

YMC EcoPrime® Buffer In-line Dilution (BID) - FAQ's

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Q. Where is YMC's EcoPrime BID system used?

A. EcoPrime BID, either in a standalone skid or integrated with LPLC, is used in downstream processing of biopharmaceuticals where large amounts of dilute buffer is required. These systems generate point-of-use buffers from buffer concentrates.

Q. What are the process benefits of YMC's EcoPrime BID platform?

A. EcoPrime BID provides the following process benefits:

- Smaller tanks, less footprint, reduced CIP volume and waste, leaner operation
- Less operator exposure to potential chemical hazards
- Reduced labor costs for buffer preparation
- Reproducible and accurate buffer compositions are achieved with dilution based on volumetric flow control
- Enables single use (concentrates in bags) increasing process scheduling flexibility
- Automation provides simplified documentation facilitating validation

Q. How is the system used, standalone or integrated with the facility tank farm?

A. YMC can supply either standalone systems that serve one or more downstream unit operations for point-of-use buffer dilution or can engineer integrated systems servicing a plant wide system or central tank farm.

Q. Which buffers are suitable for an EcoPrime BID system?

A. Any buffer concentrate that is compatible with 316L stainless steel, EPDM and PTFE. This encompasses all buffers typically used in the downstream processing of biopharmaceuticals.

Q. How standardized/off-the-shelf is the EcoPrime BID system?

A. If incorporated into a chromatography system, we have a standard product for up to 33 LPM. We can easily increase the flow capacity and design a system for up to 66 LPM based on the standard platform design.

For stand-alone BID systems, our design philosophy is to use the same components and global suppliers as are used for our standard chromatography systems wherever possible. All components (sensors, controllers...) are standard, off-the-shelf components generally accessible in all geographies.

Q. Do you have systems that are used for commercial pharmaceutical production?

A. Yes, we have designed and manufactured a number of systems to meet a variety of customer needs. We have built and installed systems going back as far as early 1990's.

Q. What is the footprint of the system?

A. The overall footprint will depend on the capacity and functional requirements of the system. The size of the system also depends on the buffer preparation strategy, is the system dedicated to one unit operation or is it for a complete downstream process with multiple unit operations?

- Our smaller skids are approximately (LxWxH) 1.5 x 1 x 1.5 meters (60 x 40 x 60 inches).
- Our largest buffer prep skid was approximately (LxWxH) 5 x 6 x 5 meters (16.5 x 20 x 16.5 feet).
- Our smallest EcoPrime LPLC system with integrated buffer inline dilution is (LxWxH) 1.8 x 0.9 x 2.0 meters (70 x 35 x 80 inches).

Q. How many buffer concentrates feed into the system as the same time?

A. EcoPrime BID base system has 4 inlets on the buffer concentrate pump and 2 inlets on the diluent/WFI pump with the option to add two more inlets to each pump.

YMC has developed in-line buffer systems with as many as five pumps and multiple inlet valves that allows for preparation of sophisticated buffer solutions. We have manufactured a BID system that prepares up to seven point-of-use buffers required for a complete downstream operation.

Q. How many buffers can be prepared at the same time?

A. Our systems produce one buffer at a time. Basic systems dilute one buffer concentrate while more complex, custom systems can be designed to handle more concentrates and blend two concentrates with WFI simultaneously.

Q. How are the stock solutions fed into the system?

A. Using appropriate tubing or hoses with an internal diameter equal to or larger than the inlet size of the pump (pump size is capacity dependent) with positive net pressure (10 - 25 psi, 0.7 – 1.7 bar) to avoid pump cavitation. Connections to the system are made with sanitary tri-clamps.

Q. How is mixing performed on the system?

A. YMC's proprietary hydraulic design, developed by modeling numerous configurations, delivers a flow path with sufficient mixing, less cross-channel interferences and lower volumetric pulsation. An optional static mixer can also be added to the system.

Q. What is the percentage of rejection of buffers when mixing a new buffer?

A. The amount of buffer rejected or sent to waste at the beginning of each new concentration is dependent on the flow rate and hold-up volume of the system. Typically, this is a very minimal amount as compared to the entire batch.

Q. How does the transition between one point-of-use buffer to another buffer happen?

A. A CIP solution adequate for cleaning is selected and flushed through the system until a pre-defined cleaning endpoint is reached. The endpoint can be based on either pH or conductivity measurement or volumetric flow. The system can then be programmed to begin a recipe to prepare the next buffer.

Q. What is the control strategy?

A. There are two primary control strategies that can be employed; volumetric flow control and pH or conductivity control.

YMC recommends volumetric flow control with pH and/or conductivity monitoring. Volumetric flow control to blend buffer constituents provides superior, reproducible buffer composition and accurate dilution because flow control is less prone to measurement drift than chemical sensors such as pH and conductivity. In addition, pH and conductivity require more frequent calibration.

The system is also capable of pH and/or conductivity control to adjust the flow rate of the buffer concentrate or diluent based on pre-defined pH/conductivity set points. This method is not our recommendation for primary control of the dilution process due to the delay in feedback control and potential for these devices to drift over time.

LEWA's ecodos® pumps with state-of-the art digital servo motors, used in EcoPrime LPLC and BID systems, deliver flow rate variation of $\leq 1\%$ across the pump flow rate range ensuring accurate volumetric flow control for buffer dilution.

Q. What dilution accuracy can be expected?

A. EcoPrime systems with ecodos metering pumps enables dilution factors up to 50 to 1 with volumetric flow error of less than 1% at the mid to high flow rate range of the skid.

Q. How is the system controlled? What is the automation/software platform?

A. EcoPrime systems are controlled using a PLC with an industrial PC-based HMI as the interface and data acquisition device and is built on Rockwell FactoryTalk® View SE. An information-rich, graphical interface displays system information and status. The software includes pre-programmed sequences for operations such as priming, dilution, system flushing minimizing operator programming errors. The user builds recipes using sequences to perform their specific operations. The system provides recipe management with access control and an audit trail for recipe modification to support 21 CFR Part 11 compliance.

Q. Our facility uses DeltaV. Is it possible to use DeltaV?

A. Yes, our EcoPrime system are frequently interfaced with and controlled with DeltaV. The user can link the system PLC to a central DeltaV DCS. This allows the user to view system operation from a remote location and continuously or intermittently download data generated by the system but not directly control the system. Alternatively, YMC can work with you to develop a complete DeltaV control solution that meets your specific needs.

Q. What information does YMC need to prepare a proposal for a BID system?

A. The following information is required:

- Will the buffer system deliver to a single unit operation or multiple unit operations?
- What are the buffers? What is the capacity of each point-of-use buffer?
- Is there a maximum time to make up each buffer? Rate of buffer consumption? Liters per hour?
- What are the critical process parameters (accuracy to pH, conductivity, ionic composition...)?
- For CIP consideration, what is the frequency of CIP, by campaign, by schedule, or by production volume?
- Describe the method used to verify buffer concentrate accuracy.

Note: No solid buffer components are allowed.

Q. Does YMC have a tool for modeling total cost of ownership of the BID systems?

A. YMC does not have an automated tool for calculation of cost of ownership. Commercially available modeling tools such as BioSolve™ Software from Biopharm Services are available. We have provided Biopharm Services with the cost information for our hardware for use with the BioSolve Software.

It is difficult to model and compare the cost of ownership without a thorough understanding of the facility's operating procedures. For example, there are often SOPs, equipment, QC, and WFI generation, etc. in place that must factor into the model for reliable estimates of total cost of ownership.

Q. Why should I consider YMC for BID?

A. YMC maintains a strong relations with LEWA, the original manufacturer of arguably the world's most accurate and reliable metering pump. Over 14,000 of these pumps have been in service on chromatography and buffer in-line dilution skids over the past 30 years. As the heart of any metering / blending system, the pump drives the accuracy and precision of any BID system. With over 15 years in the design and manufacturing of bioprocessing equipment, YMC Process Technologies understands how to best manage blending critical streams. As a GMP systems manufacturer, we have the most integrated supply chain of any buffer dilution system manufacturer. This adds up to a superior solution for our customers in technology, quality control and economy.

The future provides broader solutions for our customers

The innovation and growth of this and other EcoPrime product lines has attracted the attention of leading technology suppliers and users. YMC Co., Ltd. assumed all rights and production for the EcoPrime suite of systems in late 2018 from LEWA-Nikkiso America, Inc. This acquisition brings a broad spectrum of chromatographic resins, and columns ideal for large and small molecule purification. More about this new chapter for EcoPrime at www.ymcpt.com.

Ordering information To order the EcoPrime BID system, please contact your regional sales representative.

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