Ready-to-use fluid management solutions for chromatography systems

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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 four typical large-scale chromatography setups. These setups comprised different combinations of ReadyToProcess and AxiChrom™ columns and ÄKTA™ ready and ÄKTAprocess™ systems.

Ready-to-use plastic bags, plastic tubing, connectors and a mobile processing station provided flexible liquid-handling solutions that will simplify workloads and boost efficiency for all four configurations. The increasingly wide range of 'plug-and-play' bioprocessing components now available should thus find use in pilot and production facilities that utilize both disposable as well as fixed equipment.

Fig 1. ReadyToProcess column connected to an ÄKTA ready chromatography system. Buffer and sample management is by a combination of ready-to-use liquid handling components such as ReadyCircuit™ bags and tubing, ReadyMate™ connectors, and ReadyKart mobile processing stations.

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 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.

GE Healthcare's broad ReadyToProcess product platform brings such 'plug-and-play' options to biopharmaceutical manufacturing. Many disposable components are designed for single-use only while others can be re-used. All, however, are prepared for immediate use.

This Application note describes solutions for handling buffers and sample in a process setup for ÄKTA ready, a liquid chromatography system that operates with ready-to-use, disposable flow paths, as well as for ÄKTAprocess, a hard-piped chromatography system. Both systems operate with disposable prepacked ReadyToProcess columns or conventional columns such as the AxiChrom range that offers Intelligent Packing with verified, preprogrammed packing methods.

Process using ÄKTA ready system

System description

ÄKTA ready is a liquid chromatography system for process scale-up and production for early clinical phases. The system has a design, functionality and documentation to support its use in GLP and cGMP environments. As it operates 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 scenario illustrated in Figure 1 is a chromatographic purification process using a 10 L ReadyToProcess column. Sample and buffers are managed using ReadyCircuit, which are bags and tubing assemblies that quickly form sterile, self-contained purification modules.

Each bag is connected to the ÄKTA ready system inlet/outlets through a ReadyMate DAC 750 mini TC via a jumper with ReadyMate connectors at each end (Fig 2). Bag sizes for each solution and connection components are listed in Table 1. Figure 3 illustrates the complete operating setup.

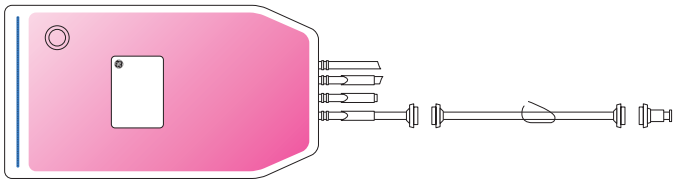

Fig 2. ReadyCircuit 20 L bag and ReadyMate connection assembly. All four bag sizes (see Table 1) use a ReadyMate ½ inch inner diameter jumper with a 3 ft length.

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

Process step	Bag description
Equilibration	100 L bag with 4 inlets
Sample	200 L bag with 4 inlets
Wash	50 L bag with 3 inlets
Elution	50 L bag with 3 inlets
Strip	20 L bag with 3 inlets
CIP	50 L bag with 3 inlets
Outlet waste	100 L bag with 4 inlets
Component	**Connection**
Jumper 7 pct	RMRM Jumper, 3/8 inch, C-FLEX, 3 ft
ReadyMate DAC 750 mini TC	To connect ReadyMate with mini TC
ReadyClamp	To secure ReadyMate connections

In general, process operators should match ReadyMate jumper diameter to the diameter of the installed flow kit or the diameter of the ReadyCircuit bag tubing. Note, however, that high flow rates and solution viscosities may mean that this recommendation needs adjusting upwards.

Choose the length of the jumper according to how the buffers are positioned to the chromatography system. In this example, ½ inch tubing in 3 ft (914 mm) lengths is used for all solutions. ReadyMate jumpers are supplied in 1, 3 and 5 ft (305, 914 and 1524 mm) lengths.

Buffers are managed using ReadyKart. Part of the ReadyToProcess platform, ReadyKart is a mobile processing station designed to simplify workloads and raise efficiency. The solution shown here includes one standard ReadyKart with a 100 L bin and a top shelf (gives two additional shelves) together with ReadyKart Mini with a 200 L bin. This combination is sufficient to handle all inlet buffers and sample.

Fifty L ReadyCircuit bags are placed in the 50 L tray to simplify all operations. The 20 L bag hangs on the adjustable standard ReadyKart buffer bag handle. The outlet comprises a standard ReadyKart with a 50 L tray for the elution bag. If desired, bags can also be used to collect waste fluid streams, but this is not included here. Table 2 lists the ReadyKart components used in this application.

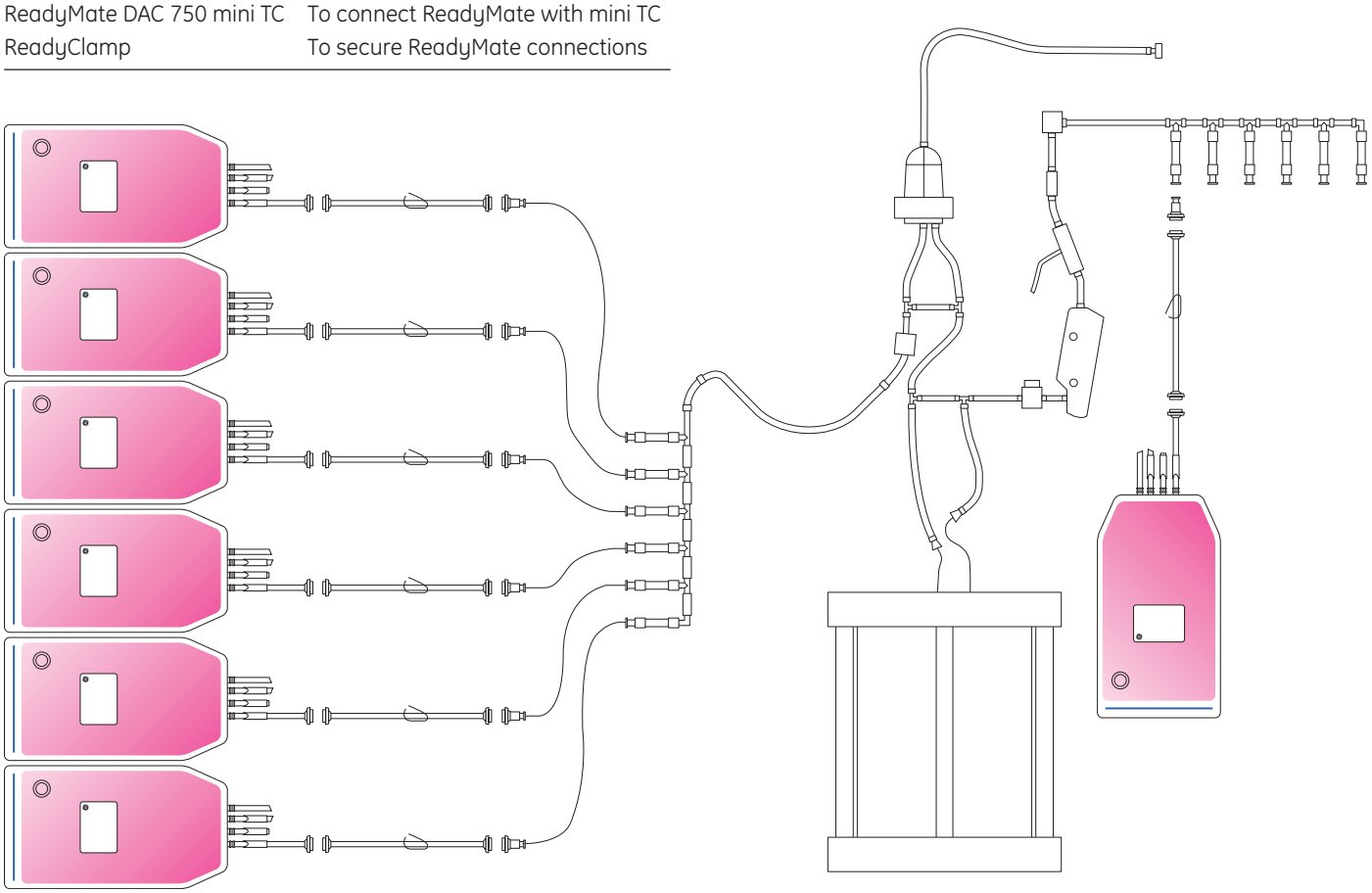

Fig 3. Complete operating setup with six bags connected to the ÄKTA ready flow kit via jumpers and ReadyMate connections.

Table 2. ReadyKart setup components used in buffer and sample management

Item/description
ReadyKart with three shelves
Top shelf assembly
ReadyKart shelf with tank hole
ReadyKart Mini frame for three shelves
ReadyKart Mini shelf no tank hole
ReadyKart 200 L Tank
ReadyKart 100 L Tank
ReadyKart 50 L Tray

As an alternative to the 10 L ReadyToProcess column shown in Figure 1, a conventional column can be used with ÄKTA ready system. In this case, the column is connected using a suitable length of tubing with mini TC connections of the same diameter as the installed system flow kit. Figure 4 shows how a conventional AxiChrom 140 column has replaced the ReadyToProcess column in the ÄKTA ready setup shown in Figure 1.

Fig 4. AxiChrom 140 column connected to an ÄKTA ready chromatography system. Buffer and sample management uses the same ready-to-use components as shown in Figure 1.

Process using ÄKTAprocess system

System description

ÄKTAprocess is an automated liquid chromatography system for process scale-up and large-scale biopharmaceutical manufacturing. Its proven stainless steel-based design can be configured to meet specific process demands. Three flow rate ranges extend up to 1800 L/h.

Liquid-handling setup

Buffer and sample management using ready-to-use bags can also be applied to a traditional hard-piped system like ÄKTAprocess. Figure 5 shows such an arrangement where the buffer assemblies for an AxiChrom 140 column are managed in exactly the same way as for the ÄKTA ready setup shown in Figure 1. Note that ReadyKart and its component parts are also used in the same manner in the 'fully traditional' setup shown in Figure 5.

Fig 5. AxiChrom 140 column connected to an ÄKTAprocess chromatography system. Buffer and sample management use the same ready-to-use components as shown in Figure 1.

Replacing the AxiChrom 140 column with a 10 L ReadyToProcess column, thereby eliminating packing and repacking from the operating procedure, results in a buffer and sample management arrangement like the setup shown in Figure 6.

Fig 6. ReadyToProcess column connected to a traditional ÄKTAprocess chromatography system. Buffer and sample management use the same ready-to-use components as shown in Figure 1.

Conclusions

Disposables and single-use equipment are finding increasing use in downstream chromatographic processes, and are especially popular in new-build pilot and production facilities.

This Application note shows that ready-to-use plastic bags and flexible plastic tubing, plus supporting liquid handling systems, are sufficiently flexible to work effectively not only with the ReadyToProcess product platform but also with more traditional columns and 'hard-piped' systems for biopharmaceutical manufacturing.

Ordering information

Product	Code number
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
200 L bag with 4 inlets	12-4102-08
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, 2 pct	28-9778-94
ReadyKart top shelf assembly	28-9778-99
ReadyKart shelf with tank hole, 1 pct	28-9779-09
ReadyKart Mini frame for three shelves	28-9778-98
ReadyKart Mini shelf no tank hole	28-9779-10
ReadyKart 200 L Tank	28-9779-03
ReadyKart 100 L Tank	28-9779-04
ReadyKart 50 L Tray, 5 pct	28-9779-07

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