

CoPrime® Biochromatography Process-Scale Systems

Fully automated, configurable systems
for biopharmaceutical manufacturing and
cGMP process scale applications

The CoPrime® biochromatography systems are designed to achieve optimum separation and purification of monoclonal antibodies, vaccines, plasma, and therapeutic proteins. The systems support rapid scale-up and are ideally suited for pilot and process scale.

The CoPrime® systems are designed based on 50 years of process knowledge and engineering expertise to provide a configurable, intuitive process-scale purification solution. CoPrime® A, B, and C sizes have an extended flow rate span and optimized performance for greater gradient accuracy and purification reproduction. The CoPrime® C (40 L) covers higher scales and allows to scale-up directly from CoPrime® B (20 L). CoPrime® A (3 L) covers pre-clinical and clinical scales.



Benefits

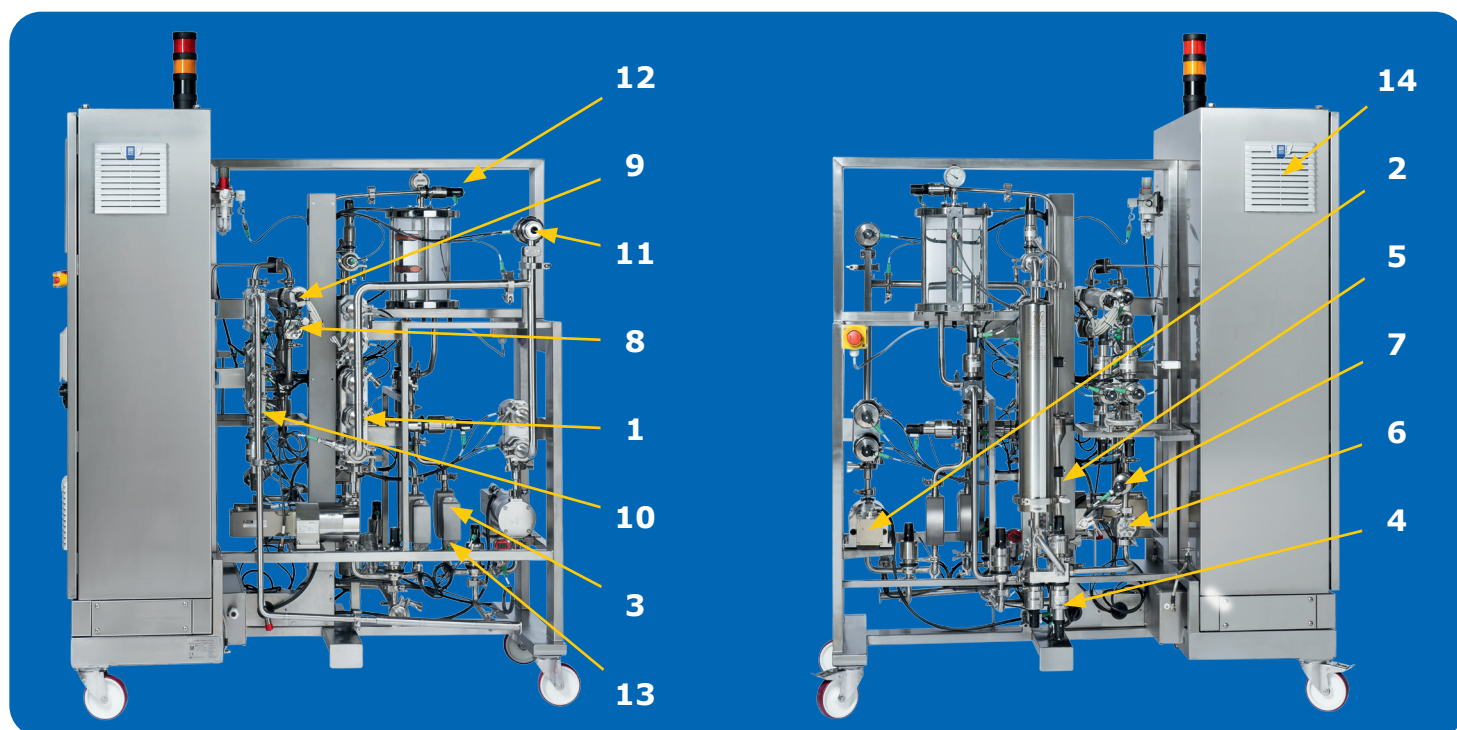
- Scalability with 3 flow rate ranges: CoPrime® A (3 L) up to 180 L/h
CoPrime® B (20 L) up to 1,200 L/h
CoPrime® C (40 L) up to 2,500 L/h
- Optimized design for very low hold-up volume
- Gradient precision across an extended flow rate window
- Consistent purified fractions over multiple cycles for optimum performance, reliability, and robustness

Configure to meet your purification requirements

Select from the options below to add to the CoPrime® base platform to best meet your unique chromatography processing requirements. Some of the options have been included in the CoPrime® size A and C base system, see table 1 for details.

CoPrime® size	CoPrime® A Biochromatography System 3 L	CoPrime® B Biochromatography System 20 L	CoPrime® C Biochromatography System 40 L
Total options	5 options	14 options	8 options
Option 1: 5 inlet ports	Included in base system	Yes	Included in base system
Option 2: 2 nd feed pump		Yes	
Option 3: mass flow meter		Yes	
Option 4: valve block for pre-column filter	Inline filter only	Yes	Yes
Option 5: valve block and pre-column filter	Not available	Yes	Yes
Option 6: pre-column pH and conductivity sensor	Yes	Yes	Yes
Option 7: HETP	Not available	Yes	Not available
Option 8: post-column pH and conductivity sensor	Included in base system	Yes	Yes
Option 9: post-column UV absorption sensor	Yes	Yes	Yes
Option 10: 5 outlet ports	Yes	Yes	Yes
Option 11: CIP manifolds	Yes	Yes	Yes
Option 12: valve position feedback-switch	Yes	Yes	Yes
Option 13: magnetic flowmeter	Not available	Yes	Not available
Option 14: system IPx5 rated	Included in base system	Yes	Included in base system

Table 1: Options for all CoPrime® system sizes.



Note: System displayed is CoPrime® Size B (20 L).

CoPrime® size A (3 L)

The CoPrime® size A base platform includes (in addition to size B base platform): 5 inlet manifold on first pump for multiple buffer processing, second pump with 2 inlets, mass flowmeters, post-column pH and conductivity sensors, and stainless steel filter hoods on the enclosure.

CoPrime® A base platform is with the post-column instrumentation 8. Option 9 can be added.

Option 6: Pre-column pH and conductivity

A conductivity sensor (with temperature compensation) and a pH sensor are fitted in the same flow cell, which is integrated in line between the filter and the column.

Option 9: Post-column UV sensor

With this option, a Kemtrak dual wavelength UV absorption sensor is proposed.

Option 10: Five outlets

Three additional ¼ in. outlet ports with Gemü® valves are added downstream of the column to separate different fractions.

Option 11: CIP manifold for cleaning the entire system (excluding the column) in CIP, from one single inlet to one single outlet

Option 12: Feedback switches on Gemü® valve

With this option, every valve is mounted with an integrated position feedback switch. Closed position is physically detected.

Note: Valve block of pre-column filter option is not available for CoPrime® size A system, but an Opticap® XL 300 inline filter can be installed in place of the spool piece.

CoPrime® size B (20 L)

The CoPrime® size B base platform includes: air sensor on product inlet line, two inlets ports, one Quattroflow® inlet pump, pressure transmitter and pressure switch on pump outlet, bubble trap with vent valve and air break, pre-column air sensor, pre-column pressure sensor and transmitter, column flow path valve block (forward, reverse or bypass), post column pressure transmitter sensor & transmitter, two outlets and drain ports, system drain line, electrical enclosure, and pressurized air supply block.

CoPrime® B base platform must be purchased with a flowmeter option (option 3 or 13) and the post-column instrumentation (options 8 and 9).

Option 1: 5 inlet manifold on 1 pump for multiple buffer processing

Option 2: Second pump with 2 inlets enabling:

- Mixing of two products with a regulated flow rate ratio (2% accuracy of the measured value from 180 L/h to 1,200 L/h)
- Linear gradient, from 10% to 90%, according to a rated slope based on flow rate or conductivity (closed control loop: 2% accuracy of the measured value on volume or 2% accuracy of the full scale on conductivity)
- Step gradient, from 10% to 90%, according to set points on flow rate or conductivity (closed control loop: 2% accuracy of the measured value on flow or 2% accuracy of the full scale on conductivity)

Option 3: Mass flowmeter

One mass flowmeter is set up between the pump and the bubble trap for monitoring and regulation of the flow fed to the column.

Note: This option includes only one flowmeter. If option 2 (second pump) is selected, the flowmeter option is to be selected twice. The mass flowmeter option excludes the mag flowmeter option.

Option 4: Valve block of pre-column filter either disposable or in a housing

Note: Filter and housing not included.

Option 5: Valve block and pre-column filter housing

Note: Stainless steel 10 or 20 in housing.

Option 6: Pre-column pH and conductivity

A conductivity sensor (with temperature compensation) and a pH sensor are fitted in the same flow cell, which is integrated in line between the filter and the column.

Option 7: HETP inlet block valve

This option enables injection of the HETP sample as close as possible to the column inlet, through a NovAseptic® divert valve.

Note: It is possible to perform an HETP sequence using an inlet port instead of the dedicated divert valve.

Option 8: Post-column pH conductivity

A conductivity sensor (with temperature compensation) and a pH sensor are fitted in the same flow cell, which is integrated in line between the column and outlet ports. Two ranges of conductivity are defined, one for the process and another for cleaning.

Option 9: Post-column UV sensor

With this option, a mono-wavelength UV absorption sensor, Optek® AF45 sensor, or a dual-wavelength with an Optek® AF46 sensor is proposed.

Option 10: Five outlets

Three additional ¾ in. outlet ports with NovAseptic® valves are added downstream of the column to separate different fractions.

Option 11: CIP manifold for cleaning the entire system (excluding the column) in CIP, from one single inlet to one single outlet

Option 12: Feedback switches on NovAseptic® valve

With this option, every valve is mounted with an integrated position feedback switch. Closed position is physically detected.

Option 13: Electromagnetic flowmeter

The performance of the flowmeter is dependent on the conductivity of the product. Product conductivity must be greater than 5 µS/cm for liquids, in general, and greater than 10 µS/cm for demineralized water.

Option 14: Filter hoods

The addition of stainless steel filter hoods on the enclosure filters and fan allows an IP rating of IPx5.

CoPrime® size C (40 L)

The CoPrime® size C base platform includes (in addition to size B base platform): 5 inlet manifold on first pump for multiple buffer processing, Second pump with 2 inlets, Mass flowmeters and stainless steel filter hoods on the enclosure.

CoPrime® C base platform can be purchased with post-column instrumentation (options 8 and 9).

Option 4: Valve block of pre-column filter either disposable or in a housing

Note: Filter and housing not included.

Option 5: Valve block and pre-column filter housing

Note: Stainless steel 30 in housing.

Option 6: Pre-column pH and conductivity

A conductivity sensor (with temperature compensation) and a pH sensor are fitted in the same flow cell, which is integrated in line between the filter and the column.

Option 8: Post-column pH conductivity

A conductivity sensor (with temperature compensation) and a pH sensor are fitted in the same flow cell, which is integrated in line between the column and outlet ports. Two ranges of conductivity are defined, one for the process and another for cleaning.

Option 9: Post-column UV sensor

With this option, a mono-wavelength UV absorption sensor, Optek® AF45 sensor, or a dual-wavelength with an Optek® AF46 sensor is proposed.

Option 10: Five outlets

Three additional 1 inch outlet ports with NovAseptic® valves are added downstream of the column to separate different fractions.

Option 11: CIP manifold for cleaning the entire system (excluding the column) in CIP, from one single inlet to one single outlet

Option 12: Feedback switches on NovAseptic® valve

With this option, every valve is mounted with an integrated position feedback switch. Closed position is physically detected.

Designed for Easy, Reliable Processing

Embedded NovAseptic® Valves on size B and C (Gemü® valves on size A)

With 20 years of proven performance, these “Aseptic by Design” valves deliver optimal performance, reliability, durability, and ease of maintenance. Our NovAseptic® connectors have no dead legs for maximum product recovery with zero hold-up volume, and are compatible with the most stringent cleanability requirements.

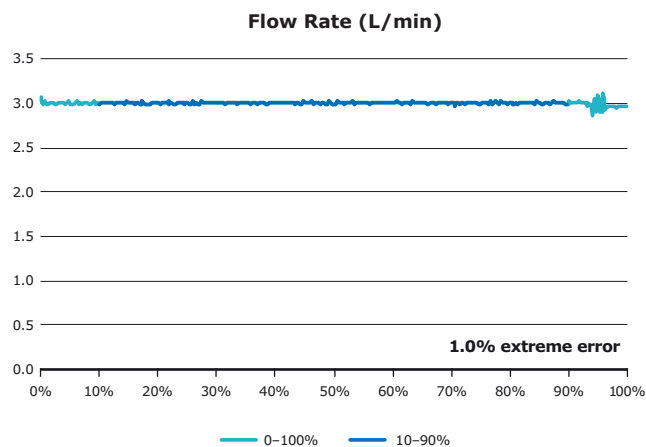
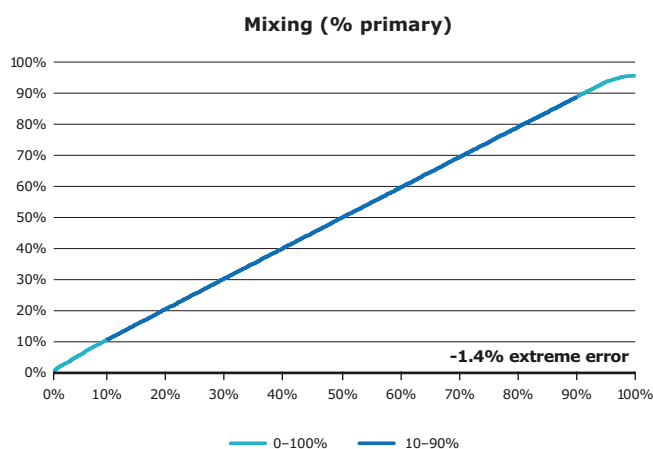
CoPrime® size B (20 L) System Robust Chromatography Performance

Gradient accuracy over extended window of operation

The system is designed to deliver gradients using optional pump-based mixing at an accuracy of $\pm 2\%$ over a 10–90% gradient mix range.

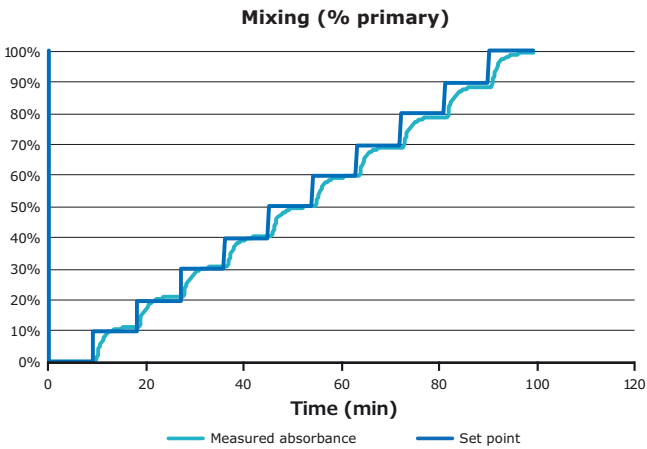
Linear Gradient per Percentage at 3 L/min

The extreme errors at 3 L/min measured on the range 10–90% are **-1.4%** on mixing and **1.0%** on total flow rate.



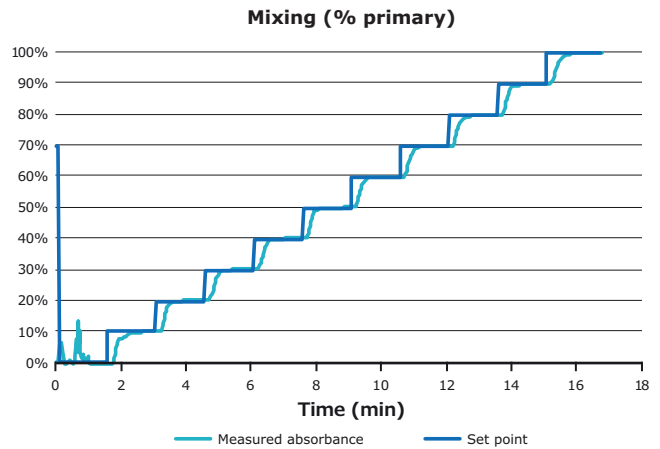
Step Gradient per Percentage at 3 L/min

The extreme errors measured on the range 10–90% are **-1.3%** on mixing and **0.0%** on total flow rate.



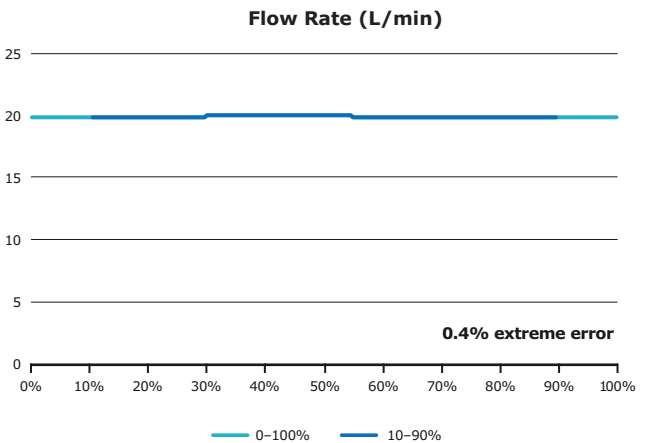
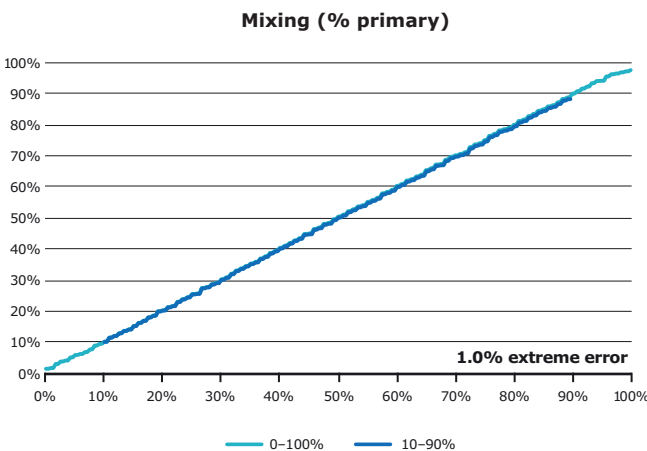
Step Gradient per Percentage at 20 L/min

The extreme errors measured on the range 10–90% are **-0.2%** on mixing and **-0.1%** on total flow rate.



Linear Gradient per Percentage at 20 L/min

The extreme errors measured on the range 10–90% are **1.0%** on mixing and **0.4%** on total flow rate.



Proven Sanitary Design with Automatic CIP Cycle and Manifold

During cleanability studies, a bovine serum solution was pumped through the system and then flushed with NaOH and WFI or RO water. The results showed a TOC less than 3 ppm.

Extensive Process Monitoring

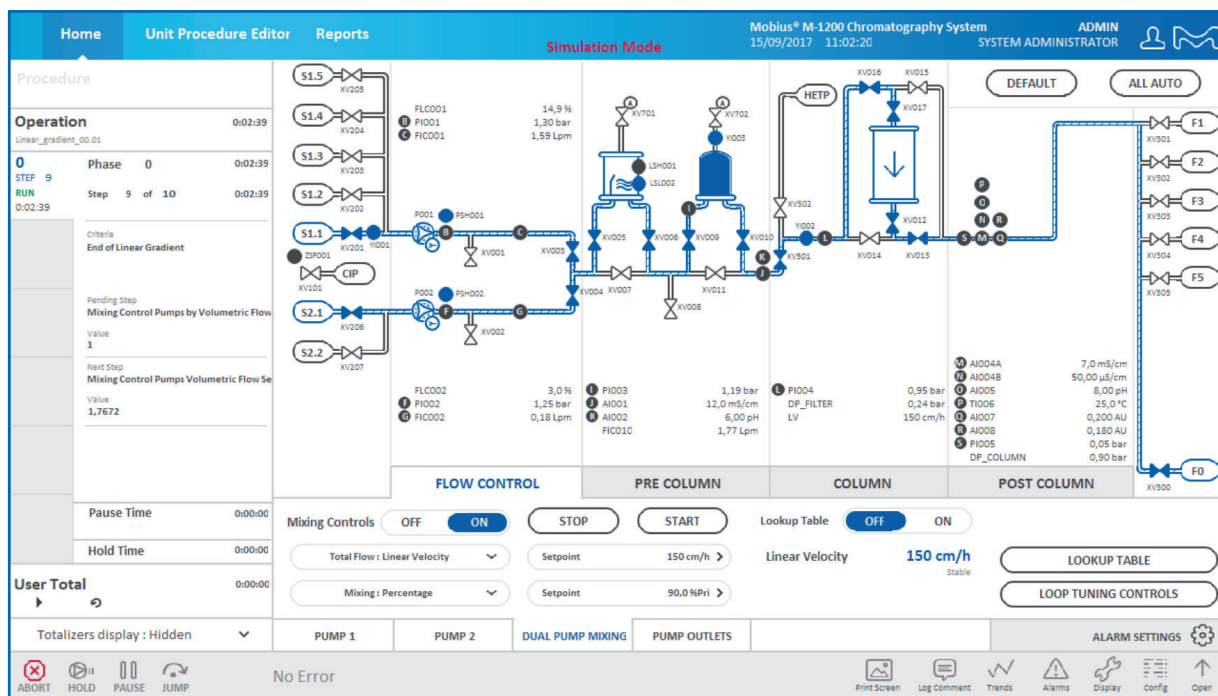
Each flow cell is specially designed to ensure complete passage of all process fluids, resulting in rapid sensor response and precise system operation. Pre-column sensors monitor the presence of air, flow, pressure, pH, conductivity, and temperature. Post-column sensors monitor UV, pH, conductivity,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

Total Process Control and Connectivity

Common Control Platform® Software (CCP®) for Multiple Unit Operations

From Mobius® bioreactors to clarification, chromatography, tangential flow filtration, and virus filtration systems, our CCP® software can provide you with one familiar interface that simplifies software management and reduces the

learning curve for new operators. This software package is available to support all application sizes, accelerating tech transfer and process scale-up.



Monitors Processes and Enables Batch Reporting

The latest version of CCP® software is powerful, intuitive and graphical; providing real-time monitoring and total in-depth control of your bi chromatography platform. Create process operations using the recipe editor, monitor the process from the home screen, and create reports for the batch using the configurable report generator.

Comprehensive and Secure Data Acquisition

CCP® software was designed to support compliance to 21 CFR part 11 and was developed under GAMP5 guidelines. The software includes an accessible audit trail and electronic signatures for verification. CCP® software is suited for manufacturing equipment from development to large-scale, using industrial computers and controllers for reliability.

Network Integration

Data transfer to the plant control system enables data collected by CCP® software to be centrally stored and managed.

Powerful Recipe Editor Simplifies Generation of Process Specific Separation Protocols

CCP® software monitors and adjusts all process parameters to ensure execution of a preprogrammed method or "recipe" using the Recipe Editor. You can quickly and efficiently configure, modify, test, and ultimately, lock these recipes for initial evaluation, repetitive process investigation, or transfer to production operations. Complex operations are easily constructed without prior programming experience.

Backup and Restoration

Backup and restoration of data can be managed via network integration.

Security Synchronization

Security synchronization allows user accounts to automatically coordinate with the networked plant control system for faster and simpler user account control and editing.

CoPrime® Systems Service

The pharmaceutical and biotechnology industries are highly regulated and, to help you navigate this challenging environment, we offer a wide range of services. These services help you save time, lower costs, and comply with regulations. For your peace of mind, all our services are performed by our global experts who have an intimate knowledge of our equipment backed by decades of experience.

Qualification Services

Our qualification services are designed to make the integration of our system into your process as seamless as possible and ensure your equipment is properly installed and functioning per your pre-defined requirements.

- Factory acceptance test (FAT)
- Installation qualification/operational qualification (IQ/OQ)
- Full test package: this service is an alternative to standard IQ/OQ for customers who wish to have tests from FAT performed again at their site
- Performance qualification support (PQ)

Training Services

Appropriate training for users is not only a GMP requirement, but it also ensures your staff has the expertise to operate and manage the system as part of your manufacturing process. Our training offering has been designed to make your staff more autonomous in managing your system and your process while saving time and money.

Our training services cover system use and programming with interactive hands-on sessions and, depending on the training you select, may also include:

- Installing the Flexware® assemblies
- Interacting with the Human Machine Interface
- Manual and automatic system operation
- Troubleshooting issues
- Creating and managing your own recipes
- Process recommendations

These trainings can be delivered either at your site or in our M Lab™ Collaboration Centers. Please contact your local representative or email ilearn@merckgroup.com to discuss our training offering.

System Service Reliance Plans

To help you ensure optimum equipment uptime while mitigating risks, we have developed a wide range of services and support that allow you to select a coverage level that best fits your needs. Our System Service Reliance Plans, a complete range of services for your systems, offer priority access to support while ensuring your equipment is properly maintained.

For additional details, please refer to the System Service Reliance Plans Data Sheet (MK_DS7881EN).

Specialized Services

Regular maintenance of your system is critical to avoid unnecessary downtime for repairs, minimize the risk of process deviations, and maintain optimum performance and compliance.

CCP® Software Recipe Design

Every process is unique and, to ensure that your system is optimized to deliver the best performance, our biomanufacturing engineers will configure your process into your own CCP® software recipe. This allows your system to run fully automatic, resulting in consistency and reduced operator error.

For catalogue numbers, please refer to the ordering information at the end of the document. For additional details, please refer to the illustrated spare parts list MK_SDS1687EN available at sigmaaldrich.com.

Repair Services and Spare Parts

Repair Services

In the event your system experiences a problem, our worldwide engineering organization will provide on-site or repair center technical support to get you back up and running as quickly as possible.

Spare Parts

Purchasing spare parts directly from us is the only way we can guarantee that you get the right parts every time, with the same level of performance as the original.

Services catalogue numbers

Catalogue numbers	Description
SSVFATCPB	CoPrime® System – FAT execution incl. protocol
SSVFATCPB2	CoPrime® System – FAT execution, qty=2, incl. protocol
SSVQUACPB1	CoPrime® System – SAT & IQ/OQ execution included protocol & travel
SSVQUACPB2	CoPrime® System dummy skid configuration – SAT execution included protocol & travel
SSVQUADOC	CoPrime® System documentation verification
SSVRPCCPB	CCP® recipe design qty 3
PTRCPBOP	CoPrime® System operator training, 1 day
PTRCPBCCP1	CoPrime® System – CCP® V.6 recipe writing, 1.5 day
PTRCPBCCP2	CoPrime® System – system use, troubleshooting and CCP® V.6 recipe writing, 3 days
PTRCPBCCP3	CoPrime® System – system use, process design, troubleshooting and CCP® V.6, recipe writing
SSVESPCPB	CoPrime® System – Essential Service Reliance Plan – execution, travel and protocol incl. protocol & travel
SSVESPCPB + SSVADCCPB	CoPrime® System – Advanced Service Reliance Plan – execution, travel and protocol incl. protocol & travel
SSVESPCPB + SSVTOCCPB	CoPrime® System – Total Reliance Plan – execution, travel and protocol incl. protocol & travel

Specifications

	CoPrime® A Biochromatography System 3 L	CoPrime® B Biochromatography System 20 L	CoPrime® C Biochromatography System 40 L
Mechanical specifications			
System dimension L x W x H, in mm (Inches)	1,513 ¹ x 864 x 1,896 (59.6" x 34.1" x 74.7") * with keyboard support	1,680 x 926 ¹ x 1,814 ² (66.2" x 36.4" x 72.9") ¹ with option 14, instead 851 ² without top flashlight	1,990 x 926 ¹ x 2,024 ² (78.4" x 36.4" x 79.5") ¹ with option 14, instead 851 ² without top flashlight
Net Weight	280 kg (full options)	410 kg (full options)	800 kg (full options)
Materials of Construction	Piping: Stainless steel 316 L Elastomer: EPDM in compliance with 21 CFR 177.2600	Piping: Stainless steel 316 L Elastomer: EPDM in compliance with 21 CFR 177.2600	Piping: Stainless steel 316 L Elastomer: EPDM in compliance with 21 CFR 177.2600
Connections			
Main line pre-pump	TC 3/4" OD 3/8"	TC 1"1/2 OD 1"	TC 1"1/2 OD 1"1/2
Main line post-pump	TC 3/4" OD 1/4"	TC 3/4" OD 3/4"	TC 1"1/2 OD 1"
Fractions lines	TC 3/4" OD 1/4"	TC 3/4" OD 3/4"	TC 1"1/2 OD 1"
CIP inlet line	TC 3/4" OD 3/8"	TC 1"1/2 OD 1"	TC 1"1/2 OD 1"1/2
Drain	TC 3/4" OD 3/4"	TC 1"1/2 OD 1"	TC 1"1/2 OD 1"1/2
Operating specifications			
Max Fluid viscosity	2 cP	2 cP	2 cP
Product Temperature Range	+4 to +30 °C	+4 to +30 °C	+4 to +30 °C
Maximum Pressure	4 barg	4 barg	6 barg
System operating temperature	+4 to +30 °C	+4 to +30 °C	+4 to +30 °C
Operating Humidity	15–60% (non-condensing)	15–60% (non-condensing)	15–60% (non-condensing)
Instrument specification and Performances			
Valves			
Pneumatic Valves	Gemü® diaphragm valves	NovAseptic® diaphragm valves	NovAseptic® diaphragm valves
Pumps			
Feed Pump P001	Quattroflow® Quaternary diaphragm pump Flow rate: 0.05 to 3 L/min	Quattroflow® Quaternary diaphragm pump Flow rate: 0.3–20 L/min	Quattroflow® Quaternary diaphragm pump Flow rate: 0.83 to 40 L/min
Feed Pump P002	Same pump, included	Same pump, optional	Same pump, included
UV			
UV sensor	Kemtrak Measurement range: 0 to 3 AU +/-0.04	Optek® Measurement range: 0 to 2 AU +/-0.04	Optek® Measurement range: 0 to 2 AU +/-0.04
OPL options	2 mm	2.5 mm 5 mm 10 mm	2.5 mm 5 mm 10 mm
Wavelengths options	Dual wavelength: 250–280 nm	Single wavelength: 254 nm 280 nm 300 nm 313 nm Dual wavelength: 254 nm, 280 nm 254 nm, 313 nm 254 nm, 300 nm 280 nm, 300 nm 280 nm, 313 nm 300 nm, 313 nm	Single wavelength: 254 nm 280 nm 300 nm 313 nm Dual wavelength: 254 nm, 280 nm 254 nm, 313 nm 254 nm, 300 nm 280 nm, 300 nm 280 nm, 313 nm 300 nm, 313 nm
Probes			
Flowmeters	Endress+hauser Range: 0,15–4 L/min +/-1% MV	Endress+hauser Range: 1–25 L/min +/-1% MV	Endress+hauser Range: 4–50 L/min +/-1% MV
Conductivity sensors	Hamilton Pre-column process range: 1–100 mS/cm +/-3% MV – 100–200 mS/cm +/-5% MV Post-column process range: 1–100 mS/cm +/-3% MV – 100–200 mS/cm +/-5% MV Post-column cleaning range: 1–50 µS/cm +/-3% MV	Optek® Pre-column process range: 0–200 mS/cm +/-4 mS/cm Post-column process range: 0.1–200 mS/cm +/-4 mS/cm Cleaning range: 0.1–50 µS/cm +/-1 µS/cm	Optek® Pre-column process range: 0–200 mS/cm +/-4 mS/cm Post-column process range: 0.1–200 mS/cm +/-4 mS/cm Cleaning range: 0.1–50 µS/cm +/-1 µS/cm
pH sensor	Hamilton Range: 0–14 pH +/-0.2	Mettler-Toledo Range: 0–14 pH +/-0.1	Mettler-Toledo Range: 0–14 pH +/-0.1

We offer an extensive portfolio of chromatography products to support your process from start to finish.

Affinity Media

Eshmuno® P Anti A/B
Eshmuno® A
Fractogel® EMD
Chelate (M)

CEX Media

Eshmuno® S
Eshmuno® HCX
Eshmuno® CPX
Eshmuno® CP-FT
Eshmuno® CPS
Eshmuno® CMX
Fractogel® EMD
SO3 (S) (M)
Fractogel® EMD
SE Hicap (M)
Fractogel® EMD
COO (M)

AEX Media

Eshmuno® Q
Fractogel® EMD
TMAE (S), (M)
Fractogel® EMD
TMAE Hicap (M)
Fractogel® EMD
TMAE Medicap (M)
Fractogel® EMD
DEAE (M)
Fractogel® EMD
DMAE (M)

Single-use Membrane Adsorber

Natrix® Q

Reversed Phase Media

LiChroprep® RP
product range
PharmPrep™
P100 RP-18e
PharmPrep™
P100 RP-8e

Prepacked Columns

MiniChrom
RoboColumn®
HiBar®
OPUS® 5 cm–80 cm
(ID)

Chromatography Columns

QuikScale®
IsoPak™
Vantage®

For additional information, please visit

sigmaaldrich.com/chrom-systems

