YMC EcoPrime Twin LPLC Platform - FAQ's

Click on any question below to be taken to the answer.

Q. For what applications is the EcoPrime Twin LPLC system best suited?

A. EcoPrime Twin LPLC is uniquely designed to perform continuous capture chromatography, traditional batch processes, and sequential chromatography steps (capture – polish, polish – polish). These modes of operation can be coupled with in-line buffer dilution for further flexibility. Substantial productivity gains are realized by using multi-column chromatography to purify product on a continuous or semi-continuous basis.

Q. There are a number of different terms that are used for multi-column chromatography, 2-PCC, 3-PCC, 4-PCC and CaptureSMB. What do these terms mean?

A. CaptureSMB is a term used by ChromaCon and YMC to describe ChromaCon's approach to 2-column Periodic Counter-Current Chromatography (PCC). Other suppliers provide systems that perform continuous chromatography with three- or four-column Periodic Counter-Current Chromatography (3-PCC, 4-PCC). Some systems employ even more columns and significantly more complicated valve arrangements.

Q. Can I use my chromatography media (resin) and columns of choice on your system?

A. Yes! The system can accept most any column or resin. We are available to provide observations on general characteristics of chromatography media and columns that leverage the EcoPrime Twin design to it's fullest.

Q. How will an EcoPrime Twin LPLC (multi-column) system meet my needs for continuous chromatography?

A. EcoPrime Twin LPLC is a simple but advanced design for multi-column chromatography. It is most applicable to those:

- Who value significant productivity gains delivered by multi-column systems but are concerned with the ever greater system and validation complexity of 3, 4, 5 or more column systems
- With pilot scale, continuous process development projects, who also want a platform that is ready for expansion to full GMP production scale
- With limited space who would benefit from having 1 unit with multiple functional capabilities
- Looking to reduce buffer volumes and the associated space for containers and bags by employing in-line dilution (optional)
- Who need the flexibility for both batch and continuous operation on the same system

Q. What benefits can I expect from the new EcoPrime Twin LPLC?

A.

- Up to 3x productivity gain or up to 50% reduction in Protein A use for a typical capture process
- Advanced simplicity with the 2-column EcoPrime Twin system that accelerates validation, simplifies maintenance, and minimizes downtime and operating expenses
- Consistent and accurate scale up of processes from analytical bench PCC (periodic counter-current chromatography) systems such as the Contichrom® CUBE from ChromaCon®
- Space and cost savings with a compact design and continuous and batch capability with one system
- Reliable uptime, based on proven pump technology with over 10,000 pumping units in chromatography systems since the 1980's

- Lower operating costs and buffer storage space with the on-board in-line buffer dilution (optional)
- Capability for additional functionality, sequential processing (capture/polish, polish/polish)

Q. Does the EcoPrime Twin LPLC platform have a reference history?

A. EcoPrime Twin 100 has been employed on actual mAb streams with great success.

A recent joint publication by Bristol Myers Squibb, ChromaCon, and YMC (formerly LEWA), *Scale-Up of Twin-Column Periodic Counter-Current Chromatography for MAb Purification*, reports on the successful scale-up from lab to pilot scale by 100x for capture of a Mab from clarified cell culture harvest with comparable process performance and critical quality attributes. The pilot scale work was performed on EcoPrime Twin whereas the lab-scale development was done with Contichrom CUBE.
http://bpi.bioprocessintl.com/scale-up-of-twin-column-periodic-counter-current-chromatography-for-monoclonal-antibody-purification

Q. What is the dynamic range of the EcoPrime Twin LPLC platform?

A. EcoPrime Twin LPLC systems have a wide flow range permitting the use of a wide range of column diameters on the same system.

- EcoPrime Twin 100 has a flow rate range of 0.004 – 0.60 L/min and accommodates column IDs of 2.5 – 10 cm.
- EcoPrime Twin 250 has a flow rate range of 0.02 – 3.0 L/min and accommodates column IDs of 5 – 20 cm.
- EcoPrime Twin 500 has a flow rate range of 0.006 – 10.0 L/min and accommodates column IDs of 8 – 45 cm.

Q. Is there a scale-up, scale-down system analog to the EcoPrime Twin?

A. Yes. We have modeled our EcoPrime Twin on the capture feature designed into the Contichrom® CUBE system by ChromaCon AG. The Twin provides seamless scale up from the Contichrom CUBE with a simple Microsoft® Excel®-based tool to translate results from one system to the other. For more information on the CUBE follow this link: Contichrom Cube

Q. Are the key components in the EcoPrime Twin LPLC easy to maintain or replace?

A. Yes. Our engineering team took pains to design the unit for maximum serviceability focusing on accessibility of components and minimizing downtime without compromising performance. A 2-column system is significantly less complex when compared to systems with more columns and therefore requires less maintenance and costly downtime. Following the recommended maintenance schedules will significantly minimize unscheduled downtime risk. Should a key component fail, it can be easily swapped out.

Q. What monitoring capabilities are available on the EcoPrime Twin LPLC?

A. Post-column pH, conductivity, and UV (dual wavelength, 280 nm and 313 nm) sensors are used to monitor the chromatographic process. Flow meters, air sensors, and pressure sensors monitor the operation of the system and can be configured to alarm should operating parameters exceed pre-set limits.

Q. What is integrated Buffer In-line Dilution (BID)?

A. The integrated BID option adds a 3rd pump to enable the ability to dilute concentrated buffers that can then be used directly in the chromatographic steps. Combining two unit operations, 2-PCC chromatography and in-line buffer dilution on the same system, reduces buffer tank footprint, frees up space in the plant, and lowers operating expense.

Q. What is sequential processing?

A. Sequential processing refers to performing two different and connected chromatography steps continuously without a hold step between the two steps. The two steps could be capture followed by a polishing step or two different polishing steps, for cation exchange or HIC followed by anion exchange chromatography. Dilution or buffer modification between the two steps is accomplished with the addition of a 3rd pump.

Q. Is the base system set up to run steam-in-place (SIP)?

A. No, but SIP is possible with our customized systems. Sanitization with 0.5 to 1N NaOH is accepted practice and can be easily performed with the clean-in-place (CIP) system manifolds. The CIP manifolds include inlets and outlets for easy hook up to facility tanks and drains and we include software to automate the process.

Q. Is the system CE compliant?

A. Yes. The EcoPrime platform systems comply with 2006/42/EC Machinery Directive, 2014/30/EC Electromagnetic Compatibility Directive, and 2014/35/EC Low Voltage Directive.

Q. What is the system automation platform?

A. EcoPrime Twin LPLC system uses PLC software to control the chromatography process, to acquire data and to provide historical trending. The system software, based on Rockwell FactoryTalk® View, provides user configurable control of all chromatographic parameters. The software runs on an industrial PC-based HMI with an information-rich, graphical interface that displays system and process information as well as historical trends putting relevant information in one place to enable efficient and informed decision-making. The system provides recipe management and full audit trail. Batch reports, in several formats, are easily generated.

DeltaV options are available as custom installations.

Q. Is the system designed to enable 21 CFR Part 11 compliance?

A. Yes. The EcoPrime LPLC platform systems are designed to enable compliance to 21 CFR Part 11.

The platform also enables users to comply with Good Manufacturing Practices (GMP) as defined by the Food & Drug Administration (FDA) with regulations 21 CFR Parts 210 and 211 that include requirements for master production and control records and batch records.

Q. Is it possible to have a demonstration of the EcoPrime Twin software?

A. Yes. We have demo software that can be presented by EcoPrime Sales Specialists via an internet connection.

Q. Is remote software support available?

A. A VPN is built in (included) but accessible only if the customer enables access on their end. When enabled by the customer, this feature allows YMC experts to remotely diagnose, troubleshoot and update software.

Q. Is a User Guide for the EcoPrime LPLC Twin available?

A. Yes. A manual that guides the user in all aspects of set up, safe operation and maintenance is included as part of a comprehensive turn over package (TOP) and conforms to the requirements of the EU Machine Directive for CE marking. The manuals for OEM equipment used in the system such as the flow meters and analytical sensors are included in the TOP.

Q. Is a Factory Acceptance Test (FAT) available?

A. Yes. FAT is available. This extensive series of wet and dry challenge tests demonstrates the system's functionality claims. An FAT is typically defined and attended by our customer and can take up to 5 days depending on the complexity of the system. An FAT can be purchased by the customer as an option.

Q. What is the approximate size of the system? Will it fit through my door?

A. Our models are designed to pass through hallways, elevators and doors that are appropriate to that scale of equipment. For instance, EcoPrime Twin 100 system which is likely to be used for process development in a laboratory environment is sized to fit most standard single doors and lab hallways (35" or 90 cm). Our pilot and production size units are bigger, and will fit most double doors and manufacturing access ways (e.g. freight elevators).

Q. What other considerations should I think of when designing my process for multi-column systems?

A. To extract optimum performance from a multi-column system, we caution users to think carefully about incorporating SOP's common on a traditional batch set up. The high productivity that users can achieve with multi-column systems don't seamlessly accommodate adoption of some traditional batch system operational conventions without some impact. The bubble trap is an example of a component that has minimal productivity impact in conventional batch system which are not as sensitive to hold-up. Therefore, we recommend users consult with the experts at YMC when contemplating multi-column installations.

Q. Can a system have both continuous capture and MCSGP (Multi-Column Solvent Gradient Purification) on the same skid?

A. No. While the Contichrom CUBE instrument has both functionalities in a combined package, these unit operations are available only as independent skids from YMC. At process scales, there are design, safety and environmental considerations that prevent combining continuous capture and MCSGP on the same skid.

YMC has elected to design both units in the most simple, stand-alone formats to minimize risk when implementing the technology in manufacturing. Qualification and operation in a manufacturing environment is not a concern with the bench-top Contichrom CUBE system.

Q. Are demo / rental systems available?

A. Yes. A limited fleet of demo / rental systems are available in the US and EU in 2017. Please contact your regional YMC Sales Specialist for more information.

Q. What is the lead time of the EcoPrime Twin LPLC?

A. The estimated lead time from issuance of purchase order to shipment for the capture version of the EcoPrime Twin 100 is 25 – 30 weeks. Addition of buffer in-line dilution (BID) and functionality for sequential processing can add 10 to 16 weeks. Larger capacity units would be slightly longer. Of course, these lead time estimates can varying depending on the number of orders being processed.

Q. I want a quote for an EcoPrime Twin LPLC continuous capture system. How long does it take?

A. Budgetary numbers are generally available in one business day. For the smaller scale EP 100, 250 and EP 500, a proposal can be generated in 8 - 10 days. Quotes for larger systems and multiple systems may take a few days longer.

Q. What is the price of EcoPrime Twin LPLC?

A. Price will be more than the standard EcoPrime (batch or single column) LPLC systems due to the additional hardware, software and 2 PCC license. In addition, this system runs both batch *and* continuous processes furthering the value of this system. With the productivity gains that are achieved, customers can expect a very favorable ROI. Unlike other multi-column systems, there are no components that require replacement after every use and the EcoPrime Twin only requires two columns versus 4 or more in other continuous systems.

Q. I have never heard of YMC Process Technologies in the context of chromatography. Are you new to this application?

A. Formerly we were LEWA Process Technologies (acquired by YMC in 2018). This Devens, MA USA based company has been in business since 2000 and supplied GMP scale chromatography system throughout the world. You can learn more about us and our history at www.ymcpt.com.

Q. Why doesn't the base EcoPrime Twin LPLC include a bubble trap?

A. YMC Process Technologies group recommends avoiding the use of a bubble trap in a multi-column process. We have found that with proper design, the system can operate quite well without a bubble trap. The EcoPrime Twin system has in-line air sensors before the pumps and before the columns. The air sensors will alarm if air enters the system protecting both the pumps (cavitation) and media in packed columns.

While a bubble trap is often used in a conventional chromatography set up, multi-column continuous chromatography systems are advanced designs with some specific operational considerations; system hold-up volume being one such consideration. Unnecessary hold-up volumes (such as the volume of a bubble trap) can influence the process performance, for example by degrading the enhanced accuracy afforded by fast-acting valves that are important to timely multi-column switching. Also, the additional hold-up volume will require larger system purge volumes that will reduce process productivity.

Ways to reduce the risk of air intrusion include:

- Optimize feed tank mixers to use minimum agitation reducing the possibility of entraining air.
- Design feed delivery system to provide a flooded inlet at all times.
- Ensure that all feed line fittings are tight.
- Install YMC recommended feed line sizes to the inlet valves and avoid unnecessary line ID changes that result in air bubble formation due to pressure changes in micro environments.
- Install YMC recommended line sizes to the chromatography columns.

With proper design, systems can operate quite well without bubble traps.

Q. Why doesn't the base EcoPrime Twin LPLC include an in-line pre-filter as a standard option?

A. In preparing continuous systems for optimum performance, we caution users to think carefully about incorporating in-line, high pressure side filters. YMC does offer a dual, parallel path filter scheme as an option for those customers who require this component and can tolerate the concerns noted below.

In addition to concerns about hold-up volume noted in the bubble trap response above, continuous production run times raise the probability of plugging the filter prior to the end of the run. This would result in having to stop the system, open the system and restart the process. Stopping and/or opening the system is not desirable in a continuous operation for obvious reasons.

Alternatively, a duplex filter could be installed allowing the in-process change of an exhausted filter. This eliminates concerns over stopping the process for filter change-out may but still result in opening the flow channel to the environment to install the back-up / parallel filter cartridge.

If buffer and/or feed filtration is required, it is recommended that pre-filters be installed by the user on the low pressure side of the pumps. These filters can be easily specified for the process requirements and can facilitate continuous operation by allowing the installation of parallel filters, especially for the feed flow path. For buffers, another option is to pre-filter the buffer prior to use on the system.

More questions? Ask us! ecoprime@YMCpt.com

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 Twin LPLC system, please contact your regional sales representative.

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