Millipore®
Preparation, Separation,
Filtration & Monitoring Products

Data Sheet

BioContinuum™ Buffer Delivery Platform

Biomanufacturing requires large volumes of buffers for downstream processing, which can often be a bottleneck. As processes evolve and intensify, additional focus has been placed on reducing bottlenecks, footprint, and capital expenditures while delivering the right buffers at the right time and specifications.

The BioContinuum™ Buffer Delivery Platform is a configurable offering of buffer concentrates, buffer dilution system, single-use assemblies and services, tailored to provide the highest level of accuracy and precision for absolute certainty in buffer preparation and management. Whether designing a new, low-overhead facility or expanding capacity at an existing facility, the BioContinuum™ Buffer Delivery Platform delivers a competitive edge by reliably supplying process buffers from point of manufacturing to point of use, utilizing a fraction of the resources and facility space.

Key Benefits

- Simplify buffer preparation and management with an integrated offering of buffer concentrates, buffer delivery system, Mobius® MyWay single-use assemblies, and services
- Reduced manufacturing footprint devoted to buffer preparation and management
- Increase speed and flexibility in buffer preparation to meet the needs of evolving manufacturing demands
- Increase operator safety by reduced handling of dry powders
- Integrated quality using Emprove® raw materials, Mobius® MyWay single-use assemblies and robust volumetric dilution control

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Sterile Filtered Buffer Concentrates

From the most common buffers used for mAb manufacturing, twenty-six have been predefined and assessed:

- Emprove® raw materials are used in their preparation to enhance quality, traceability, transparency, and performance.
- Concentrated buffers, with concentration factors up to 50x are available, allowing for significant volume and facility footprint reduction.
- Mobius® MyWay single-use assemblies to safely deliver sterile liquid to your process, your way.
- Concentrates stability data guidance is available in Mobius® single-use bags. Advanced stability studies defined and ongoing. Work with our chemical excellence team for customer stability studies.
- Reusable totes and drums are qualified for use as secondary packaging for the transport of bulk liquids and have undergone ISTA testing, ensuring the safe delivery of the prepared diluted buffer to your process unit.
- Our ready to use buffer concentrates are pre-titrated, minimizing post dilution pH adjustments.

Buffer Dilution System

Designed to streamline buffer preparation in a reduced facility footprint, our Buffer Dilution System allows you to precisely prepare accurate buffers from concentrates, reducing bottlenecks with additional flexibility that meets your timeline, specifications and quality standards.

Advanced metering pumps

The Buffer Dilution System utilizes Lewa Ecodos® metering pumps with Intellidrive® to deliver precise and accurate flow of concentrates and diluent to assure final buffer composition with minimum variability of critical quality attributes such as ionic strength, concentration, pH and conductivity. Robustness of flow control reduces in-process adjustments and facilitates validation.

Dilution factor

The advanced system design and pumps allow for dilution of low conductivity buffers up to 50:1. An accuracy of ≤±1.0% and precision ≤±0.5% is delivered for dilution ratio up to and including 20:1. This enables a single solution to prepare multiple, complex buffers while reducing warehouse space.

System options

Based on your buffer volume requirements, choosing a 17 L/min or 33 L/min Buffer Dilution System provides a wide range of flow rates and dilution capabilities to meet your process needs while minimizing facility footprint and reducing capital investment costs.

Software for Seamless and Intuitive Operation

The software was developed under GAMP 5 guidelines and enables straightforward recipe configuration, system monitoring and trend analysis of critical process parameters.

HMI for informed, real-time decision-making

An interactive touchscreen allows operators to monitor, navigate, and manually operate the system. System information includes communication and alarm status, recipe and operator information, and system device monitoring (flow rate, pressure, pH, conductivity, and temperature). Critical process parameters can be visualized in real-time with an embedded trend plot of key attributes of the dilution process. Navigation to specific software functions such as the alarm table and reporting function are accessed through a navigation bar for quick, easy access. Individual system components are also accessible from the main screen to enable manual operation to facilitate maintenance and troubleshooting.

Data integrity

All system and process parameters are trended in real-time and captured in the Process Information (PI) historian. Access to critical information such as system instrument values and equipment status ensures that the Buffer Dilution System is functioning properly during buffer preparation. Historian infrastructure and archiving ensure data integrity critical to 21 CFR part 11 compliance.

Recipe-driven operation

System operation is controlled by preprogrammed recipes using predefined sequences for all common operations such as system priming, dilution, and cleaning. Configuration of the parameters in a sequence allows creation of recipes that meet specific buffer preparation requirements. There are two levels of recipe status; “Development” status enables configuration and testing prior to locking down a recipe for production, and “Production” status ensuring that no changes are made to recipes used for final buffer production.

Built-in batch reports

Standard batch reports are provided in detailed and simple formats to meet all levels of reporting requirements. A simple report includes sequence and run details, results data, and alarm information. Detailed reports are expanded to include trend data, an events log, and more comprehensive sequence parameter information. A recipe report can also be generated that is useful for recipe transfer.

Record keeping and storage

Data and configuration files are archived in an onboard Historian database for convenient access to copy or transfer for safe, long-term storage.

Buffer Dilution System Configurations

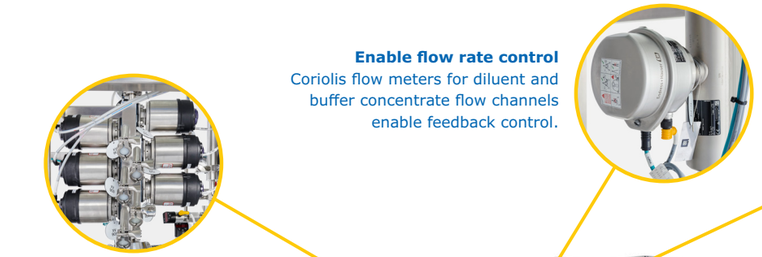
The system is designed to be configured to meet your specific needs. Our experienced team can help you select the options that best address your buffer production challenges.

The Buffer Dilution Base System

Our base system is designed to accept additional configurations to meet your individual buffer requirements. This base system includes:

- advanced metering pumps
- 2 diluent pump inlet valves
- 4 buffer concentrate pump inlet valves
- 1 buffer product outlet valve
- 1 waste valve
- buffer pump air sensor
- pH sensor
- conductivity sensor
- 3 pressure transmitters
- full process control instrumentation
- on-board operator workstation with control and monitoring software

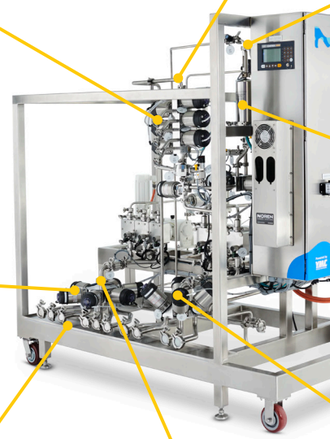
The Buffer Dilution System Options



Automate dispensing with additional outlet valves
Four additional low volume outlet valves enable direct buffer dispensing into hold tanks.

Enable flow rate control
Coriolis flow meters for diluent and buffer concentrate flow channels enable feedback control.

Provide inline mixing
Static mixer provides enhanced mixing of buffer concentrates and diluents.



Increase concentrate flexibility
Add two additional low-volume inlet valves to connect to up to six buffer concentrates for additional speed and efficiency.

Incorporate onboard filtration
A filter housing assembly ensures inline filtration and includes a filter housing, valves (filter inlet, outlet, bypass and vent), pressure transmitter and necessary tubing and fittings.

Prepare your system with CIP manifolds
CIP manifolds designed for easy cleaning of the entire system from inlet valves to outlet valves.

Ensure diluent is available
Addition of an optional diluent air sensor provides confidence that the system has all necessary fluids.

Expand your diluent options
Add two additional diluent valve inlets to expand diluent selection opportunities.

Specifications

Systems	Flow Rate Range L/min		Dilution Range	Operating Pressure	Ambient Temp. Range °C	Process Temp. Range °C	pH Range	Conductivity Range mS/cm	Skid Size (LxWxH)	Materials of Construction
	Inlet concentrate pump	Inlet diluent pump								
Buffer Dilution System 17	0.6 - 9.0	1.2 - 17.0	Up to 50:1	6 bar	4 – 25	4 – 40	2 – 13	0.001 – 500	75 x 45 x 76 in. (191 x 114 x 193 cm)	316 L stainless steel, EPDM, PVDF, and PTFE
Buffer Dilution System 33	1.2 - 17.0	2.2 - 33.0							75 x 45 x 92 in. (191 x 114 x 234 cm)	

Mobius® MyWay Single-Use Assemblies

The Mobius® MyWay program is a 3-tiered design and delivery program, developed to help drug manufacturers implement flexible manufacturing with greater speed and enhanced supply security. Rather than selling pre-configured standard designs that may not meet your needs, we have developed a program in which you have the flexibility to choose your configuration, as well as your delivery speed, based on your manufacturing needs. This allows you to cut the traditional lead time of 12 - 14 weeks down to as little as 24 hours.

Mobius® Stock (24 hrs.)

- Standard off-the-shelf assemblies
- High-volume custom assemblies with monitored raw material and finished-good supply levels

Mobius® Select (6 wks.)

- Configure-to-order assemblies from an optimized and pre-qualified component library
- The perfect balance of off-the-shelf speed and custom flexibility
- Monitored component supply levels for reliable delivery dates
- Comprehensive documentation for fast and easy implementation

Mobius® Choice (12-14 wks.)

- Highly customized solutions from our expansive component library, shipped in standard lead times
- Designs for critical and complex applications backed by our technical and engineering expertise

The Emprove® Program

Your fast track through regulatory challenges

The Emprove® Program provides three types of dossiers to support different stages of development and manufacturing operations such as qualification, risk assessment and process optimization. The dossiers consolidate comprehensive product-specific testing data, quality statements and regulatory information in a readily-available format to simplify your compliance needs.

Buffer Delivery System Services

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 unique intimate knowledge of our equipment backed by years of experience.

Service Offerings

- Factory acceptance test (FAT)
- Site acceptance test (SAT)
- Installation qualification/operational qualification (IQ/OQ)
- Performance qualification support (PQ)
- Operator & software training
- Preventive maintenance (PM)
- Corrective maintenance (CM)

Benefits

- Support regulatory compliance
- Enable smooth, successful, and efficient system implementation and integration
- Increase system efficiency and reliability
- Receive direct access to spare parts
- Training to ensure that your team can operate and troubleshoot the system
- Focus your attention on your core business

Qualification Services

Our qualification services, based on standardized risk assessment approach, are designed to make the integration of our system into your process as seamless as possible.

Factory Acceptance Test (FAT)

Duration: 3 days

Service equipment is fully tested for compliance with your technical and quality specifications – prior to delivery – to ensure acceptance of the equipment before it arrives at your site. Performing a FAT will also yield test reports that can be used throughout the remaining SAT and IQ/OQ qualification stages. The FAT includes protocol writing and execution.

Includes

- Review of executed release tests
- Visual inspection
- Mechanical, electrical & automation tests
- Completion of system documentation

Site Acceptance Test (SAT)

Duration: 3 days (SAT and IQ/OQ are performed together)

SAT and IQ/OQ are complementary services. They are performed together and cannot be ordered separately.

Serves to clearly demonstrate that performance and functionality of the system were not impacted by the transport and installation of the system on-site and that the system is ready for IQ/OQ.

Installation Qualification/Operational Qualification (IQ/OQ)

Duration: 3 days (SAT and IQ/OQ are performed together)

Ensures your system is fully documented, operational, compliant with regulatory requirements, and ready for Performance Qualification.

Includes

- Completion of as-built system documentation
- Visual inspection
- Mechanical, electrical & functional tests
- Instrumentation verification

Performance Qualification Support (PQ)

Our biomanufacturing engineers will provide you with on-site support to assist you while you perform your qualification with preparation of the equipment, dry run of your process recipe, and assistance during a real run.

Training Services

Appropriate training for users is not only a cGMP requirement, it also ensures your staff has the knowledge and expertise to operate and manage the system as part of your manufacturing process. It represents substantial time and cost savings.

Operator & Software Training

Duration: 1-2 days

cGMPs require that operators are trained on new equipment and must provide documentation of that training. Our operator training is designed for pharmaceutical and biotechnology manufacturing personnel operating upstream and downstream processing equipment. Hands-on sessions are designed to satisfy cGMP requirements and course graduates receive a certificate upon completion.

Includes

- Theoretical session: overall design, P&ID, and components identification
  - Familiarization with UI features, controls, user setpoints, analog data and alarms
  - Configuring, downloading and running pre-defined recipes
  - New recipe creation and recipe archival feature
  - Batch data and Reporting features
  - 21 CFR part 11 compliance (audit trail, security, electronic signature,..)
- Hands-on session: practice on the system
- Q&A session
- Assessment and correction
- Certificate of attendance

Maintenance & Repair 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.

Preventive Maintenance (PM)

Duration: 2 days

Frequent and routine maintenance is the most cost-effective and critical component to ensuring long-lasting performance of your system. Regular maintenance reduces repair costs, increases uptime, and is a cGMP requirement. During our maintenance visit, certified engineers will verify your equipment using established protocols to ensure documented compliance with quality requirements. Components subject to wear and tear will be replaced (with parts to be purchased separately).

Upon completion of the service, a full report of the services performed and maintenance recommendations will be provided to ensure proper operation and that the validated state of the process is maintained.

Includes

- Initial equipment status recording
- Visual inspection
- Functional checks
- Performance tests
- Parts replacement (parts to be purchased separately)
- Service report

Corrective Maintenance (CM)

In the unlikely case your system does experience a problem, our engineers will provide on-site 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.

Documentation

Mobius® 2D and 3D assemblies and storage systems, DS4579EN00

For additional information

please visit **MerckMillipore.com/Buffer-Delivery**

To place an order or receive technical assistance

please visit **MerckMillipore.com/contactPS**

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