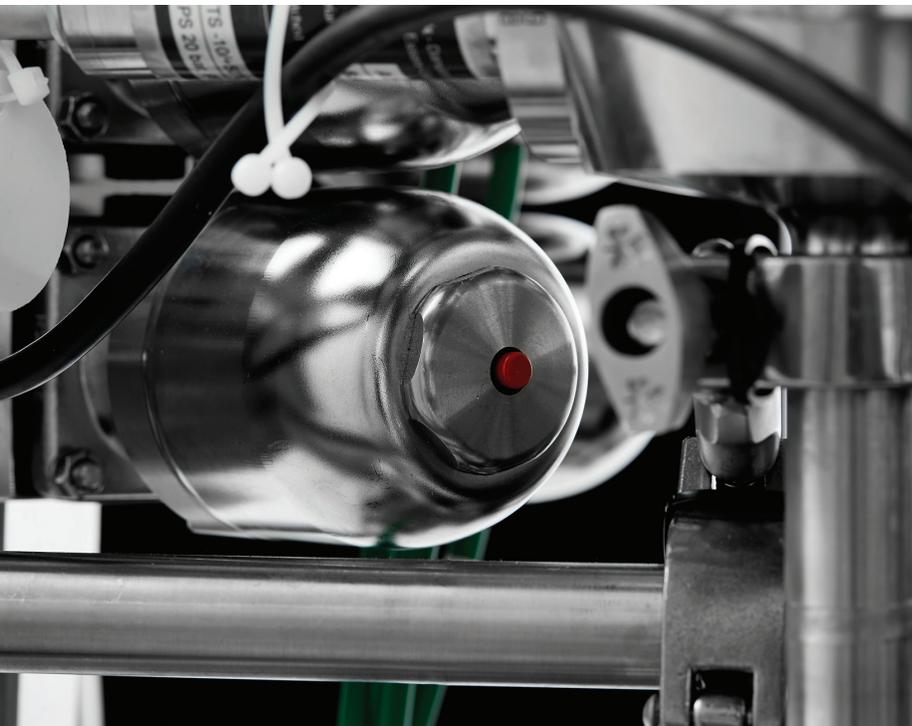
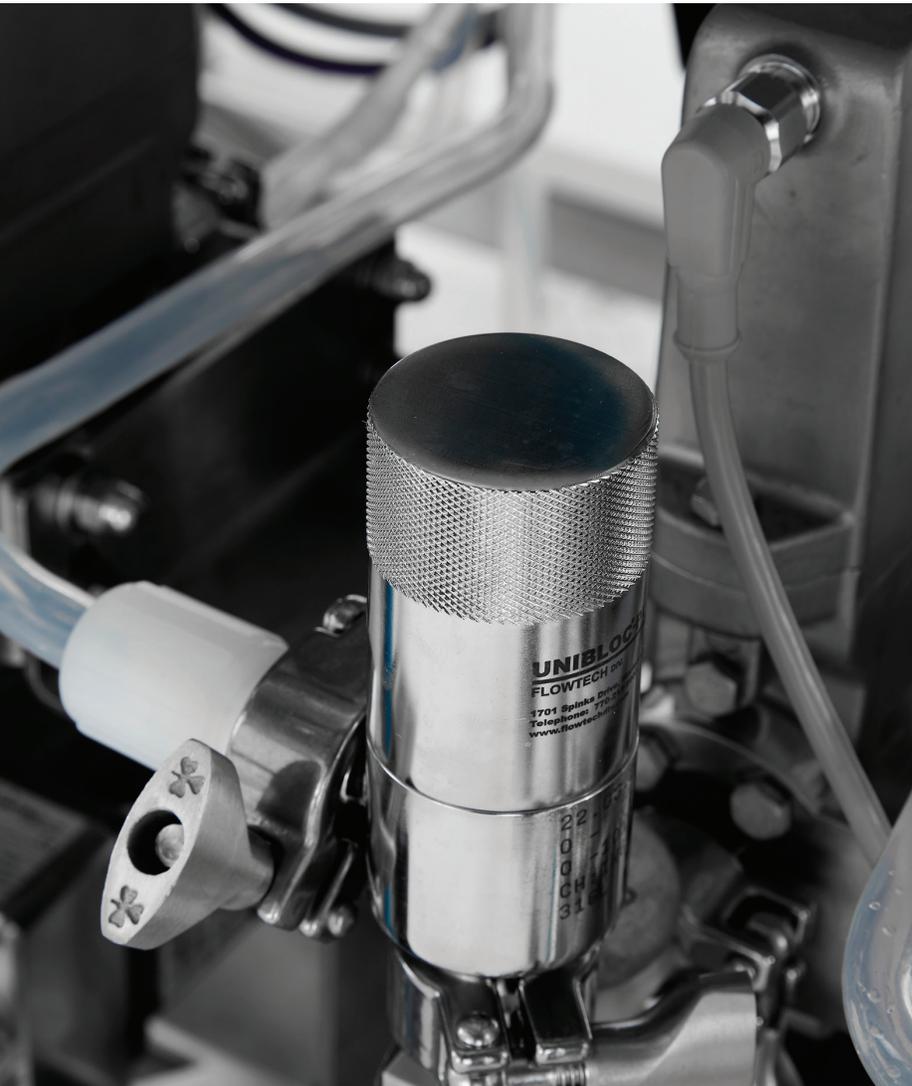


Fluid Management Solutions for IBD™ Inline Buffer Dilution and Conditioning Systems

3-Pump and 5-Pump Systems

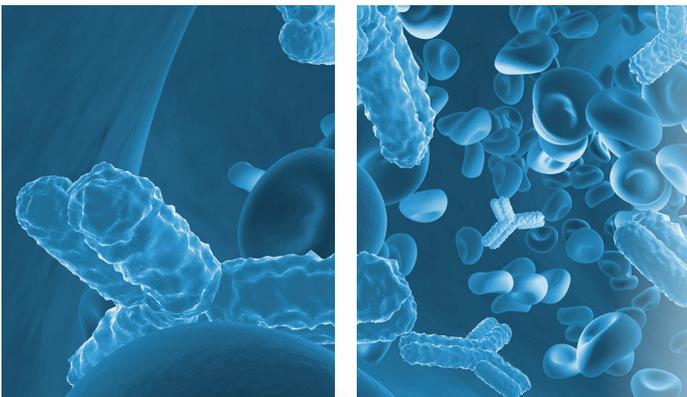




Built For You.

Asahi Kasei Bioprocess is dedicated to unlocking efficiencies and driving buffer preparation productivity in your biopharmaceutical downstream processing area.

Creating safe, affordable biologic medicines today requires increased downstream buffer production. You can move beyond these downstream bottlenecks with IBD™, our patented Inline Buffer Dilution technology now available in 3-Pump and 5-Pump configurations to give you more options that are built for you.



Accurate and Reproducible Dilution and Conditioning of Buffers

Whether your production plant is a stainless steel (SS) fed-batch facility or a single-use perfusion facility, your downstream processes demand large volumes of dilute buffers. Thousands of liters can be required for protein capture, polishing, concentration and virus removal steps, with each step needing specific buffer compositions.

IBD Inline Buffer Dilution Systems have been trusted to cost-effectively prepare millions of liters of dilute and pH-conditioned buffers just-in-time from up to 20X stock concentrate in cGMP production facilities around the world. Using our patented inline mixing technology, we offer a family of 3-Pump and 5-Pump IBD Systems that can meet almost any cost or performance need in your biopharmaceutical production plant.



The IBD™ multi-stage blending technology was awarded US Patent 8271139 in 2012.

Buffer preparation comparison

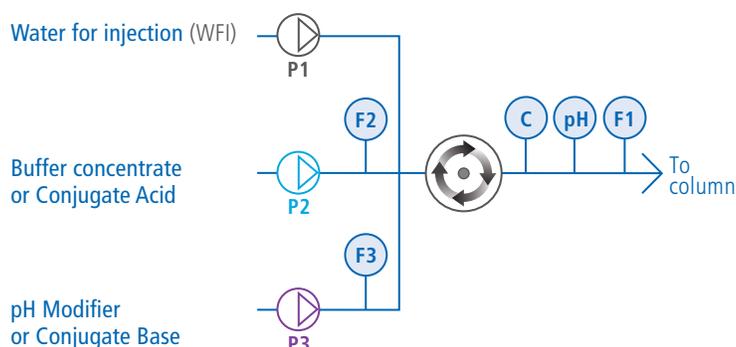
Consideration	Manual Batch Compounding	IBD Technology
Buffer prep footprint required	Large	Small (less than half)
Mode of operation	Labor-intensive	Automated
Production turnaround time from Buffer A to Buffer B	Hours	Minutes
Final conductivity and pH accuracy and precision	Relatively low	High
Buffer preparation time	Produced and released in hours	Produced and released in seconds
Regulatory acceptance	In use in cGMP manufacturing facilities	In use in cGMP manufacturing facilities
Reproducible dilution and conditioning	No	Yes
Fit for integrated or continuous processes	No	Yes
Fit for batch processes	Yes	Yes
Ancillary equipment required	Requires large capital investment of SS tanks	Can be used with single-use bags
Impact on improved protein recovery	Low	High

3-Pump IBD™ Systems for Cost-Effective Dilution and Conditioning

Our original IBD Systems are outfitted with three pumps and provide dilute and conditioned buffers constructed from up to three streams. One larger pump is used to deliver the diluent, typically WFI or purified water, into the system. The second smaller pump can deliver buffer concentrate, while the third smaller pump can deliver acid or base modifier. The system can control the blend using conductivity and pH feedback control, or alternatively mass flow control.

3-Pump IBD Systems (flow control or conductivity and pH control)

Sensors: F = Flow rate C = Conductivity pH



Final buffers that are:

+/- 0.1 mS/cm or better

+/- 0.1 pH or better



Standard Sizes for 3-Pump IBD Systems



3-Pump IBD 1K

- » 60 – 1000 L/h
- » Clinical manufacturing
- » Dilution + conditioning
- » Up to 20x dilution
- » 600 mm W x 1219 mm D x 1600 mm H



3-Pump IBD 5K

- » 500 – 5000 L/h
- » Large scale manufacturing
- » Dilution + conditioning
- » Up to 20x dilution
- » Affordable buffer production
- » 1981 mm W x 1219 mm D x 1880 mm H



3-Pump IBD 10K

- » 1000 – 10,000 L/h
- » Large scale manufacturing
- » Dilution + conditioning
- » Up to 20x dilution
- » Affordable buffer production
- » 1981 mm W x 1524 mm D x 1880 mm H



3-Pump IBD 15K

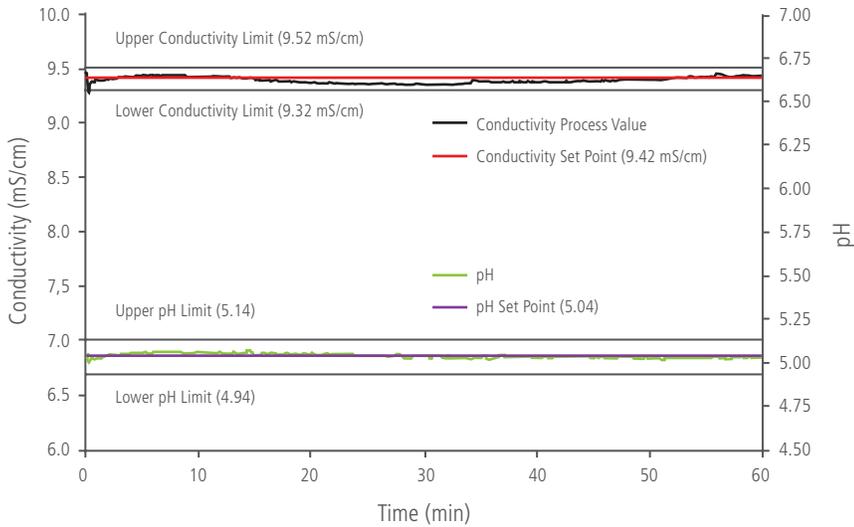
- » 1500 – 15,000 L/h
- » Largest scale
- » Dilution + conditioning
- » Up to 20x dilution
- » Affordable buffer production
- » 1981 mm W x 1524 mm D x 1880 mm H

Note: Dimensions are approximate. Customized systems for unique applications are also available.

Performance

Our 3-Pump IBD Systems reliably produce dilute and conditioned buffers from stock concentrates.

Production of ~100 mM Tris-Acetate buffer



- Concentrate 1: 1.0 M Tris-Base
- Concentrate 2: 1.0 M Acetic Acid
- Diluent: Deionized water
- Conductivity set point: 9.4 mS/cm
- pH set point: 5.0

Figure 1. Example of a 3-Pump IBD System holding conductivity set point to within ± 0.1 mS/cm and pH set point to within ± 0.1 pH units at 120 L/h.

Scalability

IBD technology has been proven at flow rates up to 15,000 L/h, demonstrating the scalability of IBD and its ability to recover quickly from process upset at scale. See Figure 2.

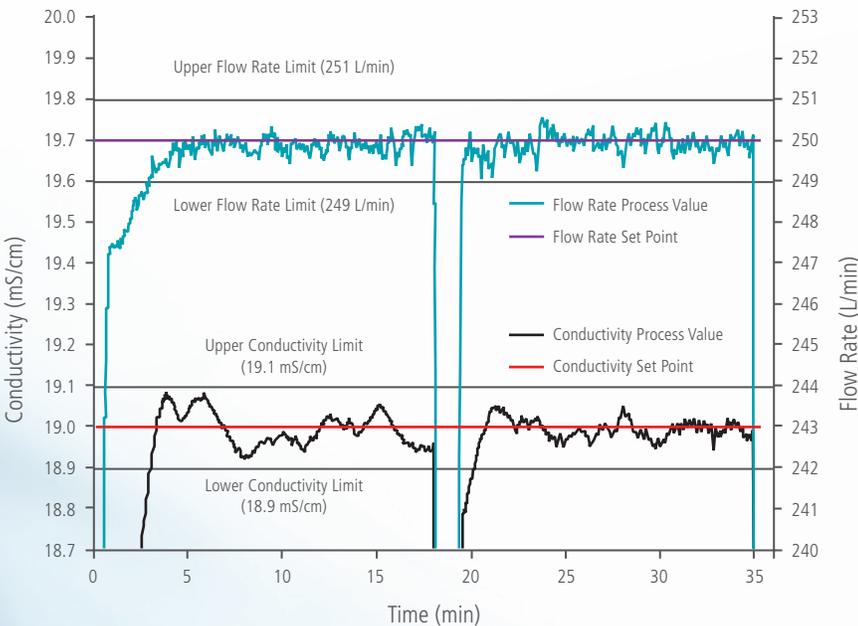


Figure 2. IBD holding conductivity set point of saline solution to within ± 0.1 mS/cm at a total flow rate of 15,000 L/h. At time 18 minutes, a 45 second hold interval was implemented to simulate a process upset and stop the system pumps. After resuming, the system came back to target set point within approximately one minute.

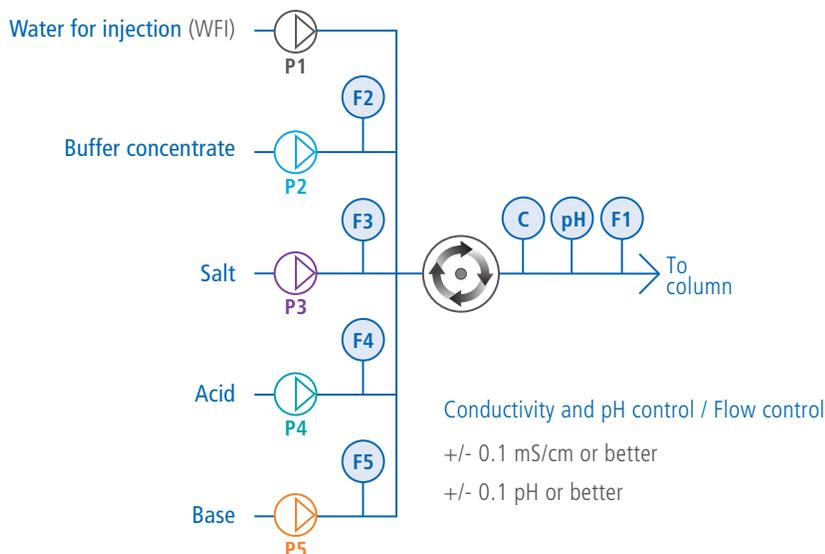


5-Pump IBD™ Systems for Complex Mixtures

Our newest 5-Pump IBD Systems can produce more complex buffers constructed from up to five streams. These systems provide the ultimate flexibility to generate mixtures using a combination of conductivity, pH and mass flow control.

5-Pump IBD Systems (flow control or conductivity and pH control)

Sensors: F = Flow rate C = Conductivity pH



New Mixer Technology

A patented dynamic inline mixer shortens the buffer response rate of IBD. The single pass mixer permits IBD to reach target setpoint within seconds, and also results in faster washout volumes so you can increase the utilization of your system. The mixer is standard on both 3-Pump and 5-Pump IBD Systems.

Standard Sizes for 5-Pump IBD Systems



5-Pump IBD 0.2K

- » 20 – 200 L/h
- » Process development
- » Dilution / conditioning / mixing
- » Up to 20x dilution
- » Maximum flexibility
- » 762 mm W x 1356 mm D x 1600 mm H



5-Pump IBD 1K2

- » 120 – 1200 L/h
- » Clinical manufacturing
- » Dilution / conditioning / mixing
- » Up to 20x dilution
- » Maximum flexibility
- » 1524 mm W x 1067 mm D x 1829 mm H



5-Pump IBD 2K0

- » 200 – 2000 L/h
- » Large scale manufacturing
- » Dilution / conditioning / mixing
- » Up to 20x dilution
- » Maximum flexibility
- » 1524 mm W x 1524 mm D x 1829 mm H

Note: Dimensions are approximate. Customized systems for unique applications are also available.

Capability: A Multiplicity of Buffers

IBD Systems have been used to produce the widest range of buffers of any comparable system on the market. Chances are that an IBD System has already produced the buffers you use in your downstream process.

What buffers can IBD produce?

Compound	Molecular Formula	Molar Mass	Solubility in Water
Trisodium citrate	$\text{Na}_3\text{C}_6\text{H}_5\text{O}_7$	258.06 g/mol (anhydrous), 294.10 g/mol (dihydrate)	Pentahydrate form: 92 g/100 g H_2O (25 °C)
Pentetic acid (DTPA)	$\text{C}_{14}\text{H}_{23}\text{N}_3\text{O}_{10}$	393.35 g mol ⁻¹	<0.5 g/100 mL at 25 °C, 100 kPa
Tris	$\text{C}_4\text{H}_{11}\text{NO}_3$	121.14 g mol ⁻¹	~50 g/100 mL at 25 °C, 100 kPa
Sodium chloride	NaCl	58.44 g mol ⁻¹	359 g/L at 25 °C, 100 kPa
Trehalose	$\text{C}_{12}\text{H}_{22}\text{O}_{11}$ (anhydride)	342.296 g/mol (anhydrous)	68.9 g per 100 g at 20 °C
Monosodium phosphate	NaH_2PO_4	119.98 g/mol (anhydrous)	59.9 g/100 mL (0 °C)
Disodium phosphate	Na_2HPO_4	141.96 g/mol (anhydrous)	7.7 g/100 mL (20 °C)
		268.07 g/mol (heptahydrate)	11.8 g/100 mL (25 °C, heptahydrate)
Trisodium phosphate	$\text{Na}_3\text{O}_4\text{P}$	163.94 g mol ⁻¹ (anhydrous)	14.5 g/100 mL (25 °C)
Histidine	$\text{C}_6\text{H}_9\text{N}_3\text{O}_2$	155.15 g mol ⁻¹	4.19 g/100 g at 25 °C, 100 kPa
Sorbitol	$\text{C}_6\text{H}_{14}\text{O}_6$	182.17 g mol ⁻¹	2350 g/L at 25 °C, 100 kPa
Mannitol	$\text{C}_6\text{H}_{14}\text{O}_6$	182.172 g mol ⁻¹	216 g/L at 25 °C, 100 kPa
Sucrose	$\text{C}_{12}\text{H}_{22}\text{O}_{11}$	342.30 g/mol	2000 g/L (25 °C)

High Viscosity Buffers

IBD Systems can also handle high viscosity fluids, such as glycerol. The 20X dilution of 100% glycerol was successfully performed at room temperature on an 3-Pump IBD 1K under both low flow (180 L/h) and high flow (1000 L/h) conditions.

5% Glycerol Blend from 100% Glycerol Stock with IBD

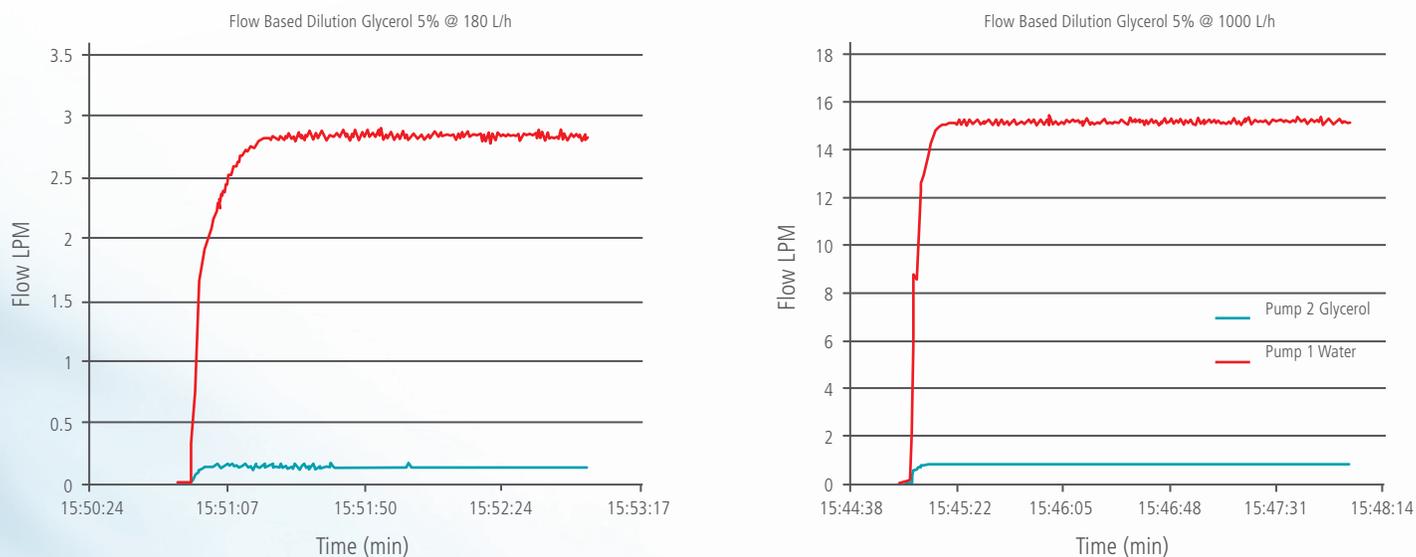
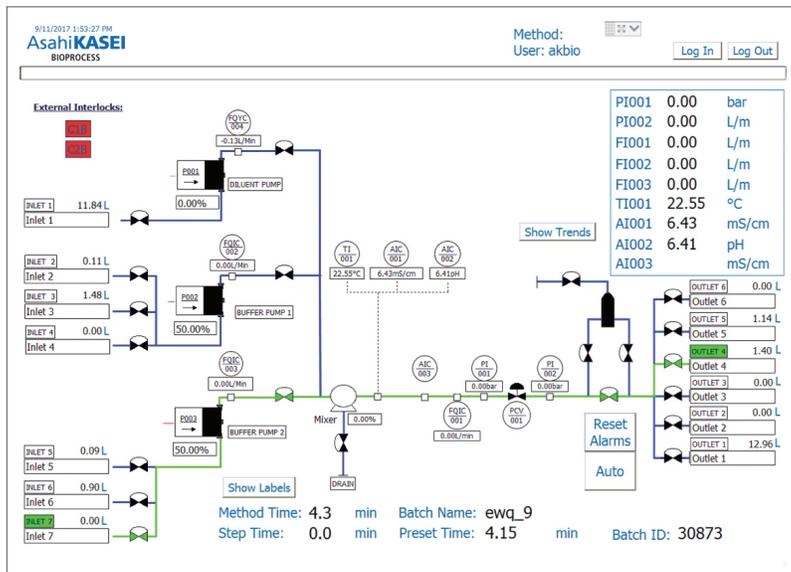


Figure 3. 100% glycerol at room temperature was successfully diluted by 20X at 180 and 1000 L/h.

Software

Our IBD Systems are implemented on a range of automation platforms built for you. Depending on the model of system you require, one or more PLC-HMI/SCADA architectures may be available.



Available automation platforms

3-Pump System	Siemens S7 PLC	Rockwell CompactLogix PLC	Delta V
IBD 1K	Standard	N/A	N/A
IBD 5K	Standard	Standard	Custom/external integrator*
IBD 10K	Standard	Standard	Custom/external integrator*
IBD 15K	Standard	Standard	Custom/external integrator*
5-Pump System	Siemens S7 PLC	Rockwell CompactLogix PLC	Delta V
IBD 0.2K	Standard	N/A	N/A
IBD 1K2	Standard	Standard	Custom/external integrator*
IBD 2K0	Standard	Standard	Custom/external integrator*

All standard IBD Systems include a robust and validated PLC platform with 21CFR Part 11 compliant HMI/SCADA. Standard systems are also OPC-compatible for simple transfer of historized data to your plant historian.

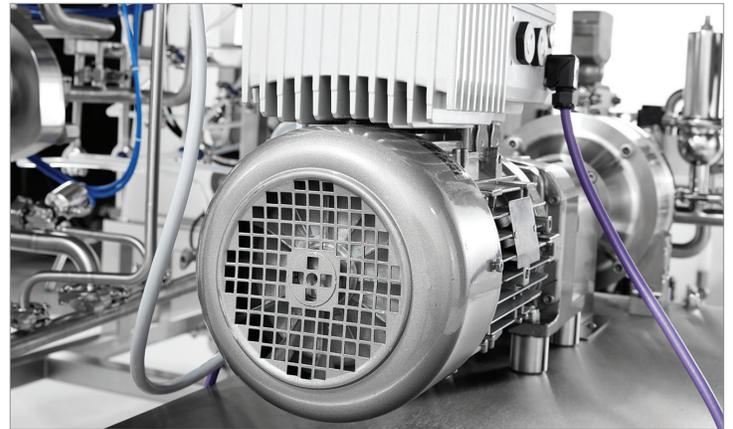
*Operational commands and data transfer from our PLC platform can easily be made available to your DeltaV system. Alternatively, a fully integrated DeltaV solution can be developed by your local integrator or with the support of AKBA's integrator.

DeltaV is a trademark of Emerson Process Management.

IBD Standard Options

Systems in the IBD Family are each available with the following options:

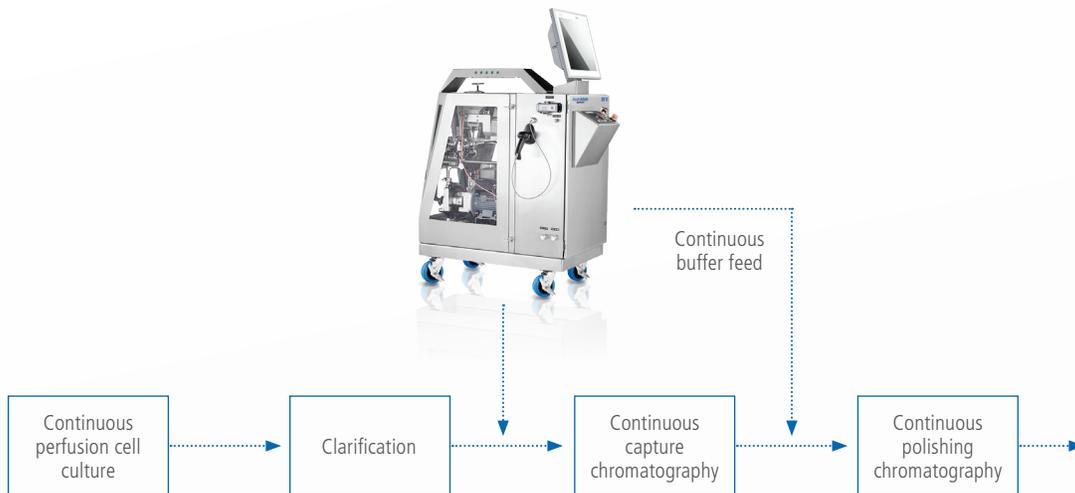
- » Second conductivity sensor
- » Second pH sensor
- » Temperature control (heat exchanger)
- » 0.2 µm sterilizing grade outlet filter
- » 2, 4 or 6 total outlets
- » Reagent Tracker
- » CIP manifolds
- » Forward pressure regulator for WFI



Continuous Processing

While IBD Systems have been in use in traditional batch processing for over a decade, they are now being implemented into integrated and continuous processes to support continuous buffer supply.

- » Deliver buffers continuously to downstream continuous process
- » IBD "Scheduler" function allows production of multiple process buffers unattended and sequentially, just-in-time to feed continuous chromatography systems



Technology designed to move you beyond your downstream processing bottlenecks.

IBD Reagent Tracker

Simplifying Buffer Composition Tracking

Since its launch, our IBD technology has produced millions of liters of high-quality, consistent buffers for downstream processing steps. Now with the new Reagent Tracker option, it is easier than ever to achieve error-free labeling on diluted buffer bags and totes.

Use the provided bar code scanner to scan information on individual bar-coded stock reagents that you connect to the IBD system. Through the IBD software, select your pre-programmed buffer recipe, and the system will produce your target buffer to the required formulation. Print the generated buffer label on the wireless label printer, and affix it to your buffer bag.

Reagent Tracker Features:

- » Bar code scanner for reading labeled stock solution information into the system
- » Wireless printer for generating 4" x 6" labels for the final buffer formulation
- » Labels print standard with the Method Name, Batch ID and Date of Manufacture
- » Labels are customizable to include other information such as Date of Expiry



+

POST BATCH REPORT

Method Name:
200mM NaCl + 50mM Tris (EQ Buffer B)
Batch ID: 1412
Date: 8/25/2016

COMPONENTS

Inlet 1: Water for Injection 270.0L
Inlet 5: 2M NaCl + 500mM Tris 29.9L
Inlet 7: 0.5M HCl 0.1L



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A Decade of Implementation Experience

With our deep experience installing IBD Systems in a myriad of plants around the world, our engineers bring a wealth of knowledge to ensure that your implementation is trouble-free.

Examples of Common Pitfalls	AKB Solution
Inconsistent WFI supply	WFI break tank with level detection
Fluctuating pressures of incoming WFI feed	Forward pressure regulation valves
Varying ΔP downstream of IBD System (buffer hold tank head; downstream filters, etc.)	<ul style="list-style-type: none"> » Ensure backpressure regulation valve is upstream of divert valve » Size pumps for the discharge pressure at the buffer hold point, not at the pump discharge
Chemical compatibility concerns with concentrates	Polymeric lines, other alloys such as AL6XN, Hastelloy
Temperature fluctuations	Shell-and-tube, tube-in-tube, or U-tube heat exchangers
pH measurement readings	Prevent mechanical "shock" (water hammer, etc.)

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Technical Support and Warranty Information

A reliable technical support network is available throughout the United States, Europe and Asia.

We offer an extendable 1-year warranty, service contracts and a personalized level of service for peace of mind and timely support when you need it.

For more information, please visit:

www.ak-bio.com

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