Ready-to-use fluid management solutions for cross flow filtration systems

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Ready-to-use fluid management solutions for cross flow filtration systems

A selection of fluid management components from GE Healthcare's ReadyToProcess platform of disposable and single-use equipment was used to arrange buffer and sample management solutions for two large-scale filtration setups. The first was conventional cross flow ultra filtration on UniFlux™ 10 system, the second, cross flow micro filtration on UniFlux 30.

Ready-to-use plastic bags, plastic tubing, connectors and mobile processing stations provided flexible liquid-handling solutions that will simplify workloads and boost efficiency for both systems. The increasingly wide range of 'plug-and-play' bioprocessing components now available should thus find use in pilot and production facilities running large-scale filtration applications.

Introduction

Interest in disposables and single-use bioprocessing equipment has increased over recent years. Today, new-build pilot and production facilities are often based on a flexible platform where unit operations such as filtration occupy only a small footprint. To minimize space, for example, ready-to-use plastic bags and flexible plastic tubing increasingly replace fixed stainless steel buffer tanks and piping. In addition, using bags to manage buffer handling reduces the cleaning effort required as well.

GE Healthcare's broad ReadyToProcess product platform brings such 'plug-and-play' options to key unit operations within biopharmaceutical manufacturing. Many disposable items are designed for single-use only while others can be re-used. Examples include ReadyCircuit™, ReadyMate™, and ReadyKart components.

This Application note describes two examples of cross flow filtration setups where disposables for buffer and sample management as well as for filters are combined with traditional filtration systems.

Fig 1. UniFlux 10 cross flow ultra filtration setup for concentrating a target protein 10-fold. Items also shown include ReadyKart mobile processing stations, disposable bags and ReadyCircuit and ReadyMate connection assemblies.

Cross flow ultra filtration with UniFlux 10 system

System description

UniFlux filtration systems incorporate cross flow filters and high performance hardware in a single, easy-to-set up system. A range of sizes from pilot to production-scale is available, as is a standard range of recirculation tanks with volumes ranging from 5 to 600 L. A specific UNICORN™ control system allows automation of the total cross flow filtration process. UniFlux 10 is the smallest of four UniFlux filtration system sizes.

Liquid-handling setup

The filtration scenario illustrated in Figure 1 shows UniFlux 10 in a conventional cross flow ultra filtration setup for concentrating a target protein 10-fold. Diafiltration was also used to change the buffer conditions, and this was followed by a further 2-fold concentration. Buffers and sample are introduced via the system inlet manifold. Table 1 lists connection items used in the process. Figure 2 shows the connection assemblies.

Table 1. ReadyCircuit items used in the process described for UniFlux 10 filtration system

Description	Comment
Inlet manifold	
20 L bag, 3 inlets	Water
50 L bag, 3 inlets	Sample
50 L bag, 3 inlets	Conditioning and diafiltration buffer
4-way tee	3/8 in C-FLEX tubing, system without inlet manifold
RMRM Jumper (3 pct)	3/8 in C-FLEX tubing, 3 ft, system with inlet manifold
Outlet manifold, sample collection	
5 L bag, 3 inlets	Concentrated and conditioned sample
5 L bag, 3 inlets	Flush of concentrated and conditioned sample
3-way tee	3/8 in C-FLEX tubing
Outlet manifold, permeate waste collection	
100 L bag, 4 inlets	Permeate waste
RMRM Jumper	3/8 in C-FLEX, 3 ft
ReadyMate DAC 750 mini TC	Connect ReadyMate with mini TC, 10 pack
ReadyClamp	To secure ReadyMate connections/25 pack

Each solution is delivered in a disposable bag that is connected to the system via a tubing jumper and a ReadyMate DAC 750 mini TC connector located on the inlet manifold (Fig 2).

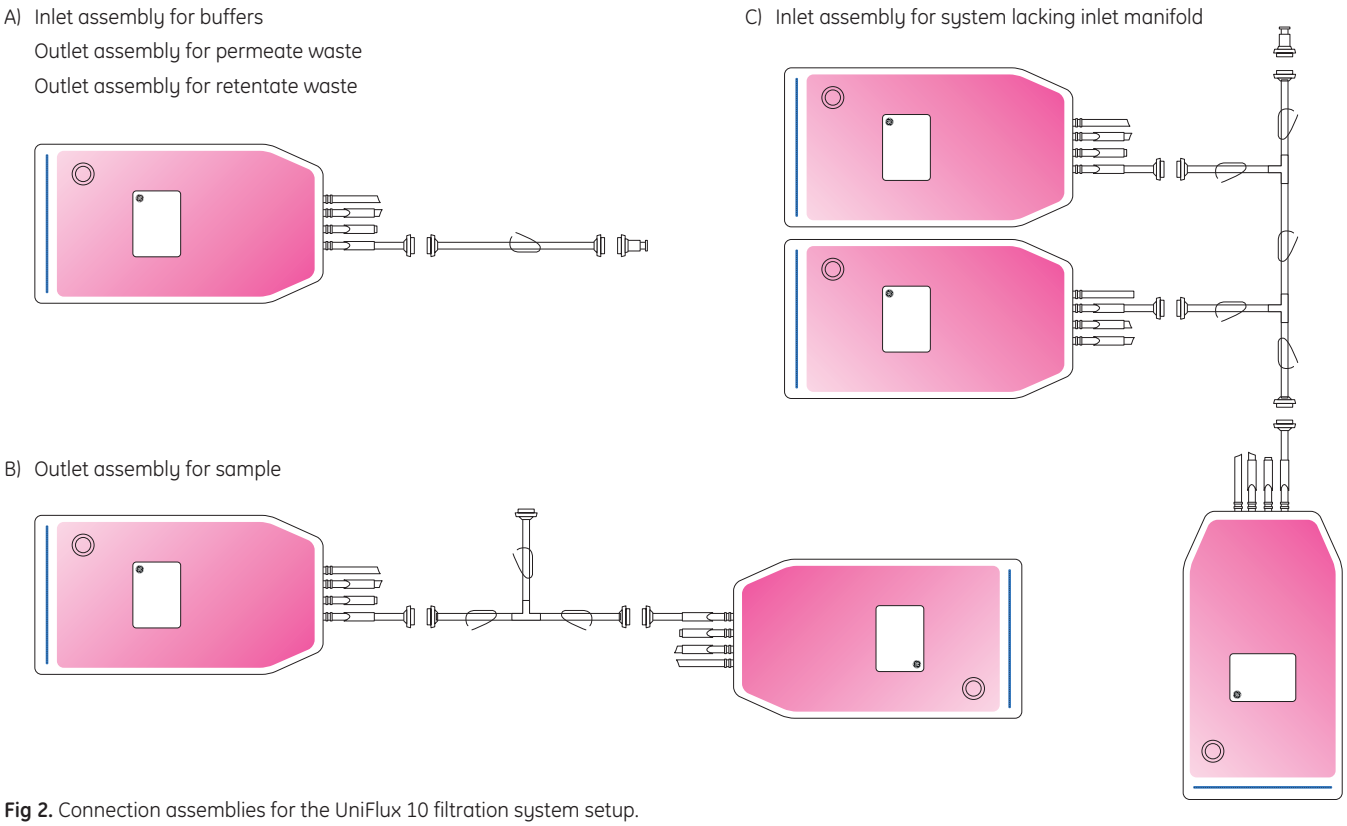

Fig 2. Connection assemblies for the UniFlux 10 filtration system setup.

In general, users should select the same jumper inner diameter as the bag outlet tubing as long as the flow rate and solution viscosity do not set a limitation. In this example, all jumpers were 3 ft in length. However, depending on the distance between the bags and system, three standard tubing lengths are available to secure connectivity, 1, 3 and 5 ft (305, 914 and 1524 mm).

Systems without inlet manifolds can be connected to bags using 4-way tees. These 4-way tees are in turn connected to the system transfer pump (including the pump tubing and tubing to the system) using a ReadyMate DAC 750 mini TC.

Product is recovered from UniFlux 10 filtration system via a 3-way tee connected to the system via a tubing jumper and a ReadyMate DAC 750 mini TC. To minimize dead volume, keep the length and diameter of the jumper as short and small as possible. Connect one leg of the 3-way tee to a bag for concentrated sample and the other to a bag for system rinse. If the rinse is to be pooled directly with the product, just use one bag connected with a ReadyMate DAC 750 mini TC.

Both permeate and retentate waste outlet assemblies are constructed in the same way, which helps users who want to collect permeate, retentate buffer and water rinse. The bag is connected to a jumper that is in turn connected to the system using a ReadyMate DAC 750 mini TC. Ensure that the jumper has the same inner diameter as the bag, and that its length will reach between the system and the bag location. In the example shown in Figure 1, only permeate waste is included in the set up.

ReadyKart mobile processing stations are used to manage the buffers. The UniFlux 10 setup shown in Figure 1 comprises one standard ReadyKart with a 100 L tank plus an extension kit for two additional shelves as well as one ReadyKart Mini. Table 2 lists the ReadyKart items required.

Table 2. ReadyKart mobile processing station components used in the UniFlux 10 system setup

Description
ReadyKart with three shelves, 2 pct
ReadyKart shelf with tank hole
ReadyKart 100 L Tank
ReadyKart 50 L tray, 2 pct
ReadyKart 1-5 L tray, 2 pct

Processors can use this example as a staring point for designing a fluid management process for a new UniFlux 10 ultrafiltration application. Changing buffer volume or increasing tubing jumper length can be easily managed with help of the product information found in Tables 1 and 3. As noted above, the actual assemblies will change depending on the system configuration, i.e. whether or not a transfer pump is included.

The above example has not taken CIP into account. However, expanding the number of legs in the inlet manifold to introduce another bag with the same set up as the other buffers will easily accommodate CIP.

Cross flow micro filtration with UniFlux 30 system

System description

UniFlux 30 system is the next size up from UniFlux 10. Its maximum recirculation flow rate is 60 L per min at 4 bar compared to 10 L per min for UniFlux 10, and tank capacity is 50 or 100 L (5 or 10 L for UniFlux 10). Like UniFlux 10, UniFlux 30 incorporates cross flow filters and high performance hardware in a single filtration system.

Liquid-handling setup

The application scenario used for UniFlux 30 system is a cross flow micro filtration process for a cell culture expressing an extracellular target protein. To maximize recovery, the product is concentrated 10-fold and diafiltered 4 times.

A 10 L bag with four inlets is used (in hanging mode) as the recirculation vessel (see Fig 3 and Table 3). UniFlux 30 is configured with an inlet manifold. The bags holding the liquids to be introduced into the system are assembled and connected to the system via a jumper and a ReadyMate DAC 750 mini TC. Use a jumper with the same inner diameter as the bag tubing.

Fig 3. UniFlux 30 micro filtration setup for concentrating an extracellular target protein 10-fold. Items also shown include ReadyKart mobile processing stations, disposable bags and ReadyCircuit and ReadyMate connection assemblies.

As with the UniFlux 10 cross flow ultra filtration scenario, ReadyKart mobile processing stations are used to manage the buffers. Table 4 lists the ReadyKart items required for UniFlux 30. Figure 4 shows the connection assemblies.

Table 3. ReadyCircuit components used in the micro filtration process shown in Figure 3

Description	Comment
Inlet manifold	
20 L bag, 3 inlets	Water
100 L bag, 4 inlets	Sample
50 L, 3 inlets	Conditioning and diafiltration buffer
4-way tee	3/8 in C-FLEX tubing, system without inlet manifold
RMRM Jumper (3 pct)	3/8 in C-FLEX tubing, 3 ft, system with inlet manifold
Recirculation manifold	
10 L bag, 4 inlets	Recirculation vessel
RMRM Jumper (2 pct)	1/2 in C-FLEX, 1 ft
Permeate manifold	
200 L bag, 4 inlets	Sample collection
RMRM Jumper	1/2 in C-FLEX, 3 ft
10 L bag, 3 inlets	Permeate waste collection
Retentate outlet manifold	
20 L bag, 3 inlets	Retentate waste collection
RMRM Jumper	1/2 in C-FLEX, 3 ft
Used in all three manifolds	
ReadyMate DAC 1500 TC	Connect ReadyMate with system TC, 10 pack
ReadyMate DAC 750 mini TC	Connect ReadyMate with mini TC, 10 pack
ReadyClamp	To secure ReadyMate connections/25 pack

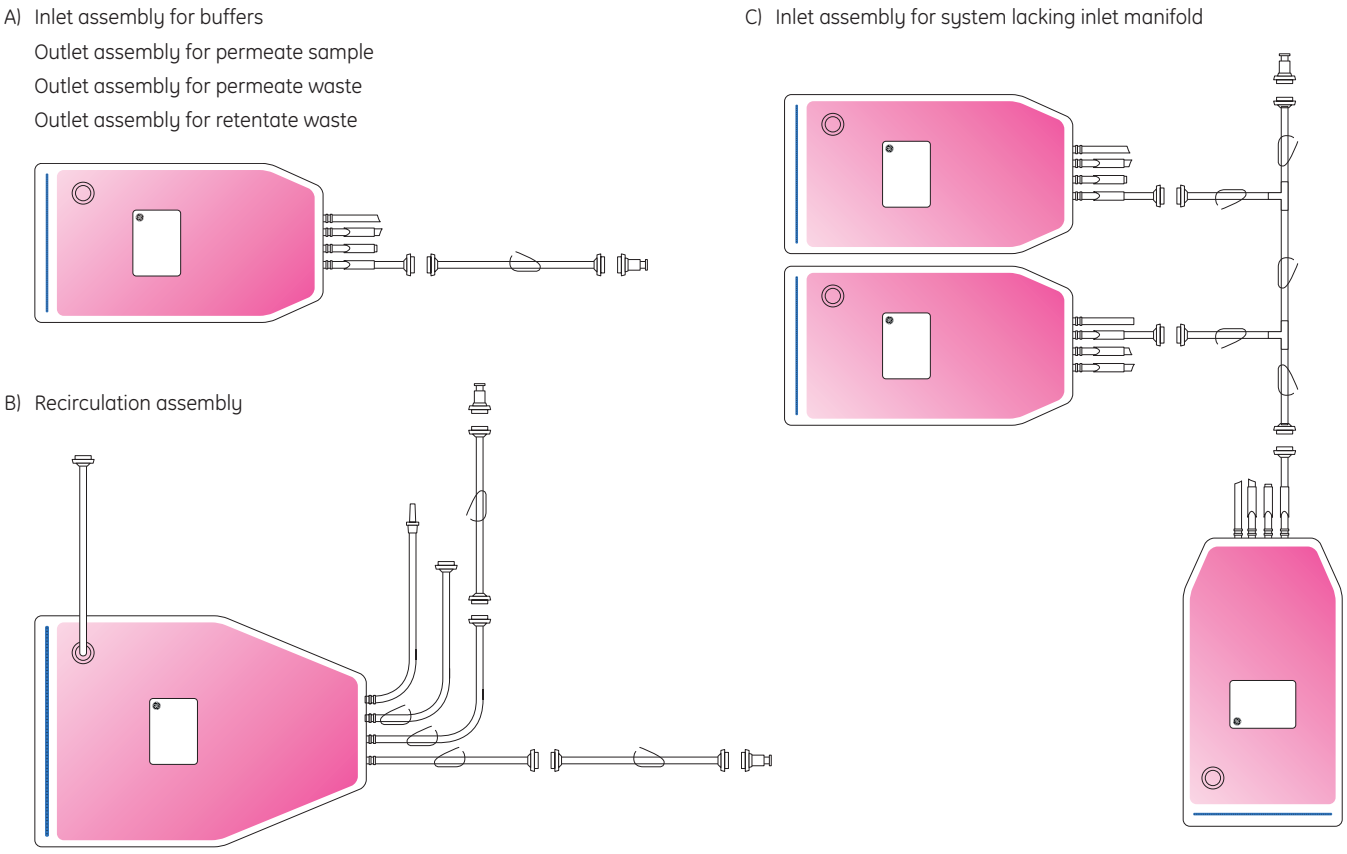

Fig 4. Connection assemblies for the UniFlux 30 filtration system setup.

Table 4. ReadyKart mobile processing station items for the UniFlux 30 setup

Description
ReadyKart with three shelves
ReadyKart top shelf assembly
ReadyKart shelf with tank hole, 2 pct
ReadyKart Mini with three shelves
ReadyKart Mini shelf with tank hole
ReadyKart 200 L Tank
ReadyKart 100 L Tank
ReadyKart 50 L tray

Due to limited space, only two buffers can be connected to the inlet manifold at the same time. However, by removing tubing once the first buffer has been delivered and fitting new tubing in its place, an extra buffer can be added to the system.

For systems with a transfer pump instead of an inlet manifold, bags holding solutions to be introduced to the system are connected via a tubing jumper to a 4-way tee. This tee is connected to the tubing pump using a ReadyMate DAC 750 mini TC. A tubing jumper is connected from the transfer pump to one of the inlets on the recirculation bag using ReadyMate DAC 750 mini TC. The jumper should have the same diameter as the diameter of the bag tubing and a length sufficient to reach the bag (3 or 5 ft).

The recirculation bag is connected to UniFlux 30 via a tubing jumper (1 ft if possible to minimize hold up volume) of the same inner diameter as the bag and a ReadyMate DAC 1500 TC. The retentate return is connected in the same way, but might require a longer tubing jumper than the recirculation bag.

Permeate is collected by connecting a 3-way tee where one inlet is dedicated to the permeate waste and the other to product collection. Both bags are connected to the 3-way tee using jumper tubing with the same inner diameter as the dedicated bag (Fig 4). Retentate is collected in a single 20 L bag via a 3 ft tubing jumper and a ReadyMate DAC 1500 TC. Although everything will go to waste, the retentate needs to be collected separately for decontamination prior to release to minimize the risk of genetically modified organisms (GMO) leaking.

The cross flow membrane is connected to UniFlux 30 system using two ReadyMate DAC 1500 TC connections on the feed and retentate positions.

This example has not taken CIP into account since the membrane is ReadyToProcess and the system has therefore to be cleaned separately.

Conclusions

Disposables and single-use equipment are finding increasing use in unit operations such as ultra and micro filtration. They are especially popular in new-build pilot and production facilities for biopharmaceutical manufacturing.

This Application note demonstrates that plastic bags, flexible plastic tubing and liquid handling systems from GE Healthcare's ReadyToProcess product platform are sufficiently flexible to work effectively with a range of traditional filtration system operations.

Ordering information

Note that UniFlux filtration systems can be ordered through GE Healthcare's configurator. For assistance in placing your order, please contact your local GE Healthcare representative.

Product	Code number
5 L bag with 3 inlets	12-4102-20
10 L bag with 3 inlets	12-4102-22
10 L bag with 4 inlets	12-4102-23
20 L bag with 3 inlets	12-4102-24
50 L bag with 3 inlets	12-4102-28
100 L bag with 4 inlets	12-4102-06
RMRM Jumper 0.25 in × 3 ft C-FLEX, 1 pct	12-4101-15
RMRM Jumper 0.375 in × 3 ft C-FLEX, 1 pct	12-4101-18
RMRM Jumper 0.5 in × 1 ft C-FLEX, 1 pct	12-4101-20
RMRM Jumper 0.5 in × 3 ft C-FLEX, 1 pct	12-4101-21
RMRM Jumper 0.5 in × 3 ft Reinforced Silicon, 1 pct	12-4101-36
4RMT Jumper 0.25 in × 6 ft C-FLEX, 1 pct	12-4101-73
3RMT Jumper 0.375 in × 6 ft C-FLEX, 1 pct	12-4101-64
PSIL Jumper 0.375 in i.d. × 0.563 in o.d., 1 pct	28-9794-32
PSIL Jumper 0.375 in i.d. × 0.625 in o.d., 1 pct	28-9794-34
ReadyMate DAC 750 Mini TC, 10 pct	28-9366-95
ReadyMate DAC 1500 TC, 10 pct	28-9568-89
ReadyClamp, 25 pct	28-9366-90

Product	Code number
ReadyKart with three shelves, 2 pct	28-9778-94
ReadyKart top shelf assembly	28-9778-99
ReadyKart shelf with tank hole	28-9779-09
ReadyKart shelf no tank hole, 1 pct	28-9779-08
ReadyKart mini with three shelves	28-9779-97
ReadyKart mini shelf with tank hole	28-9779-10
ReadyKart 50 L Tray, 2 pct	28-9779-07
ReadyKart 10-20 L Tray	28-9779-06
ReadyKart 1-5 L Tray, 2 pct	28-9779-05
ReadyKart 100 L Tank	28-9779-04

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