

# ÄKTA readyflux

## SINGLE-USE FILTRATION SYSTEM

ÄKTA readyflux is an automated single-use filtration system for pilot- and small-scale manufacturing (Fig 1). The system is intended for crossflow (also called tangential flow) filtration applications in both upstream and downstream workflows.

### Bring confidence to filtration with ÄKTA readyflux

- Easy method preparation and flexible automation methods require no programming expertise and free up time for other activities.
- Quick installation of single-use flow path (incl. sensors) reliably guided using installation wizard.
- Innovative and compact design with low minimum recirculation volume for high concentration factors and product recovery.
- Flexible use of both filter cassettes and hollow fiber filter cartridges for microfiltration and ultrafiltration operations.
- ReadyMate™ Flow Kit, together with ReadyToProcess™ hollow fiber cartridges, enables closed system operations.

ÄKTA readyflux provides excellent filtration capabilities in a compact design. The system features a single-use flow path that minimizes cross-contamination risk, reduces the need for cleaning, and shortens the batch change-over time. The system features verified methods and extensive monitor and control capacities. Using the phase editor of the UNICORN™ system control software, automation methods are easily created to fit your application. The system offers flexibility by allowing the use of both filter cassettes and hollow fiber filter cartridges and a wide range of disposable bags. Additional equipment can be connected, using the external I/O interface, and be incorporated in the ÄKTA readyflux automation methods.

ÄKTA readyflux is suitable for use in a cGMP environment, and the system can be connected to other single-use equipment. In upstream applications, for example, ÄKTA readyflux can be connected to Xcellerex™ XDR stirred-tank bioreactor systems or rocking WAVE Bioreactor™ systems for use in clarification of cell culture feed. Used together with the ÄKTA ready chromatography



Fig 1. ÄKTA readyflux single-use filtration system.

system in a connected process, ÄKTA readyflux can be used for concentration and buffer exchange in downstream applications. Xcellerex XDUO mixer system or ReadyCircuit 2-D Hanging Pillow Bags can be used as a recirculation reservoir when working with ÄKTA readyflux.

## System overview

ÄKTA readyflux puts the application in focus. The system is floor-standing and can easily be rolled in and out of the production facility. The system can be used with both filter cassettes and hollow fiber filter cartridges. The UNICORN software provides intuitive and flexible method creation, system control, and process evaluation to simplify your filtration tasks. Colors used in the process picture of the software to identify the different sections of the flow path are also shown on the system to facilitate installation of the flow path.

## Flow Kit

The Flow Kits include single-use pump head and tubing, as well as sensors for pressure, conductivity, temperature, flow, UV, and pH (depending on choice of Flow Kit, see Ordering information). The Flow Kit is available with Tri-Clamp™ connectors or with ReadyMate connectors for aseptic connection. The Flow Kit is supplied gamma irradiated. Flow Kit with ReadyMate connectors are supplied with a sterile claim.

The flow path is delivered in separate sections for feed, retentate, and permeate (Fig 2). The Flow Kit can be installed using the installation wizard of the UNICORN software. Installation can be performed in less than 15 min. A barcode scanner can be used to identify the installed flow path, and the instructions of the wizard ensure correct and easy installation of the Flow Kit. A report is generated upon completed installation. An installation test can be performed to ensure proper functionality of sensors.

The flow path has been designed to enable low minimum working volumes for high concentration factors and is sloped to ensure maximized product recovery.

## Transfer line

The transfer line has three inlets: one for buffers, one for product, and one for air. A peristaltic pump is used to transfer buffer to the recirculation line. The pump can also be used for automated fed-batch operation and diafiltration. An air sensor allows for complete loading of sample and prevents air from entering the system. An air filter is included in the transfer line and is used to filter air during sample recovery by air blow down.

## Recirculation line

The recirculation line has three inlets to be used for liquids for flushing, filter cleaning, and storage of the filter. The ÄKTA readyflux recirculation pump is of diaphragm type for low shear, and the single-use pump head is integrated in the flow path. Pressure sensors are located in the feed line and in the retentate line along with sensors for conductivity and temperature. Product can be recovered through the low-point port. The retentate pressure control valve is used to control

transmembrane pressure (TMP) during ultrafiltration. For in-line integrity testing, omitting the need to dismantle and reassemble the filter in the filter holder, the system provides a port for connection of an integrity test instrument.

## Permeate line

Permeate line includes sensors for pressure, conductivity, temperature, flow, UV, and pH (depending on choice of Flow Kit, see Ordering information) to control and monitor the filtration run. A peristaltic pump can be used for permeate flow control during microfiltration operation.

## Reservoirs

A wide range of disposable reservoirs can be fitted to the ÄKTA readyflux system. 2D bags with volumes up to 20 L and 3D bags with volumes ranging from 50 to 1000 L can be used with the system. Bagkart can be used for 2D bags (Fig 3), and 3D bags are used with XDUO mixer system with integrated load cells. When 3D bags are used with XDUO Mixing System, in-bag pH measurement, mixing, and temperature can be monitored by the UNICORN software. 2D and 3D bags can also be used with user-supplied load cell of choice. The load cell is connected to the UNICORN software that displays bag weight for Cytiva's 2D and 3D bags or customer reservoir of choice.



Fig 3. ÄKTA readyflux system with Bagkart (left) and Fluxkart (right).

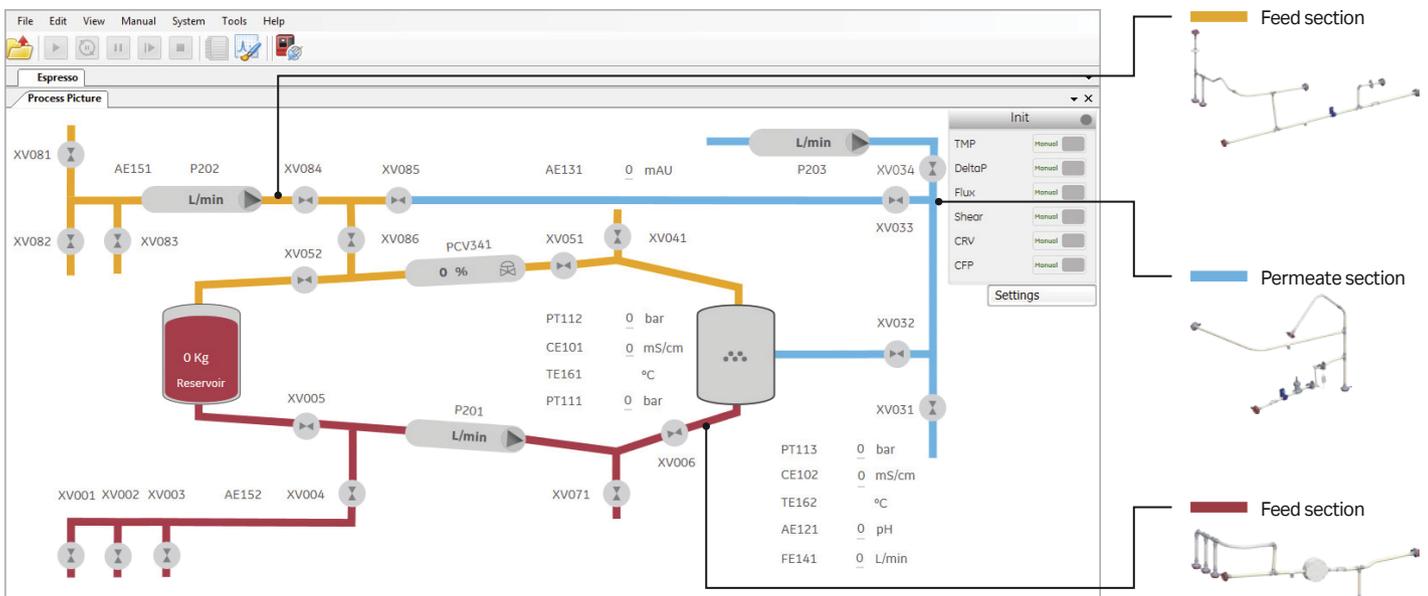


Fig 2. In the process picture of the UNICORN software, the flow path sections are displayed with different colors to facilitate Flow Kit installation.

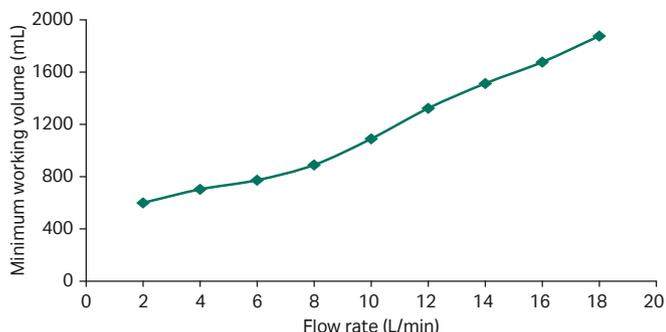
## Designed for low minimum recirculation volume

### Hold-up volume

System hold-up volume refers to the volume of liquid in the filtration system and is independent of the filter used. To obtain the total hold-up volume, the filter hold-up volume needs to be added to the hold-up volume of the Flow Kit. System and filter should be selected for the lowest hold-up volume compatible with other performance requirements of the process. ÄKTA readyflux has a system hold-up volume of < 400 mL, of which typically about 30 mL or less is non-recoverable liquid.

### Minimum working volume

The system's minimum working volume represents the minimum fluid volume in the recirculation line required to operate the system at the desired crossflow rate without drawing air into the feed line. The minimum working volume is determined by the design of the system (reservoir, feed and retentate tubing), the filter hold-up volume, and the crossflow rate. When designing a filtration process, minimum working volume needs to be considered to ensure that the target recirculation volume is not less than the system's minimum working volume. For ÄKTA readyflux, the minimum working volume at different feed flow rates for a BSA solution of 5 g/L is displayed in Figure 4.



**Fig 4.** Minimum working volume (recirculation line excl. filter) at different feed flow rates with ÄKTA readyflux. Here, a BSA solution of 5 g/L was used.

## Comprehensive control with UNICORN software

UNICORN system control software is based on an integrated controller and an intuitive user interface. To facilitate handling, the interface uses the familiar Windows® environment. The run sequence is determined by the end-user for control of a specific process. A graphical interface helps you create the process sequence. Conventional line programming can be performed by advanced users. The UNICORN software contains the tools needed to perform almost any type of crossflow filtration process at different scales, from setting up and running a method to evaluating the data.

The software includes four modules:

**Method Editor:** provides an easy interface to create or modify methods.

**System Control:** allows performing and monitoring the run in real time.

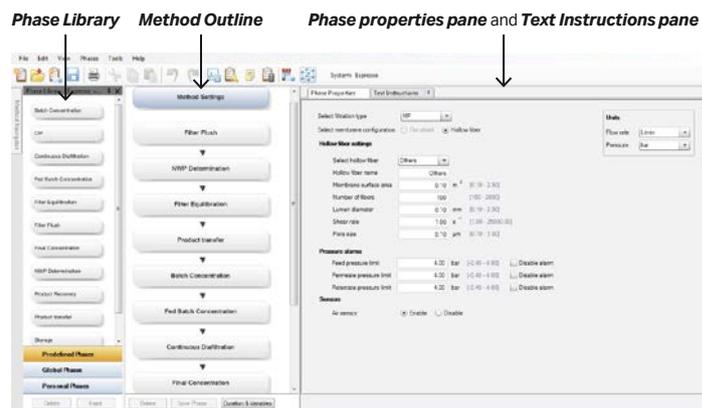
**Evaluation:** supports data analysis and report generation.

**Administration:** used to set up user access, view logs, and manage the built-in SQL Server® database tools.

External user audits have shown that the UNICORN development process offers good adherence to the framework, principles, and practices described in GAMP™ 5 and that the functionality of the product is acceptable for use in a cGMP regulated environment in a manner that complies with 21 CFR Part 11. The UNICORN software uses a standard for open platform communication (OPC), allowing for real-time and historical data access as well as third-party software control. A Profibus™ node is available for connection to external programmable logic controller (PLC)/distributed control system (DCS).

### Method creation

The **Method Editor** provides a range of predefined methods for ultrafiltration and microfiltration applications as well as for filter cleaning and storage and allows you to create or adjust methods to suit your application needs (Fig 5). The module features built-in application support and contains all instructions needed to control a run. The interface provides easy viewing and editing of the run parameters.



**Fig 5.** Automated methods can quickly and easily be created by dragging and dropping phases in the **Method Editor** of the UNICORN software.

The UNICORN software includes a library of predefined phases for creating or editing your own methods. Each phase reflects a step in the process, such as filter equilibration, product transfer, batch concentration, or continuous diafiltration. A method is created or edited by dragging-and-dropping phases from the **Phase Library** to the **Method Outline** and by entering process parameters in the **Phase Properties** pane. A wide range of control options and monitors are available to ensure that the process is run according to set specifications and that the batch is completed on time.

Parameters for hollow fiber filter cartridges from Cytiva are predefined in the software. By selecting the cartridge in the **Phase Properties** pane, filter parameters (e.g., filter area and lumen diameter) are automatically programmed into the method. For other types of filters, such as filter cassettes, filter parameters are filled in by the user.

For added flexibility, advanced users can edit programming instructions directly in the **Text Instructions** pane.

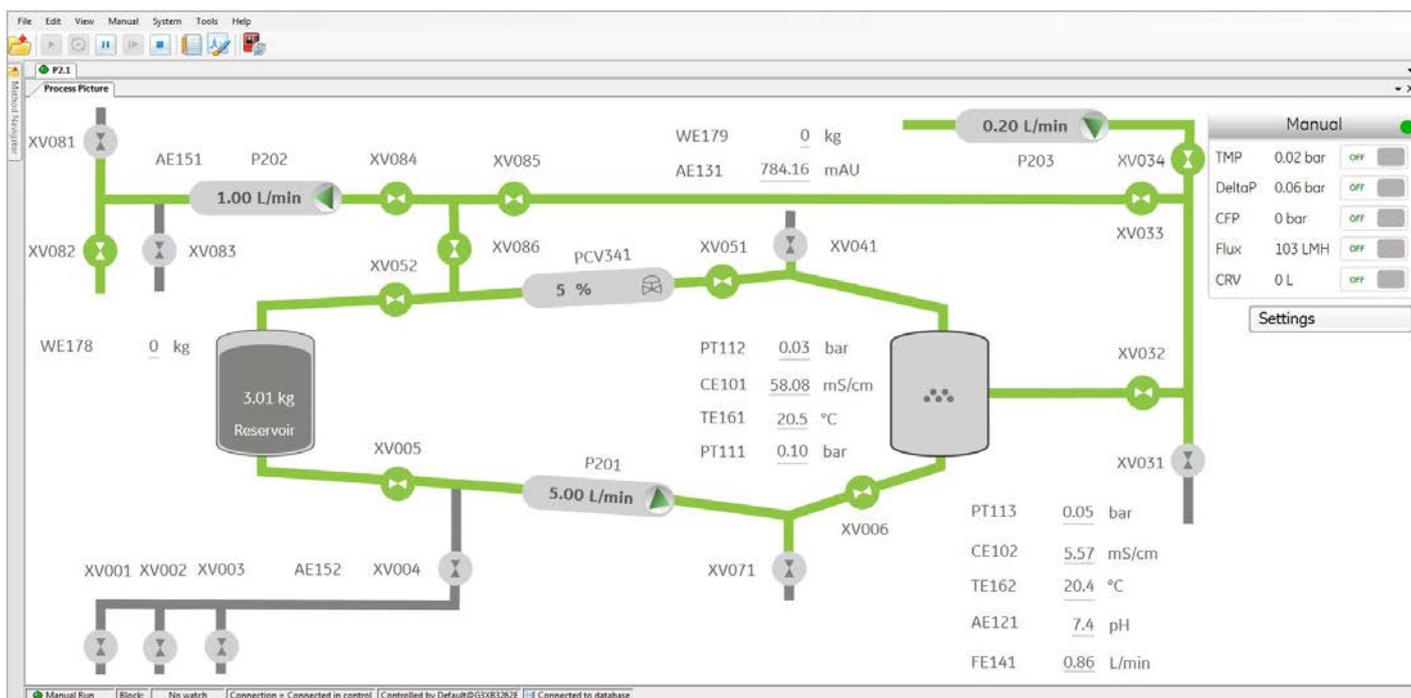


Fig 6. Process picture in the UNICORN software.

## System control

The **System Control** module is used to start, monitor, edit, and control a run in real time. Features of the **System Control** module include:

- Full control during manual or programmed runs. Parameters can be changed at any time and are included in the run log.
- Real-time flow scheme showing the current flow path, valve positions, and monitor values (Fig 6).
- Allowing control of up to three instruments, with an individual layout for each system.
- **Method Queue** function to enable unattended operation of multiple methods in queues.

ÄKTA readyflux features the following control parameters:

- Automated feedback control of the filtration process (e.g., TMP, delta pressure, flux, constant retentate volume).
- Filtration-specific end point monitoring during different run modes (e.g., concentration factor, permeate flux, retentate volume, conductivity).
- Automated maintenance alerts based on component-defined run hour limits.

## Evaluation

With UNICORN 7, the **Evaluation** module provides a simplified user interface optimized for most commonly used workflows such as quick evaluation and comparison of results (Fig 7). The **Evaluation** module features:

- Simplified interface, including single-click operations with instant feedback for operations.
- Preview of results for quick evaluation of data.
- Comparison of results in overlay and tile view.
- Sorting of results according to running parameters to see trends in data.

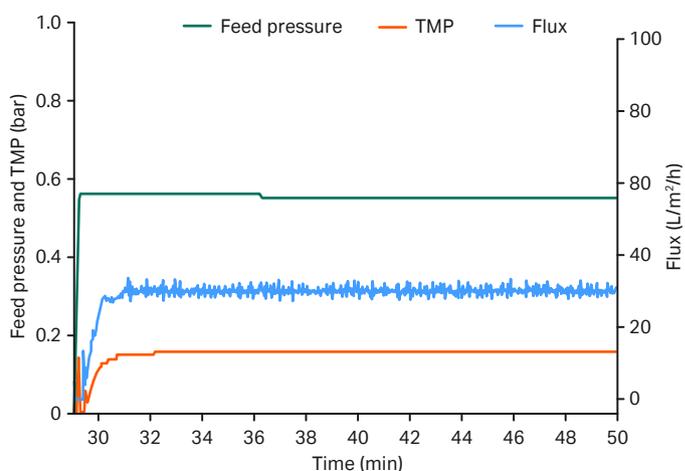
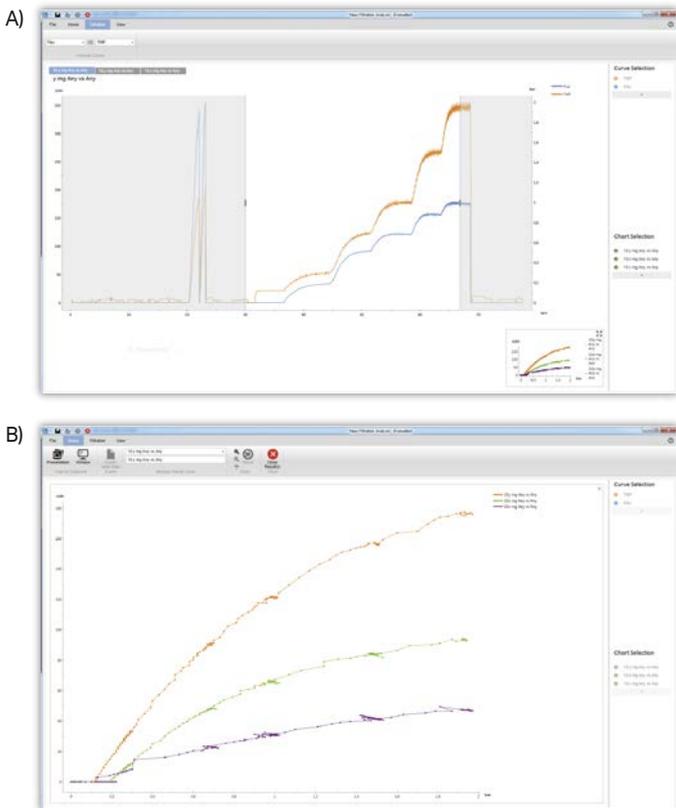


Fig 7. Example of user-selected curves. Run data are captured in real time and easily evaluated using the Evaluation module post a run.

ÄKTA readyflux supports a number of crossflow evaluation algorithms for analysis of generated results:

- **Process optimization** is used to analyze process characterization experiments in which a series of set points are tested. The plot is used to visualize flux versus TMP (Fig 8).
- **Diafiltration time optimization** allows identifying the concentration factor for which the least time is required to complete the diafiltration.
- **Capacity plot** can be used to evaluate capacity of the filter.
- **Normalized water flux (NWF):** The membrane permeability can be tested using the NWF function. This test is performed to ensure that the filter cleaning process is still effective and to determine the lifetime of a filter. The test enables the user, not only to automatically calculate the NWF from a result file, but also to plot results from multiple cycles on a single plot.

- **Any vs any:** Any vs any is used to graphically display data from any two curves generated during concentration, buffer exchange, or cell culture clarification. The analysis provides the possibility to plot any process parameter captured as a curve from a filtration system.



**Fig 8.** Flux vs TMP curve. (A) Run data plotted in UNICORN result file. (B) Graph for flux vs TMP generated in Evaluation module.

## Regulatory

### Robust and hygienic design

All wetted polymer materials and/or pressure holding parts have been tested and classified according to USP <88> Class VI; Biological Reactivity Tests in vivo and are free from animal-derived components or in compliance with EMA 410/01, Rev.3. Used materials are traceable back to their production batches.

The flow path is produced and packed under controlled conditions in clean room environment (class ISO 7) using validated procedures. The ÄKTA readyflux Flow Kit is delivered in double plastic bags to protect against contamination. The Flow Kit is gamma irradiated (27.5 to 40 kGy). The Flow Kit with ReadyMate connectors has undergone sterile and bioburden testing.

### 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 readyflux concept, including the single-use Flow Kit. The Flow Kit for ÄKTA readyflux is supported with an extensive documentation package.

- **Product documentation:** provides information about the materials used in wetted parts. Product documentation is delivered with the ÄKTA readyflux Flow Kit. Extensive system documentation, such as drawings and schematics, is delivered with the ÄKTA readyflux.
- **Validation guide:** includes a description of the Flow Kit manufacturing process, qualification tests, and extractable information.
- **Release documentation:** ÄKTA readyflux is delivered with a functional test protocol. The Flow Kit is 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.

## Filters

ÄKTA readyflux can be used with both hollow fiber filter cartridges and filter cassettes. For closed system operations, ReadyToProcess hollow fiber filters are recommended. ReadyMate connectors allow aseptic connection of the filter to the system. Hollow fiber filter cartridges are connected to the system using an adjustable filter holder. Most commercially available filter cassettes can be used with the system. The Fluxkart can be used to fit cassette holders of choice.

## System specifications

System specifications are listed in Table 1.

**Table 1.** ÄKTA readyflux system specifications

<b>General specifications</b>	
Dimensions, main system (W × H × D)	1100 × 1520 × 880 mm
Weight, main system	280 kg
Dimensions, Bagkart (W × H × D)	910 × 1550 × 810 mm
Weight, Bagkart	87 kg
Dimensions, Fluxkart (W × H × D)	720 × 1000 × 450 mm
Weight, Fluxkart	40 kg
Software	UNICORN 7.1 or later version
Control system	100–240 V~
AC voltage frequency	50/60Hz
Max. power consumption	1 kVA
Ingress protection	IP45
Compressed air interface	5.5–7 bar, 50 NL/min, oil- and particle-free
Weight scale connector	Bagkart
Analog inputs	Recirculation weight, transfer weight and permeate weight
Profibus interface	Xcellerex XDM S UF and XDUO mixers

## Recommended operating condition

Ambient temperature	4°C to 32°C
Liquid temperature	4°C to 50°C
Liquid pressure	-0.4 to 4 bar
Fluid density	800 to 1200 kg/m <sup>3</sup>
Fluid viscosity	
Recirculation	5-fold of water viscosity
Permeate	1.3-fold of water viscosity

## Flow rates

Feed pump	0.2 to 18 L/min
Transfer pump	0.5 to 6 L/min
Permeate pump	0.05 to 1.6 L/min

## Flow Kit specifications

Tubing diameter (i.d.)	
Feed and retentate	12.7 mm (1/2 in)
Transfer, permeate and drain	9.5 mm (3/8 in)
Inlet manifold diameter (i.d.)	12.7 mm (1/2 in)
Pump tubing diameter (i.d.)	
Transfer	9.5 mm (3/8 in)
Permeate	6.4 mm (1/4 in)
Connectors, type / size	TC 25 or ReadyMate connectors
No. of fluid inlets / outlets	3-May
No. of air inlets	2

Sensor specifications	Range	Accuracy
Flow rate range, feed	0.2 to 18 L/min	± 0.2 L/min or ± 12% of reading, whichever is greater*
Flow rate range, permeate	0.05 to 1.6 L/min	± 0.05 L/min of reading after calibration
Flow rate range, transfer	0.5 to 6 L/min	± 0.4 L/min or ± 10% of reading, whichever is greater*
Pressure (feed, retentate, and permeate)	-0.4 to 4 bar g	± 0.1 bar for full scale or ± 5% of reading, whichever is greater
Flow, permeate	0.05 to 6 L/min	0.05 to 2 L/min shall be ± 0.05 L/min of reading 2 to 6 L/min shall be ± 0.1 L/min of reading
UV	0.01 to 1.0 AU	Deviation from linearity ± 5% <sup>†</sup>
Conductivity (retentate and permeate)	0.1 to 200 mS/cm	± 0.15 mS/cm for full scale or ± 7% of reading, whichever is greater <sup>‡</sup>
pH	3 to 10	± 0.3 of reading
Temperature (retentate and permeate)	4°C to 50°C	± 1.0°C when ambient and liquid temperature are same
Weight	0 to 25 kg	± 50 g or ± 0.1% of reading, whichever is greater

\* Calibration can improve accuracy for the usage range.

<sup>†</sup> Valid for 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.

<sup>‡</sup> Accuracy can be improved by configuring the output signal to usage range. Valid for max. temperature difference of 5°C between liquid and ambient temperature. Valid at actual temperature (no temperature compensation).

## Filter specification for ÄKTA readyflux

Hollow fiber filter cartridges	
Max. no. of cartridges	2
Cartridge size	5, 6, 8, or 9
Filter cassettes	
No. of cassette holders	1
Total filter area (depending on application parameters)	0.46 to 2.5 m <sup>2</sup> *

\* Filter area based on a feed flow of 6–8 L/min/m<sup>2</sup>

## Ordering information

Product	Description	Product code
ÄKTA readyflux	Main instrument	29151000
Bagkart	Bag trolley for 2-D bags with integrated load cell	29151500
Fluxkart	Filter trolley for usage with filter cassettes	29245919
Flow Kit RM, ÄKTAreadyflux	Flow path with ReadyMate connectors, pump head and tubing, and sensors for pressure (F, R P), conductivity and temperature (R), and flow (P)	29187381
Flow Kit TC, ÄKTA readyflux	Flow path with Tri-Clamp connectors, pump head and tubing, and sensors for pressure (F, R P), conductivity and temperature (R), and flow (P).	29187383
Flow Kit plus RM, ÄKTA readyflux	Flow path with ReadyMate connectors, pump head and tubing, and sensors for pressure (F, R P), conductivity and temperature (R, P), flow, UV, and pH (P)	29187382
Flow Kit plus TC, ÄKTA readyflux	Flow path with Tri-Clamp connectors, pump head and tubing, and sensors for pressure (F, R P), conductivity and temperature (R, P), flow, UV, and pH (P)	29151600
HF filter holder	For 1 filter	29258287
HF filter holder	For 2 filters	29256166
Air sensor	Air bubble detection in additional feed inlet	29003879
Bar code reader	Scanning of flow kit serial numbers	29269812
UNICORN 7 Filtration	Software license	29270760
IQ/OQ documentation	Installation and operational qualification documentation of ÄKTA readyflux	29214963
IQ/OQ Performance	Installation and operational qualification performance of ÄKTA readyflux	28992657

F = feed, R = retentate, P = permeate

<b>Fittings and accessories</b>	<b>Description</b>	<b>Product code</b>
ReadyMate, 10 L bag	Disposable 10 L hanging bag for feed, recirculation or permeate	12410222
ReadyMate, 20 L bag	Disposable 20 L hanging bag for feed, recirculation or permeate	12410224
ReadyMate, Jumper, 0.5 in × 1 feet	AdvantaPure™ reinforced tubing connecting size 5 and 8 cartridges to retentate	12410135
ReadyMate, Jumper, 0.5 in × 2 feet	AdvantaPure reinforced tubing connecting size 6 and 9 cartridges to retentate	RC2017-0061
ReadyMate, Jumper, 0.38 in × 0.5 feet	AdvantaPure reinforced tubing connecting size 5 and 8 cartridges to permeate	RC2017-0062
ReadyMate, Jumper, 0.38 in × 1.5 feet	AdvantaPure reinforced tubing connecting size 6 and 9 cartridges to permeate	RC2017-0063
ReadyMate, Jumper Y manifold, 0.38 in × 0.5 feet	AdvantaPure reinforced tubing connecting both cartridge permeate outlets to permeate	12410194
TC, 10 L bag	Disposable 10 L bag for feed, recirculation or permeate	RC2017-0073
TC, 20L bag	Disposable 20 L bag for feed, recirculation or permeate	RC2017-0074
1.5 to 0.75 in TC, Jumper, 0.5 in × 1 feet	AdvantaPure reinforced tubing connecting size 5 and 8 cartridges to retentate	RC2017-0066
1.5 to 0.75 in TC, Jumper, 0.5 in × 2 feet	AdvantaPure reinforced tubing connecting size 6 and 9 cartridges to retentate	RC2017-0067
0.75 in TC, Jumper, 0.38 in × 1 feet	AdvantaPure reinforced tubing connecting size 5 and 8 cartridges or cassette holder to permeate	RC2017-0068
0.75 in TC, Jumper, 0.38 in × 2 feet	AdvantaPure reinforced tubing connecting size 6 and 9 cartridges or cassette holder to permeate	RC2017-0064
0.75 in TC, Jumper, 0.38 in × 3 feet	AdvantaPure reinforced tubing connecting cassette holder to permeate	RC2017-0065
0.75 in TC, Jumper Y manifold, 0.38 in × 0.5 feet	AdvantaPure reinforced tubing connecting both cartridge permeate outlets to permeate	RC2017-0069
ReadyMate to 0.75 in TC, Adapter	Disposable aseptic connector converting ReadyMate to TC	28936695

## Related literature

<b>Title</b>	<b>Literature code</b>
Cross flow filtration method handbook	29085076
UNICORN 7 system control software, data file	29135786
Concentration and buffer exchange using the automated, single-use ÄKTA readyflux system, application note	KA291161017AN
Connected polishing and concentration under one automation method, application note	KA985271017AN
Single-use workflow for recovery of a domain antibody from E. coli culture feed in an automated manner	A667181017AN
ÄKTA readyflux, operating instructions	29175550
ÄKTA readyflux, software guide	29296551
Xcellerex XDUO Mixer, data file	29048366

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