MILLIPORE

DATA SHEET

K-Prime® 40-I, 40-II, and 40-III Biochromatography Systems

- *Broad flow rate range expands processing capabilities*
- *New Batch Reporting features conform to regulatory requirements*
- *Recipe Editor facilitates protocol transfers for clinical trials and small scale manufacturing*
- *Designed for use in small volume and process development applications as well as clinical and early production*

Small and production scale systems for developing protein and bio-engineered product separations requiring flow rates from 20 mL to 10 L per minute

The K-Prime biochromatography systems are designed for separating and purifying proteins and bio-engineered products. These advanced systems span a wide range of flow rates, delivering sharp separations in applications from small-scale pilot processes through commercial production. All K-Prime systems are designed to make process scale-up as easy as possible.

Scale-up Overview

Development
- Method discovery
- Media evaluation
- Material prep
- Material evaluation

Pilot
- Optimize method
- Clinical material manufacturing

Production
- Method execution
- Material manufacturing

Figure 1. *Transferring separations from small to production scale systems is critical in the success of all new products.*

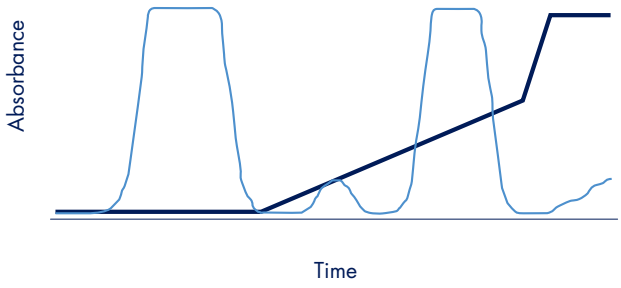
Optimized for Process Development, Pilot, and Small to Intermediate Production Scale Applications

Operating at a flow rate of either 20 to 500 mL/min., 0.1 to 3 L/min. or 1 to 10 L/min. and a pressure rating of up to 7 bar (102 psig), the K-Prime biochromatography systems are designed for use in process development, pilot, clinical trial and production-scale manufacturing. These compact systems support a variety of chromatographic techniques, including ion exchange, affinity, hydrophobic interaction and gel filtration. They accommodate a broad range of column diameters, depending on the process application.

Extended Chromatographic Capabilities Improve Results

Many features, including automated buffer mixing and enhanced UV monitoring, ensure each K-Prime system delivers high product recovery and purity for cost-effective separations. Automated gradient formation provides exceptional control for linear and isocratic mixing, which are essential for ensuring precise elution profiles. Multiple wavelength sensing improves the system's capacity to monitor the process stream and control the elution process.

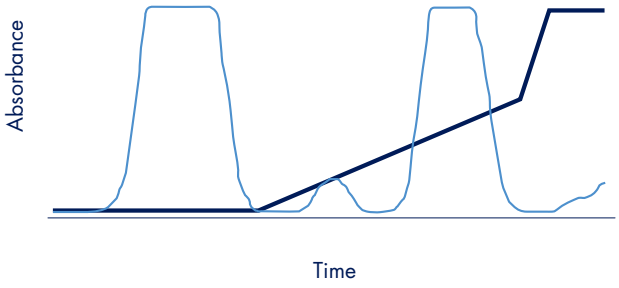
K-Prime 40-I System



Gradient profile		Time	HETP (cm)	ASYM
Loading	0%	5 CV	0.031	1.12
Elution	0 – 60%	7 CV		
Wash & elute	60 – 90%	1 CV		

Figure 2.

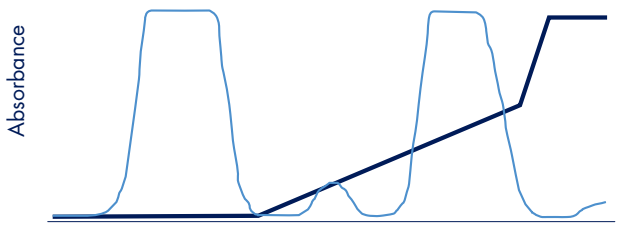
K-Prime 40-II System



Gradient profile		Time	HETP (cm)	ASYM
Loading	0%	5 CV	0.035	1.15
Elution	0 – 60%	7 CV		
Wash & elute	60 – 90%	1 CV		

Figure 3.

K-Prime 40-III System



Gradient profile		Time	HETP (cm)	ASYM
Loading	0%	5 CV	0.032	1.2
Elution	0 – 60%	7 CV		
Wash & elute	60 – 90%	1 CV		

Figure 4.

User-friendly CCP® Automation Software

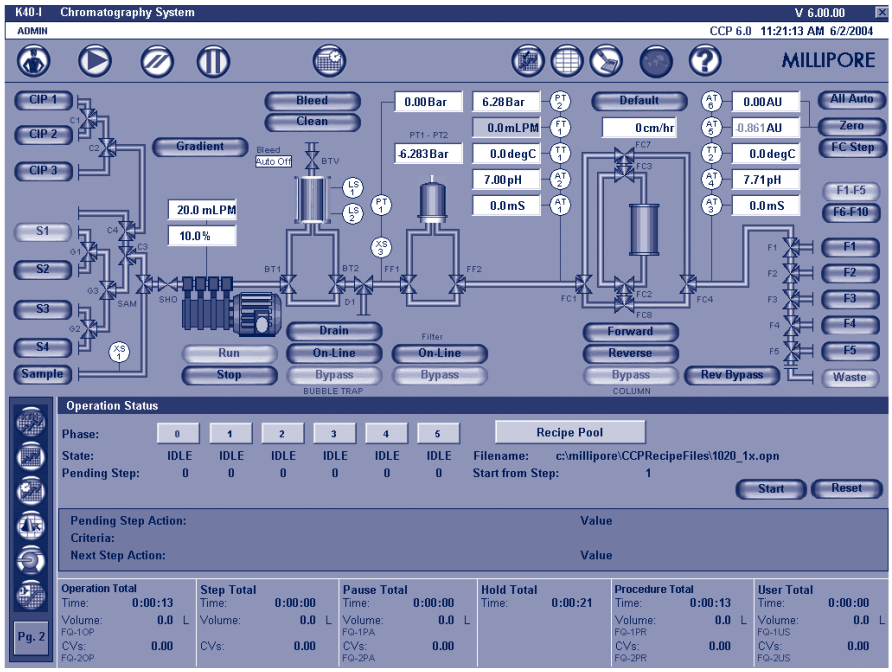
The Common Control Platform®, (CCP) software, is a robust, industry-recognized platform used to accelerate application development and production. The CCP software establishes a common platform capable of controlling and linking Millipore chromatography and TFF solutions. It is designed to allow data to be conveniently archived to networked systems, and recipes to be rapidly scaled from developmental systems to production capacity unit operations.

The software, through a touch-screen user-interface, brings push-button simplicity to the task of developing and executing complex and repetitive separation protocols. In addition, the software:

- Delivers a range of control features to help you optimize your process.
- Offers full-manual or automatic control.
- Integrates easily into your plant network for sharing results and data.
- Includes a powerful Recipe Editor which allows the user to create customizable separation recipes that are configured quickly and easily.
- Ensures acquisition of all process data.
- Generates comprehensive batch reports that meet regulatory requirements.

In combination with superior performing hardware built into all K-Prime systems, the software delivers a robust and full-featured solution designed for today's ultra-pure separation needs.

CCP User Interface



K-Prime 40-I, 40-II and 40-III Biochromatography Systems

Complete and Advanced Purification Solutions for Biopharmaceutical Applications

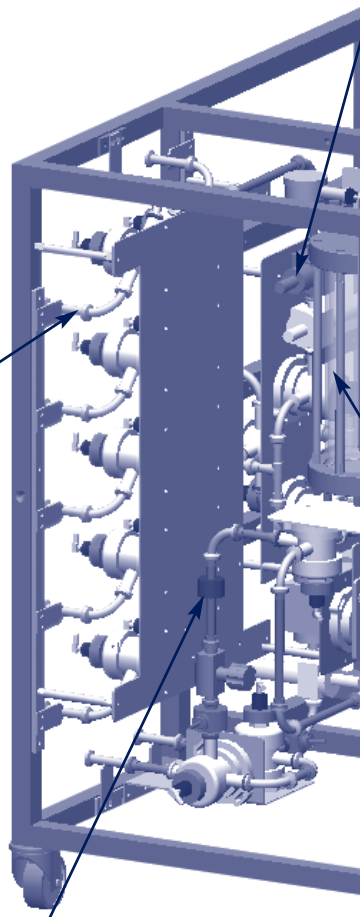
Technical Innovations in All K-Prime Systems Deliver Optimized, Robust Chromatographic Performance

Specialized Piping and Valves Offer Efficient and Reliable Separations

The system's bio-inert pipework is configured to minimize hold-up volume, eliminate unswept areas and assures system cleanability. All piping and system components are easily accessible for maintenance and calibration. The innovative application of unique, three-way, PTFE (Teflon® resin) valves give the system its versatility and durability. Used in many locations throughout the system, these specialized valves enable superior process stream management, eliminate the use of tees, and guarantee extremely long life. Sturdy, stainless steel connections placed at system boundaries add robustness and reliability.

Automated Gradient Mixing Allows Precise Separation Control

A gradient mixing system controls both buffer mixing and mixing valve cycling to form highly accurate and reproducible isocratic or linear gradients. Mixing valves are positioned before the system pump and are capable of producing up to 6 different buffer combinations. This methodology ensures greater precision of absorptive-based chromatographic separations, lowers processing costs, and reduces reservoir requirements.



Clean Fraction Collection

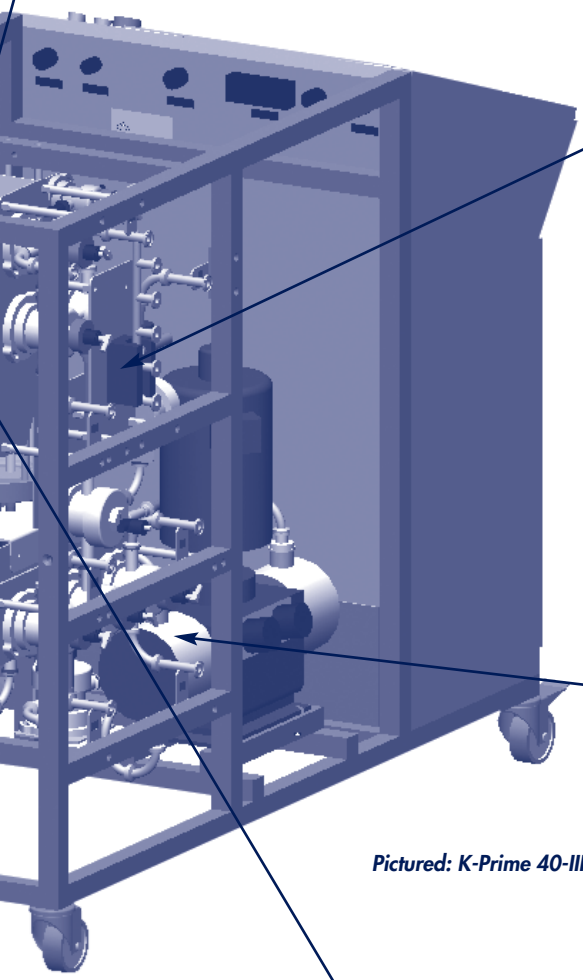
Users may configure the K-Prime systems with three, five or ten fraction collection ports, and fraction waste port. Radial diaphragm valves assure complete diversion of all product to the collection vessel and eliminate the potential for diffusional contamination that may occur with weir-diaphragm or other types of valve arrangements.

Extensive Process Monitoring

Each flow cell is specially designed to ensure complete passage of all process fluids, resulting in rapid sensor response and precise system operation. Pre-column sensors monitor the presence of air, flow, pressure, pH, conductivity and temperature. Post-column sensors monitor UV, pH, conductivity and temperature. All sensing elements are constructed of materials that conform to FDA guidelines and are contained within distinct flow cells for easy access and maintenance.

Improved Monitoring/Control with High Performance UV Detector

The unique internal geometry of the flow cell ensures accurate measurement of the entire process stream across a broad range of absorbance. For improved process monitoring and greater control K-Prime Systems are capable of monitoring two wavelengths simultaneously, within a single flow cell. This optional feature broadens column eluent visibility and improves the capability to fractionate product, resulting in higher purity and recovery.



Pictured: K-Prime 40-III System

Accelerated, Simplified and Dependable Cleaning

An optional three-valve manifold may be added to the system to either control additional buffer solutions or control the introduction of cleaning solution during clean in place (CIP) operations. CIP valves direct cleaning solutions to each buffer inlet port and throughout the system. They can either be actuated manually or controlled via automated cleaning recipe commands. When the proximity sensor detects the CIP inlet manifold, the control system automatically enables the CIP inlets ports for cleaning operations. This feature assures the system is properly cleaned prior to resuming separations.

Control Flow Throughout the Separations

The system pump is a highly efficient positive displacement duplex diaphragm type with an operating flow range of 20–500 mL/min. (40-I), 0.1–3 L/min. (40-II) or 1 to 10 L/min. (40-III), and maximum discharge pressure of 7 bar. A high-precision flow meter monitors the flow during the purification operation, allowing users to precisely adjust pump speed and flow rate.

Column Protection Ensures Reliable Performance

Each system is equipped with a bubble trap that both prevents air from reaching the column and dampens flow pulsation. Level sensors monitor air in the bubble trap and signal the software to both trigger an alarm and shut down the pump in the event of excess air accumulation. Flow within the bubble trap promotes mixing and prevents liquid stratification due to variations in liquid density. To avoid sample dilution during product loading, the bubble trap can be by-passed. The K-Prime 40-III system can be configured with a stand alone bubble trap or a bubble trap with a separate filter.

CCP—State-of-the-Art Automation Software

Fast, Functional Platform

The Common Control Platform features an intuitive, graphical software interface designed to operate and interface with all K-Prime Systems. It allows access to tools used for: developing, monitoring, and controlling complex separation applications; generating comprehensive batch reports; and sharing information across a network.

Quickly Create Separation Protocols Using Touch-Sensitive Screens

A touch-sensitive interactive display allows users to quickly create and launch custom procedures and operations. Process graphic screens display a wide range of information including: active flow path, process sensor readings, alarm status set point values, as well as system-generated messages.

Compliance ready with FDA Guideline 21 CFR Part 11 For Electronic Records and Electronic Signatures

The K-Prime systems include CCP software. CCP software's powerful batch reporting feature meets the technological requirements of FDA's 21 CFR Part 11[1] for electronic signatures and electronic records. The batch reporting feature includes capabilities for electronic signing, auditing files, and rendering data files unalterable. It utilizes industry recognized ANSI/ISA-S88.01-1995 standards for batch operation nomenclature, and is consistent with the most current industry terminology.

Tools Monitor Processes and Compare Batches

CCP software's batch reporting feature continuously monitors key system data to ensure consistent processing. Powerful post-run analysis tools track separation processes and allow batch-to-batch chromatogram comparisons. Functions such as HETP and Asymmetry calculations reveal how well columns are packed prior to separation processing. Copies of batch records may be exported to third party programs for further analysis.

Customize Recipes Easily

Users may schedule events based on time, volume, column bed volume, or any combination of conditional events based on sensor outputs or process-initiated prompts. CCP software displays the execution status of recipes and procedures together with data trends and process values that provide users with relevant information for optimizing their process.

Securely Share Your Knowledge

CCP software is OPC[2] compliant, Microsoft® Windows® compatable, and incorporates the iFIX® SCADA® technology. Secure access, definable for multiple user levels, allows access to only those parts of the system appropriate to user function. Secure data acquisition provides a comprehensive audit trail for process reporting and regulatory compliance. With an optional system-integrated UPS (uninterruptible power supply), recipes downloaded into the PLC and all process data is secure– even in the event of power failure.

Meets GAMP Standards

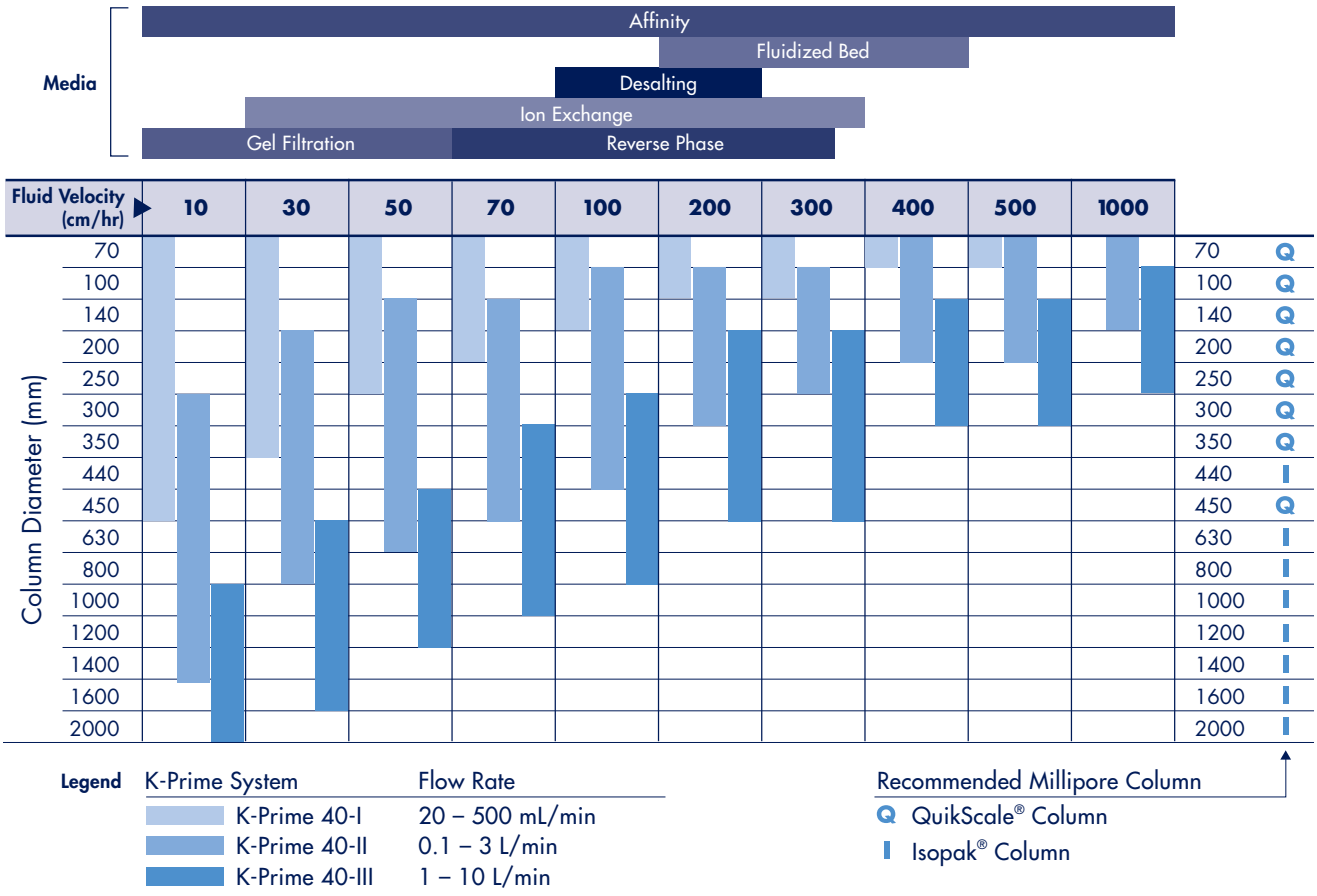
CCP software was developed in a facility registered to the applicable ISO® 9000 Quality Systems Standard. Millipore has adopted and follows the GAMP guidelines for automated equipment for the pharmaceutical manufacturing industry. Millipore is routinely audited by external agencies. You, the customer, are welcome to visit or audit our manufacturing facilities to observe our Quality Management System in operation.

Multilingual

A multi-language option displays the main screen, recipe editor and extensive portions of the batch report file in eight languages.

[1] 21 CFR Part 11 provides criteria under which the FDA will consider electronic records equivalent to paper records and electronic signatures equivalent to hand-written signatures. It applies to any records in electronic form created, modified, maintained, archived, retrieved, or submitted under any agency records requirement.

[2] OPC = OLE for Process Control.
OLE = Object Linking and Embedding



Chromatography Applications

The K-Prime systems are ideally suited to a broad range of process development applications and production chromatography applications.

For more detailed information on system and column sizing, please contact your Millipore Application Specialist.

Your Source for All of Your Chromatography Media and Column Needs

Millipore specializes in providing media for high-throughput affinity applications at process scale. Millipore also provides media for other chromatography techniques, including normal and reversed phase, ion exchange, gel filtration, and affinity separations. To optimize efficiency, capacity and cost, customers may select media in a range of particle and pore sizes. On request, Millipore provides customers with full regulatory support information (including Drug Master File numbers) on nearly all Millipore media.

Millipore columns represent state-of-the-art, automated packing and media-handling applications. The columns are ideal for development, pilot or production purification in the pharmaceutical biotechnology industry. Sanitary design, ease of assembly, and pneumatically assisted axial compression make these columns especially applicable for use with the more rigid, higher resolution chromatographic media. For ultimate expansion to industrial process scale, Millipore's standard and custom columns range in size from 70 mm up to two meters in diameter. They permit direct scale-up of pilot performance with assurance of continued high efficiency.

Validation Support and Documentation

The K-Prime systems utilize components and process wetted materials that are proven suitable for biotech and pharmaceutical applications. To ensure the system can be installed and commissioned quickly and reliably, each unit is subjected to a broad range of pre-shipping tests.

All test results are recorded and included within an extensive documentation package that accompanies each system.

System documentation includes:

- User documentation
- Materials and chemical compatibility data
- Comprehensive system parts list
- Sub-component manuals
- Spare parts recommendations
- Maintenance recommendations

Warranty

The system warranty may be extended to a full 2 years, providing one of the longest warranties in the industry.

Specifications

Flow Rate[3] per minute	**40-I** 20–500 mL (1.2–30 L/hr)	**40-II** 0.1–3.0 L	**40-III** 1–10 L
Pressure Rating	Up to 7 Bar (102 psig)		
Temperature Range			
Ambient:	+2 to 30 °C		
Flow Stream (temperature range for operating at maximum pressure rating):	+2 to 30 °C		
Process Connection Type	3/4 inch sanitary clamp (accommodates both 3/4 in. and 1/2 in. fittings)		
Pipework Inside Diameter	**40-I** 3 mm bore	**40-II** 10 mm bore pre-pump 6 mm bore post-pump	**40-III** 10 mm bore
Buffer/Solvent Inlets	Four inlets with gradient capability		
Gradient Capability	Two component buffer Isocratic or linear mix; six binary mix combinations		
Mix range:	10–90%		
Accuracy:	± 2% FS of either buffer		
Reproducibility:	± 1%		
Hold-up Volume	**40-I**	**40-II**	**40-III**
Buffer to Waste:	75 mL	250 mL	1.45 L
Sample to Column:	35 mL	150 mL	1.2 L
Bubble Trap (Full):	550 mL	550 mL	2.0 L
Humidity	5–95% (non-condensing)		
Utility Requirements			
Compressed Air:	≥ 6 bar instrument air filtered to ≤ 5 micron, –20 °C dew point, oil free.		
Maximum Consumption:	~8 L/min (0.3 SCFM)		
Electrical Supply[4]*:*	Single Phase 100, 120, 240 volts 50/60 Hz		
Power Consumption:	~1 kVA		
Connection:	Push fit socket for 10 mm OD tube on cabinet		
Fraction Ports	3 or 5 or 10		
Dimensions	**40-I and 40-II**		**40-III**
Height:	1270 mm (50 in)		1270 mm (50 in)
Width:	686 mm (27 in)		686 mm (27 in)
Depth:	1042 mm (41 in)		1499 mm (59 in)
Uncrated Weight	**40-I** 170 kg (375 lbs)	**40-II** 190 kg (419 lbs)	**40-III** 260 kg (573 lbs)
Wetted Materials	316 L SST, PP, EPDM, Teflon resin, PFA, PVDF, TPX, Quartz, Titanium, Santoprene® elastomer and CHEM-SURE™ (K-Prime 40-III only)		
Electrical Enclosure	IP 56 (NEMA 4X)		

[3] Under specified conditions. Refer to user manual.

[4] Voltage configured at time of order.

To Place an Order or Receive Technical Assistance

For additional information call your nearest Millipore office:
In the U.S. and Canada, call toll-free **1-800-MILLIPORE (1-800-645-5476)**
In the U.S., Canada and Puerto Rico, fax orders to **1-800-MILLIFX (1-800-645-5439)**
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