# Ready-to-use fluid management for inline conditioning (IC) large-scale chromatography systems

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GE Healthcare
Life Sciences

Application note 29-0257-24 AA ReadyToProcess™

# Ready-to-use fluid management for inline conditioning (IC) large-scale chromatography systems

**There is an increasing interest in IC systems because they; (i) are relatively customizable; (ii) reduce the need for large storage tanks, and (iii) are economical. These features combine well with ready-to-use plastic bags, plastic tubing, connectors, and a mobile processing station to provide flexible liquid-handling solutions that simplify your workload and boost efficiency. We used a selection of fluid management components from GE Healthcare Life Sciences ReadyToProcess platform of disposable and single-use equipment to arrange buffer and sample management solutions for a large-scale inline conditioning chromatography setup.**

**Fig 1.** ReadyToProcess column connected to a BioProcess IC system. Buffer and sample management was achieved by a combination of ready-to-use liquid-handling components such as ReadyCircuit bags and tubing, ReadyMate™ Disposable Aseptic Connectors (DAC), and ReadyKart mobile processing stations.

## Introduction

The increasing demand for disposables and single-use bioprocessing equipment have led to the building of pilot and production facilities that are often based on a flexible platform in which individual units tend to occupy a relatively small footprint. In addition, modern methods for producing biopharmaceuticals require increased buffer supplies delivered at precise times, at appropriate concentrations, and flow rates. In response to these demands, the biopharmaceutical industry has developed state-of-the-art technologies such as IC as an alternative to large storage tanks and this allows for the use of ready-to-use plastic bags and flexible plastic tubing instead of fixed stainless steel buffer tanks and piping.

We have developed a broad ReadyToProcess product platform that allows you to take advantage of plug-and-play features in biopharmaceutical manufacturing.

This application note describes solutions for handling buffers and samples in a process setup for BioProcess™ or ÄKTAprocess™ system for IC. The IC system can be operated with either conventional columns, (e.g., AxiChrom™ range), which offers intelligent packing with preverified packing methods or disposable prepacked ReadyToProcess columns. The IC system can also be used for buffer delivery to other systems like ÄKTA™ ready or ÄKTAprocess that delivers buffer directly to the system or into bags that are connected to the system.

Figure 1 shows a chromatographic purification setup using a ReadyToProcess 10 L column. ReadyCircuit™, (i.e., bags and tubing assemblies that quickly form sterile, self-contained purification modules), were used to handle the samples and buffers.

## Liquid-handling setup

Each bag was connected to the IC system inlet/outlet through a ReadyMate DAC 750 mini TC via a jumper with ReadyMate DACs at each end. A 2 in ULTA™ Prime SG capsule was connected to the bag for buffer filtration (Fig 2).

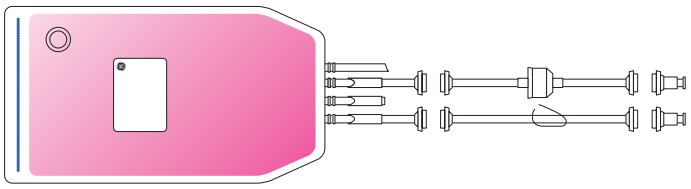

**Fig 2.** ReadyCircuit 20 L bag and ReadyMate connection assembly. All four bag sizes (see Table 1) use a ReadyMate DAC 3/8 in inner diameter jumper with a 3 ft length. A 2 in ULTA Prime SG capsule with a 3/8 in tubing terminating with ReadyMate connectors was connected to the bag for buffer filtration.

The bag sizes for each solution and connection components are listed in Table 1.

**Table 1.** Bags and connection components used in the buffer and sample management setups

| Process step | Bag description |
|---|---|
| Water | Stainless steel tank |
| Base component 1 | 20 L bag with 3 inlets |
| Acid component 1 | 10 L bag with 3 inlets |
| Salt | 50 L bag with 3 inlets |
| Clean-In-Place (CIP) | 10 L bag with 3 inlets |
| Base component 2 | 5 L bag with 3 inlets |
| Acid component 2 | 5 L bag with 3 inlets |
| Outlet* | 50 L bag with 3 inlets |
| **Component** | **Connection** |
| ULTA Prime SG capsule | Connected with 3/8 in C-Flex® and ReadyMate |
| Jumper 8 pcs | RMRM Jumper, 3/8 in, C-Flex, 3 ft |
| ReadyMate DAC 750 mini TC | Connect ReadyMate with mini TC |
| ReadyClamp | To secure ReadyMate connections |

* Only sample collection, not waste

As an alternative to making connections using the components in Table 1, you can use custom-made ReadyCircuit solutions (Fig 3). The bag sizes and connection components for each solution are listed in Tables 1 and 2.

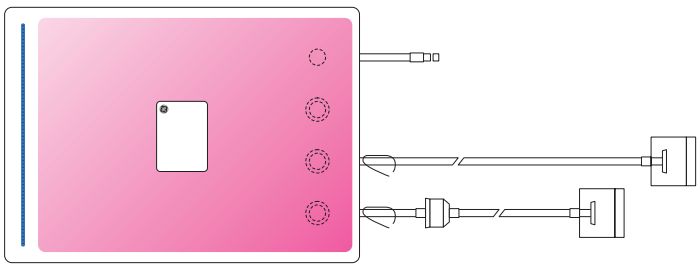

**Fig 3.** Custom-made ReadyCircuit 50 L bag and ¾ TC connection assemblies. All the four bag sizes (see Table 2) use a ReadyMate 3/8 in inner diameter jumper with a 5 ft length. A 2 in ULTA Prime SG capsule was connected to the bag for buffer filtration.

**Table 2.** Custom bags used in the buffer and sample management setups. All the bags have two inlets with a 5 ft 3/8 in C-Flex tubing, ¾ TC connectors, and a buffer filter on one inlet

| Process step | Bag description |
|---|---|
| Water | Stainless steel tank |
| Base component 1 | 20 L bag |
| Acid component 1 | 10 L bag |
| Salt | 50 L bag |
| CIP | 10 L bag |
| Base component 2 | 5 L bag |
| Acid component 2 | 5 L bag |
| Outlet | 50 L bag |

In general, we recommend that you match each ReadyCircuit jumper diameter to the diameter of the installed flow kit or the diameter of the ReadyCircuit bag tubing. However, you might have to adjust this recommendation according to the flow rate and viscosity of the solution you use.

You may choose the length of the jumper according to the position of the buffers in the chromatography system. In this example shown in Figure 4, we used a 3/8 in tubing in 3 ft (914 mm) for all the solutions. ReadyMate jumpers are supplied in 1, 3, and 5 ft (305, 914, and 1524 mm) lengths. For a custom made ReadyCircuit bags the length is defined by your specification.

ReadyKart is part of ReadyToProcess platform. It is a mobile processing station designed to simplify workloads and increase efficiency. In this particular application, we used ReadyKart to control the buffer system. The setup shown here includes two ReadyKart standard—one for the inlet side and the other for the outlet side of the system together with ReadyKart mini and a 200 L bin. This combination is sufficient to handle all inlet buffers and sample.

The 50, 20, and 10 L ReadyCircuit bags were placed in trays to simplify all operations. The 5 L bags hang on the adjustable standard ReadyKart buffer bag handle. The outlet comprises a standard ReadyKart with a 50 L tray for the elution bag. You may use the bags to collect waste fluid streams. ReadyKart components used in this application are listed in Table 3.

**Table 3.** ReadyKart setup components used in buffer and sample management

| Item/description |
|---|
| ReadyKart with three shelves, 2 pct |
| ReadyKart mini with three shelves |
| ReadyKart mini shelf with tank hole, 2 pct |
| ReadyKart 200 L Tank |
| ReadyKart 50 L Tray, 2 pct |
| ReadyKart 10, and 20 L Tray, 2 pct |

## Application of BioProcess or ÄKTAprocess liquid chromatography systems for IC with a ReadyToProcess column

### *System description*

The IC system is available in multiple configurations and the critical process parameters can be controlled by conductivity, pH, or flow, or by a combination of these three. The Programmable Logic Controller (PLC) within UNICORN™ control software, which is independent of the IC system configuration complexity (see UNICORN data file 18-1156-35) confers automation on the system.

The key components of an IC design include:

- At least five pumps selected according to dilution requirements (concentrates of the corresponding acid and base that are used in combination with water for injection (WFI) and salt to generate the correct buffer. The sample is added through a separate line. Each component is delivered via separate pumps to allow best performances and control)
- A dedicated flow meter attached to each pump to ensure a fast, well-controlled response at the start of a new buffer mix
- An optional mixer depending on the properties of the fluids being mixed
- A conductivity monitor to verify the quality of the mixing (any other appropriate inline monitor can be used)

The complete operating setup is shown in Figure 4.

## Process using BioProcess or ÄKTAprocess liquid chromatography systems for IC with an ÄKTA ready system

### *System description*

ÄKTA ready is a liquid chromatography system for process scale-up and production for early clinical phase research. The system has a design, functionality, and documentation to support its use in GLP and cGMP environments. Since it is operated with ready-to-use, disposable flow paths, the need for cleaning between unit operations/products/batches is eliminated and no development and validation of cleaning procedures is required. Using ÄKTA ready system with ReadyToProcess columns avoids the risk for cross-contamination.

### *Liquid-handling setup*

The buffer and sample management of an IC system can also be used to deliver buffers to an ÄKTA ready system by connecting the outlets of the IC system to the inlets of ÄKTA ready. As an alternative to direct delivery to ÄKTA ready system from the IC system, the buffers can be prepared and delivered into bags using the IC system, and the bags can then be connected to ÄKTA ready for use in a process step.

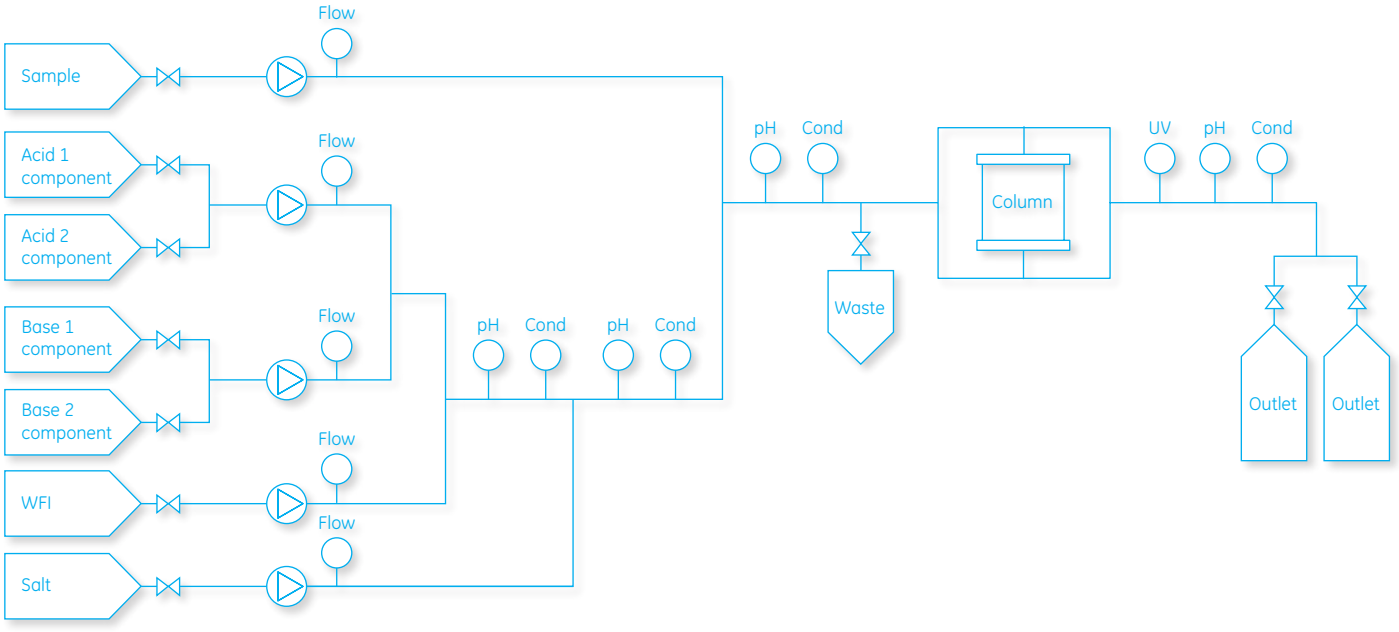


**Fig 4.** A flow scheme for a typical system designed for IC.

## Conclusions

The incorporation of disposables and single-use equipment in downstream chromatographic processes, especially in new pilot and production facilities, provides the following advantages:

- Increased process efficiencies through the elimination of CIP, steam-in-place (SIP), and reduction of WFI
- Improved cost savings from the reduction in the number and size of chemical storage tanks, use of ReadyToProcess products, and IC.

## Ordering information

| Product | Code number |
|---|---|
| 200 L bag with 4 inlets | 12-4102-08 |
| 50 L bag with 3 inlets | 12-4102-28 |
| 20 L bag with 3 inlets | 12-4102-24 |
| 10 L bag with 3 inlets | 12-4102-22 |
| 5 L bag with 3 inlets | 12-4102-20 |
| RMRM Jumper 0.375 in × 3 ft C-FLEX, 1 pct | 12-4101-18 |
| ReadyMate DAC 750 mini TC | 28-9366-95 |
| ReadyClamp | 28-9366-90 |

| Product | Code number |
|---|---|
| ReadyKart with three shelves | 28-9778-94 |
| ReadyKart mini with three shelves | 28-9778-97 |
| ReadyKart mini shelf with tank hole | 28-9779-10 |
| ReadyKart 200 L Tank | 28-9779-03 |
| ReadyKart 50 L Tray | 28-9779-07 |
| ReadyKart 10, and 20 L Tray | 28-9779-06 |

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