ÄKTA ready™ systems

SINGLE-USE CHROMATOGRAPHY SYSTEMS

The ÄKTA ready™ system family consists of a range of single-use liquid chromatography hardware options that are built for process scale-up and manufacturing (Fig 1). The systems operate with ready-to-use, disposable flow paths that are available in two sizes for each system option—high or low flow—providing a wide operating flow rate range. The disposable flow path removes the need for cleaning between products/batches, and no development and validation of cleaning procedures is required. When used together with ReadyToProcess™ columns, the risk for cross-contamination is minimized. Replacing flow paths between batches is fast and intuitive, enabling fast campaign changeover while minimizing the risk for operator errors.

This range includes the ÄKTA ready system (with isocratic or gradient capability), ÄKTA ready variable UV, and ÄKTA ready extended chromatography systems. Each option provides different levels of functionality and performance. The flow paths for all hardware options are made of biocompatible material that is well suited for use in a GMP-regulated environment and easily disposed of. ÄKTA ready chromatography systems are controlled by UNICORN™ software or DeltaV software, including a complete installation guide and documentation for installation of flow kits and columns.

We can also provide modified versions of the ÄKTA ready system with additional features upon request or with other control software.

Fig 1. ÄKTA ready extended chromatography system.

ÄKTA ready systems provide the following benefits:

- Improved process economy and productivity due to the fully disposable flow path and easy campaign changeover.
- Simplified equipment installation and validation takes less time to obtain production capacity.
- No need for system cleaning validation and minimized risk of cross-contamination between products/batches.
- Extensive product documentation to facilitate implementation in GMP environment.

After completion of a purification run, the columns and flow path (i.e., a flow kit and a gradient section) are disposed of, minimizing the risk of cross-contamination, which can speed processes up considerably due to fewer operations. The flow path can be changed quickly, with a downtime of less than 1 h for a changeover, saving time in manufacturing and allowing better utilization of capital investment while lowering start-up cost and utility consumption.

Each system comprises an ÄKTA ready chromatography unit, UNICORN or DeltaV control software, and a disposable ÄKTA ready flow path including sensors and detection flow cells. Comprehensive hardware and flow path documentation are provided. Users can execute installation and operation qualification (IQ/OQ) protocols or can have these done by a certified Cytiva specialist. An optional component test checks that the kit has been correctly installed and that sensors are functional prior to start operating the system.

System capacity

ÄKTA ready low and high flow kits are available for all system versions and allow a wide range of flow rates—from 3 L/h 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 (~ 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, ~10 L column volume and higher), allows flow rates of up to 510 L/h.

ÄKTA ready system configurations

ÄKTA ready single-use chromatography systems are available in four standard configurations (Table 1):

- **ÄKTA ready system (isocratic and gradient capability)** provides essential functionality in chromatography operations with isocratic or gradient capability (Fig 2).
- **The ÄKTA ready variable UV system** includes gradient capability, three variable UV wavelengths, and an integrated pH electrode in the flow kit.
- **The ÄKTA ready extended system** provides additional functionalities compared to ÄKTA ready variable UV system.

Other configurations of the system are also available upon request.

Table 1. High-level comparison of functionality across ÄKTA ready systems

	ÄKTA ready		ÄKTA ready variable UV	ÄKTA ready extended
	Isocratic	Gradient		
Essential functionality	•	•	•	•
Gradient capability		One inlet	One inlet	Six inlets
Three variable UV wavelengths			•	•
Integrated pH electrode in flow kit			•	•
Pre-column conductivity and air sensors				•
Automated air trap				•
Up/down flow on column				•
Integrated HMI*				•

*Human-machine interface

ÄKTA ready system (isocratic and gradient configurations)

The isocratic and gradient versions of the ÄKTA ready system have the functionality and sensor capability needed for most common chromatography operations. Isocratic systems can also be upgraded to gradient capability. The systems have a visual installation aid integrated into the software. Typical applications include mAbs and recombinant protein purification.

Fig 2. ÄKTA ready gradient system.

The configuration of the ÄKTA ready system (isocratic and gradient) is shown in Figure 3. Six inlets are available for the isocratic pump and one for the gradient pump. The pumps deliver fluid to the column via a pressure sensor (P) and the air trap. There are two sets of valves between the pump and the column: the air trap valves allow bypassing of the air trap, and the column valves allow bypassing of the column. The air trap has a manual air vent valve. After the column, the fluid passes through a second pressure sensor (P), where an electrode (pH) can be inserted (optional). Thereafter, the fluid continues through a flow meter (F), which includes an infrared (IR) temperature sensor (T), a conductivity cell (C), and a UV cell (UV). The last sensor in the path shown in Figure 3 is a third pressure sensor (P). After the sensors, the fluid continues via the outlet tubing to the outlet manifold, where valves divert the fluid to either waste or fraction collection.

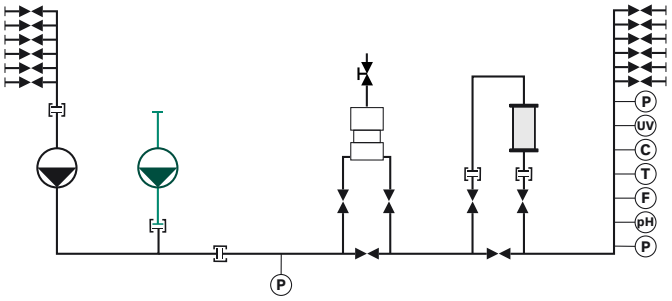

Fig 3. Flow chart for ÄKTA ready (isocratic and gradient configurations) and ÄKTA ready variable UV systems. Note that the green pump is not included in the isocratic system configuration.

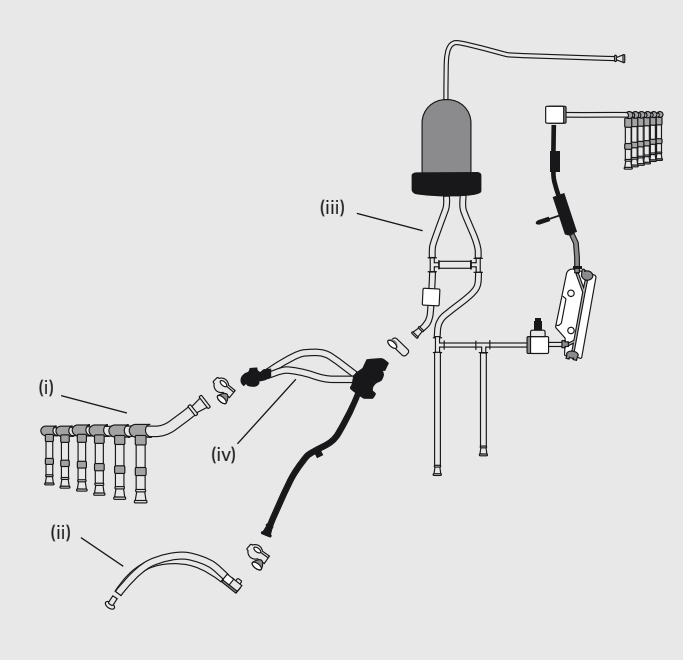

Fig 4. Flow kit with gradient section for ÄKTA ready system, showing inlet (i), pump tubing (ii), main section (iii), and gradient section (iv).

Each flow kit consists of three separate parts: the inlet manifold (i), the pump tubing (ii), and the main section (iii). These are assembled when the flow kit is connected to the system. A gradient section (iv), together with a flow kit, is required to run gradient elution. It should be inserted in the main pump position (Fig 4). Step-by-step installation guidance and documentation are provided by the UNICORN installation wizard.

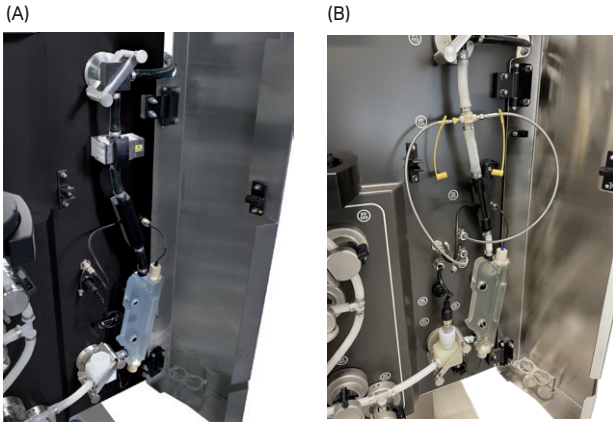

Fig 5. (A) Post-column sensors on ÄKTA ready chromatography system (isocratic and gradient configurations) displaying pressure, flow and temperature, conductivity, UV, and final pressure flow cell. (B) Post-column sensors on ÄKTA ready variable UV system displaying the two different sensor units: integrated pH electrode and three-wavelength UV cell.

ÄKTA ready variable UV system

Compared to ÄKTA ready system (isocratic and gradient), the ÄKTA ready variable UV chromatography system incorporates two different types of sensors in the system: a three-wavelength variable UV sensor and an integrated single-use pH electrode in the flow path (Fig 5B). The UV sensor can measure any three wavelengths in the range of 206–700 nm simultaneously during processing. The software can also calculate UV absorbance ratios during processing—for instance, the absorbance ratio of 260 nm and 280 nm can be useful when separating empty from full adeno-associated virus (AAV) capsids. To enable closed processing, the pH electrode is integrated into the flow kit. Flow kits with aseptic connectors must be used in this scenario. The pH sensor is pre-calibrated and the calibration constants are easily entered into the software at installation.

The flow kit functionality, including combination with gradient section, is the same as for the ÄKTA ready system (isocratic and gradient) described above and shown in Figure 3. However, the UV and pH sensor cells in the flow kit have a different design (Fig 5B).

ÄKTA ready extended system

Compared to the ÄKTA ready system (isocratic and gradient) and ÄKTA ready variable UV system, the ÄKTA ready extended system is designed with extra features to provide more flexibility in processing. Like the ÄKTA ready variable UV system, the extended system has a three-wavelength UV sensor and single-use pH electrode. In addition, the system has an integrated HMI and PROFIBUS connectivity to Xcellerex™ XDUO single-use mixing systems. This enables monitoring of sensors and control of the agitation on up to five Xcellerex XDUO mixers.

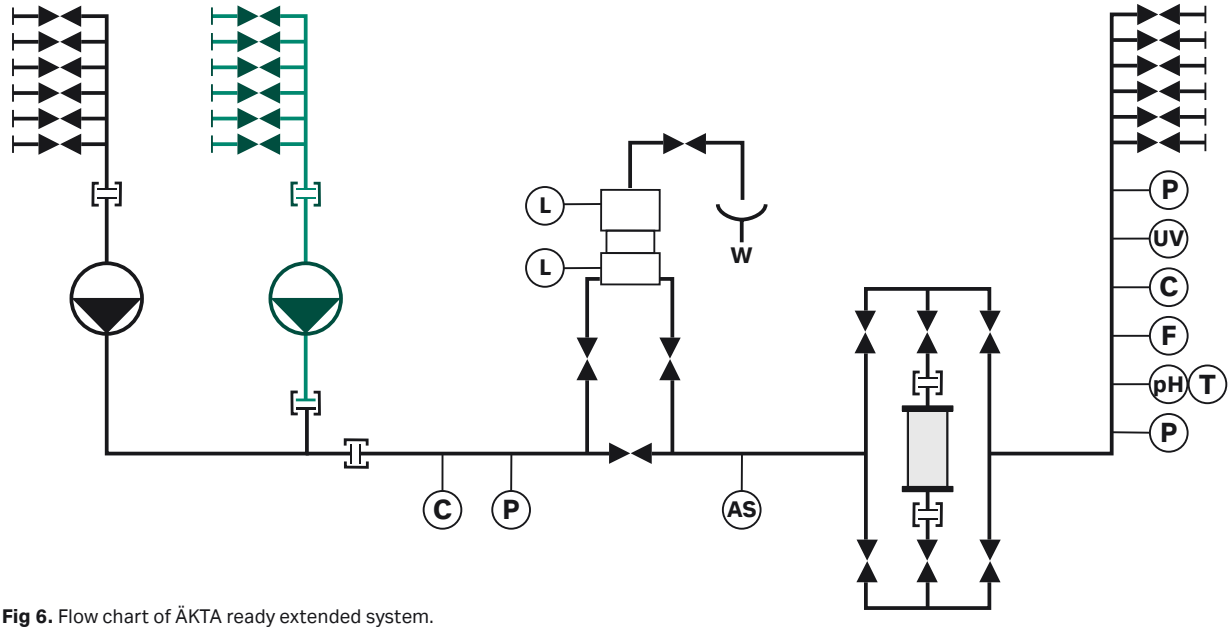

Fig 6. Flow chart of ÄKTA ready extended system.

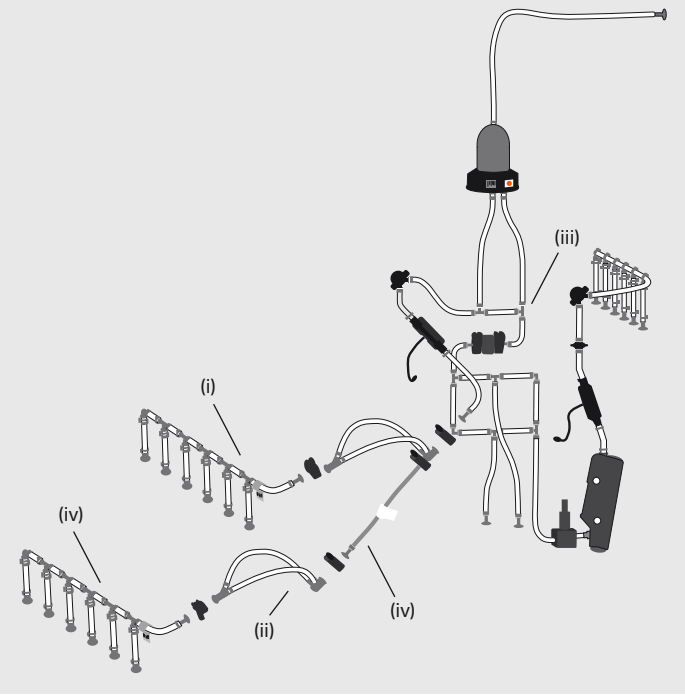

Fig 7. Flow kit with gradient section for ÄKTA ready extended system, showing inlet (i), pump tubing (ii), main section (iii), and gradient section with six additional inlets (iv).

The configuration of the ÄKTA ready extended system is shown in Figure 6. There are six inlets on the isocratic pump and six additional inlets on the gradient pumps. There is a conductivity sensor (C) directly located after the pumps that is used to monitor pre-column conductivity and can also be used for gradient control. A pressure sensor (P) is located after the conductivity sensor for safety and to measure the delta pressure over the chromatography column. The air trap is fully automated with two level sensors located on the chromatography unit. These control the fill and stop fill function of the air trap. A pre-column in-line air sensor (AS) can be activated to prevent introduction of air into the column. The column valve assembly can run up or down flow, or it can be bypassed. Post-column sensors include a pressure sensor (P) with integrated pH electrode (pH) with integrated temperature sensor (T), followed by a flow meter (F) and conductivity (C) and ultraviolet (UV) sensors. A pressure sensor (P) is located before the six outlets to protect the operation from tubing blockage. The optional gradient section can be combined with the flow kit (Fig 7). The gradient runs can be controlled based on conductivity feedback or by mass flow.

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 8 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 maintained again at constant flow rate of 50 L/h (C).

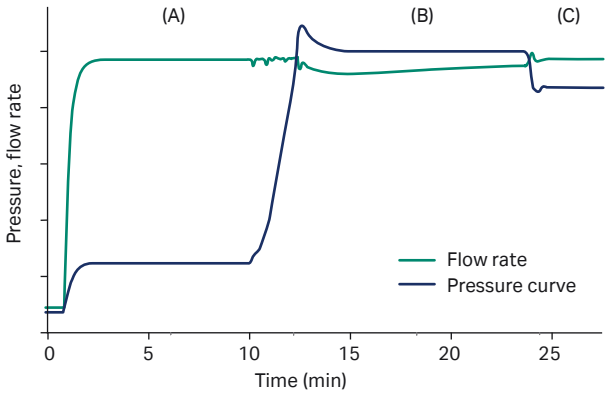

Fig 8. Control features of ÄKTA ready system flow rate (green curve) and pressure (blue curve). The figure shows the initial flow rate control (A); regulated flow rate to achieve constant pressure (B); and return to flow rate control (C).

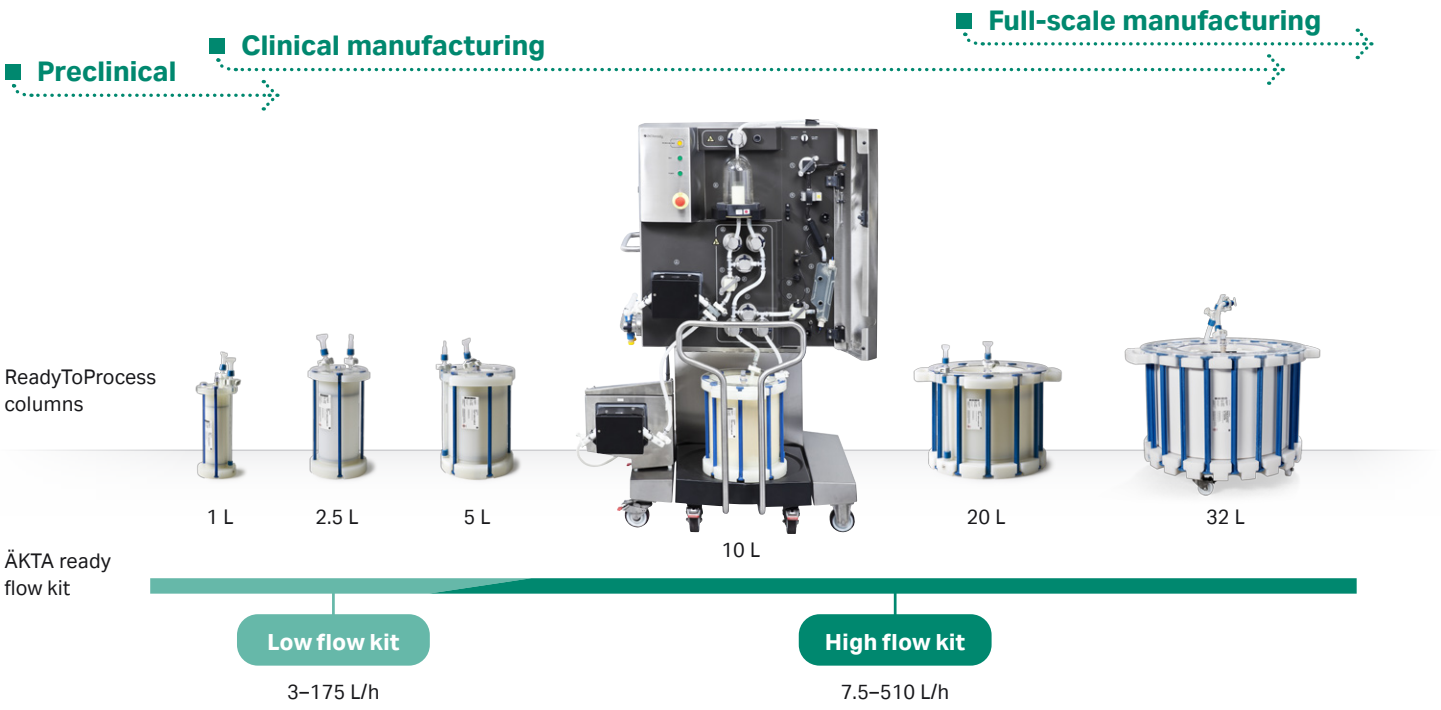

Fig 9. Consistency in column geometry allows for convenient scaling of ReadyToProcess columns, from 1 L to 32 L columns with 20 cm bed height.

Flow kits

ÄKTA ready flow kits are resistant to common chemical agents used in protein recovery, including buffer solutions for adsorption, elution, and washing, as well as regeneration and cleaning solutions.

All materials are 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. All the materials are listed under Specifications. Flow kits are available with a choice of aseptic connectors. See the ordering table for more details.

All flow kits are produced under controlled conditions and packed in a clean room environment (class ISO 7) using validated protocols. The pump tubing elements (in flow kits and gradient sections) are autoclaved. The other flow kit parts are gamma irradiated. To protect against contamination, and for easy transfer into the clean room, flow kits are delivered in double plastic bags.

Product documentation and services

Regulatory authorities expect manufacturers of pharmaceuticals to qualify equipment before use in production. Rigorous documentation is an integral part of the ÄKTA ready concept, including the single-use flow kit. Both the ÄKTA ready hardware and flow kits are supported with an extensive documentation package.

- Product documentation provides information about the materials used in wetted parts. Specific product documentation is available for flow kits. Extensive system documentation, such as drawings and schematics, is delivered with the ÄKTA ready system.
- Validation guide includes a description of the flow kit manufacturing process, qualification tests, wetted materials, and extractable information.
- Release documentation is delivered with a functional test protocol. Flow kits are also delivered with a certificate of quality, including product release criteria.
- The system can be delivered with installation and operational qualification (IQ/OQ) documentation and the qualification can be performed by certified Cytiva specialists.

Comprehensive control with UNICORN software

The ÄKTA ready system (isocratic or gradient) includes an installation wizard with instructions for correct and easy attachment. You can use UNICORN software's installation wizard to set up the flow kit and check functionality control of the flow paths before starting a batch run. A report is generated with completed installation procedures, including instructions from the installation guide, traceability to flow path, process information, and results from the component test. The installation guide also contains instructions and reports for column installation.

External, independent audits have shown that the UNICORN software development process provides 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.

The UNICORN software communicates via OLE for Process Control (OPC), allowing for real-time and historical data access as well as third-party software control. The ÄKTA ready extended chromatography system can also be connected to Xcellerex XDUO mixers where process data can monitored and agitation controlled. The ÄKTA ready system can be delivered with other software, such as DeltaV software, on request.

ReadyToProcess columns

ReadyToProcess columns are available with a range of BioProcess™ chromatography resins in several different diameters. 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 operation, the columns can also be used for preclinical studies and full-scale manufacturing (Fig 9). The columns can be used in chromatographic applications for separation of proteins, endotoxins, DNA, plasmids, and viruses.

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

Reproducible results with scalability

ÄKTA ready chromatography systems are designed for process scale-up and small- scale production. Methods can be developed at laboratory scale and then scaled up to the ÄKTA ready system. In addition, the process developed for ÄKTA ready systems can be transferred to the ÄKTA process™ system for production with conventional clean and reused technology if desired. Most ÄKTA™ systems use the same UNICORN control software, so methods can be scaled quickly and easily.

Scale-up studies

A study was performed to verify that similar results from protein separation experiments can be obtained 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. We used HiScale™ 16/40 columns packed with Capto™ S ion-exchange resin (20 cm bed height) and three sizes of ReadyToProcess prepacked columns: 5 L Capto S resin (178/200), 32 L Capto S resin (450/200), and 57 L Capto S resin (600/200) (Fig 10).

The results shown in Figure 10 indicate that scale-up from HiScale 16/40 to ReadyToProcess columns was possible and that the results were similar regardless of the chromatography system used.

A study was conducted to compare gradient elution performance on ÄKTA ready gradient system and an ÄKTAprocess™ (now replaced by ÄKTA process CFG system) chromatography system. BSA and lactoferrin were separated through gradient elution on 2.5 L and a 10 L ReadyToProcess columns. Figure 11 indicates comparable results for ÄKTAprocess (A) and ÄKTA ready gradient (B) systems.

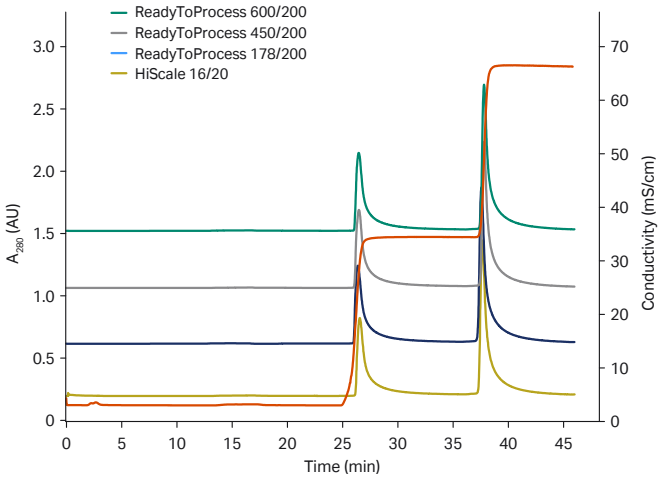

Fig 10. Stacked chromatogram from ÄKTA pure™, ÄKTA ready, and ÄKTA ready XL systems comparing step elution on four different columns (the HiScale 16/40 column was packed with Capto S chromatography resin was run on an ÄKTA pure system). The elution buffers were 50 mM sodium acetate, 0.3 M NaCl, pH 5.0 and 50 mM sodium acetate, 0.65 M NaCl, pH 5.0. The elution steps were 3 column volumes (CV) each. The height of the UV-curves has been normalized based on the height of the first peak.

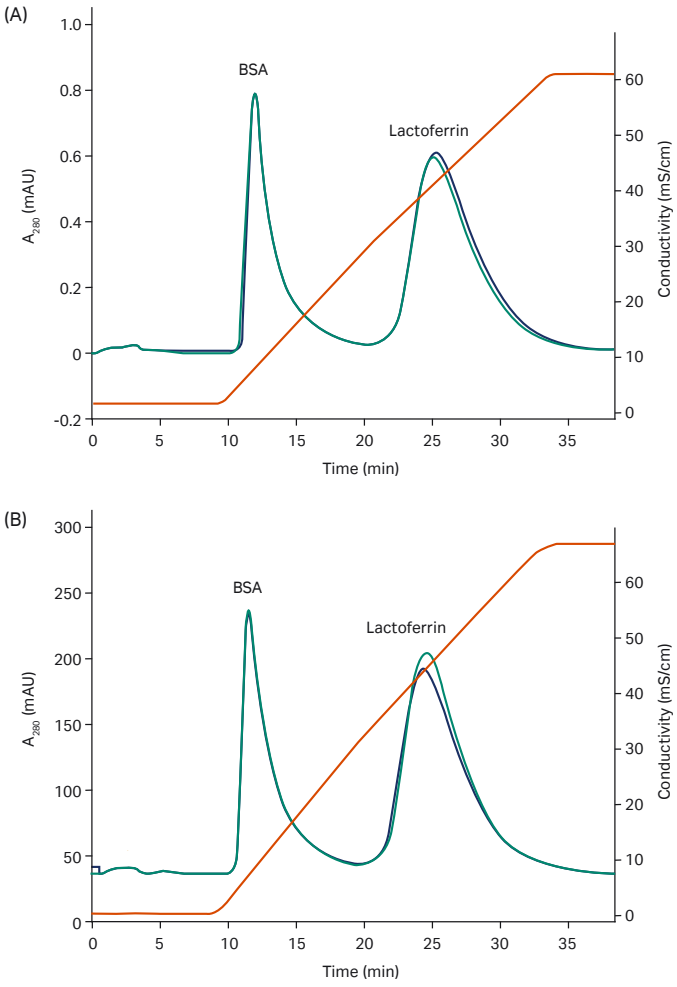

Fig 11. Chromatogram from ÄKTAprocess (now replaced by ÄKTA process CFG system) (A) and ÄKTA ready gradient (B) systems comparing gradient elution on 2.5 L and 10 L Capto S resin ReadyToProcess columns. The equilibration buffer was 50 mM sodium acetate, pH 5.0 and the elution buffer was 50 mM sodium acetate, 0.65 M NaCl, pH 5.0. The elution was performed over 10 CV followed by 100% elution buffer for 3 CV. The gradient is based on gradually changing the pump speed over time, which creates a volumetric gradient with ± 2% linearity. When conductivity is measured, linearity is ± 4% due to the non-linear relationship to the salt concentration.

Specifications

General specifications

	ÄKTA ready (isocratic and gradient)	ÄKTA ready variable UV	ÄKTA ready extended
General specifications W × H × D	1000 × 1650 × 800 mm (isocratic) 1160 × 1650 × 800 mm (gradient)	1140 × 1670 × 840 mm	1060 × 1760 × 1000 mm
Weight (kg)	230 (isocratic) 250 (gradient)	258	360
Ingress protection	IP45, pump head IP25		IP55, pump head IP25
Compressed air interface	5.5–10 bar, 50 NL/min, oil- and particle-free		

Sensor specifications

Flow rate accuracy†	**High flow kit:** ± 5% actual value at flow‡ ≥ 40 L/h ± 10% actual value at flow < 40 L/h **Low flow kit:** ± 5% actual value at flow‡ ≥ 20 L/h ± 10% actual value at flow < 20 L/h
Pressure sensor:	
Range	0–5 barg
Accuracy	± 0.20 barg
Conductivity sensor:§	
Range	0–150 mS/cm
Accuracy	± 5% full scale¶

	ÄKTA ready (isocratic and gradient)	ÄKTA ready variable UV	ÄKTA ready extended
Temperature sensor:			
Range	2°C to 40°C	2°C to 40°C	2°C to 30°C
Accuracy	± 3°C	± 3°C	± 2°C
UV sensor:		3-wavelengths	3-wavelengths
Range	0.01–1.0 AU	0–2 AU	0–2 AU
AU linearity	± 5%	± 2%††	± 2%††
pH sensor:			
Range	pH 2–12	3–10	3–10
Accuracy	± 0.2 pH at calibration temperature**	± 0.3	± 0.3

† Flow meter cells for high flow and low flow kits are designed with different flow path geometries
‡ 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
§ Temperature compensation optional
¶ Valid at actual temperature (no temperature compensation)
** Temperature compensation not available
†† Valid for 250–700 nm, 2% linearity 0–1 AU for 206–250 nm

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:	
Low flow kit	3–175 L/h
High flow kit	7.5–510 L/h
Pump speed:	
Low flow kit	225 rpm (100%)
High flow kit	340 rpm (100%)
Max. pressure,peristaltic pump	4.0 bar
System pressure rating:	
High-pressure flow path, upstream column	5.0 bar
High-pressure flow path, downstream column	2.0 bar
Low-pressure outlet manifold	0.95 bar
Low-pressure inlet manifold	0.6 bar
Flow gradient	10%–90% gradient buffer with ± 4% linearity, up to 3 bar
Conductivity gradient (ÄKTA ready extended system)	10%–90% gradient buffer with ±2% linearity, up to 3 bars
Gradient flow range:	
Low flow kit	20–175 L/h
High flow kit	40–510 L/h

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) (ALL), PEEK (ALL), Polycarbonate (PC) (AseptiQuik), Silicone (AseptiQuik & Presto), Polyethersulphone (PES) (Presto)
Pressure cell	PP, Ethylene propylene diene monomer (EPDM)
Flow meter body	Polymethylpentene (TPX)
Air sensor (ÄKTA ready extended system)	PP
Air trap	Polyamide (PA), transparent; PP
pH electrode:	
Isocratic and gradient systems	Polyoxymethylene (POM), ceramics (junction), glass
Variable UV and extended systems	Polysulfone (PSU), high density polyethylene (HDPE), glass, Loctite M121HP, porous zirconia, Polyvinylpyrrolidone (PVP)
pH electrode housing	PSU
pH electrode dummy	PP
Conductivity cell	PP, titanium
UV cell:	
Isocratic and gradient systems	PP
Variable UV and extended systems	PEEK, quartz, titanium
Sealing materials	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

Ordering information

ÄKTA ready systems (with isocratic and gradient capability)

Chromatography system	Product code
ÄKTA ready isocratic system (including trolley)	28906261
ÄKTA ready gradient system (including trolley)	29032038
ÄKTA ready system with gradient upgrade	29032784

Flow kits	Sanitary clamp	Kleenpak™ Presto sterile connectors	AseptiQuik
Low flow kit	28930182	30033878	29417228
High flow kit	28930183	30033882	29388250
Gradient low flow section[1]	29021085	30033885	29398155
Gradient high flow section[2]	29021086	30033884	29417678

Flow kits with other connectors can be made available upon request.

[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.

IQ/OQ qualification	Product code
IQ/OQ performance	29748404
IQ/OQ protocol	29748350
IQ/OQ binder	28933443
Commissioning and qualification performance 4 days	28992657

ÄKTA ready variable UV system

Chromatography system	Product code
ÄKTA ready variable UV (including trolley)	On request

Flow kits	Sanitary clamp	Kleenpak Presto sterile connectors	AseptiQuik
Low flow kit	29511188	30033889	29424571
High flow kit	29511193	30033887	29645508
Gradient low flow section[1]	29021085	30033885	29398155
Gradient high flow section[2]	29021086	30033884	29417678

Flow kits with other connectors can be made available upon request.

[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.

IQ/OQ qualification	Product code
IQ/OQ document type B	29310217
IQ/OQ performance type B	28992658

ÄKTA ready extended system

Chromatography system	Product code
ÄKTA ready extended system CE	30012249
ÄKTA ready extended system ETL	30012250

Flow kits	Sanitary clamp	Kleenpak Presto sterile connectors	AseptiQuik
Low flow kit	29487803	30033890	29660555
High flow kit	29477427	30033891	29660540
Gradient low flow section[1]	29490879	30033892	29709714
Gradient high flow section[2]	29184612	30033894	29699095

Flow kits with other connectors can be made available upon request.

[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.

IQ/OQ qualification	Product code
IQ/OQ document type B	29310217
IQ/OQ performance type B	28992658

ÄKTA ready system accessories

Description	Product code
Low flow test kit (excludes ÄKTA ready extended system)	28933680
High flow test kit (excluded ÄKTA ready extended system)	29006727
UV conductivity test tools	28933688
Pressure calibration tool	28932942
Temperature kit	28938864
Industrial UV-Cell PEEK (for ÄKTA ready variable UV and extended systems)	28959578
RTP column trolley	28937588
Air sensor (external clamp-on)	29003879
Air sensor with sanitary clamp connection (inline for ÄKTA ready extended system)	29744338
Air sensor with AseptiQuik connection (inline for ÄKTA ready extended system)	29751526

Related literature

Description	Document code
ReadyToProcess columns product list	CY1797
ReadyToProcess columns data file	CY11724
Extractables studies for single-use systems used in antibody-drug conjugate manufacturing	CY13922
Scale-up and process economy calculations of a dAb purification process using ready-to-use products	CY13817
ÄKTA ready system site preparation guide	29135897

cytiva

cytiva.com/AKTAready

For local office contact information, visit cytiva.com/contact

CY10671-18Jun26-DF

danaher