differential between the liquid level and the ATF Device pump. These values will affect the initial pressure control (PC_SP) and flow control (Orifice) values, which will help the algorithm, achieve steady state faster.

This screen is useful when configurations can vary significantly (i.e. ATF4 Device or ATF4 MC Device that can be either mounted to side of a Stainless Steel bioreactor or through the top). Otherwise, it is recommended to keep the values at 0.

Field	Description
Vessel Pressure	Enter bioreactor vessel pressure of bioreactor
Height Differential	Enter the height differential between the liquid level and ATF Device pump.

Buttons	Description
Previous	Navigates backwards to the previous screen within the Basic Setup screens loop.
Next	Navigates forward to the next screen within the Basic Setup screens loop.
Menu	Navigates to Menu for access to other screens

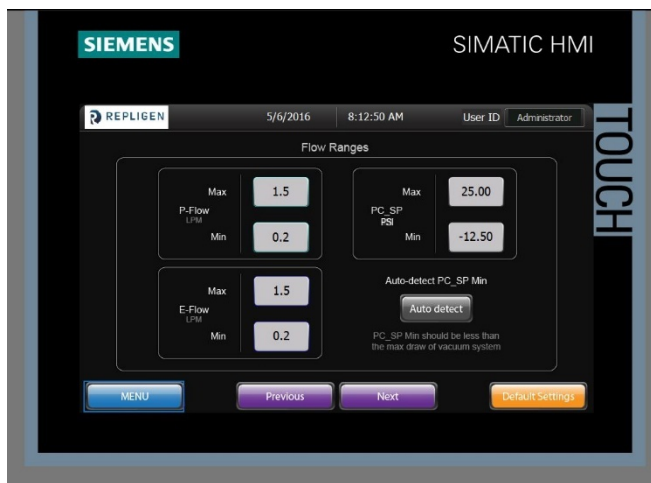
Figure 26. Controller Configuration



Buttons	Description
Auto Restart	Press ON to allow the controller to continue its previous status, following a power failure. Press OFF to allow the controller status to default to STOPPED status, following a power failure.
Control Mode	Press AUTO to allow the controller to automatically adjust the pressure control (PC_SP) and flow control (Orifice) values. Press MANUAL to deactivate the control algorithm and keep current the pressure control and flow control values or as defined by the user.
Pressure Unit	Select desired unit.
Previous	Navigates backwards to the previous screen within the Basic Setup screens loop.
Next	Navigates forward to the next screen within the Basic Setup screens loop.
Menu	Navigates to Menu for access to other screens

The Bioreactor Configuration screen enables the user to configure the controller Auto Restart option, Control Mode, and Pressure Unit.

Figure 27. Flow Ranges



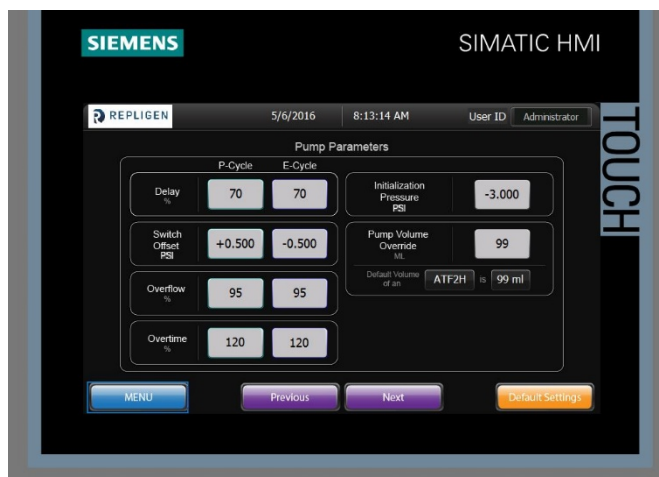
The Flow Ranges screen enables the user to define the P-Flow and E-Flow ranges, depending on the ATF Device size selected. The Pressure Control (PC_SP) range is also defined on this screen. The user has the option of pressing the “Default Settings” button and the fields will be populated with the Repligen recommended settings.

Field	Description
P-Flow Max	Maximum limit for P-Flow rate, based on size of ATF Device
P-Flow Min	Minimum limit for P-Flow rate, based on size of ATF Device
E-Flow Max	Maximum limit for E-Flow rate, based on size of ATF Device
E-Flow Min	Minimum limit for E-Flow rate, based on size of ATF Device
PC_SP Max	Maximum operating limit for PC_SP during the Pressurization cycle, typically 25 to 30 psi. This value must be lower than the pressure set on the Second Stage pressure gauge.
PC_SP Min	Minimum operating limit for PC_SP during the Exhaust cycle, typically -12.5 to -14.7 psi. This value must be lower than the vacuum generated by the vacuum source.

Buttons	Description
Auto Detect	Press this button to set the PC_SP Min automatically, based on the maximum vacuum draw.
Default Settings	Press this button to automatically populate the fields with Repligen recommended values.
Previous	Navigates backwards to the previous screen within the Basic Setup screens loop.
Next	Navigates forward to the next screen within the Basic Setup screens loop.
Menu	Navigates to Menu for access to other screens

When a new P-Flow and/or E-Flow Set Point is changed by the user, the settings for PC_SP and FC_SP Orifice will automatically switch to preset default values based on the Starting Algorithm. See section on Algorithms for greater detail. The preset values provide the controller with start settings which minimize the number of pump cycles needed for the controller to tune the Device to reach desired flow rates.

Figure 28. Pump Parameters

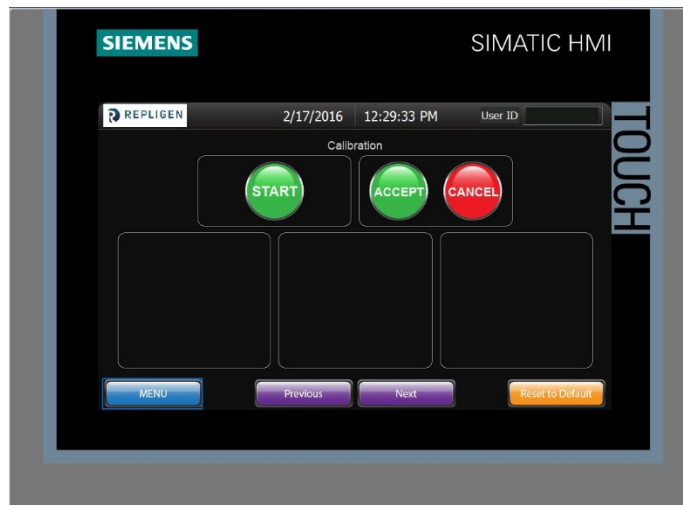


The Pump Parameters screen enables the user to define the parameters which ultimately determines when the Pump switches between Pressure and Exhaust cycles. The field values entered will depend on the objective of the process.

Field	Description
Delay (%)	Set the time point (in % of calculated cycle time) for sampling P2 (sP2).
Switch Offset (bar/psi)	Pressure Offset increment (PSI) added to sP2 (during the P- cycle) or subtracted from sP2 (during the E-cycle), which set the Cycle Switch Point between Pressure and Exhaust cycles.
Overflow (%)	Contingency switch based on pressure “overflow” - Set as a percentage of P1 pressure. For $P2 \geq$ than Overflow (%) of P1, a cycle change is forced. It provides a High Limit (Pressure) and Low Limit (Exhaust) in case P1-P2 is < the Switch Offset and the Primary Method of switching cannot work.
Overtime (%)	Contingency switch based on cycle “overtime”. Set at a percentage greater than 100% of the calculated Cycle time. If the Primary method fails, a cycle change is forced at Overtime (%) of the calculated cycle time.
Initial Pressure (-bar/psi)	Prior to starting, P2 must reach this negative pressure which assures that the pump is fully exhausted, and the diaphragm is at its starting point.
Default Settings	Press this button to automatically populate the fields with Repligen recommended values.
Previous	Navigates backwards to previous screen within the Advanced Setup screens loop.
Next	Navigates forward to the next screen within the Advanced Setup screens loop.
Menu	Navigates to Menu for access to other screens

10.3 Advanced Setup Screens

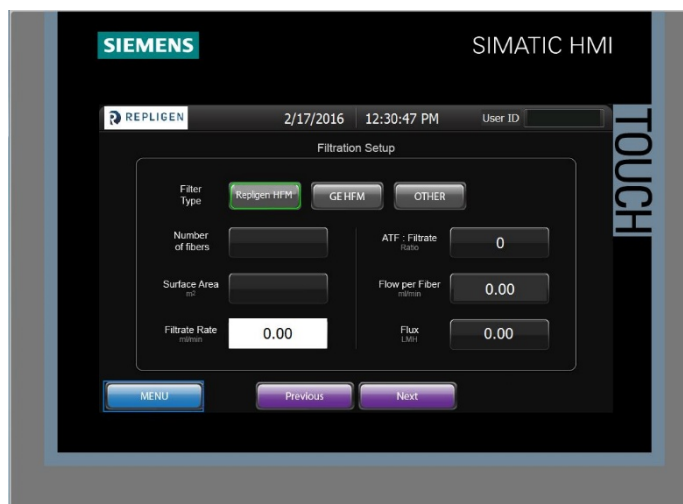
Figure 29. Calibration



The Calibration screen enables the user to perform a two-point calibration on the pressure, which ensures the accuracy of P1 and P2 measurements. The calibration procedure is explained in Section 8.5.

Buttons	Description
START	Press to start calibration
ACCEPT	Press after 2 nd calibration point is captured, to accept new calibration values.
CANCEL	Press to cancel calibration at any time.
Capture	Press to confirm new calibration value for each point.
Reset to Default	Press to reset calibration to factory default values.
Previous	Navigates backwards to the previous screen within the Advanced Setup screens loop.
Next	Navigates forward to the next screen within the Advanced Setup screens loop.
Menu	Navigates to Menu for access to other screens

Figure 30. Filtration Setup

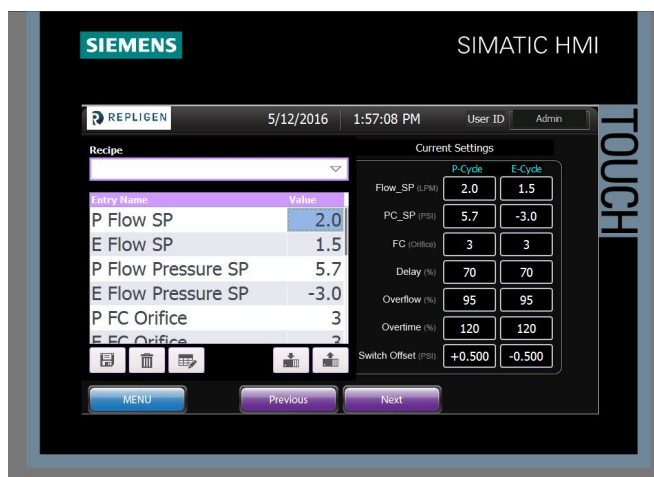


The Filtration Setup screen enables the user to define the current filtration setup, and see important scale-up parameters including the ATF rate to Filtration rate ratio, Flow per fiber, and Flux.

Currently, an external pump cannot be controlled by the C24. The filtrate rate is manually entered to see the scale-up parameters.

Field	Description
Number of fibers	Displays number of fibers based on Filter Type selection, and ATF Device selected.
Surface Area	Displays total filter surface area based on Filter Type selection, and ATF Device selected.
Filtrate Rate	Enter value of filtration rate. This value must be updated to reflect actual value on external pump, in order to show accurate scale-up parameter values.
ATF:Filtrate Ratio	Displays ratio between ATF Device flow rate and Filtrate rate. Note: The higher this value, the better the self-cleansing effect inherent of the ATF Device.
Flow per Fiber	Displays the volume of flow per fiber within the HFM.
Repligen HFM	Select when using Repligen Spectrum® Hollow Fiber module
GE HFM	Select when using approved GE hollow fiber module
Other	Select when using other hollow fiber module
Previous	Navigates backwards to the previous screen within the Advanced Setup screens loop.
Next	Navigates forward to the next screen within the Advanced Setup screens loop.
Menu	Navigates to Menu for access to other screens

Figure 31. Recipes

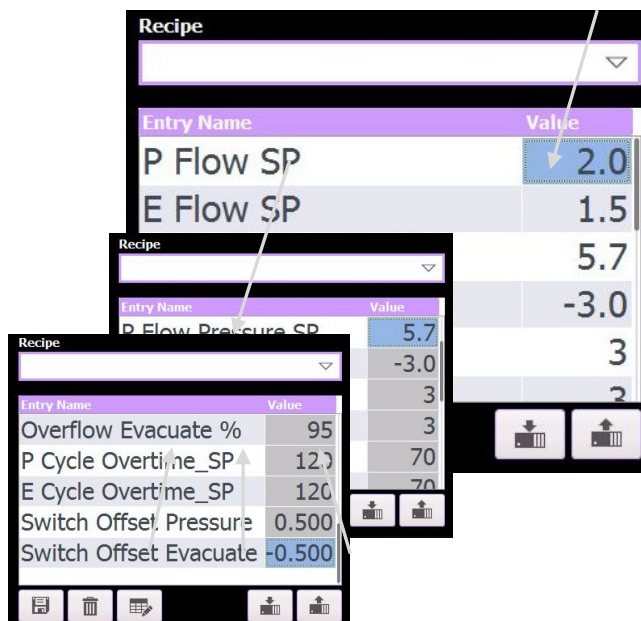


The Recipes screen enables the user to create simple recipes, which can be saved and edited as needed. When the START button is pushed on the Main screen, the user is given the option of executing any saved recipe.

Field	Description
Recipe Interface	Provides access to recipes: Including Recipe name, Parameters, Save, Delete, Rename, download and upload button interface.
Flow_SP	Current settings of orifice values for P and E-cycle. (View only)
PC_SP	Current settings of starting pressure value for P and E-cycle. (View only)
FC_SP	Current settings of starting Orifice value for P and E-cycle. (View only)
Delay	Current settings of Delay value for P and E-cycle. (View only)
Overflow	Current settings of Overflow “Switch Limit” value for P and E-cycle. (View only)
Overtime	Current settings of Overtime value for P and E-cycle. (View only)
Switch Offset	Current settings of Switch Offset value for P and E-cycle. (View only)

Buttons	Description
Recipe Interface	Described on the following page allows recipe parameter entry and loading to “Current Settings”
Previous	Navigates backwards to the previous screen within the Advanced Setup screens loop.
Next	Navigates forward to the next screen within the Advanced Setup screens loop.
Menu	Navigates to Menu for access to other screens

Recipe Interface: Fourteen (14) parameters can be manually entered by pressing in the value entry box highlighted in blue below. Press in the left section of the value entry box to avoid inadvertently activating the right slider bar.



To view lower parameters, it is recommended to press on the Entry Name parameters and drag the list up. Upper parameters can again be viewed by dragging the list back down.

Save	Delete	Rename		Download	Upload
------	--------	--------	--	----------	--------

To create a new recipe, simply press the Recipe entry box. The Alpha-Numeric keypad appears. Type in a recipe name and press “Enter”. The name appears in the Recipe box. Populate the recipe parameters either by entering values as described above, or by pressing the upload button to capture the “Current Settings”.

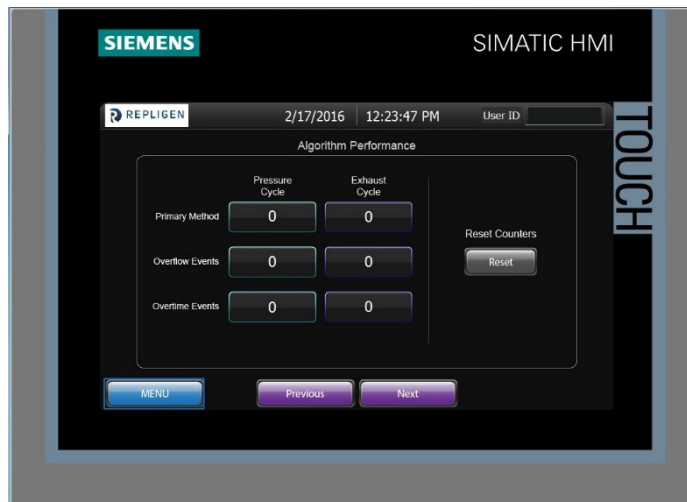
Press the Save button. The recipe is saved and can be loaded when starting the ATF. Additionally, recipe parameters can be downloaded to the “Current Settings” by pressing the Download button.

Buttons	Description
Recipe	Pull down drop box of existing recipes.
Save (icon)	Push to save a new recipe or overwrite an existing recipe that was edited.
Delete (icon)	Push to delete an existing recipe
Rename (icon)	Rename Recipe Name.
Download (icon)	Populates the “Current Settings” with recipe values shown in recipe table.
Upload (icon)	Populates recipe table with “Current Settings”.

The download button can be used to view all recipe values. Remember that the current settings are the parameters running the ATF; so, caution should be exercised when performing recipe downloads to “Current Settings.”

10.4 Admin Screens

Figure 32. Algorithm performance



The Algorithm Performance screen enables the user to see how well the controller is functioning according to the control algorithms. The information is especially valuable in troubleshooting potential problems and making the proper adjustments to the control parameters so that the controller functions properly, such that the XCell ATF® Device pump is achieving a full volume displacement.

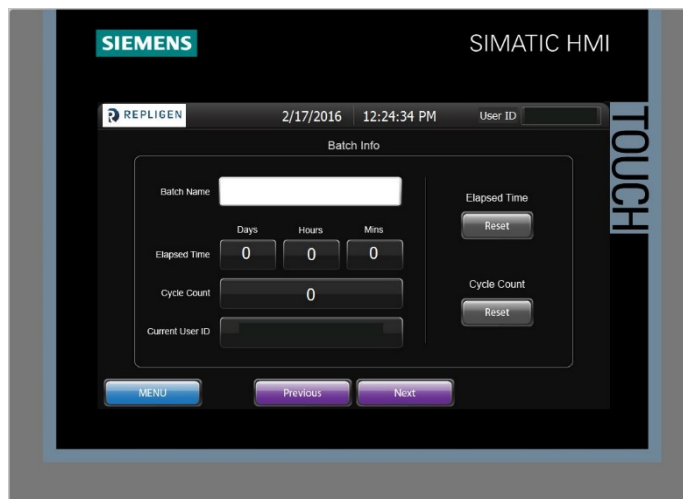


NOTE: That this function is available in Automatic mode only.

Field	Description
Primary Method	Displays the number of cycles completed under the Primary Method of the control algorithm.
Overflow Events	Displays the number of cycles that resulted from Overflow contingency switch.
Overtime Events	Displays the number of cycles that resulted from Overtime contingency switch.

Buttons	Description
Reset Counters	Push to reset all of the algorithm counters (recommended at start of a new perfusion run)
Previous	Navigates backwards to the previous screen within the Admin screens loop.
Next	Navigates forward to the next screen within the Admin screens loop.
Menu	Navigates to Menu for access to other screens

Figure 33. Batch Info



The Batch Info screen enables the user to define a batch name and monitor time and cycle count for a specific batch. The Batch name will appear on the main screen. The elapsed time and cycle count can be reset for each new batch.

Field	Description
Batch Name	Enter desired batch name. This batch name will also be displayed on Main screen.
Elapsed Time	Displays the number of days, hours and minutes that have elapsed since last reset.
Cycle Count	Displays the number of cycles completed since last reset.
Current User ID	Displays the current user level.

Buttons	Description
Elapsed Time Reset	Push to reset elapsed time counter.
Cycle Count Reset	Push to reset cycle count
Previous	Navigates backwards to the previous screen within the Admin screens loop.
Next	Navigates forward to the next screen within the Admin screens loop.
Menu	Navigates to Menu for access to other screens

Figure 34. Passwords



The Passwords screen is accessible by all fully configured users. All configured users can change their own password. Members of the Administrator group can change passwords of any user, as well as add new users and modify all credentials displayed in the Passwords table.

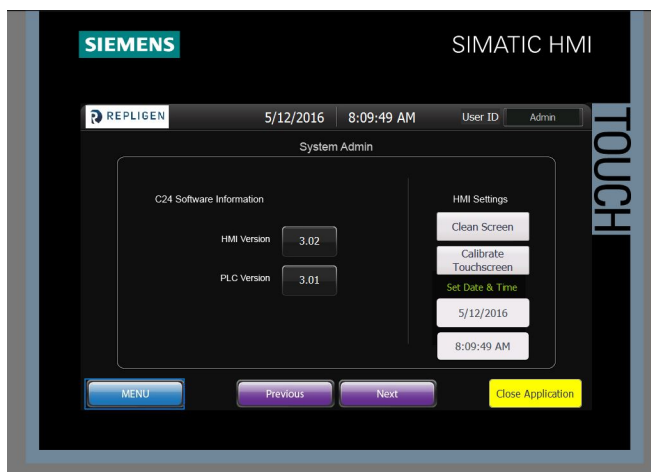
The XCell™ C24 Controller comes with the Admin User and Password (“111111”) configured. The above listed users are preconfigured without passwords. Activating these other users is accomplished by specifying a password for the user by members of the Administrator group. Additional users can be added by Administrator group members.

Buttons	Description
Previous	Navigates backwards to the previous screen within the Admin screens loop.
Next	Navigates forward to the next screen within the Admin screens loop.
Menu	Navigates to Menu for access to other screens

Members of the group “Users” experience the password screen as shown below. Only their username is shown. The password can be changed by selecting the Password section of the table and completing the entries of the Change password dialog.



Figure 35. Device Admin

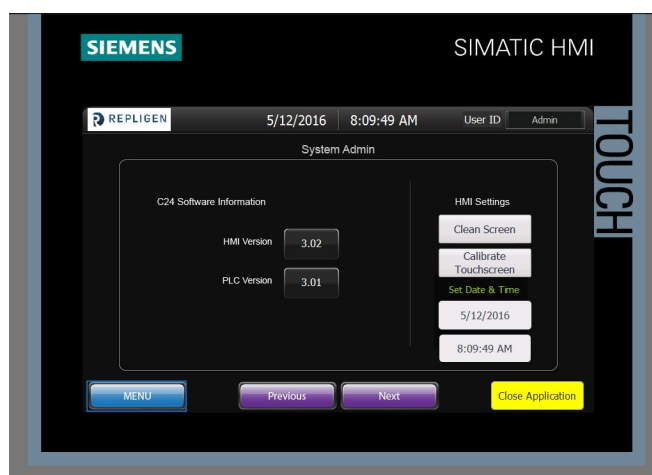


The Device Admin enables the user to see the current HMI and PLC version installed on the XCell™ C24 Controller. This screen also provides access to adjust the physical HMI settings and date and time.

Field	Description
HMI Version	Displays the current HMI version installed.
PLC Version	Displays the current PLC version installed.

Buttons	Description
Clean Screen	Push to run a utility that disables the touch screen for 30 seconds, allowing the screen to be wiped and cleaned.
Calibrate Touchscreen	Push to run a utility that recalibrates the touch locations on the screen.
Date (shown as 5/12/2016)	Push to edit the Device Date. (Alpha-Numeric keypad pops up)
Time (shown as 8:09:49 AM)	Push to edit the Device Time. (Alpha-Numeric keypad pops up)
Previous	Navigates backwards to the previous screen within the Admin screens loop.
Next	Navigates forward to the next screen within the Admin screens loop.
Menu	Navigates to Menu for access to other screens
Close Application	Closes the C24v3 HMI application allowing access to other Device parameters, such as IP Address set up.

Figure 36. Date/Time Change (Two methods)



1. Within the XCell™ C24 Controller (v3) HMI application: Navigate to the Device Admin screen. Press the button displaying the Device date and/or time to edit the date via Alpha-Numeric keypad.
2. From the Windows CE Settings:
 - a. From the Device Admin screen, press the “Close Application” button.
 - b. The run time program will shut down and Start Center V13.0.1.0 will be displayed in the middle of the screen.
 - c. Press Settings.
 - d. In the upper left of the screen, press Date/Time.
 - e. Set the Date and Time, the Time Zone, and whether to use Daylight Savings Time.
 - f. Press Apply.

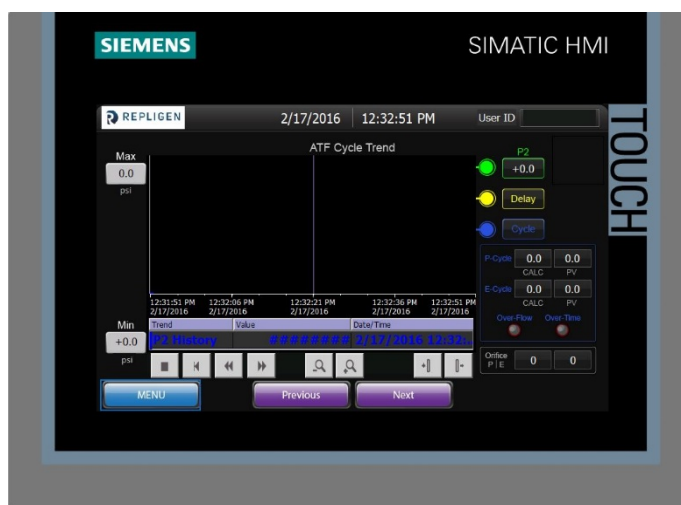
10.4.1.1 Set/Change IP Address of HMI

1. HMI IP Address setting:
 - a. Select settings from the start menu, select network and dial up connections, then select PN_X1.
 - b. From this interface, the IP Address, Subnet Mask and all other Ethernet Properties can be adjusted.
2. PLC IP Address setting:
 - c. Select settings from the start menu (or go back to the setting screen) and select Service & Commissioning.
 - d. Select IP config by pressing the right arrow to reveal the 5th tab.
 - e. From the Service & Commissioning screen, press the assign IP button.
 - f. On the following screen select network, scan and start. “Scan is running” appears at the bottom of the window.
 - g. After the scan is complete, the S7-1200 device should appear. Select the S7-1200 device and the device fields populate with the current configuration.
 - h. From this interface, the IP Address, Subnet Mask and all other Ethernet Properties can be adjusted.
 - i. Once the values have been entered, select device, download and IP to assign the address to the device. “IP suite settings could be assigned” appears at the bottom of the window.
 - j. Exit out of the assign IP
3. Set Connection between HMI and PLC:
 - k. From the Service & Commissioning screen, press the set connection button.

- l. On the following screen press the Find Online button. After the scan is complete, the S7-1200 device should appear. Select it, and the IP Address box below contains the PLC’s address. Note: It can also be entered manually.
 - m. Press OK to accept and close the window.
 - n. Press Save to set the connection. “Save is successful” appears at the bottom of the window.
 - o. Close the window to exit.
 - p. Close the Service & Commissioning window.
 - q. Close the Settings Window.
4. Start the program again and ensure that ‘#####’ do not appear in the main screen fields.

10.5 Trending Screens

Figure 37. ATF Cycle



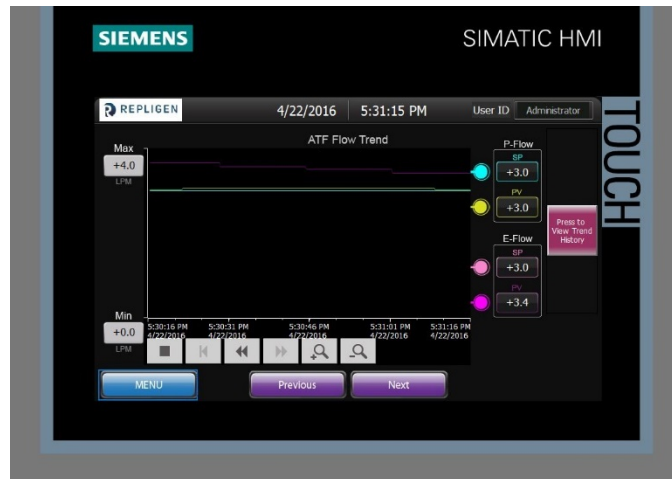
The ATF Cycle trending screen enables the user to monitor real-time information about the XCell ATF® Device cycle, including P2, Delay, and Cycle time (calculated and actual PV).

Pressure values are displayed with PSI engineering units.

Field	Description
Trend graph	Displays real-time trend values. Touch anywhere in this field to display history value at that point
Max	Enter maximum value for the chart Y Axis
Min	Enter minimum value for the chart Y Axis
P2	Displays P2 real-time value.
P-Cycle CALC	Displays calculated cycle time for the P-Cycle
P-Cycle PV	Displays actual cycle time for the P-Cycle
E-Cycle CALC	Displays calculated cycle time for the E-Cycle
E-Cycle PV	Displays actual cycle time for the E-Cycle
Orifice P and E	Displays the current orifice values for the P-cycle and E-cycle

Buttons	Description
Color ink wells	Touch to toggle on or off the color-specific trend line.
Previous	Navigates backwards to the previous screen within the Trending screens loop.
Next	Navigates forward to the next screen within the Trending screens loop.
Menu	Navigates to Menu for access to other screens

Figure 38. ATF Flow Rate



The ATF Flow Rate trending screen enables the user to monitor real-time information about the ATF Device Flow rate.

Field	Description
Trend graph	Displays real-time trend values. Touch anywhere in this field to display history values at that point
Max	Enter maximum value for the chart Y Axis
Min	Enter minimum value for the chart Y Axis
P-Flow SP	Displays current P-Flow Set point
P-Flow PV	Displays current P-Flow Process Value
E-Flow SP	Displays current E-Flow Set point
E-Flow PV	Displays current E-Flow Process Value

Buttons	Description
Color ink wells	Touch to toggle on or off the color-specific trend line.
Trend History	Touch to display historical data trend; zoomed in.
Previous	Navigates backwards to the previous screen within the Trending screens loop.
Next	Navigates forward to the next screen within the Trending screens loop.
Menu	Navigates to Menu for access to other screens

Figure 39. ATF Flow Rate History (zoomed in)

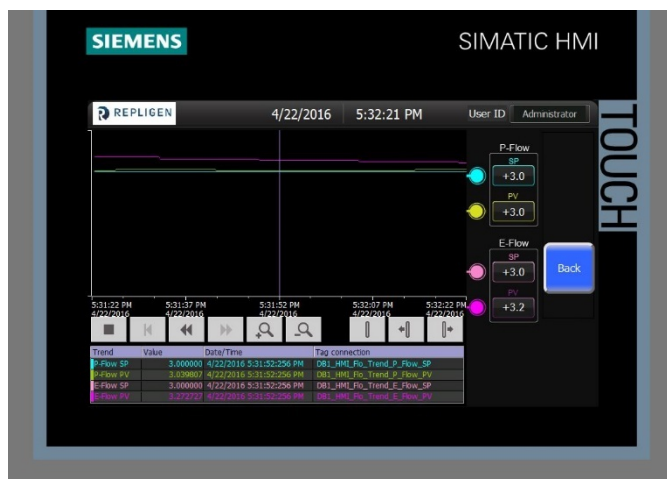
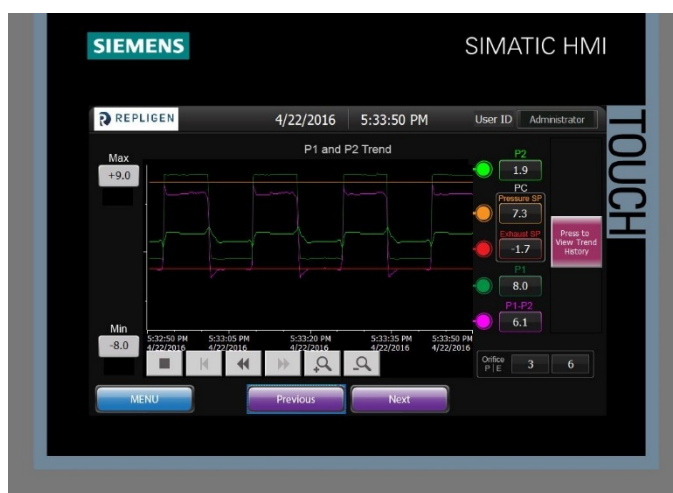


Figure 40. P1 and P2 Trend



The P1 and P2 trending screen enables the user to monitor real-time information about the important control pressures: Pump Diaphragm pressure P2 as a tool for setting the correct parameters for detecting fully inflated/fully exhausted pump diaphragm.

Field	Description
Trend graph	Displays real-time trend values. Touch anywhere in this field to display history value at that point
Max	Enter maximum value for the chart Y Axis
Min	Enter minimum value for the chart Y Axis
P2	Displays P2 real-time value.
PC_SP (Pressure)	Displays the current Pressure Control setpoint for the P-cycle, set by the algorithm.
PC_SP (Exhaust)	Displays the current Pressure Control setpoint for the E-cycle, set by the algorithm.
P1	Displays the actual Pressure Control process value (also known as PC_PV)
P1 – P2	Displays the difference between P1 and P2, which is the pressure drop across the Orifice.
Orifice P and E	Displays the current orifice values for the P-cycle and E-cycle

Buttons	Description
Color ink wells	Touch to toggle on or off the color-specific trend line.
Trend History	Touch to display historical data trend; zoomed in.
Previous	Navigates backwards to the previous screen within the Trending screens loop.
Next	Navigates forward to the next screen within the Trending screens loop.
Menu	Navigates to Menu for access to other screens

Figure 41. P1 and P2 Trend History (zoomed in)

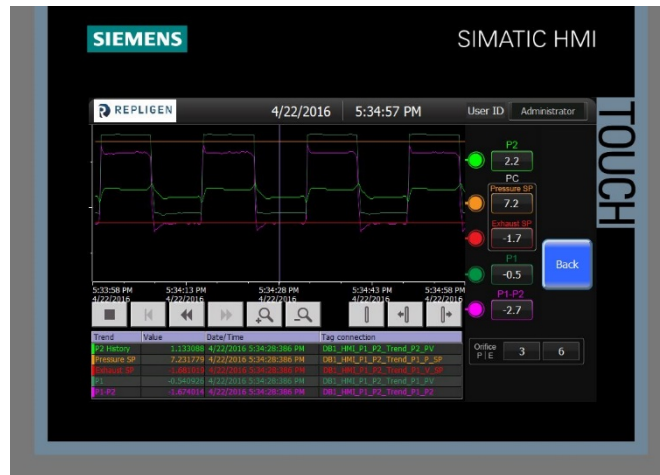
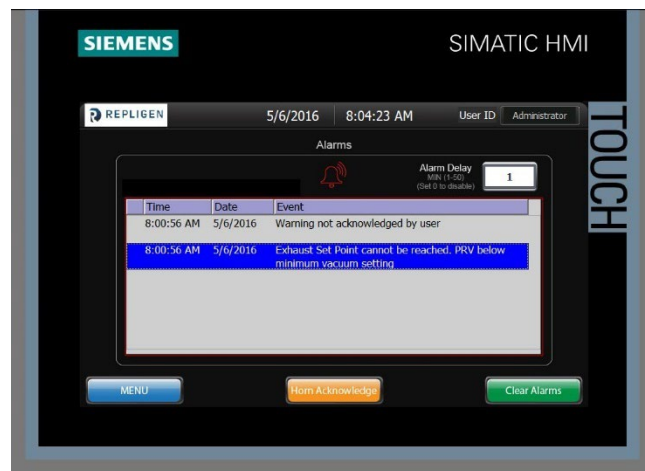


Figure 42. Alarm Screen



Any logged in user can view the XCell™ C24 Controller Warnings and Alarm conditions:

- All Alarms/ Warnings are displayed with Time/Date stamping and full description of condition.
- Both Alarms and Warnings will activate the (optional) audible horn located inside the XCell™ C24 Controller cabinet.
- An Alarm condition will automatically stop the pump cycling action, while a Warning condition allows the pumping cycling action to continue.

Field	Description
Warning Acknowledge Delay Timer (min)	Enter delay time in minutes to stop ATF Device function if Warning is not acknowledged. NOTE: Entering a “0” value disables the Delay Timer feature.

Buttons	Description
Clear Alarms	Press to remove Warning/Alarm messages
Horn Acknowledge	Press to silence horn inside the C24 controller.

The XCell™ C24 Controller Warnings and Alarms are shown in [Appendix 2](#).

11. Appendix 2—Information for Remote Data Logging

Tag name	Description	PLC Address	Offset	Type
DL_P1	PRV Feedback from Transducer	%DB10.DBD0	0.0	Real
DL_P2	Pressure Reading at the Pressure Transducer	%DB10.DBD4	4.0	Real
DL_PRV1	Pressure Setpoint during Pump State 2	%DB10.DBD8	8.0	Real
DL_PRV2	Pressure Setpoint during Pump State 5	%DB10.DBD12	12.0	Real
DL_PFLOW	Calculated pressure flow rate	%DB10.DBD16	16.0	Real
DL_EFLOW	Calculated Exhaust flow rate	%DB10.DBD20	20.0	Real
DL_PFLOWSP	Pressure Flow Setpoint	%DB10.DBD24	24.0	Real
DL_EFLOWSP	Exhaust Flow Setpoint	%DB10.DBD28	28.0	Real
DL_FLOR	Pressure Cycle Orifice setting	%DB10.DBW32	32.0	Word
DL_EXOR	Exhaust Cycle Orifice Setting	%DB10.DBW34	34.0	Word
PP_PFLOWSP*	Pressure Setpoint LPM	%DB11.DBD0	0.0	Real
PP_EFLOWSP *	Exhaust Flow Setpoint LPM	%DB11.DBD4	4.0	Real
PP_Bioreactor Pressure	Bioreactor Pressure	%DB11.DBD8	8.0	Real
PP_Bioreactor_Height_Diffe	Bioreactor Height Differential	%DB11.DBD12	12.0	Real
PP_PFLOWMAXSP	Max Pressure Flow Setpoint LPM	%DB11.DBD16	16.0	Real
PP_PFLOWMINSP	Min Pressure Flow Setpoint LPM	%DB11.DBD20	20.0	Real
PP_EFLOWMAXSP	Max Exhaust Flow Setpoint LPM	%DB11.DBD24	24.0	Real
PP_EFLOWMINSP	Min Exhaust Flow Setpoint LPM	%DB11.DBD28	28.0	Real
PP_PRV1MAX	Flow Regulator Value Max Value	%DB11.DBD32	32.0	Real
PP_PRV2MIN	Exhaust Regulator Value Min Value	%DB11.DBD36	36.0	Real
PP_FDFOFST *	Flow Driving Force Offset for switching	%DB11.DBD40	40.0	Real
PP_EDFOFST *	Exhaust Driving Force Offset for switching	%DB11.DBD44	44.0	Real
PP_P2SWPCT *	Flow P2 percentage to switch	%DB11.DBD48	48.0	Real
PP_EBUSWSP *	Flow P2 percentage to switch	%DB11.DBD52	52.0	Real
PP_P_Cycle_Overtime_SP *	P-Cycle - Overtime SP (%)	%DB11.DBD56	56.0	Real
PP_V_Cycle_Overtime_SP *	V-Cycle - Overtime SP (%)	%DB11.DBD60	60.0	Real
PP_Init_Pressure_SP	Initialization Pressure Set Point	%DB11.DBD64	64.0	Real
PP_PUMPVOL	Pump Diaphragm Volume	%DB11.DBD68	68.0	Real
PP_FTDP *	Flow Time Delay Percentage	%DB11.DBD72	72.0	Real
PP_ETDP *	Exhaust Time Delay Percentage	%DB11.DBD76	76.0	Real
PP_STATUSREG	Pump Status Register	%DB11.DBW80	80.0	Word
PP_PUMPSTATE	Pump State	%DB11.DBW82	82.0	Word
PP_MODELNO	Pump Model No	%DB11.DBW84	84.0	Word
PP_AutoRestartEnabled	Allow Pump to restart after a power cycle	%DB11.DBX86.0	86.0	Bool
PP_Manual_Automatic_Mode	Device in manual or automatic mode	%DB11.DBX86.1	86.1	Bool
PP_Units_PSI_Bar	Pressure displays in PSI or Bar	%DB11.DBX86.2	86.2	Bool
PP_Default_Pump_Parameters	Load default setup values	%DB11.DBX86.3	86.3	Bool

* Recipe Parameters (See Recipe Screen section for more on Recipes).

Figure 43. Input/Output List

Tagname	Description	PLC Address	Type	Engineering			
				Range		Decimal Places	Units
				Low	High		
Spare		%I0.0	DI				
Spare		%I0.1	DI				
Spare		%I0.2	DI				
Spare		%I0.3	DI				
Spare		%I0.4	DI				
Spare		%I0.5	DI				
Spare		%I0.6	DI				
Spare		%I0.7	DI				
Spare		%I0.8	DI				
Spare		%I0.9	DI				
Spare		%I0.10	DI				
Spare		%I0.11	DI				
Spare		%I0.12	DI				
Spare		%I0.13	DI				
Horn	Optional signal for external horn	%Q0.0	DO				
Sol_A	Orifice Valve A	%Q0.1	DO				
Sol_E	Orifice Valve E	%Q0.2	DO				
Sol_F	Orifice Valve F	%Q0.3	DO				
Sol_G	Orifice Valve G	%Q0.4	DO				
Spare	Spare	%Q0.5	DO				
Sol_B	Orifice Valve B	%Q0.6	DO				
Sol_C	Orifice Valve C	%Q0.7	DO				
Sol_D	Orifice Valve D	%Q1.0	DO				
DO_Harvest_Pump	Optional signal for external pump	%Q1.1	DO				
RAW_P2_PV_1	P2 Pressure Transducer Raw Signal	%IW64	AI	-14.7	30.00	2	PSI
RAW_PRV1_PV_1	PRV1 Pressure Feedback Signal	%IW66	AI	0.00	30.00	2	PSI
Spare	Spare	%QW64	AO				
Spare	Spare	%QW66	AO				
RAW_P1_CV	Analog output to PRV1	%QW80	AO	0.00	30.00	2	PSI

Figure 44. Setpoint List

Tagname	Description	PLC Address	Engineering			
			Range		Decimal Places	Units
			Low	High		
PFLOWSP	Pressure Flow Setpoint (Pump Model Dependent)	DB1.PFLOWSP	0.2	10.0	1	LPM
EFLOWSP	Evacuate Flow Setpoint (Pump Model Dependent)	DB1.EFLOWSP	0.2	10.0	1	LPM
PRV1	Pressure Control Setpoint	DB1.PR1V1	0.1	1.7	1	Bar
			1.5	24.7		PSI
PRV2	Evacuate Control Setpoint	DB1.PR1V2	-0.9	-0.1	1	Bar
			15	-1		PSI
FLOR	Pressure Orifice Number Setpoint	DB1.FLOR	0	31	0	na
EXOR	Evacuate Orifice Number setpoint	DB1.EXOR	0	31	0	na
Bioreactor_Pressure	Bioreactor Vessel Pressure	DB1.Bioreactor_Pressure	-0.68	0.682	3	Bar
			-9.900	9.900		PSI
Bioreactor_Height_Diffe	Height Differential in Centimeters	DB1.Bioreactor_Height_Diffe	-199	999	0	cm
PFLOWMAXSP	Pressure Flow Setpoint Range Maximum	DB1.PFLOWMAXSP	1.0	10.0	1	LPM
PFLOWMINSP	Pressure Flow Setpoint Range Minimum	DB1.PFLOWMINSP	1.0	10.0	1	LPM
EFLOWMAXSP	Exhaust Flow Setpoint Range Maximum	DB1.EFLOWMAXSP	1.0	10.0	1	LPM
EFLOWMINSP	Exhaust Flow Setpoint Range Minimum	DB1.EFLOWMINSP	1.0	10.0	1	LPM
PRV1MAX	Pressure Control Setpoint Range Maximum	DB1.PR1V1MAX	0.07	2.07	2	Bar
			1.00	30.00		PSI
PRV2MIN	Pressure Control Setpoint Range Minimum	DB1.PR1V2MIN	-1.03	-0.07	2	Bar
			-15.00	-1.00		Psi
FTDP	Pump Pressure Cycle Delay	DB1.FTDP	0	100	0	%
ETDP	Pump Evacuate Cycle Delay	DB1.ETDP	0	100	0	%
FDFOFST	Pump Pressure Cycle Switch Offset Pressure	DB1.FDFOFST	0.000	0.682	3	Bar
			0.000	9.900		PSI
EDFOFST	Pump Evacuate Cycle Switch Offset Evacuate	DB1.EDFOFST	-0.68	0.000	3	Bar
			-9.900	0.000		PSI
P2SWPCT	Pump Pressure Cycle Overflow	DB1.P2SWPCT	50	100	0	%
EBUSWSP	Pump Evacuate Cycle Overflow	DB1.EBUSWSP	50	100	0	%
P_Cycle_Overtime_SP	Pump Pressure Cycle Overtime	DB1.P_Cycle_Overtime_SP	100	150	0	%
V_Cycle_Overtime_SP	Pump Evacuate Cycle Overtime	DB1.V_Cycle_Overtime_SP	100	150	0	%
Init_Pressure_SP	Pump Initialization Pressure	DB1.Init_Pressure_SP	-0.68	0.000	3	Bar
			-9.900	0.000		PSI
PUMPVOL	Pump Volume Override	DB1.PUMPVOL	0	999	0	ml
Filter_Fibers	Number of Fibers SP	DB1.Filter_Fibers	0	99999	0	na
Filter_Surface_Area	Surface Area SP	DB1.Filter_Surface_Area	0.000	9.999	3	m ²
Filtrate_Rate	Filtration Rate	DB1.Filtrate_Rate	0	99	2	ml/min
WATSP	Warning Acknowledge Time SP	DB1.WATSP	0.00	50.00	0	min

Figure 45. Alarm List

Tagname	Description	PLC Address	Alarms			
			Severity	Enable	Alarm Delay	Action
ALARM_B0	Warning not acknowledged by user	%M7.0	Alarm	Alarm Delay Timer setpoint greater than zero	1 Minute or greater	System Halt
ALARM_B1	Main Power Loss (120/220) while Pump was running	%M7.1	Alarm	Pump is Running	NA	System Halt
WARN_B0	Pressure Flow Set Point cannot be reached.	%M8.0	Warning	Pump is Running	NA	Warning
WARN_B1	Exhaust Flow Set Point cannot be reached.	%M8.1	Warning	Pump is Running	NA	Warning
WARN_B2	Exhaust Set Point cannot be reached. PRV above maximum vacuum setting	%M8.2	Warning	Pump is Running	NA	Warning
WARN_B3	Exhaust Set Point cannot be reached. PRV below minimum vacuum setting	%M8.3	Warning	Pump is Running	NA	Warning
WARN_B4	Warning - System Automatically Restarted after Power Failure.	%M8.4	Warning	Pump is Running	NA	Warning

12. Appendix 2— The XCell™ C24 Controller (v3) available orifice combinations

Table 8. Orifice Sizes

Orifice	Size
A	15K
B	7.5K
C	2K
D	.75K
E and F	2X 5/32 Open
G	1/8 Open

Orifice Combinations Available to the user for manual entry.

Highlighted cells indicate Orifice combinations actually used by controller defaults.

Table 9. Controller Defaults

Step	Orifice						Flow @ 3psi
0	A						0.2
1	A	B					0.7
2	A		C				1.9
3	A	B	C				2.4
4	A			D			4.2
5	A	B		D			4.7
6	A		C	D			6.0
7	A	B	C	D			6.4
8	A				E & F		12.2
9	A	B			E & F		12.8
10	A		C		E & F		14.1
11	A	B	C		E & F		14.2
12	A			D	E & F		16.1
13	A	B		D	E & F		16.3
14	A		C	D	E & F		17.8
15	A	B	C	D	E & F		18.0
16	A					G	22.5
17	A	B				G	23.2
18	A		C			G	24.4
19	A	B	C			G	25.1
20	A			D		G	26.6
21	A	B		D		G	27.0
22	A		C	D		G	28.0
23	A	B	C	D		G	28.5
24	A				E & F	G	32.5
25	A	B			E & F	G	33.5
26	A		C		E & F	G	35.0
27	A	B	C		E & F	G	35.0
28	A			D	E & F	G	36.0
29	A	B		D	E & F	G	37.0
30	A		C	D	E & F	G	38.0
31	A	B	C	D	E & F	G	38.0

13. Appendix 3 – XCell ATF® 2 Device and XCell ATF® 4 Device exploded drawings and parts List

Figure 46. Exploded View of the XCell ATF® 2 Device

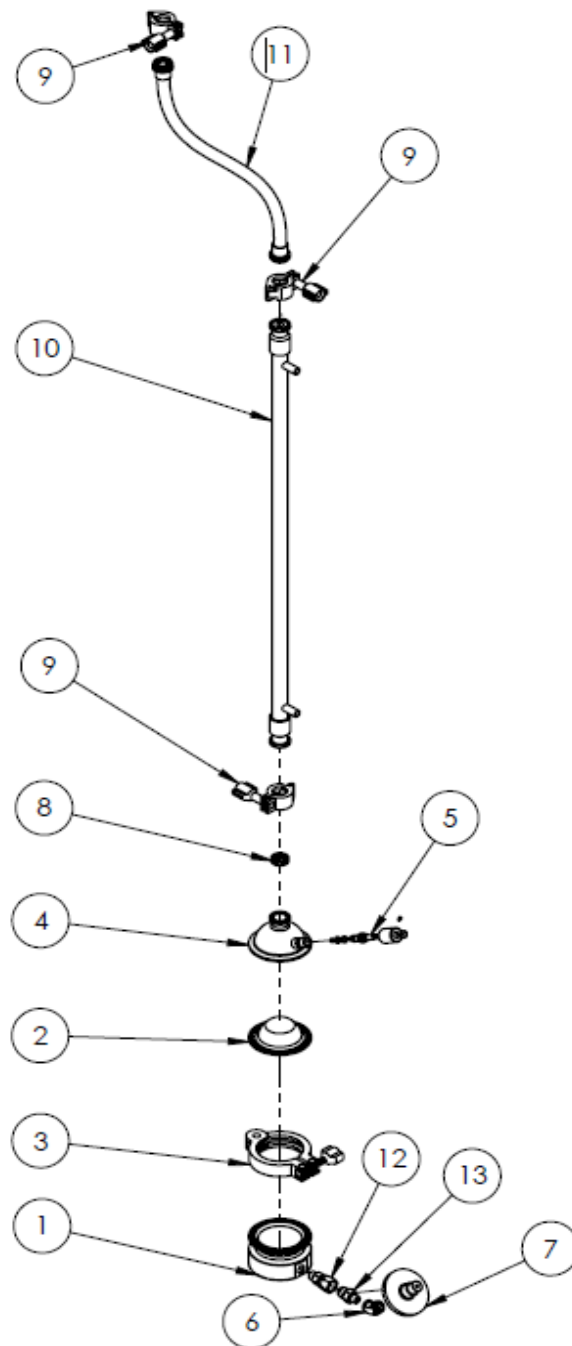
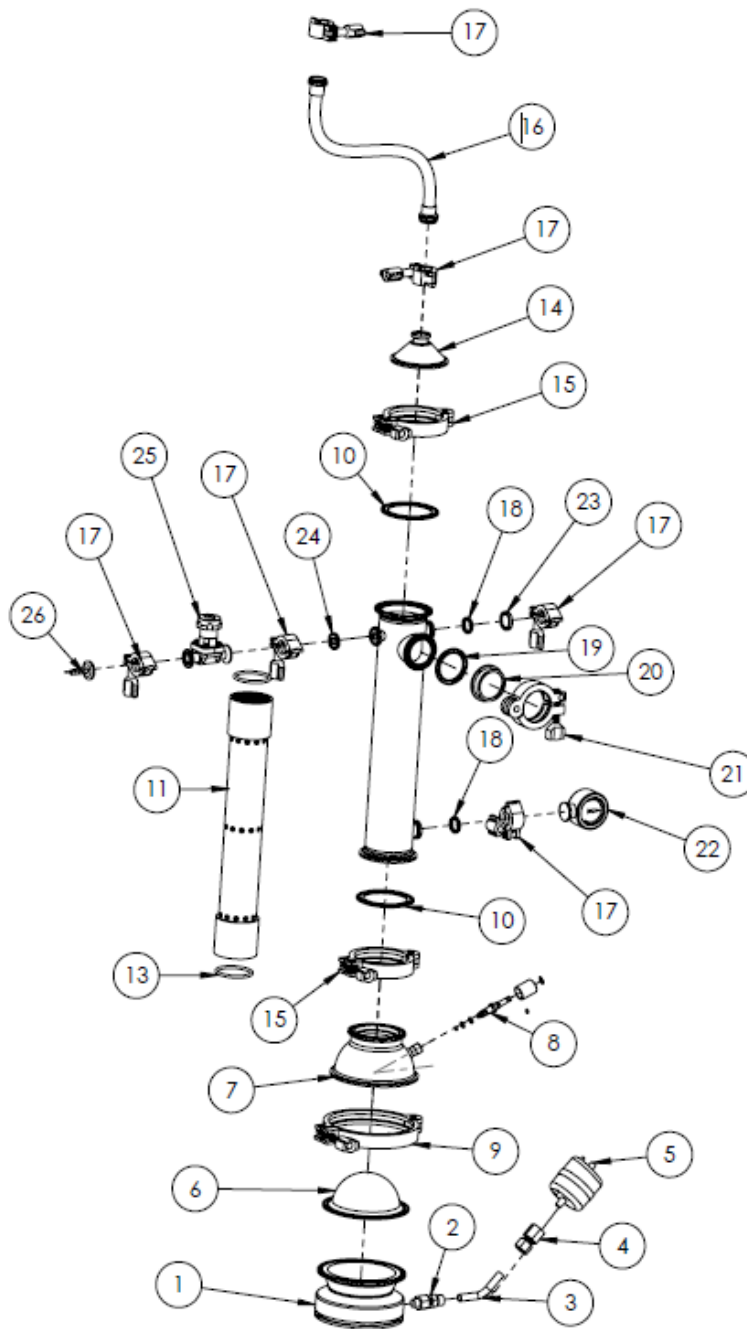


Figure 47. Exploded View of the XCell ATF® 4 Device



14. Appendix 4— XCell ATF® Device for Microcarriers

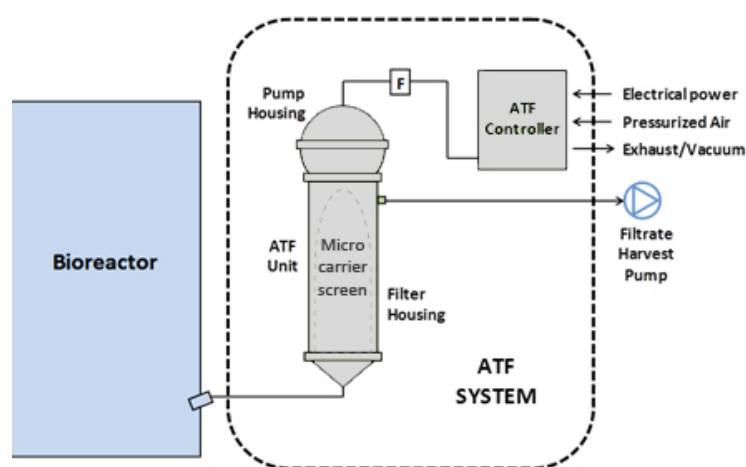
Key Differences

There are a number of key differences between the XCell ATF® Device for Microcarriers and the XCell ATF® Device used for suspension cells.

14.1 Configuration

ATF-MC Devices are all inverted, whereby the diaphragm pump sits above the filter housing. This configuration allows Microcarriers to be pushed back into bioreactor and prevents Microcarriers from accumulating inside ATF unit due to gravity. [Figure 48](#) shows a schematic of the XCell ATF® Device for Microcarriers relative to the bioreactor. Note the relative position of the Microcarrier screen – the opening is at the reducer, towards the path to the bioreactor.

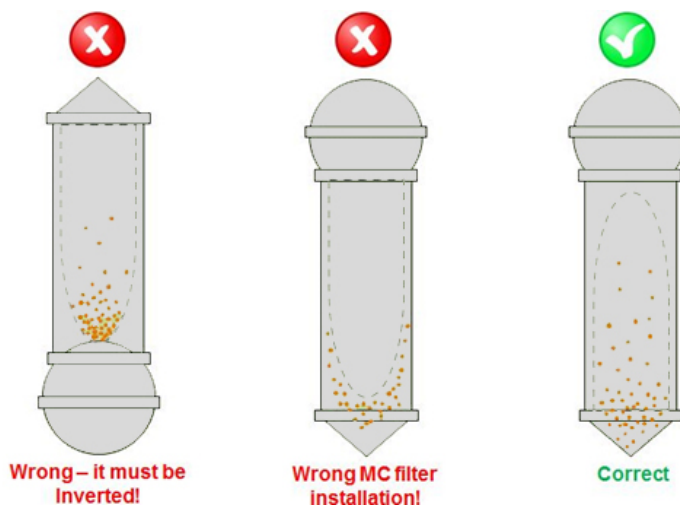
Figure 48. XCell ATF® Device for Microcarriers



14.1.1 Common mistakes

Below illustrate some common mistakes in the configuration of the XCell ATF Device for Microcarriers. The configuration on the left is not inverted, so the Microcarriers will accumulate inside the ATF unit. The configuration in the middle shows the ATF properly inverted, but the Microcarrier screen is not installed correctly, and the Microcarriers may get stuck between the screen and the module itself. The configuration on the right shows the correct configuration.

Figure 49. Common mistakes



14.2 The XCell ATF® Device -MC Screen module

The XCell ATF® Device for Microcarriers relies on a 70µm screen rather than hollow fibers. Most of the common Microcarriers available on the market are within a size range of 125 – 250 microns, so a 70 µm screen is sufficient for almost all applications. The screen is composed of polysulfone and all of the materials used in the module are USP Class VI compliant. The ATF Microcarrier screen module is designed with a special flow path to reduce fouling and attachment. Like the hollow fiber modules (HFM), the ATF Microcarrier screen is warranted for only one autoclave cycle.

Figure 50. XCell ATF® 2 Device Microcarrier screen modules

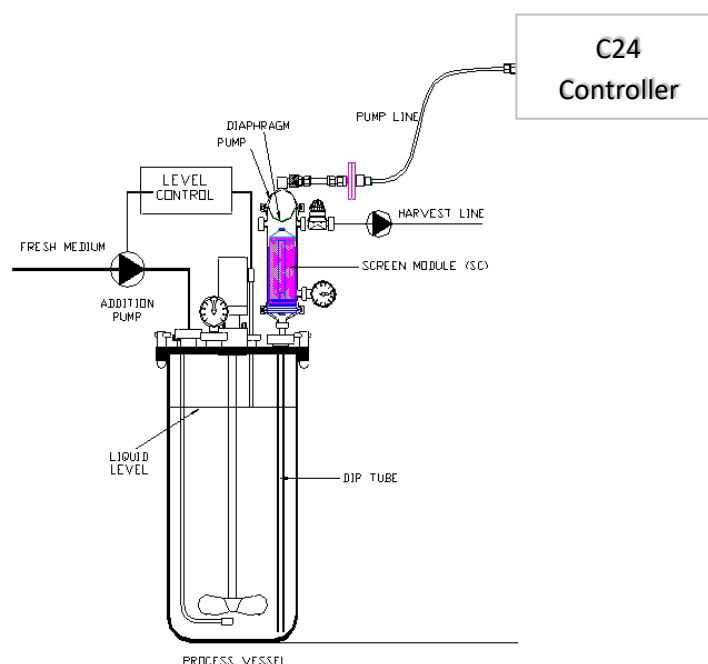


14.3 Connection to bioreactor

As with all XCell ATF® Devices, the XCell ATF® MC Devices can be connected to almost any bioreactor, whether glass, stainless steel or single-use bioreactors. It is important to use the appropriate bioreactor port and a sufficient connection.

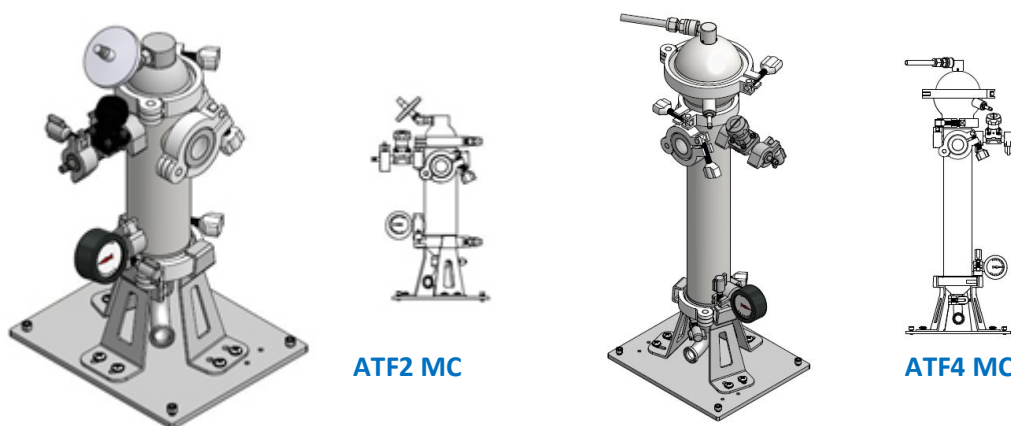
[Figure 51](#) illustrates the XCell ATF® 2 Device Microcarrier Device connected to a glass bioreactor through the headplate. In this setup, the XCell ATF® 2 Device MC unit is mounted directly onto the standard dip-tube via tri-clamp connection. This entire assembly is autoclaved together. The XCell ATF® 2 Device MC has significant weight relative to the glass bioreactor, so this top-heavy setup is not recommended for smaller glass bioreactors (i.e. <5L) nor single-use bioreactors.

Figure 51. The XCell ATF® 2 Device-MC Device connected to glass bioreactor



If the XCell ATF® 2 Device MC is too top heavy for the bioreactor, it can alternatively be mounted on a stand, placed on a shelf above the head plate, and connected to the dip tube using our standard silicone tubing. [Figure 52](#) illustrates the XCell ATF® 2 Device MC unit mounted on a separate stand. This assembly can be autoclaved together, or the silicone tubing can be connected using quick connectors or disposable sterile connectors. The same would be done with an The XCell ATF® 4 Device-MC Device which is always mounted on a separate stand

Figure 52. The XCell ATF® 2 MC and XCell ATF® 4-MC Device mounted on individual stand



[Figure 53](#) illustrates how the XCell ATF® 4 MC Device or other larger scale the XCell ATF® MC Devices would be connected to a stainless steel bioreactor. The larger XCell ATF® MC Device units would be mounted on a separate stand and positioned close the bioreactor for the connection through an appropriate side port. The XCell ATF® MC Device unit would be autoclaved separately; the bioreactor would be Steamed-In-Place and the connection between the two would be steam sterilized through the bi-valves.

Figure 53. XCell ATF® 4 Device MC Device mounted to a stainless steel bioreactor

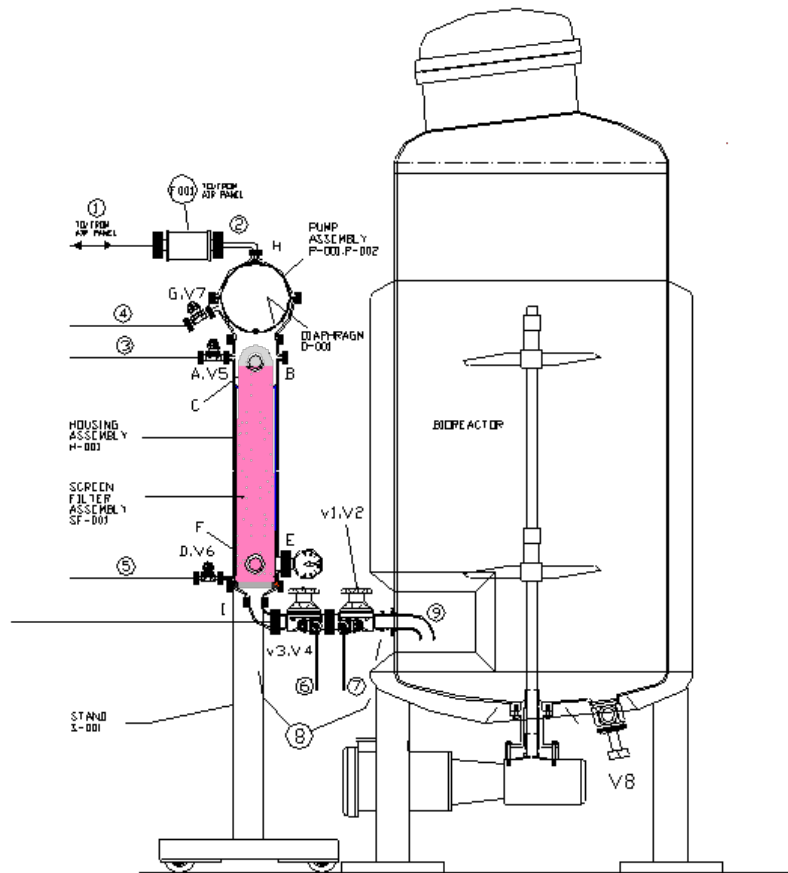


Figure 54 shows a schematic of how an ATF MC Device would attach to a single-use bioreactor (SUB). The ATF MC unit is autoclaved with a T connector in-line to accommodate a vent filter and a disposable sterile connector. This will allow steam penetration through the entire Device during autoclaving. Once sterile, the Device can then be connected to the SUB via the complementary sterile connector. However, many SUBs have ports that do not have sufficient cross section. In this case, as shown below, an adapter that includes a Y connector would be used to access two or more ports on the SUB to match the total cross-sectional area of the main ATF line. Table 10 is a table that shows the maximum length and ID of the connection, for each ATF MC scale.

Figure 54. Schematic of XCell ATF® MC Device connected to Single-use Bioreactor

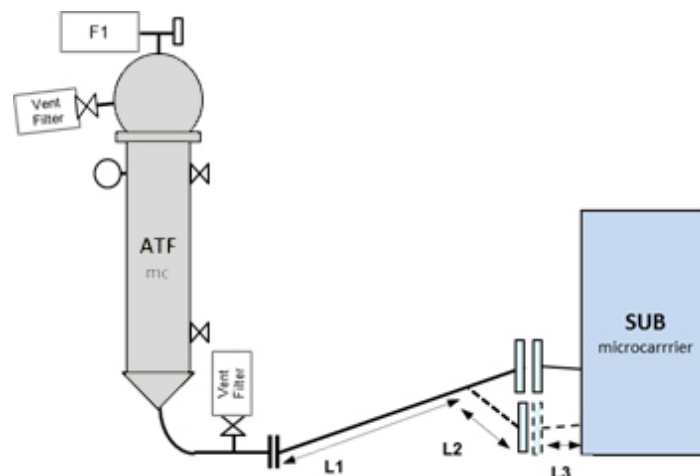


Table 10. Specifications for maximum connection length and internal diameter

Model	L1		L2		L3		Total
	Length	ID	Length	ID	Length	ID	
XCell ATF® 2	< 14"	3/8"	n/a	n/a	< 5.7"	3/8"	< 19.7"
XCell ATF® 4	< 14"	½"	n/a	n/a20	< 5.7"	½"	< 19.7"
XCell ATF® 6	< 20"	1"	< 10"	2 x ¾"	< 9.4"	¾"	< 39.4"
XCell ATF® 8	< 20"	1"	< 10"	2 x ¾"	< 9.4"	¾"	< 39.4"
XCell ATF® 10	< 20"	1.5"	< 10"	2 x 1" or 4 x ¾"	< 9.4"	1"	< 39.4"

The specifications above must be met in order for the XCell ATF® Device to be able to achieve the full range of flow rates, at minimal shear and residence time.

14.4 Controller settings

The XCell™ C24 Controller version 2.0 and C410 version 2.0 are not programmed with default XCell ATF® MC starting values for PRV, Orifice (C24), or PV (C410), for defined ATF flow rates. Because the XCell ATF® MC Device is inverted relative to the bioreactor, the default values should be different from the XCell ATF® Devices used for suspension. These default starting values are simply a starting point from which the controller will tune itself automatically to achieve the desired flow rate. Therefore, the C24 v2.0 and C410 v2.0 can still be used with the XCell ATF® MC Devices. However, it will take longer for the controller to achieve a stable state since it may be farther from the proper values for a given ATF flow rate. The new XCell™ C24 Controller (v3) software is programmed with the appropriate starting values for the XCell ATF® 2 Device MC and XCell ATF® 4 Device MC. The XCell™ C410 Controller (v3) update, will also be programmed with the appropriate starting values for the XCell ATF® 4 Device MC, XCell ATF® 6 Device MC and XCell ATF® 10 Device MC.

14.5 Operation

It is important to ensure that the ATF MC filtration unit is airtight. This can be confirmed by a pressure test (pressurizing through a sterile vent filter). Then the XCell ATF® MC Device filtration unit can be connected to the bioreactor via SIP connection or Single-use connection. Once the XCell ATF® MC Device is sterile connected to the bioreactor, the ATF must be primed with liquid. This is done through the filtrate line.

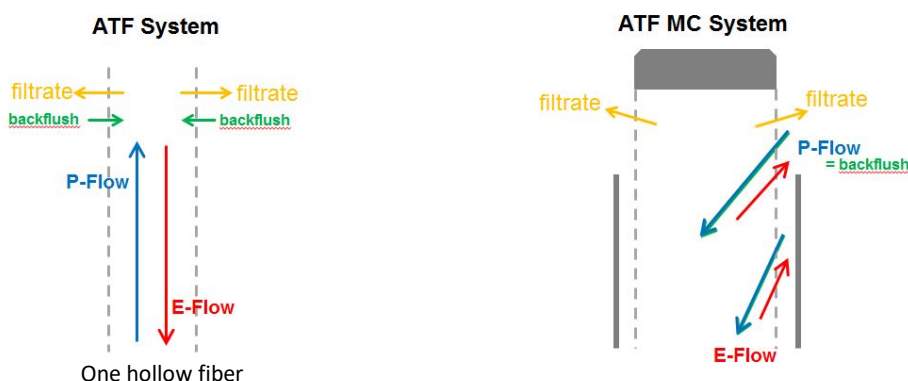
1. Attach the filtrate line to a peristaltic pump and set to desired flow rate.
2. On the XCell™ controller (C24 or C410) set the ATF P-flow and E-flow to desired Flow rate. Remember that the P-cycle flow rate should be at least 2x (preferably 4x) the E-cycle flow rate plus the filtrate rate.
3. Start the XCell ATF® Device.
4. Start the Filtrate pump.
5. Calculate the time necessary to prime the hold-up volume based on your filtrate flow rate.
6. Once you see the liquid in the sight glass on the XCell ATF® Device, the ATF is being primed properly.
7. If you do not see liquid in the sight glass within the calculated time, the ATF is not being primed. This can be indication of a leak, which means that sterility may have been broken, and the ATF filtration unit may need to be re-autoclaved and pressure tested.

Once the XCell ATF® Device is activated, it is important to keep it running throughout the entire process. If the XCell ATF® Device is turned off, there will be no means for the Microcarriers to return back to the bioreactor. Even when the filtrate flow is stopped, it is recommended that the XCell ATF® Device remain active.

14.6 Backflush Action

There are some inherent differences between the XCell ATF® Device and the XCell ATF® Microcarrier Device in how it achieves its backflushing effect. In the XCell ATF® Device used for suspension, the diaphragm pushes/pulls the fluid tangential to the hollow fibers, resulting in sweeping of the membrane as well as backflush due to changes pressure differentials. Whereas in the XCell ATF® Device for Microcarriers, the backflush action is more complex due to the design of the ATF Microcarrier Screen module. [Figure 55](#) illustrates this difference.

Figure 55. Backflush action differences



Due to the design of the ATF Microcarrier Screen Module, the backflush action is localized primarily at the top region and ensures a more optimal flow path to minimize microcarrier residence time. In the XCell ATF® Device, typically P-flow and E-flow are set to be equal. The backflush action can happen during either cycle, but primarily during the E-flow cycle. But in the XCell ATF® MC Device, the backflush action happens only during the P-flow cycle. Ideally, there should be a net flow of fluid in the P-flow direction, towards the bioreactor. In order to achieve this, it is recommended that the P-flow cycle should be at least 2x to 4x that of the E-flow rate *plus* the filtration rate.

14.7 Conversion between XCell ATF® Device for suspension and MC use

The XCell ATF® Device used for suspension can be converted for MC use, with the exception of the XCell ATF® 2 Device. The XCell ATF® 2 MC is completely different from the XCell ATF® 2 Device used for suspension; in that it requires a stainless steel housing to accommodate the MC screen. Therefore, the XCell ATF® 2 Device is not interchangeable.

Figure 56. XCell ATF® 2-MC



The XCell ATF® 4 Device MC can be distinguished from the XCell ATF® 4 Device used for suspension by the fact that it does not have an integrated base to the Pump Air-side hemisphere see [Figure 57](#). However, since the filter housing is the same, the XCell ATF® 4 Device can still be used for MC use by simply inverting the unit and using a stand to secure it to that position. The standard stand for the XCell ATF® 4 Device MC (as shown below) may not be adequate for an inverted XCell ATF® 4 Device with integrated base and additional measures must be taken to stabilize the unit.

Figure 57. XCell ATF® 4 Device MC



In the larger scale XCell ATF® Devices (XCell ATF® 6 Device and XCell ATF® 10 Device), the suspension and MC versions have the same parts. So, to use as an MC Device requires only an MC screen and a separate stand to keep the unit inverted, see [Figure 58](#).

Figure 58. XCell ATF® 10 Device MC configuration



14.8 General Specifications

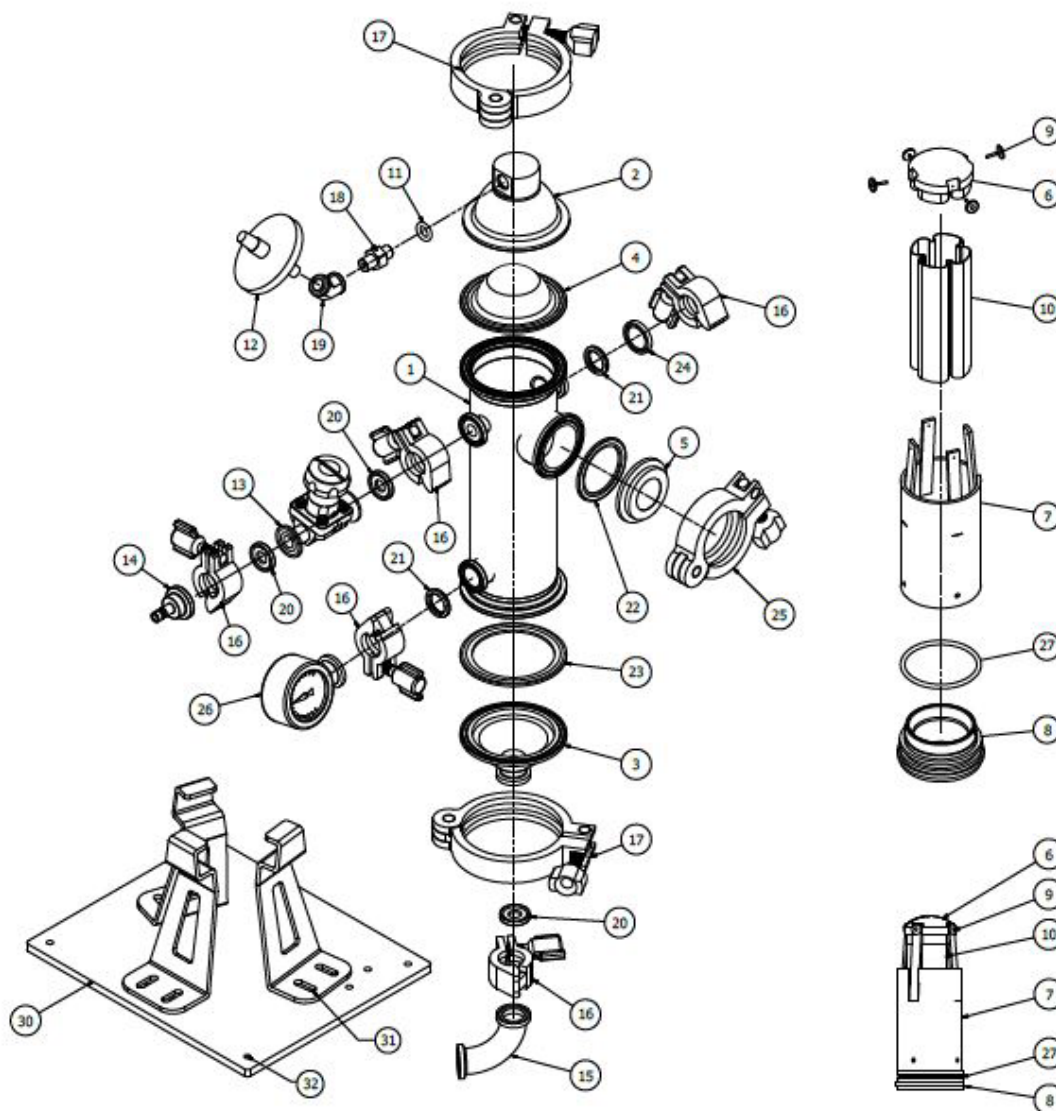
The following table shows the general specification for each ATF Microcarrier Device. Note that the recommended bioreactor working volume is just a guideline - actual capacity and vessel size depend upon process conditions.

Table 11. General specifications for ATF Microcarrier Device

	Pump Displacement Vol (L)	ATF Flow Rate Range (LPM)		Recommended Bioreactor Working Vol (L)		Microcarrier Screen SA (m ²)	Approx. Device Holdup Vol (L)
ATF2 MC	0.1	0.2	1.5	3	20	0.024	0.5
ATF4 MC	0.4	1.5	10	20	100	0.053	1
ATF6 MC	1.3	5	20	100	300	0.1305	4
ATF10 MC	6	20	80	300	1000	0.244	16.7

14.9 Parts List and Exploded View

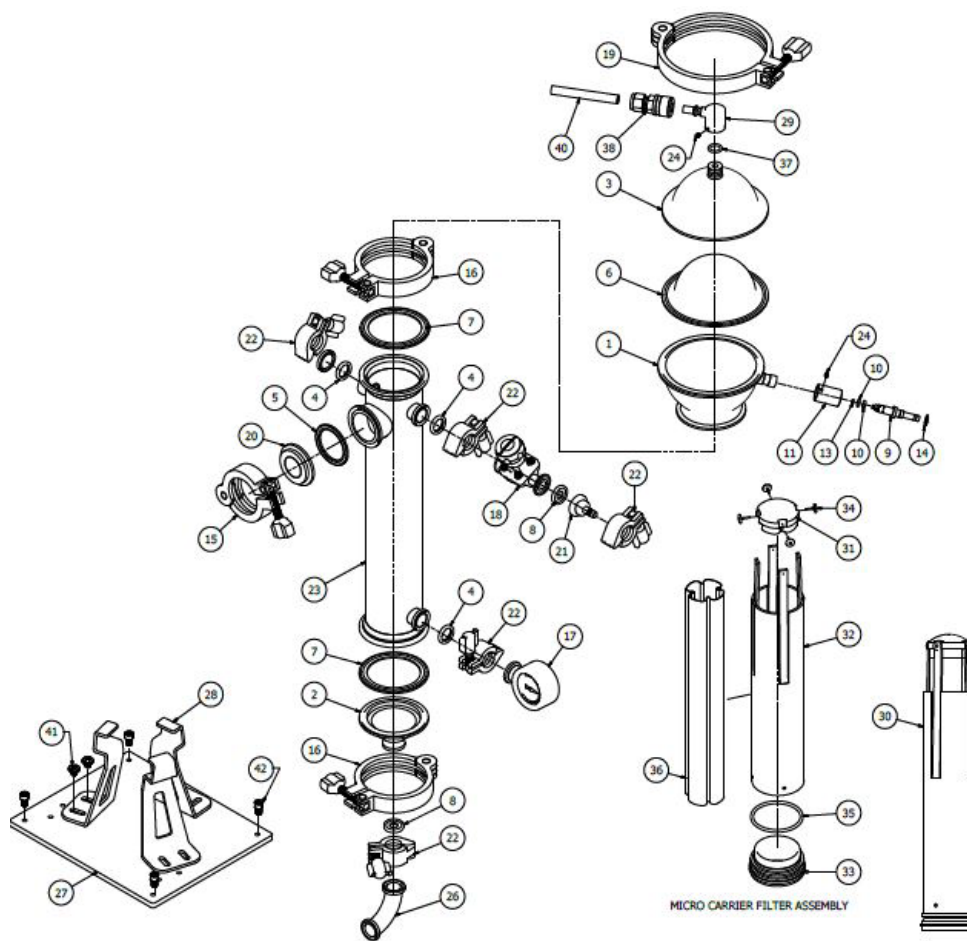
Figure 59. XCell ATF® 2 Microcarrier Device Parts List and Exploded View



PARTS LIST				
ITEM	PART NUMBER	DESCRIPTION	QTY	MATERIAL
1	A2-MC-H1	Filter Housing	1	316 L SS
2	A2:MC-T-0001	A2 MC Pump Top	1	316 L SS
3	A4:R1	Reducer	1	316 L SS
4	D2:S1	Diaphragm, 50 Durometer	1	SILICONE
5	TC:W2-1.5	Window, Sanitary 1.5" TC, Removable Window	1	316 L SS
6	MC:F2-Top	Micro Carrier Filter 2 TOP	1	Polysulfone
7	MC:F2-SLV	Micro Carrier Filter Sleeve	1	Ploysulfome
8	MC:F2-Base	Micro Carrier Base	1	Ploysulfome
9	MC:F2-Pin	Micro Carrier Pin	4	316 L SS
10	MC:F2-Screen	Micro Carrier Screen	1	
11		O-Ring - Supplied with Item 18	1	EPDM
12	F:Air2	Air Filter, Hydrophobic	1	
13	V1:S-1/2N	Sanitary Diaphragm Valve, 1/2" TC Ends	1	316 L SS
14	TC:BRB1	ROUND 1" OD x 1 1/4" Lg	1	316 L SS
15	TC:EL-1/2S	ELL -Short 90 deg, 1/2" TC Ends	1	316 L SS
16	SC:0.75	CLAMP, SANITARY	5	304 SS

17	SC:2.5	Clamp, Sanitary, 2 1/2" TC	2	304 SS
18	A:AIR-M	Air Inlet Straigh Thread / Male Pipe Adapter (1/8 Str Thd x 1/8 NPT)	1	304 SS
19	A2:AIR-F	Air Inlet Assembly 45 Deg Female Pipe Elbow, 1/8 NPT	1	304 SS
20	SG:05-E	Sanitary Gasket 1/2"	3	EPDM
21	SG:075-E	Sanitary Gasket, 3/4 TC - Pharm-Class VI	2	EPDM
22	SG:1.5-E	Sanitary Gasket, 1.5 TC - EPDM	1	EPDM
23	SG:2.5-E	Sanitary Gasket, 2.5" TC	1	EPDM
24	TC :CAP	Cap, Sanitary 3/4" TC	1	316 L SS
25	SC:1.5	Clamp, Sanitary, 1.5" TC	1	316 L SS
26	TC:PG-W3/4	Pressure Guage, 3/4 TC 30PSI-30" Hg	1	316 L SS
27	O:227-5	O-RING, 2 1/8" ID x 2 3/8" OD x 1/8" Wall	1	Silicone
29	A2 Stand Leg	A2 Stand Leg	3	Generic
30	A2 Stand Base	A2 Stand Base	1	Generic
31	MC-91772A533	Pan Hd Philips Machine Screw - 1/4-20 X 1/4 Lg	6	18-8 SS
32	MC-92196A535	Hex Socket Hd Cap Screw, 1/4-20 x 3/8" Lg	4	18-8-SS
33	MC-F2-ASM	MC-F2 Filter Assembly	1	

Figure 60. XCell ATF® 4 Microcarrier Device Parts List and Exploded View



PARTS LIST				
ITEM	PART NUMBER	DESCRIPTION	QTY	MATERIAL
1	A4:P-B-1	Pump Hemisphere (Liquid Side)	1	316 L SS
2	A4:R1	Reducer	1	316 L SS
3	A4:MC-P-T1	A4 MC Pump Top	1	316 L SS
4	SG:075-E	Sanitary Gasket, 3/4 TC - Pharm-Class VI	3	EPDM
5	SG:1.5-E	Sanitary Gasket, 1.5 TC	1	EPDM
6	D4:S1	Diaphragm, 50 Durometer	1	Silicone
7	SG:2.5-E	Sanitary Gasket, 2.5 TC	2	EPDM
8	SG:05-E	Sanitary Gasket 1/2"	2	EPDM
9	SMP:SMP3-S	Sampler Stem	1	316 L SS
10	O:009-E	O-Ring, Sampler Stem	2	EPDM
11	SMP:SMP3-K	Sampler Knob	1	440 C SS
12	TC:CAP-3/4	Cap, Sanitary	1	316 L SS
13	O:004-E	O-Ring, Sampler Plug	1	EPDM
14	SMP:SMP3-SR	Sampler Snap Ring	1	316 L SS
15	SC:1.5	Clamp, Sanitary, 1.5" TC	1	304 SS
16	SC:2.5	Clamp, Sanitary, 2 1/2" TC	2	304 SS
17	TC:PG-W3/4	Pressure Gauge, 3/4 TC 30PSI-30" Hg	1	316 L SS
18	V1:5:1/2N	Sanitary Diaphragm Valve, 1/2" TC Ends	1	316 L SS
19	SC:4.0	Clamp, Sanitary 4" TC	1	304 SS
20	TC:W2-1.5	Window, Sanitary 1.5" TC, Removable Window	1	316 L SS
21	TC:BRB1	1/4" Hose Barb Adapter, Sanitary, 1/2" TC End to 1/4" ID	1	316 L SS
22	SC:0.75	Clamp, Sanitary	5	304 SS
23	A4:H1	Filter Housing	1	316 L SS
24	MC:92845A140	#6-32 x 3/16 3/16 Lg Hex Soc Set Scr- Pilot Pt	4	18-8 SS
25		Left Blank		
26	TC:EL-1/25	ELL-Short 90 deg, 1/2" TC Ends	1	316 L SS
27	A2:Stand Base	A2 Stand Base	1	304 SS
28	A2:Stand Leg	A2 Stand Leg	3	304 SS
29	A:AIR-P1	Pump Air Inlet Cap with Quick Connect	1	316 L SS
30	MC:F2-ASM	MC-F2 Filter Assembly	1	
31	MC:F4-Top	Micro Carrier Filter Top	1	Polysulfome
32	MC:F4-SLV	Mico Carrier Filter Sleeve	1	Polysulfome
33	MC:F4-Base	Micro Carrier Filter Base	1	Polysulfome
34	MC:F2-Pin	Micro Carrier Filter Pin	4	316 L SS
35	O:227-5	O-Ring, 2 1/8" ID x 2 3/8" OD x 1/8" Wall	1	Silicone
36	MC:F4-Screen	Micro Carrier Screen	1	PES
37	O:111-E	O-Ring, 3/32 CS x 7/16 x 5/8 OD (MC Filter)	1	EPDM
38	QC3:AIR2	Air Inlet Line- Quick Disconnect 1/4 x 3/8 Comp	1	304 SS
40	TU:SS-3/8 OD	Tubing, Air Inlet Line 3/8" OD SS Tube x .25 Lg	1	304 SS
41	MC-91772A533	Pan Hd Philips Machine Screw - 1/4-20 X 1/4 Lg	6	18-8 SS

15. Appendix 5—EU Declaration of Conformity

The XCell™ C24 Controller (v3) for XCell ATF® 2 Device and XCell ATF® 4 Device operation has been assessed for CE regulations, refer to Declaration of Conformity provided with the Device for details.

Sample Nameplate

The XCell ATF® Device with XCell™ C24 Controller, software (v3) has been marked legibly and indelibly with following information:

- Name and address of the manufacturer
- The serial number
- Designation of series or type
- CE mark
- Year of construction
- Rated voltage (+/- 10%), full load amperage, and frequency
- Short-circuit Interrupting rating of the equipment
- The weight of the equipment
- Identification number of the electrical schematics

Figure 61. A sample controller nameplate is shown below



General Information and handling Instructions

1. Repligen XCell ATF® Device is rated for acceptable sound levels (60 dBA)
2. Weight of XCell™ C24 Controller is 25 lbs (11.3kg)
3. Complete Device visual inspection for damage or potential risk to the operator, surrounding personal, or equipment on a semi-annual basis
4. Annual Safety Inspection

- Conduct a vacuum Device leak assessment
- Replace the air filter between the XCell ATF® Device and the XCell™ C24 Controller
- Inspect air and vacuum connections to the XCell™ C24 Controller
- Inspect that all components inside of the XCell™ C24 Controller are secured and intact
- Inspect enclosure for damage, locks and hinges for performance, and the external electrical connection
- Inspect the ATF Device housing components, especially the internal and sealing surfaces for damage, rust, cracks, scoring.
- Perform a pressure hold test of the XCell ATF® Device

15.1 Handling Instructions



TRANSPORTATION: The XCell™ C24 Controller weighs 25 lbs (11.3 kg). Care should be taken when lifting and transporting the unit and use of a cart is recommended.



VOLTAGE: Hazardous voltage inside, disconnect power before opening. Device must stay connected to the power cord in order to function as intended. This product must not be used with a detachable power cord that is not provided by Repligen.



SERVICE: All cords/ wires must be grounded properly per product safety requirements of CE mark.

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