LEWA EcoPrime Twin LPLC Platform - FAQ's

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Q. For what specific application is the EcoPrime Twin LPLC system suited?

A. EcoPrime Twin LPLC is uniquely designed for capture chromatography steps. Substantial productivity gains are realized by using multi-column chromatography to process streams on a semi-continuous or continuous basis. LEWA can also provide 2-PCC technology for the polishing step on a case specific basis.

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

A. Yes! We are not a media or column supplier so we have no business incentive to guide you to a specific media. We are available to provide observations on general characteristics of medias that leverage the EcoPrime Twin design to it's fullest.

Q. Will an EcoPrime Twin LPLC (multi-column) system meet my needs?

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

- Who value significant productivity gains allowed 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 a range of 2 conventional skids
- 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 90% 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 single unit flow range that is equivalent to 2 conventional skids
- Lower opex and tank space with the on-board in-line buffer dilution (optional)
- Reliable uptime, based on proven pump technology with over 10,000 pumping units in chromatography systems since the 1980's

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 recommended flow rate range of 0.033 – 0.524 L/min and accommodates column IDs of 2.5 – 10 cm.
- EcoPrime Twin 250 has a recommended flow rate range of 0.131 – 2.09 L/min and accommodates column IDs of 5 – 20 cm.
- EcoPrime Twin 500 has a recommended flow rate range of 0.295 – 10.6 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. Other bench units also provide data that can be scaled to the EcoPrime Twin. For more information on the Contichrom CUBE: www.chromacon.ch

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

A. LEWA recommends avoiding 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 does have multiple in-line air sensors. The air sensors will alarm if excess 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 unique operational considerations; system hold-up volume being one such consideration. Unnecessary hold-up volumes (such as the bubble trap) may 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.

LEWA can offer a bubble trap as an option for those customers who require this component and can tolerate potential performance degradation.

Ways to reduce air entrainment include:

- Optimizing feed tank mixers to minimum agitation required and thus minimizing 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 LEWA recommended feed lines sizes to the pump inlet valves and avoid unnecessary line ID changes that result in air bubble formation due to pressure changes in micro environments
- Install LEWA 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?

A. In preparing continuous systems for optimum performance, we caution users to think carefully about incorporating in-line, high pressure side filters. LEWA 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 but still results 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.

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

A. The enhanced 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. Is the system set up to run steam-in-place (SIP)?

A. No. SIP is only possible with our custom systems. Sanitization with 0.5 to 1N NaOH is accepted practice and can be easily performed with the clean-in-place (CIP) system option. The CIP option includes manifolds with 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 2006/95/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 a 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. The software can generate system documentation such as Alarm Tables and I/O and Interlock Lists to facilitate system qualification.

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

A. EcoPrime Twin 100 has been employed on actual mAb streams with great success. These programs are confidential so results are not public, however we have carried out testing at an academic 3rd party site where results are in the process of being published. This technology was built on the ChromaCon AG patented approach which has been operating successfully for many years at the benchtop level. Further, the Twin system was modeled in great part on the very successful platform of EcoPrime LPLC which has been in the market for some time now and has installations throughout the world.

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. For the EcoPrime Twin Platform, we will perform a functional release test that is similar to a Factory Acceptance Test but abbreviated since the product is standardized and aspects of the design were verified as part of the development process. We provide a certificate to the customer that indicates each unit passed the functional release test. 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. 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 LEWA 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 22 to 26 weeks. Addition of buffer in-line dilution (BID) and functionality for integrated processing can add 10 to 16 weeks. Larger capacity units would be slightly longer. For 2-PCC technology for the polishing step, the system lead time can be up to 38 weeks. 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 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 7 - 9 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 LPLC systems due to the additional hardware, software and 2 PCC license. In addition, this system runs both batch *and* continuous processes with a flow range 2X that of conventional systems furthering the value of this system. With 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 2 columns versus 4 or more in other continuous systems.

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

A. LEWA has supplied over 14,000 pumps to chromatography systems since the late 1980's. We are a key component to the vast majority of the leading LPLC systems supplied over the past 4 decades. Additionally, we have built many chromatography systems based on customer provided specifications over the 30 years. Our recent acquisition by Nikkiso Co Ltd provides additional global presence and financial strength. We are part of a $1.4B US global company with a 50 year history!

Q. Are there other considerations in designing 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 take all care to consult with the experts at LEWA when contemplating multi-column installations.

Q. Can a system have both CaptureSMB and MCSGP 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 LEWA. A few of the consideration making these available as separate unit operations for CaptureSMB and MCSGP GMP applications:

- The added complexity in components and piping to support MCSGP (a 4 pump system) on top of the more streamline (2 pump) CaptureSMB adds risk to GMP validation.

- Most users will prefer to have unit operations that are independent of each other in a “continuous” production environment.
- Change control of software is made more cumbersome with novel steps that are at different stages of design maturity.
- The license for each of the patented technologies has slightly different terms, potentially restricting some use.
- More piping and components for MCSGP complicates the CIP on a more straightforward CaptureSMB system.
- Cost of combining the two modes on a single platform is likely less economic than two separate skids, and lengthen the lead times, FAT and IQOQ.

In conclusion, LEWA has elected to keep both units to the most simple, stand-alone format to minimize risk that is not as sensitive in non-GMP bench top discovery equipment.

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