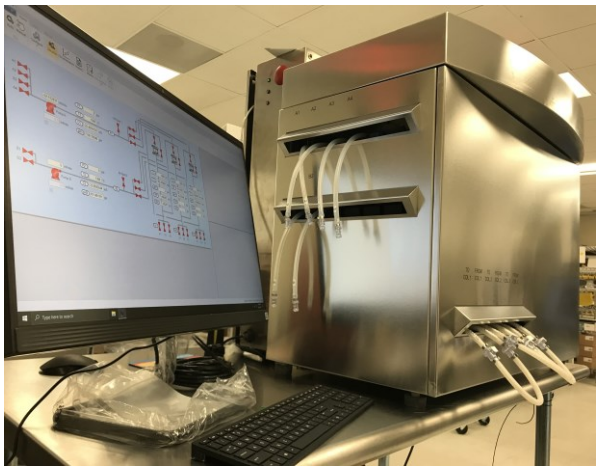
# QuantaSep® Fusion CC Elite 300

## A 3 Column Continuous Capture Systems with In-Line Buffer Blending with exchangeable (single-use) flowpaths

**The QuantaSep Fusion CC Elite 300 is a fully integrated Process Chromatography Continuous Capture plus Buffer making skid** capable of a flow rate range of 0 ml/min to 300 ml/min. Sepragen QuantaSep Continuous Chromatography System is designed to automate the purification of biopharmaceuticals in a laboratory environment. High precision hardware is combined with the most powerful and flexible software to run and control either manually or via a pre-defined protocol; a continuous chromatographic run using multiple columns. In addition, the user has immediate insight into the chromatographic process.

The integrated Tri-Column Continuous chromatography system enables continuous chromatography to be performed by enabling two simultaneous continuous processes, loading and non-load to be performed simultaneously, so harvest is always being loaded while at the same time the product is also being eluted. The way this is done is Harvest is pumped on to the first column while the "flow-through" from this column is directed through the second column while contemporaneously the "non-load steps" i.e. wash, elution regeneration and equilibration buffers are pumped through the third column. Once loaded to maximum capacity, the first column passes into non-Load phase (wash, elute, regenerate, equilibrate) and product is eluted out of the first column. Column 2 in turn becomes the "leader" column in the "load" step and "flow-through" from column 2 is now directed to column 3 which becomes the "follower" column for loading. The cycle then repeats.



The QuantaSep® Tri-Column Continuous Chromatography Capture System is an integrated compact process chromatography system capable of providing flow ranges of 0-100 ml/min and 0-300 mL/min. Either of the two sizes of flow-paths (which comes pre-assembled) can be installed in the system easily within 30 minutes. The system has capabilities of (1) Running chromatography functions on 3 sequential and alternating capture columns in such a way that continuous feed is maintained, (2) Producing Buffers from stock acid and Base concentrated buffer components, Salt and water and (3) Being used in multi-product campaigns by exchanging product contact flow path. The Buffer making functions include enabling use of different recipes of buffers made from a combination of each of the four fluid components.

- ✓ Continuous Production 24/7 Now!
- ✓ Improve Process Economics
- ✓ Increase Plant throughput
- ✓ Increase Resin Utilization
- ✓ Eliminate Buffer Prep
- ✓ No Cleaning Validation
- ✓ Reduce Space & FTE's
- ✓ Multi-product production with little downtime

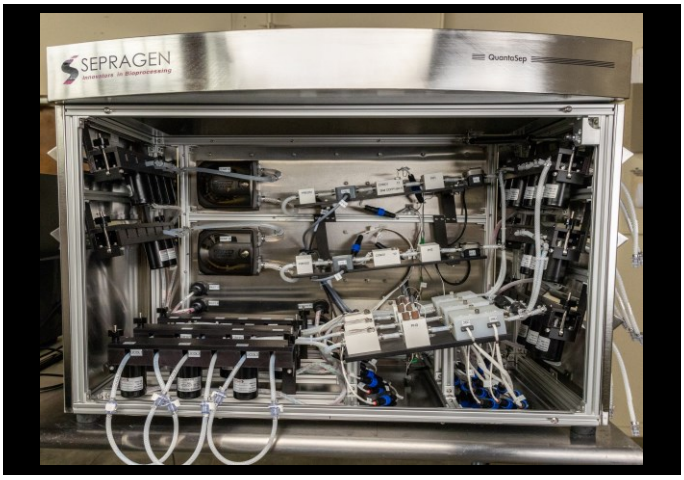
# The QuantaSep® Fusion CC Elite 300 Hardware

The Fusion CC Elite 300 is composed of the fluid handling module and the electronic module integrated into a single unit. The fluid handling module contains all the fluid handling components such as Pumps, valves, sensors and interconnecting tubing. The Control and Electronic module contain the PLC, I/O modules, power supplies, transmitters etc. The Fusion Elite 300 is compatible with 1M NaOH and 20% alcohol for CIP operations and is operable at 40C for cold room processing. The fluid flow path is mounted inside an enclosed stainless steel cabinet with a trough to which a leak detector is attached to prevent any loss of your sample.

The Industrial computer on which the SCADA based control software resides and controls the Instrument via a PLC can be operated from a distance to provide for remote control. The software operates in a MS Windows environment and is 21CFR11 compliant.

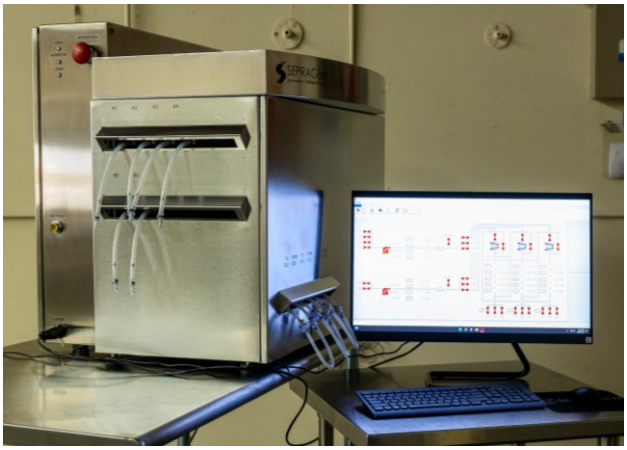
## Removable Flowpath

The flowpath of this system is designed for easy removal. This eliminates the need for cleaning validation. Issues related to cross-contamination in switching columns or products are substantially minimized when the flowpath can simply be replaced. Pinch valves and peristaltic pumps enable easy changing of the pre-fabricated tubing assembly along with the integrated sensor block, which can be easily removed and replaced as well.




## Controls Module

The controls module contains all power supplies, transformers, valve activation pneumatics, brainboards, sensor controls and circuit boards, alarm controls, sensor electronics including A/D and D/A converters, and fuse assembly. The external chart recorder interface, status LED's, an emergency stop switch, cables, computer interface, fuse blocks, etc. are included as well.



## The Hardware

The entire flow path, i.e. peristaltic pumps, with ultrasonic flowmeters, electrically-actuated pinch valves, sensors, and tubing are housed in an open stainless steel compartment with an intrinsic leak sensor. All frames and brackets are made of anodized aluminum. The fluid compartment is isolated from the Power and the Control and has easy access for operation use such as preventative maintenance and/or flow path change-over.

**Skid Enclosure, Controller & Electronics:** The PLC, I/O, transmitters, signal conditioners, pump motors, motor drivers/VFD's, Power Supplies are all housed in a Stainless Steel enclosure (NEMA 4 optional).

**Valves:** All valves used are tubing pinch valves. Standard sized quick-connect fittings are used for external bag/buffer/harvest connections.

**Pumps:** Two peristaltic pumps draw the selected Sample or buffer into the system and deliver at precisely controlled flow rates for accurate delivery. Pump accuracy is +/-3%. The discharge of both pumps passes through a corresponding flowmeter, pressure sensor, pre-column pH, conductivity (optional) and air sensor and is then connected to the columns together with in-line check valves to ensure unidirectional flow.

**Flowmeters:** 2 Flowmeters with accuracy range of +/-0.1% to +/-1% (depending on flowrate) are used. Connections are all FDA compliant plastics with elastomeric seals.

**Inline Sensors Pre and Post Column:** Inline sensors measure pH (range 1-14, accuracy ±0.1pH), Conductivity (High Range 0-200 mS, accuracy ± 5% FS and Low Range 0-25mS ±2) and UV 280 nM, Range 0-2 Au, +/- 0.1 Au, to verify appropriate conditions post column.

**Air Sensor / Active Air Trap:** The detection of bubbles greater than or equal to 60% of the I.D. of the tubing trigger the opening of a valve to remove the air

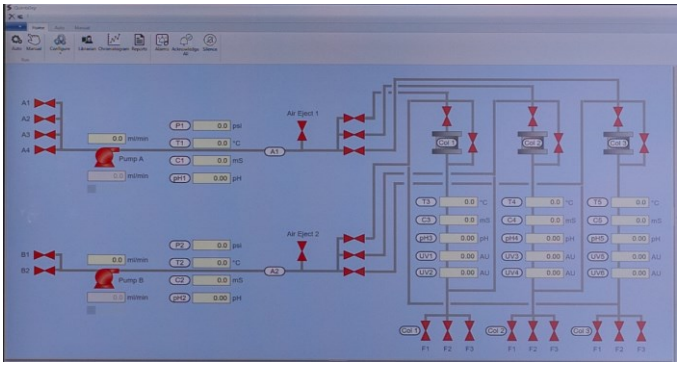
**Temperature:** Thermocouple is available for temperature sensing (range 0-40°C, accuracy ±1% FS) to verify separation conditions.

**Pressure Transducer:** The pressure transducer actively monitors the back pressure for any system overpressure alarms (0-50 psi range, accuracy ±1.0 psi) and pauses the system.

# The QuantaSep® Software

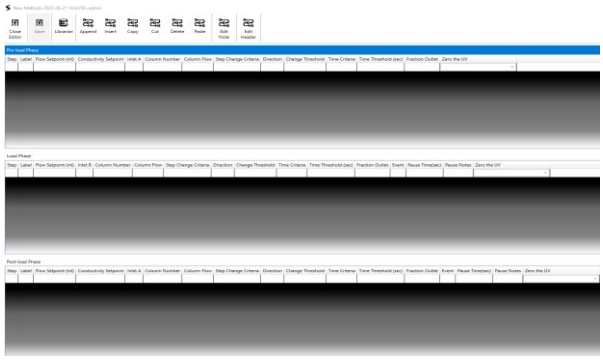
## The Right Combination of Simplicity and Power

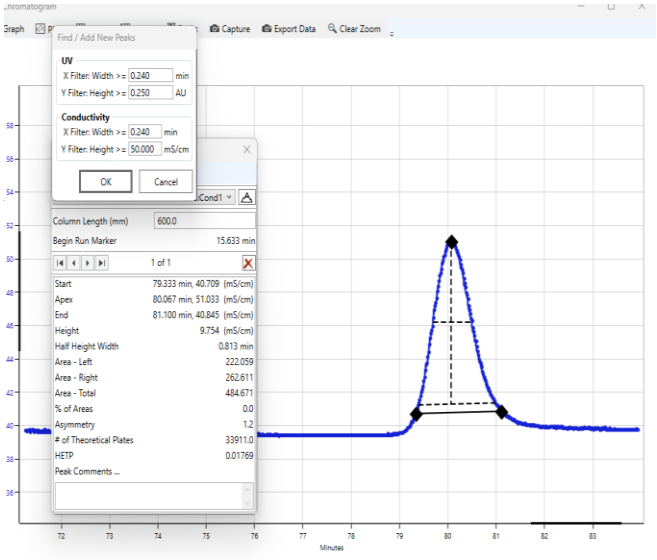
The simplicity of the QuantaSep® interactive graphical user interface gives the system its efficiency and power by making it easy to use and learn. The main screen displays a flow diagram of the system with all the main components and their real time status quickly and easily. By simply clicking the mouse, you can open or close a valve, stop or start a pump, set new flow rates, collect fractions and perform other system operations all from your work station. Click on the icon for Chromatogram or the event log to view.



## Intuitive Protocol Design

Programming is simple. It is as simple as filling out a table. Open the method editor table by clicking on the icon on the tool bar. Then key in steps in the table by selecting various conditions, stepping through different buffers and changing buffer or fraction steps based on UV, conductivity, pH or air. Simply click on the gradient box and choose your gradient profile. Click on the event box and zero the UV baseline before you load your product or program in a pause before you start eluting your product!






## CGMP Documentation and Data Analysis

All events manual or automatic (including deviations) are recorded to the batch log. Reports consisting of the method, buffers used, all alarms and events, chromatogram data, and analysis can be printed or archived as part of the batch log. The Instant Data Analysis helps do a quick check of an ongoing process against baseline data hence preventing possible losses. levels for audit purpose and batch tracking.

**Alarm History Screen:** The operator can view all active, acknowledged, and unacknowledged alarms with their associated timestamp for any system variable on a single screen.

**Chromatogram Screen:** This screen displays live trend of the process parameters for each column such as UV, Conductivity, PH, pressure, and flow rate set point. The x-axis will be displayed in time or volume units. Additionally, the screen provides a method to plot all of the available process variables, setpoints, and outputs on a single screen. The user will be able to choose as many as 6 variables per batch and trend them based on time or volume. The user is also able to easily print trends.

**Events Log:** This screen displays the actual operation step being performed by the system for comparison to the method via a time stamped sequential event log.

## Security

The multi-levels of password protection restrict access to the system. For instance, an operator may have provision to run a method but not change the parameters; only the supervisor may be given that responsibility. In another instance, only the QA or metrology group may have access to setting calibration parameters. The security administrator in the software can enable all this and more.

# Fluid Handling Module / Flow Path Specs

## General

- Pumps
  - Two peristaltic pumps draw the selected process fluids into the system and deliver at precisely controlled flow rates for accurate delivery. Pressure attainable is 3 bar. Pump accuracy is +/-3%. Pump flowmeter is +/-1% accuracy.
  - The discharge of both pumps passes through a corresponding flowmeter, pressure sensor, pre-column pH, conductivity (optional) and air sensor and is then connected to the columns together with in-line check valves to ensure unidirectional flow.
- Valves
  - All valves used are tubing pinch valves.
  - Standard sized quick-connect fittings are used for external bag/buffer/harvest connections.
- Pressure Transducer
  - The pressure transducer measure process pressure for any system overpressure alarms (0-50 psi range, accuracy ±1.0 psi).
- Air Sensor
  - The detection of bubbles of greater than or equal to 60% of the I.D. of the tubing.
- Sensors
  - Inline sensors measure pH (range 1-14, accuracy ±0.1pH), Conductivity (High Range 0-200 mS, accuracy ± 5% FS and Low Range 0-25mS ±2) and UV 280 nM, Range 0-2 Au, +/- 0.1 Au, to verify appropriate conditions post column.
- Safety features
  - "Active air trap" minimizes "bubble trap dilution"
  - Optional pre-column filter with differential pressure sensors
  - Leak and pressure alarms
  - Built in safety interlocks
  - Software method checks
  - Software security prevents unauthorized operation and tempering
- Temperature
  - Thermocouple (RTD preferred) available for temperature sensing (range 0-40°C, accuracy ±1% FS) to verify separation conditions.
- Flowmeters
  - 2 Flowmeters with accuracy range of +/-0.1% to +/-1% (depending on flowrate) are used. Connections are all FDA compliant plastics with elastomeric seals.
- Materials of Construction of Wetted Materials
  - All product contact materials are FDA compliant/inert.

## General

- Pump A (Peristaltic) 0-300 ml/ min ± 5%
- Pump B (Peristaltic) 0-300 ml/ min ± 5%
- Flow Rate
  - 1.6mm 0-100ml/min
  - 3.2mm 30-300ml/min.
- Gradients 10-90% of ratio ± 7%
- Mixing Turn down 30:1
- Valves Pinch valves
- System Volume
  - 1.6mm flowpath 25ml
  - 3.2mm flowpath 100ml
- System Pressure 50 psi
- Air Bubble Eject Size >.60% ID of tubing
- UV Sensor
  - Three detectors, one at egress of each column
  - Wavelengths: 260 nm & 280 nm
  - Path Length: 0.5cm standard
  - Range: 0 – 4.0 AUFS
  - Accuracy: ± 5% of Reading
- Conductivity Sensor
  - Five, one for buffer and one for feed line; 1 after each column
  - High Range: 0 – 200 mS ± 5% Full Scale
  - Low Range 0-25mS/cm ±2
- PH Sensor
  - 5 – Buffer, Feed, and after each column
  - Range: 1 – 14 ± 0.1 pH Pressure Sensor Range 0-100 psi;
  - Accuracy ± 1psi
- Inlet
  - 4 Pump A
  - 2 Pump B
- Fraction Selection 9 (3 per column)
- Column 3 In from Feed or Previous Column/Forward to next Column and Flow through to Collection)
- Pre-filter 1

## Flow Path Materials

- USP Grade VI - Polypropylene, PTFE, Platinum Cured Reinforced Silicone, EPDM

## Chemical Compatibility

- 1M Sodium Hydroxide, 19% Alcohol
- Operating Temperature 4 °C - 30°C

## Utilities Requirement

- Power Requirement 8 A @ 110 VAC @ 50-60 Hz

## Physical Dimensions

- 36" wide x 24" deep x 36" tall

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SEPRAGEN
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