# ÄKTA™ ready system

ÄKTA ready is a liquid chromatography system built for process scale-up and manufacturing (Fig 1). It is part of the ReadyToProcess platform, a suite of plug-and-play, ready-to-use solutions for bioprocessing. The system operates with ready-to-use, disposable flow paths that are available separately in High and Low Flow Kits. As a benefit, the need for cleaning between products/batches is eliminated and no development and validation of cleaning procedures is required. Replacing flow paths between batches is fast, and when used together with ReadyToProcess columns, the risk for cross-contamination is removed.

The ÄKTA ready system is biocompatible and hygienic, and is well-suited for use in a GMP regulated environment. ÄKTA ready system is controlled by UNICORN™ software, including a complete guide and documentation for installation of Flow Kits and columns. ÄKTA ready system is available in two versions: for either isocratic or gradient elution.

### ÄKTA ready system provides the following benefits:

- Simple exchange of the complete flow path eliminates the need for system cleaning including method development and validation
- Improved economy and productivity due to simple procedures, and low downtime between products/batches
- Risk for cross-contamination between products/batches is eliminated
- Scalable processes using UNICORN software
- Accompanied by extensive product documentation

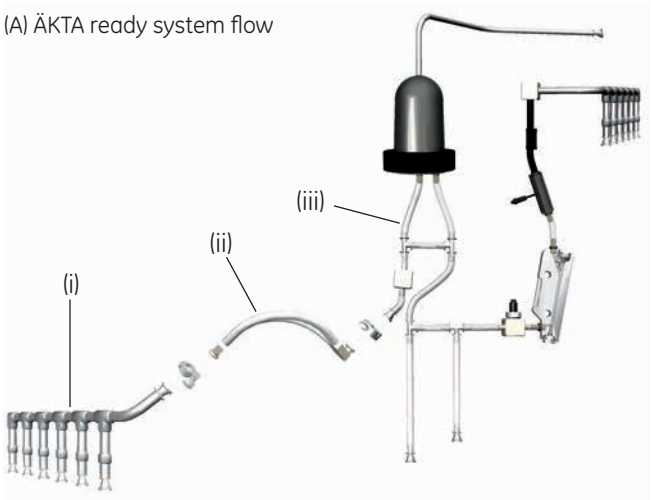
After completion of a purification task, the columns and flow path (i.e., ÄKTA ready Flow Kits and Gradient Flow Section) can either be disposed of or reused for multiple chromatographic cycles of the same batch.

The ReadyToProcess concept can speed processes considerably due to fewer operations; there is no need to establish and validate cleaning procedures, and no complex setup. The flow path can be changed quickly, with a downtime of less than 1 h. This saves time, capital investment, start-up cost, and costs for labor and utility consumption.

**Fig 1.** ÄKTA ready is a chromatography system using a disposable flow path. It allows users to speed up process scale-up and cleaning between product batches is no longer required. ÄKTA ready system for gradient elution is displayed.

## System design and description

ÄKTA ready system is available in two versions: for either isocratic or gradient elution. The system comprises an ÄKTA ready chromatography unit, UNICORN software, and a disposable ÄKTA ready flow paths including sensors and detection flow cells. The system can be Installation and Operation Qualification (IQ/OQ) qualified by the customer or by a certified specialist. An Installation Wizard supported by UNICORN assists the user during the whole installation/replacement of the flow paths. A component test can subsequently be performed to check that the kit has been correctly installed and that sensors are calibrated.



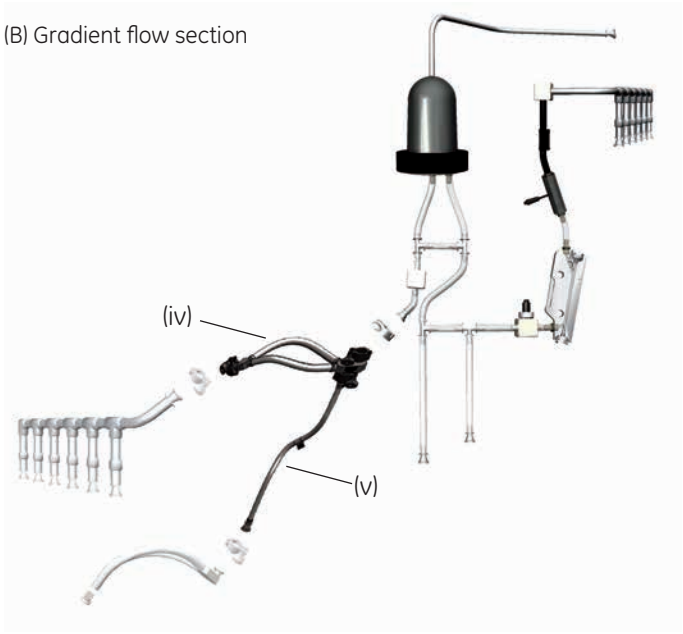




**Fig 2.** (A) ÄKTA ready Flow Kit (i) inlet manifold, (ii) pump tubing, and (iii) main flow path. (B) Gradient flow section (iv) pump tubing, and (v) tubing.

## ÄKTA ready Flow Kits

ÄKTA ready system works with two Flow Kits with different diameters to allow a wide range of flow rates, from 3 to 510 L/h. The Low Flow Kit (small diameter) manages flows of up to 175 L/h using columns typically less than 20 cm in diameter (approx. 5 L column volume). The Low Flow Kit enhances system performance at low flow rates. The High Flow Kit (large diameter) typically used with larger columns (diameter > 20 cm, approx. 10 L column volume and higher) allows flow rates up to 510 L/h. Each Flow Kit consists of three separate parts (Fig 2A), the inlet manifold, pump tubing, and the main flow path, which are easily assembled when the Flow Kit is connected to the system. An extra flow section, comprising a pump tubing and a jumper tube, is required to run gradient elution (Fig 2B). Step-by-step guidance and documentation is provided by the UNICORN Installation Wizard.

The configuration of the ÄKTA ready Flow Kits is described in Figure 3A. Inlet valves (i) select the appropriate inlet tubing for sample or buffer. The pump (ii) delivers fluid to the column (vii) via a pressure sensor (iii) and the air trap (v). There are two sets of valves between the pump and the column: the air trap valves (iv), allow bypassing of the air trap (Fig 3B); and the column valves (vi) allow bypassing of the column. The air trap has a manual air vent valve (not shown).

After the column (vii), the fluid passes through a second pressure sensor (viii), which is integrated with a pH electrode (optional). The fluid then continues through a flow meter (ix), which includes an IR temperature sensor, a conductivity cell (x), and a UV cell (xi) (Fig 3C). The last sensor in the path is a third pressure sensor (xii). After the sensors, the fluid continues via the outlet tubing to the outlet manifold (xiii), where valves divert the fluid to either waste or fraction collection.

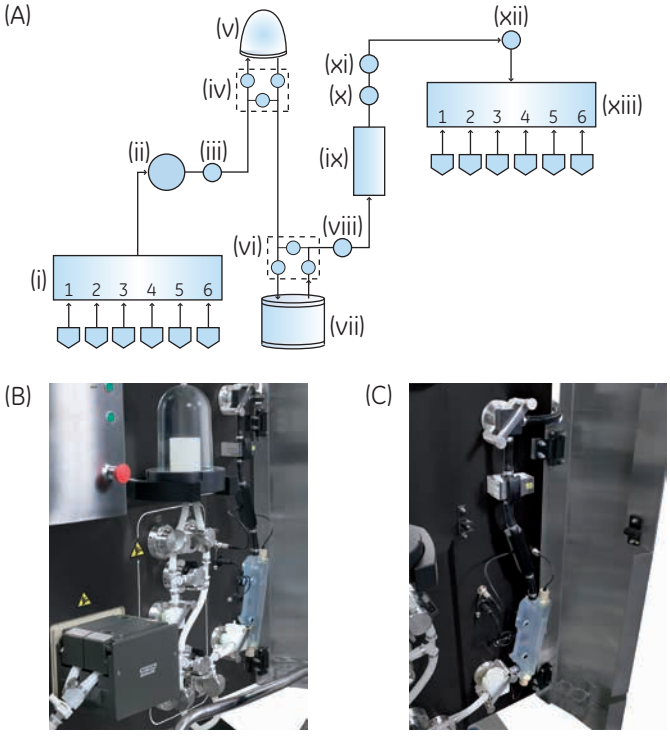



**Fig 3.** (A) Configuration of ÄKTA ready Flow Kits. (B) Location of air trap on ÄKTA ready system. (C) Temperature sensors, flow meter, conductivity sensors, and UV cell.

## Pressure and flow control

This feature allows for continued processing when running at constant flow rate and the pressure increases above the set maximum pressure. The system will use this function to automatically regulate the flow rate to a defined pressure set point. The chromatogram in Figure 4 shows the principle of the pressure-flow control function. Initially, the system is run at constant flow rate (50 L/h) (A). When pressure increases above the defined set point (1.0 bar [14.5 psi, 0.1 MPa]), the system regulates the flow rate to achieve constant pressure (B). As the pressure decreases, the flow rate increases until reaching the set point and is then maintained again at constant flow rate of 50 L/h (C).

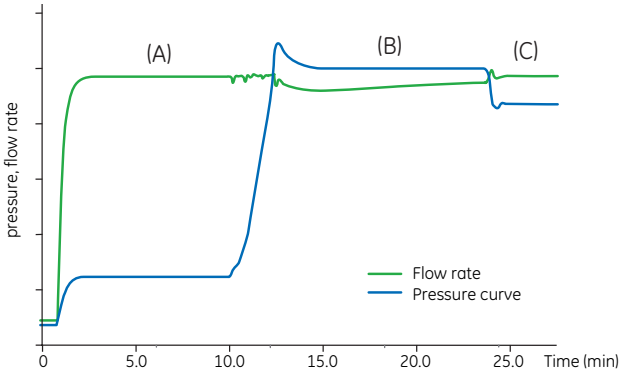



**Fig 4.** Control features of ÄKTA ready system flow rate (green curve) and pressure (blue curve). The figure shows the initial flow rate control (A); regulated flow rate to achieve constant pressure (B); and return to flow rate control (C).

## Robust and hygienic design

The ÄKTA ready system is resistant to chemical agents used in protein recovery, including buffer solutions for adsorption, elution and washing, and to regeneration and cleaning solutions.

All material is of proven quality, and the entire flow path is disposable. All wetted materials are fully biocompatible (USP class VI) and the materials used are traceable back to their production batches. The materials are listed under Specifications.

The flow paths are produced under controlled conditions and packed in clean room environment (class ISO 7) using validated protocols. The Flow Kit pump tubing and the Gradient Flow Section are autoclaved (121°C for 15 min). The other Flow Kit parts are gamma irradiated (27.5 kGy) except for the pH sensor. To protect against contamination, ÄKTA ready flow paths are delivered in double plastic bags. The level of colony forming units (CFU) and endotoxins in the flow paths were tested prior to gamma irradiation/heat treatment in the development of the production process.

## Regulatory product documentation and services

Regulatory authorities expect manufacturers of pharmaceuticals to qualify equipment before use in production. Process safety is an integral part of the ÄKTA ready concept and this includes the exchangeable, replaceable flow paths. The ÄKTA ready flow paths are supported with an extensive documentation package.

- **Product documentation** – Provides information about the materials used in the wetted parts with full traceability, containing certificates including USP Class VI and animal origin statements. This information is delivered with the ÄKTA ready Flow Kits.
- **Validation Guide** – Includes a description of the manufacturing process, qualification tests, and extractables information. Validation Guides can be downloaded from www.gelifesciences.com/rsf
- **Validation documentation** – ÄKTA ready system is delivered with a functional test protocol. Each Flow Kit is also delivered with a test protocol for component and pressure testing.
- **Fast Trak Validation** – Offers a comprehensive range of documents and also specialist services to support the validation on-site.

## Comprehensive control with UNICORN software

The Installation Wizard of UNICORN software performs the setup and checks functionality of the flow paths. The Installation Wizard consists of instructions for correct and easy attachment, and an installation and function test of the flow paths and sensors. A report is generated with completed installation procedures including instructions from the Installation Wizard, traceability to flow path, process information, and results from the component test. The Installation Wizard also contains instructions and reports for column installation.

External, independent audits have shown that the UNICORN development process shows good adherence to the framework, principles, and practices described in GAMP 5 and that functionality of the product is acceptable for use in a GMP regulated environment in a manner complying with 21 CFR Part 11.

UNICORN communicates via OLE for Process Control (OPC), allowing for real-time and historical data access as well as third-party software control.

## ReadyToProcess columns

ReadyToProcess columns are available with a range of BioProcess™ chromatography media (resins) in four different sizes: 1 L, 2.5 L, 10 L, and 20 L (Fig 5). The columns are prepacked, presanitized, and prequalified. The columns are designed for purification of biopharmaceuticals for clinical phase I and II studies. Depending on the scale of operations they can also be used for full-scale manufacturing and preclinical studies. The columns can be used in chromatographic applications for separation of proteins, endotoxins, DNA, plasmids, and viruses.

**Fig 5.** ReadyToProcess columns are easily connected to ÄKTA ready or other chromatography systems and can be disposed of after completed production.

ReadyToProcess columns make several steps redundant in downstream processing (column packing, column qualification [HETP and asymmetry tested], sanitization and cleaning validation), to ensure that significant time can be saved. ReadyToProcess columns are closed units and the design allows easy disposal after completed production.

The most common BioProcess media are available in the ReadyToProcess format, see Ordering information. Sepharose™ 6 Fast Flow and Capto™ media can be requested by contacting your local sales representative.

## Reproducible results with scalability

ÄKTA ready system is designed for process scale-up and small-scale production. Method development can be performed at laboratory scale and then scaled up to ÄKTA ready system. In addition, the process developed for ÄKTA ready system can be transferred to ÄKTAprocess™ system for use in large-scale production. Most ÄKTA systems use the same UNICORN control software, methods can therefore quickly be scaled up.

The media used in ReadyToProcess columns are also available as bulk media. Fast method development can be achieved using PreDictor™, Tricorn™, or XK columns. After optimizing the purification at laboratory scale, the process can be scaled up by keeping the residence time constant in order to maintain capacity. This can be achieved by increasing the column diameter and keeping the mobile phase velocity and sample-to-bed volume ratio constant.

## Scale-up studies

A study was performed to verify that the results of a protein separation experiment give the same result regardless of column size or chromatography system used. A mixture of two proteins, bovine serum albumin, BSA, ($M_r$ 66 000) and lactoferrin ($M_r$ 90 000), was applied to columns of different sizes, and eluted. The elution peaks in the resulting chromatograms were compared. The columns used were: XK 16/40 packed with Capto S; BPG 100 packed with 1.5 L Capto S (both to a bed height of 20 cm); ReadyToProcess: Capto S 2.5; Capto S 10; and Capto S 20 (Fig 6).

The results shown in Figure 6 indicate that scale-up from an XK 16/40 to the ReadyToProcess columns was possible and the results were similar regardless of the chromatography system used.

A study was conducted to compare gradient elution performance on ÄKTA ready gradient and ÄKTAprocess. BSA and lactoferrin were separated through gradient elution on 2.5 L and a 10 L ReadyToProcess columns. Figure 7 indicates comparable results for ÄKTAprocess (A) and ÄKTA ready gradient (B) systems.

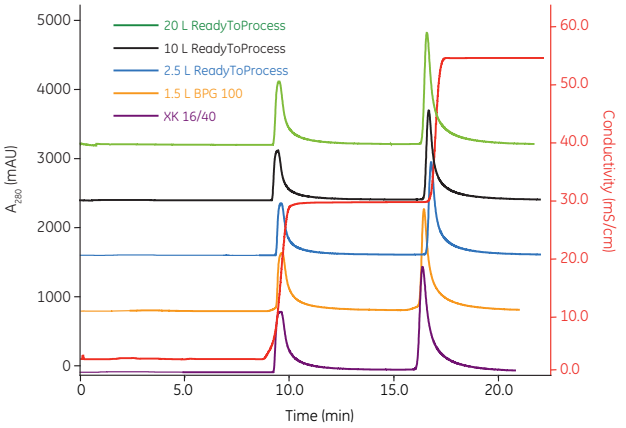



**Fig 6.** Stacked chromatogram from ÄKTA ready comparing step elution on five different columns (the XK 16/40 packed with Capto S chromatography medium was run on an ÄKTA system). The elution buffers were 50 mM sodium acetate, 0.3 M NaCl, pH 5.0 and 50 mM sodium acetate, 0.65 M NaCl, pH 5.0. The elution steps were 3 column volumes (CV) each.

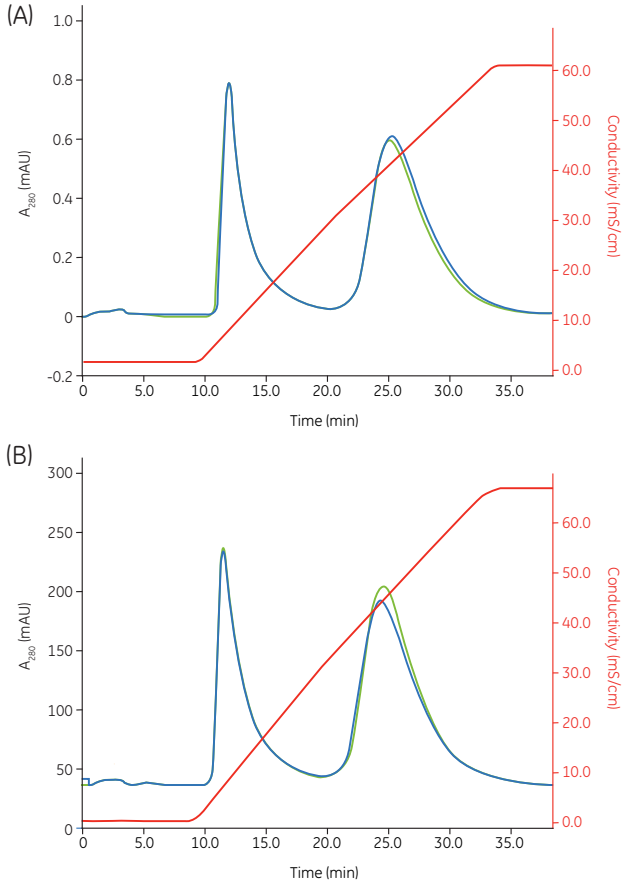



**Fig 7.** Chromatogram from ÄKTAprocess (A) and ÄKTA ready gradient (B) comparing gradient elution on 2.5 L and 10 L Capto S ReadyToProcess columns. The equilibration buffer was 50 mM sodium acetate, pH 5.0 and the elution buffer was 50 mM sodium acetate, 0.65 M NaCl, pH 5.0. The elution was performed over 10 CV followed by 100% elution buffer for 3 CV.

# Specifications

## General specifications

| | |
|---|---|
| W × H × D | 1000 × 1650 × 800 mm and 1160 × 1650 × 800 mm (gradient) |
| Weight | 230 kg and 250 kg (gradient) |
| Control system | UNICORN v5.20 or higher version of UNICORN 5 |
| Instrument input voltage | AC Voltage, 1× 100/120/200–208/220–230/240 V, ± 10%, 50/60 Hz |
| Max. power consumption | 1 kVA |
| Ingress protection | IP45 |
| Compressed air interface | 5.5–7 bar, 50 Nl/min, oil- and particle-free |

## Operating conditions

| | |
|---|---|
| Surrounding temperature | 2°C to 30°C |
| Fluid temperature | 2°C to 40°C |
| Fluid density | 950–1050 kg/m$^3$ |
| Fluid viscosity | 1.0–1.3-fold water viscosity at actual temperature, max. 2.5 cP |

## System capacity

| | |
|---|---|
| Volumetric flow rates | 7.5–510 L/h High Flow Kit<br>3–175 L/h Low Flow Kit |
| Pump speed | 340 rpm (100%) High Flow Kit<br>225 rpm (100%) Low Flow Kit |
| Max. pressure, peristaltic pump | 4.0 bar |
| System pressure rating | 5.0 bar (high-pressure flow path, upstream column)<br>2.0 bar (high-pressure flow path, downstream column)<br>0.95 bar (low-pressure outlet manifold)<br>0.6 bar (low-pressure inlet manifold) |
| Gradient range | 10% to 90% gradient buffer with ± 4% linearity, up to 3 bar |
| Gradient flow range | 40–510 L/h High Flow Kit<br>20–175 L/h Low Flow Kit |

## Sensor specifications

| Sensor | Acceptance range | Measurement error[1] |
|---|---|---|
| Pressure | 0–5 bar g | ± 0.20 bar g |
| Flow (high flow kit)[2] | 7.5–510 L/h | ± 5% actual value at flow[3] 40 L/h[3]<br>± 10% actual value at flow < 40 L/h[3] |
| Flow (low flow kit)[2] | 3–175 L/h | ± 5% actual value at flow[3] 20 L/h[3]<br>± 10% actual value at flow < 20 L/h[3] |
| Conductivity[4] | 0–150 mS/cm | ± 5% full scale[5] |
| pH[6] | pH 2–12 | ± 0.2 pH at calibration temperature<br>Drift: ± 0.025 pH units/h (20°C, pH 4)<br>Flow rate sensitivity: ± 0.1 pH unit |
| UV | 0.01–1.0 AU | Deviation from linearity ± 5%[3, 7] |
| Temperature | 2°C to 40°C | ± 3°C[3] |

[1] Max. error, valid within acceptance range under operation conditions
[2] Flow meter cells for high flow and low flow kits are designed with different flow path geometries
[3] Valid for liquid with density of water and 1.0 to 1.3-fold the viscosity of water at the actual liquid temperature; and max. temperature difference of 10°C between liquid and ambient temperature
[4] Temperature compensation optional
[5] Valid at actual temperature (no temperature compensation)
[6] Temperature compensation not available
[7] Cell length 1.8 mm ± 0.2 mm

## Wetted materials

| | |
|---|---|
| Tubing | Silicone, platinum cured, reinforced tubing in high-pressure flow path |
| Pump tubing | Composite of expanded Polytetrafluoroethylene (PTFE) and platinum-cured silicone |
| Connectors | Polypropylene (PP), Polyetheretherketone (PEEK) |
| Flow meter body | Polymethylpentene (TPX) |
| Air trap | Polyamide (PA), transparent; Polypropylene (PP) |
| pH electrode | Polyoxymethylene (POM), ceramics (junction), glass |
| pH electrode dummy | Polypropylene (PP) |
| Conductivity cell | Polypropylene (PP); Titanium |
| UV cell | Polypropylene (PP) |

Sealing materials Ethylene propylene diene monomer (EPDM); fluoroelastomer (FKM); thermoplastic elastomer (TPE)

## Material compliance

USP <88> Class VI Test for biocompatibility
Animal free or complies with the conditions in EMA/410/01

# Site preparation guide

## 1. Containers

The ÄKTA ready system is shipped in a container with the following dimensions:

| | |
|---|---|
| W × H × D | 1150 × 1900 × 1100 and 1350 × 1900 × 1100 (gradient) |

## 2. Uncrating the system

Space and tools needed to uncrate the system:

Floor space 3800 × 1100 mm
13 mm Hexagonal tool
Phillips bits no. 2
Electrical screwdriver
Knife

## 3. Transportation route

Doors, corridors, and elevators should have a minimum width of 90 cm and a minimum height of 200 cm to allow transport of the system to the production area.

## 4. Lifting device

A forklift capable of carrying up to 400 kg is needed.

## 5. Power supply requirements

| | |
|---|---|
| Supply voltage: | 100, 120, 200–208, 220–230, or 240 VAC ± 10%, 50/60Hz |
| Max power consumption: | 1000 VA |
| Max branch circuit protection: | 16 A |

## 6. Air supply requirements

| | |
|---|---|
| Compressed air pressure: | 5.5-7.0 bar (oil- and particle-free) |
| Compressed air supply: | Minimum 50 Nl/min Male air hose connector for 7.5 mm hose |

### 7. Service access area

To allow service and maintenance, leave 1 m of free space around the system.

| | |
|---|---|
| Area needed: | 2800 × 3000 mm and<br>2800 × 3160 mm (gradient) |

### 8. Operating room climate

| | |
|---|---|
| Ambient temperature: | 2°C to 30°C |
| Relative humidity: | 20% to 95%, noncondensing |

### 9. Transport and storage requirements

| | |
|---|---|
| Ambient temperature: | –25°C to 60°C |
| Relative humidity: | 20% to 95%, noncondensing |

### 10. Connectors

Two TC-clamps with gaskets for the appropriate size of inlet and outlet.

### Pretreatment of Flow Kits (wetted components)

Assembly of cleaned parts in ISO class 7 clean room.

The complete Flow Kit is gamma irradiated (27.5 kGy), except for pump tubing and pH electrode. The pump tubing is autoclaved (121°C, 15 min).

## Ordering information

### System

| Product | Code number |
|---|---|
| ÄKTA ready including Column Trolley and UNICORN | 28-9062-61 |
| ÄKTA ready gradient including Column Trolley and UNICORN | 29-0320-38 |
| Gradient upgrade ÄKTA ready | 29-0327-84 |
| Legacy gradient upgrade kit ÄKTA ready | 29-1032-17 |

### Flow Kits

| Product | |
|---|---|
| ÄKTA ready Low Flow Kit | 28-9301-82 |
| ÄKTA ready High Flow Kit | 28-9301-83 |
| ÄKTA ready Gradient Low Flow Section[1] | 29-0210-85 |
| ÄKTA ready Gradient High Flow Section[2] | 29-0210-86 |

### IQ/OQ qualification

| Product | |
|---|---|
| IQ/OQ Document | 28-9334-43 |
| IQ/OQ Performance | 28-9499-80 |
| ÄKTA ready Low Flow Test Kit | 28-9336-80 |
| ÄKTA ready UV Cond. Test Tools | 28-9336-88 |
| ÄKTA ready Pressure Calib. Tool | 28-9329-42 |
| Temp Kit | 28-9388-24 |

### ÄKTA ready accessories

| Product | |
|---|---|
| Column Trolley | 28-9218-80 |
| ÄKTApilot Air Inlet Filter | 18-1169-58 |
| ÄKTApilot pH Electrode, including O-ring and nut | 18-1168-77 |
| Air Sensor | 29-0038-79 |

### ReadyToProcess columns

| Product | Pack size | Code number |
|---|---|---|
| ReadyToProcess Capto Q 1 | 1 L | 28-9510-90 |
| ReadyToProcess Capto Q 2.5 | 2.5 L | 28-9017-23 |
| ReadyToProcess Capto Q 10 | 10 L | 28-9017-24 |
| ReadyToProcess Capto Q 20 | 20 L | 28-9017-25 |
| ReadyToProcess Capto S 1 | 1 L | 28-9510-93 |
| ReadyToProcess Capto S 2.5 | 2.5 L | 28-9017-29 |
| ReadyToProcess Capto S 10 | 10 L | 28-9017-30 |
| ReadyToProcess Capto S 20 | 20 L | 28-9017-31 |
| ReadyToProcess Capto adhere 1 | 1 L | 28-9511-09 |
| ReadyToProcess Capto adhere 2.5 | 2.5 L | 28-9017-14 |
| ReadyToProcess Capto adhere 10 | 10 L | 28-9017-15 |
| ReadyToProcess Capto adhere 20 | 20 L | 28-9017-16 |
| ReadyToProcess MabSelect SuRe™ 1 | 1 L | 28-9511-10 |
| ReadyToProcess MabSelect SuRe 2.5 | 2.5 L | 28-9017-17 |

[1] To obtain a complete gradient low flow path a low flow kit has to be ordered together with the gradient low flow section

[2] To obtain a complete gradient high flow path, a high flow kit has to be ordered together with the gradient high flow section

## *ReadyToProcess columns continue*

| Product | Pack size | Code number |
|---|---|---|
| ReadyToProcess MabSelect SuRe 10 | 10 L | 28-9017-18 |
| ReadyToProcess MabSelect SuRe 20 | 20 L | 28-9017-19 |
| ReadyToProcess Phenyl Sepharose 6 FF (low sub) 1 | 1 L | 28-9511-11 |
| ReadyToProcess Phenyl Sepharose 6 FF (low sub) 2.5 | 2.5 L | 28-9017-35 |
| ReadyToProcess Phenyl Sepharose 6 FF (low sub) 10 | 10 L | 28-9017-36 |
| ReadyToProcess Phenyl Sepharose 6 FF (low sub) 20 | 20 L | 28-9017-37 |
| ReadyToProcess Capto MMC 1 | 1 L | 28-9511-18 |
| ReadyToProcess Capto MMC 2.5 | 2.5 L | 28-9291-20 |
| ReadyToProcess Capto MMC 10 | 10 L | 28-9291-21 |
| ReadyToProcess Capto MMC 20 | 20 L | 28-9291-22 |
| ReadyToProcess Q Sepharose FF 1 | 1 L | 28-9511-25 |
| ReadyToProcess Q Sepharose FF 2.5 | 2.5 L | 28-9290-76 |
| ReadyToProcess Q Sepharose FF 10 | 10 L | 28-9290-79 |
| ReadyToProcess Q Sepharose FF 20 | 20 L | 28-9290-82 |
| ReadyToProcess SP Sepharose FF 1 | 1 L | 28-9510-97 |
| ReadyToProcess SP Sepharose FF 2.5 | 2.5 L | 28-9291-05 |
| ReadyToProcess SP Sepharose FF 10 | 10 L | 28-9291-06 |
| ReadyToProcess SP Sepharose FF 20 | 20 L | 28-9291-07 |
| ReadyToProcess DEAE Sepharose FF 1 | 1 L | 28-9511-26 |
| ReadyToProcess DEAE Sepharose FF 2.5 | 2.5 L | 28-9291-14 |
| ReadyToProcess DEAE Sepharose FF 10 | 10 L | 28-9291-15 |
| ReadyToProcess DEAE Sepharose FF 20 | 20 L | 28-9291-16 |
| ReadyToProcess MabSelect™ 1 NS | 1 L | 28-9511-28 |
| ReadyToProcess MabSelect 2.5 NS | 2.5 L | 28-9415-22 |
| ReadyToProcess MabSelect 10 NS | 10 L | 28-9415-23 |
| ReadyToProcess MabSelect 20 NS | 20 L | 28-9415-24 |
| ReadyToProcess Q Sepharose XL 1 | 1 L | 29-0326-70 |
| ReadyToProcess Q Sepharose XL 2.5 | 2.5 L | 29-0005-45 |
| ReadyToProcess Q Sepharose XL 10 | 10 L | 29-0156-16 |
| ReadyToProcess Phenyl Sepharose 6 FF high sub | 1 L | 28-9511-97 |
| ReadyToProcess Phenyl Sepharose 6 FF high sub | 2.5 L | 28-9291-08 |
| ReadyToProcess Phenyl Sepharose 6 FF high sub | 10 L | 28-9291-09 |
| ReadyToProcess Phenyl Sepharose 6 FF high sub | 20 L | 28-9291-10 |
| ReadyToProcess CM Sepharose Fast Flow 2.5 | 2.5 L | 28-9291-17 |
| ReadyToProcess CM Sepharose Fast Flow 10 | 10 L | 28-9291-18 |
| ReadyToProcess CM Sepharose Fast Flow 20 | 20 L | 28-9291-19 |

ReadyToProcess columns are supplied in 20% ethanol (ReadyToProcess Capto S columns are supplied in 20% ethanol, 0.2 M sodium acetate, pH 5.5). Other Sepharose 6 FF and Capto media not listed above can be requested by contacting your local sales representative.

# *Literature*

## Application notes

| | |
|---|---|
| Efficiency test of ReadyToProcess columns | 28-9198-21 |
| Purification of a monoclonal antibody using ReadyToProcess columns | 28-9198-56 |
| A flexible antibody purification process based on ReadyToProcess products | 28-9403-48 |

## Data files

| | |
|---|---|
| ReadyToProcess columns | 28-9159-87 |
| UNICORN control system | 18-1156-35 |

GE Healthcare Bio-Sciences AB
Björkgatan 30
751 84 Uppsala
Sweden

**www.gelifesciences.com/readytoprocess**


GE Healthcare UK Limited, Amersham Place, Little Chalfont, Buckinghamshire, HP7 9NA, UK
GE Healthcare Europe, GmbH, Munzinger Strasse 5, D-79111 Freiburg, Germany
GE Healthcare Bio-Sciences Corp., 800 Centennial Avenue, P.O. Box 1327, Piscataway, NJ 08855-1327, USA
GE Healthcare Japan Corporation, Sanken Bldg., 3-25-1, Hyakunincho, Shinjuku-ku, Tokyo 169-0073, Japan

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