

Downstream Purification Process for

Biologics



Essential Chromatography, Global Health

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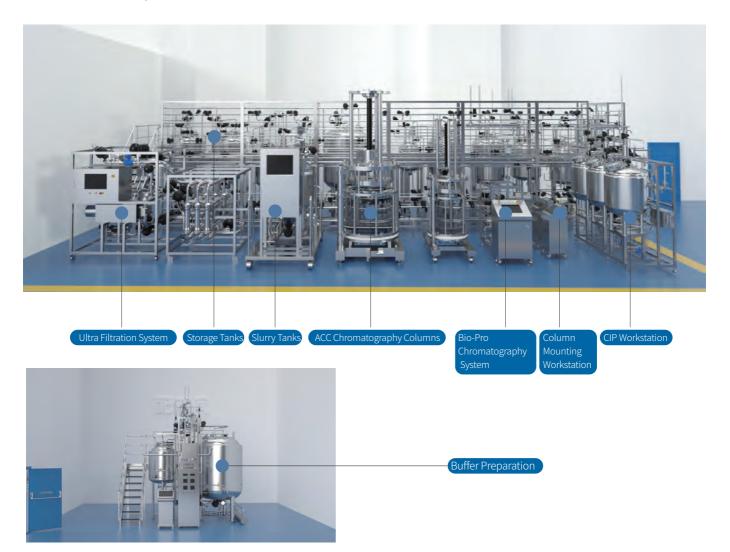
Smart Plant Design & DSP Solution

For downstream purification process, Hanbon can provide turnkey services through EPC or more flexible models, including and not limited to: sample pre-treatment module, chromatography module, ultrafiltration module and complete the design of the system automation control, utility engineering, etc.. The selection, supply, installation and construction of the corresponding production line equipment, as well as the provision of validation documents to meet GMP and FDA requirements.

The intelligent solution is based on the DCS+Batch platform, which is different from the current common PLC and SCADA platform and is an automatic control system that can obtain data centrally, manage centrally, control centrally and batch processing and batch control system. The introduction of this system enables the production line to form a complete controlled and reliable operation as a whole, with full process automation, consistent process, less manual participation, and deep integration of informationization and automation.

The DCS system can eliminate information silos and establish a "highway" for interconnecting the underlying equipment, allowing real-time data collection, monitoring, simple control and unified archiving, and production line level/workshop level/plant level data can be transparently displayed as the data base for the upper ERP and MES.

The BATCH processing control system is based on the BATCH flexible batch control software that complies with the ISA-88 standard, making the production steps clearer, streamlining the operators and allowing flexible application of new processes and methods. BATCH control system well separates the operation content and operation authority of automation personnel and process personnel, which greatly improves the confidentiality of production, while automatically creating a complete batch log, all operation information is reflected in the production log and batch report, which meets the requirements of FDA 21 CFR Part 11.





Chromatography System

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Bio-Lab[®] laboratory chromatography system is an efficient, fast and reliable automatic equipment independently developed by Hanbon. It can be used for the rapid purification of protein, peptide and nucleic acid and other biological molecules from the level of microgram to gram. The system adopts modular design and intelligent software, combined with different specifications of chromatography column, which can meet the purification requirements of various biological macromolecules in the laboratory.



Product Features

High performance system pump, detector, mixer and all kinds of control valves ensure high accuracy and repeatability as well as achieving purification results more quickly.

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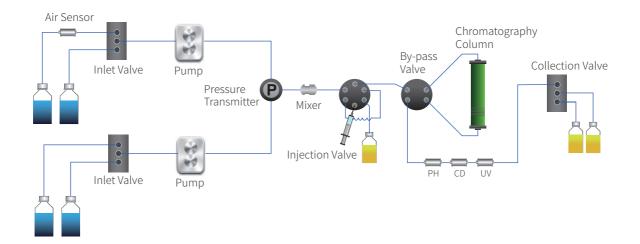
- Modular design is very convenient for system maintenance and can also realize the flexible configuration updating along with system software, which can meet different accounts login
- Stacked design of tubes can minimize dead volume and all the wetted tubes and parts have good biological compatibility, which will protect protein in all the processes.
- The software conforms to GLP/GMP and FDA 21CFR Part11 requirements
- Good user operation experience, satisfactory multi-level user permissions and complete audit tracking requirements.
- The comprehensive validation documentation system (DQ/IQ/OQ/PQ) supports your GMP/FDA audit

Three Types Available

Bio-Lab30

Bio-Lab100 Bio-Lab300

Bio-Lab® chromatography system flow path







Bio-Lab® Standard Configuration Parameter

Model	Bio-Lab 30	Bio-Lab 100	Bio-Lab 300					
System Pump	Binary piston pump, PEEK, titanium alloy or 316 L stainless steel, good biological compatibility; pump head self-washing function prevents pollution and salting out, and electronic pressure fluctuation compensation measures provide excellent gradient accuracy and repeatability for lab chromatography system to ensure the reproducibility							
Flow Rate Range(ml/min)	0~30 0~100 0~300							
Pump-max pressure(MPa)	≤30	≤20	≤15					
System-max pressure		1.3Mpa (Customized 0-8Mpa)						
Flow Rate Accuracy		±1.0%						
Gradient Model	Linear, isocratic, and s	epwise elution gradients which mod	ify the gradient ratio online					
UV Detector	Two channel UV detector, deuterium lamp (standard), tungsten lamp (optional)							
Wavelength Range(nm)	190-400							
Absorbance Range(Au)	-5~5							
Wavelength Accuracy	±1nm							
Conductivity Detection Range		1~999 mS/cm, Tolerance $\pm 3\%$						
pH Detection Range	0~	14, Tolerance \pm 0.05pH, 0.01pH Res	olution					
Valve	Standard: 2-channel inlet valv	e*2、Column position valve、Injection	n valve 2-channel collection valve					
Sensor	Air sensor and Pressure transmitter							
Mixer(ml)	0.6、2、5、10							
Software Workstation	– – – – – – – – – – – – – – – – – – –							
Power(kw)	1	1	1					
Dimensions (cm)	450*585*604	450*585*604	620*550*675					
Joint specification	1/16",1/8" 1/16",1/8" 1/8",1/4",3/16"							

Bio-Lab® Optional Configuration Parameter

Detector	
UV Detector Differential Refractive Detector	Ecom four-channel detector, 200-800nm RI-501、RI-502、RI-504
Valve	Electromagnetic/ Rotor valve
Inlet Valve Multifunctional Column Position Valve	4- channel inlet valve or 8- channel is optional4-channel column position valve or 6-channel of8-channel is optional
Outlet Valve	4- channel outlet valve or 8- channel is optional

Sample Pump	High accuracy piston pump
Flow Rate Range(mL/min)	0-30/0-100/0-300
Sensor	
Airsensor	Optional dual branch Air sensor
Pressure sensor	Optional post-column Pressure
	Sensor

Bio-Pro® Pilot & Process Chromatography System



▲ Pilot Chromatography System



Process Chromatography System



Process Chromatography System(Multi-pump diaphragm pump)

Pilot and Industrial Scale

Bio-Pro[®] automatic chromatography system is applied to the pilot and industrial production of bio-pharmaceutical purification process. Based on the requirements of ASME BPE and GMP, the system adopts an integrated module design, which can realize multi configurations according to the specific requirements of customers. In this system, many processes can be manually or automatically carried out, stable and reliable, such as conditioning, injection, flush, elution, auto-collection, CIP, etc. Besides, we can provide you with complete verification documents which are consistent with GMP.

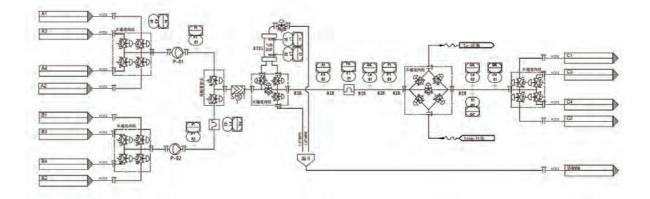
Product Features

- Key parts are from imported top brands, stable and reliable
- ASME BPE pipeline design; the inner wall electric throwing(Ra
 4um); automatic welding
- Wetted material meets USP Class VI and FDA standards.
- The system control software is developed on C# platform, which meets the requirements of FDA 21 CFR Part 11
- Complete GMP verification documents and service
- Database to store data, and mature data remote backup storage strategy





Standard Gradient System P&ID Drawing



System Parameter Table

Model	Bio-Pro 60	Bio-Pro 180	Bio-Pro 600	Bio-Pro 1200	Bio-Pro 2500	Bio-Pro 4400		
Infusion pump	High-accuracy constant-flow pump	Sanitary quaternary diaphragm pump						
Flow range(L/h)	1~60	1~180 6~600 10~1200 50-2500 150~5000						
Flow accuracy(L/h)	1% or 5ml/min	1% or 0.5L/h	1% or 1.5L/h	1% or 3L/h	1% or 5L/h	1% or 10L/h		
Tubing	1/4"TC (OD6.35 X ID4.57)	3/8"TC (OD9.53 X ID7.75)	1/2"TC (OD12.7 X ID9.4)	3/4"TC (0D19.05 X ID15.75)	1"TC (OD 25.4 X ID 22.1)	1½" TC (OD38.1 X ID34.8)		
Tubing material		SS 316L(ASME BPE), Electro polishing Ra≤0.4um						
System pressure(bar)		6						
UV-Vis Detector(nm)	Fixed wavele	Fixed wavelength 280nm / adjustable wavelength with 4 channels 200-400/200-800nm						
Conductivity range		0.1uS/cm~300mS/cm(0.1uS/cm~500mS/cm)						
pH range		0~14						
Power supply		220VAC 50Hz 380VAC 50Hz						
Working temperature		4~40 °C						
Compression air(bar)	5~7							
Size(mm)	1400x750x1300/ 1100*700*1200	1370x700x1200	1470x750x1350	1470x750x135	1350 1800×1200×1800			
Weight(kg)	265 /220	230	280	295	630	700		





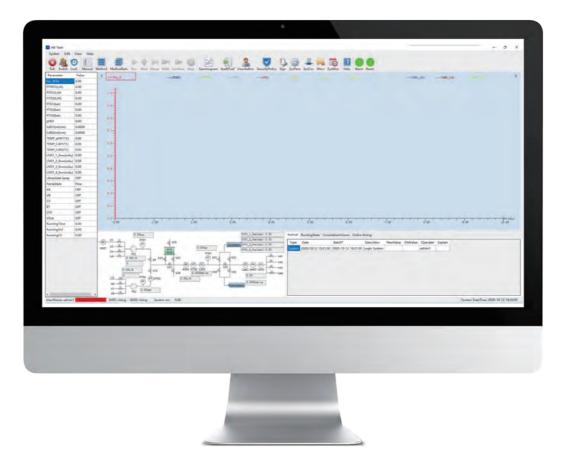
Bio-Pro System Software

The system software can track production process and set parameters, including flow rate, valve switching, injection time, elution time, collection conditions, etc. It can run automatically according to the preprogram or can run manual mode with user-defined process and parameters. Designed according to the requirements of GMP and FDA 21 CFR Part11, the software has audit trail, electronic record, electronic signature, multi-level password management and other functions.

- Monitor all running parameters; set 4 levels alarm, such as pressure, flow rate, etc.
- Good operation interface to achieve various functions
- Multi-mode operation: debug mode, manual mode, automatic mode
- Multi-level authorization administration

- Multi-task hyper-threading data processing; fast response and processing
- Complete audit trail function and data operation log
- In accordance with GAMP 5, FDA 21 CFR Part11, electronic signature and electronic records

Software Interface





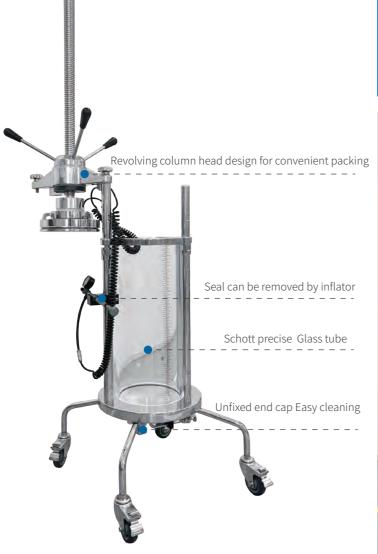


MCC[®] Manual Chromatography Column

MCC[®] adopts the compression way by manual screw to load packing materials, with the advantages of concise configuration , easy for cleaning and manual operation, applied to the switching among diversified products. The chromatography column has compact structure, convenient operation and stable performance. It can meet the requirements of most chromatography packing materials, and has good column packing effect and high column performance from the pilot to the large-scale production in demand.MCC[®] includes 2 designs ----MCC-B(manual sealing) and MCC-Q(automatic sealing, pneumatic deblocking), for the various requirements from different users.

Product Features

- Imported Schott finishing glass tube with high strength, easy to seal
- Column head sideslip design, no need for manual handling
- The frit can be replaced directly at the bottom without the need to disassemble the cylinder.
- Original and highly reliable column head sealing---manual or automatic
- Convenient, reliable and safe operation
- No dead zone in flow path, excellent cleaning performance
- Imported wetted material, according with USP Class VI and FDA
- GMP validation files and best services







Configuration Parameter

Item	MCC-70	MCC-100	MCC-140	MCC-200	MCC-300	MCC-400	MCC450		
Column Tube ID(mm)	70	100	140	200	296	400	450		
Column Height(mm)		500/ 750/ 950							
	0~450		50~450						
Packing Height(mm)	200~700			300	0~700				
	400~900			500)~900				
Max Work Pressure(bar)		6 3							
Mesh Size(um)		10/ 23(PP) or 10/20 (SS316L) 10/ 20(SS316L)							
Working Temperature		4~40							
Operation Mode				Manual					
Inlet & Outlet Diameter (mm)		"TC 3/8" TC 1/2" TC 5x ID4.57) (OD9.53x ID7.75) (OD12.7x ID9.4)							
Weight (kg)	28/30/32	34/37/40	42/47/52	57/64/71	146/156/166	191/206/221	259/271/280		
Maximum height(mm)	1550 1800 2000	1670 1920 2120	1670 1920 212	0 1670 1920 2120	1840 2090 2290	1890 2140 2340	1890 2140 2340		
Lengthxwidth (mm)	500x500	650x650	700x700 700x700		800x800	950x950	1000x1000		
Column loading volume (L)	1.0	2.0	4.0 8.0		18.0	18.0 31.0			

Notes: 1. Imported acrylic column tubes are used for MCC400 and MCC450 chromatography columns;
 2. Chromatography columns with height and air pressure requirements can be customized;
 3.The recommended column height is half of the available maximum height







ACC®Automatic Axial Compression Chromatography Column

ACC[®] series automatic axial compression column is specially designed for bio-pharmaceutical purification. The smart packing method can ensure each packing effect is consistent and chromatography results are repeatable, which can reduce the risk caused by the large difference in packing effect of each batch during production and can avoid the dependence on operators. ACC series is applied to most types of chromatography packing material and the corresponding packing methods in the bio-pharmaceutical industry to meet the production requirements of diversified products.

Product Features

- Key components are international top brand
- Patented piston seal design, better sealing performance.
- Patented piston exhaust structure design, convenient and quick
- Scientific distributor structure design to ensure the average distribution of liquid.
- SHigh precision servo motor drive with high operation accuracy to ensure
- Sanitary design, no dead angle; Wetted material: consistent with the USP VI
- the cylinder can be rotated to facilitate the removal and cleaning of the frit.
- The software of column mounting workstation meets the requirements of





Configuration Parameter

Model	ACC300	ACC400	ACC450	ACC600	ACC800	ACC1000	ACC1200	ACC1400	ACC1600	ACC2000
ID (mm)	300	400	450	600	800	1000	1200	1400	1600	2000
Tube height (mm)		600								
Recommended packing height (mm)					50-	300				
Recommended packing volume (L)	3~20	6~37	8~47	14~84	25~150	39~235	56~339	77~461	100-603	157~942
Max working pressure (bar)						4				
Frit pore size (µm)	10、20(SS316L)									
Working temperature(°C)					4	~40				
Axial compression method				Automa	tic - electric	motor axial co	ompression			
Inlet and outlet diameter (mm)	3/8" TC (OD:9.5 ID:7.75)	1/2" (OD:12.7		3/4" TC (OD:19.1 ID:15.8)		" TC .4 ID:22.1)	1.5" (OD:38.1		2.0' (OD:50.8	TC ID:47.5)
Compressed air (bar)					Ę	5~7				
Weight (kg)	305	415	555	880	1985	3675	6000	6715	8300	15000
Power (KW)	2.5	2.5	2.5	5	7	7	7	9	9	10
External dimension (cm)	70x70	72x72	73x73	90x90	145x115	162x128	186x150	206x170	230x200	280x247
Max maintenance height (cm)	235	240	253	253	279	283	318	335	362	362
Transport height (cm)	160	172	181	182	209	209	260	280	282	285

Notes: Other diameter, height, and pressure-resistant chromatography columns can be customized.



Automatic Slurry Tanks

Automatic slurry tank of Hanbon is used for rapid mixing of homogenate, replacement of new packing material with ethanol, adjustment of homogenate ratio, and collection of packing material during column removal. It is equipped with a specially designed low shear force agitator for mixing solid-liquid mixture, which can realize rapid mixing without damaging the packing material, and is a powerful auxiliary for realizing high column efficiency packing of chromatography column. We recommend that all automatic chromatography columns should be homogenized by automatic slurry tank.

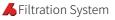


Product Features

- In accordance with GMP requirements, manufactured according to ASME BPE standard
- All wetted materials are made from SUS316L, Ra ≤0.4um, electro polished, the material not in contact with the liquid is SUS304, Ra≤0.8um
- Low shear force agitator can not cause damage to the packing material, and compressed air can be used for stirring.
- The replacement function of homogenate buffer can be used, such as replacement from preservation solution (20% ethanol, NaOH solution) to column packing buffer solution (such as WFI), or vice versa
- It can adjust the proportion of homogenate
- With weighing module, spray ball, over-pressure protection
- Two or three frits are designed at the bottom and side to accelerate the liquid change rate of slurry tank
- Caster is added at the bottom of the equipment, which is convenient to move
- The volume of slurry tank can be customized







Bio-Lab Automatic Tangential Flow Filtration System

Bio-Lab TFF automatic tangential flow filtration system is an easy-to-use automatic UF/DF system for harvesting, clarification or concentration, and liquid exchange at the R&D and pilot level for antibodies, vaccines, and nucleic acid drugs in biopharmaceuticals. It adopts fully automatic and intelligent design with automatic TMP control for automatic concentration, isovolume wash filtration, automatic collection and automatic data recording. Two models are available, Bio-Lab TFF18/180 to meet the needs of different membrane materials.

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Product Features

Highly integrated product with reasonable flow path layout to reduce system dead volume

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- Fully automatic design, automatic TMP control, automatic concentration and filtration
- Automatic data recording and backup, no risk of data loss
- Open design, easy to operate
- Compatible with many mainstream membrane packages (Millipore/Pall brands)

Configuration parameters

Model	Bio-Lab TFF18	Bio-Lab TFF180
Circulation pumps	Peristaltic pumps	Diaphragm pumps
Circulation pump flow rate	0-300ml/min	1-180L/H, Flow accuracy±1%
Liquid replenishment pump	Peristaltic pumps	Peristaltic pumps
Charge pump flow rate	0-300ml/min	1-90L/H
Maximum system withstand pressure	2Bar	6Bar
pH range	0-14	0-14
Conductivity range (mS/cm)	0.1µS/cm~300mS/cm	0.1µS/cm~300mS/cm
Piping material	PFA Hard pipe	SS316L (ASME BPE) ,Electric tossingRa≤0.4μm
Circulation tank	500ml	4L
Waste liquid tank	/	4L
Balance accuracy	Weighing range6200g, Reading Accuracy0.01g, Standard: two units	Weighing range10200g, Reading Accuracy0.01g, Standard: two units
Power supply	220V	220V
Compressed air	7bar	7bar

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Note: Configuration can be adjusted according to user needs

Bio-TFF Automatic Tangential Flow Filtration System



▲ Ultra Filtration System



▲ Deep filteration system

Bio TFF system is an easy-to-use automatic ultrafiltration UF / DF system, which is suitable for biomedical process development, pilot small-scale production. Bio TFF system adopts innovative and intelligent design, which can not only improve process extremely low minimum operating volume, but also maximum ultrafiltration concentration multiple and optimal We have done the experiment for many times on the buffer system used in common bio- pharmaceutical purification, such as phosphate system, acetate, citrate system, Tris-HCl system and so on, which achieved excellent online dilution effect. The steady time ≤ 1 min ,pH ± 0.05 , conductivity ± 0.05 or 1% (take large value) solution with high accuracy in the actual experiment research and performance, but also achieve product recovery function.

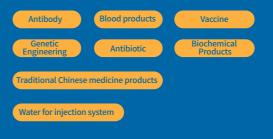
We can provide ultrafiltration / microfiltration system for clamp for Millipore / Pall / Sartorius membrane or GE/ Pall / Repligen hollow fiber column.

Product Features

- Sanitary design, conforming to GMP and ASME BPE requirements.
- Quattroflow quaternary diaphragm pump, low shear force, low pulse
- Automatic TMP control, automatic concentration, equal

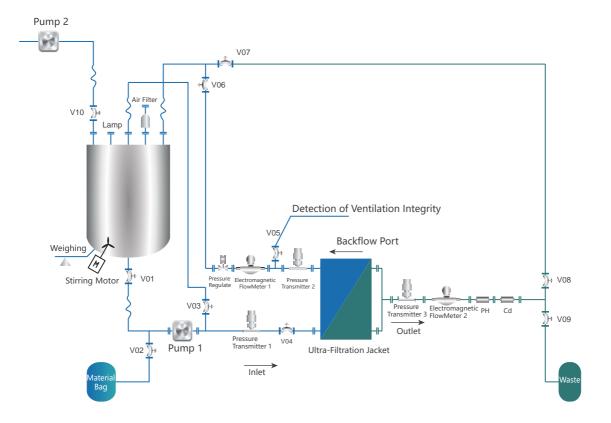
- GMP validation files and services.

Application Area





P&ID Drawing of Filtration System



Configuration Parameters

Item	Bio-TFF600	Bio-TFF1200	Bio-TFF2500	Bio-TFF4400	Bio-TFF9000	Bio-TFF20000		
Circulating pump	Sar	nitary quaternary o	Sanitary rotor pump					
Pump rate (L/H)	6~600	10~1200	50-2500	150~5000	300~9000	600~20000		
Filtration area (m ²)	0.1~2.5	0.5~2.5	0.5~5	0.5~10	1~20	2~40		
Pipeline	1/2"TC	3/4"TC 1"TC	1"TC	1½" TC	2" TC	3" TC		
pH range	0~14							
CD range (mS/cm)	0.1uS/cm~300mS/cm							
Tubing material	SS316L(ASME BPE), Ra≦0.4µm							
Solvent mixing tank (L)		Optional (20/30/50/100 and others)						
Fluid infusion pump	Optional							
System pressure (bar)	≤6							
Power	220/380VAC 50Hz							
Compressed air (bar)	5~7							

Notes: Hanbon can also provide the ultrafiltration system Bio-HF with the hollow fiber column. This configuration parameter table is also applied to the hollow fiber ultrafiltration system. Larger specifications of ultrafiltration system can be customized

Software Instruction

The software meets the requirements of GAMP5 and FDA 21 CFR Part 11. According to the process, operation parameters can be prepared, including the liquid volume, system flow, inlet\backflow\outlet pressure, TMP control, \triangle P, liquid weight inside the tank, etc. Each parameter in the process of the equipment has a special file record, and the chromatogram is drawn in real time for reference of the operator.

- Monitor all running parameters, set level 4 alarm, such as pressure, conductivity, etc
- Good operation interface, convenient to realize various functions.
- Multi-mode operation---- debugging mode, manual mode and automatic mode
- Comply with GAMP5 and FDA 21 CFR Part 11, conform to electronic signature record.
- The system is divided into four levels of operation authority to avoid arbitrary change of process parameters by operators.
- The system can edit the method to realize automatic CIP, concentration, filtration and other functions.
- Complete audit trail function, perfect data operation log.



UF/TFF Cassette Holder

- Adaptive for mainstream brands membrane such as Millipore /PALL/Sartorius.
- Special flow inlet and outlet design ensures the system can be cleaned thoroughly
- Standard 316L material, standard Tri-Clamp connection.
- Various configuration can realize customized processing from research and development to pilot production scale.



▲ Vertical film bag fixture



▲ Horizontal film bag fixture



▲ Deep filteration fixture (Single layer)



▲ Deep filteration fixture (Double layer)



▲ Deep filteration fixture (Single layer)



▲ Deep filteration fixture (Double layer)



Buffer Inline Dilution&Conditioning System

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Bio-con inline buffer dilution system solves the demand for the accuracy and repeatability of the complex buffer soluiton in the biopharmaceutical process. In addition, it can reduce the quantity of the liquid / storage tank, save the manpower and materials, and thus reduce the production cost.

Technical Advantage

Eliminate human errors, reduce liquid distribution time, improve efficiency and the accuracy of liquid dosing.

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- Real time monitoring and accurate feedback on concentration / flow rate, pH and conductance.
- The real-time curve record, complete audit trail.
- Reduce the single-use invested cost and the cost of cleaning validation.

The new building

- Reduce 60% area of liquid dosing and storage
- Reduce 90% volume of the dosing and the storage tank
- Reduce 60% staff
- Reduce the 70% cost of dosing time.

The built factory

- Reduce the cost of cleaning and verification of liquid dosing and storage tank
- Increase the accuracy of the liquid dispensing and reduce the labor cost
- Increase the scale of liquid dosing and 3 times of the productive power



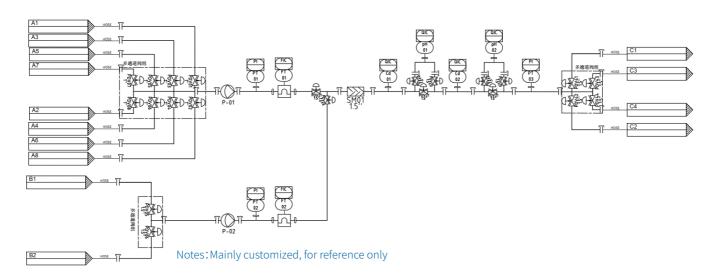


Technical Principle

The basic principle of Bio-Con inline buffer dilution system is to mix a variety of concentrated buffers, including acid, alkali, salt and so on, with the injection water to make the buffer solution needed. According to the specific use conditions, different concentration can be accurately controlled. And in this system, the stability of the control parameters can be reached within 1min.



The Bio-Con inline buffer dilution system can also be integrated into a Bio-Pro chromatography system or the Bio-TFF tangentialflow filter system, which can continuously complete the process of liquid dispensing + chromatography or liquid dispensing + tangential flow, and the overall control and data record will increase the convenience for the customer purification process.



P&ID Drawing of Bio-Con

Liquid Dosing Experiment

We have done the experiment for many times on the buffer system used in common bio- pharmaceutical purification, such as phosphate system, acetate, citrate system, Tris-HCl system and so on, which achieved excellent online dilution effect. The steady time ≤ 1 min ,pH ± 0.05 , conductivity ± 0.05 or 1% (take large value) solution with high accuracy in the actual experiment

Single-use System



Single-use System

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We can also provide single-use ultrafiltration system, including system pump head, pipeline, pressure sensor, flowmeter, pH,conductivity, UV, etc., all of which are single-use replaceable components. All components are designed with aseptic pre packaging in advance, which can be directly disassembled and packaged before use and installed after CIP verification. It is especially suitable for the application of multiple CDMO or multiple products on the same line.





Product Features

- All wetted parts can be directly replaced, fast and convenient
- FDA and USP VI certificates for non-stainless steel wetted parts
- A compact design, minimum recyclable volume and higher concentration multiple

◀ Single-use Chromatography System

▲ Single-use Ultrafiltration System

About Hanbon

Jiangsu Hanbon Science & Technology Co., Ltd. was established in 1998 as a high-tech enterprise that integrates research and development, production, and sales, with liquid chromatography products as its core. It has formed an industrial cluster of liquid chromatography analysis instruments, preparation liquid chromatography , simulated moving bed continuous chromatography systems, supercritical liquid chromatography equipment, chromatographic silica, and biochemical products using chromatography technology as a separation method. It is a leading manufacturer of liquid chromatography purification equipment domestically and internationally.



Jiangsu Hanbon Science & Technology Co., Ltd.

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