

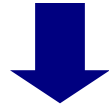


kSep[®] Technology AusBiotech 2010

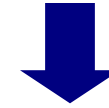


THE SCIENCE TO SUCCEED.

KBI Biopharma, Inc.



Biopharmaceutical Contract
Development Services



Development and
Commercialization of
the kSep[®] Technology



Who We Are

- KBI is a Contract Development and Manufacturing Organization
- Founded in 1997
- RTP-area location
- 34 acre campus. 140,000 ft² facility
- Began contract operations in July 2004



We enhance biologics drug value for our clients through rapid and efficient development of scalable and robust processes that result in quality products



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kSep[®] Technology - Introduction

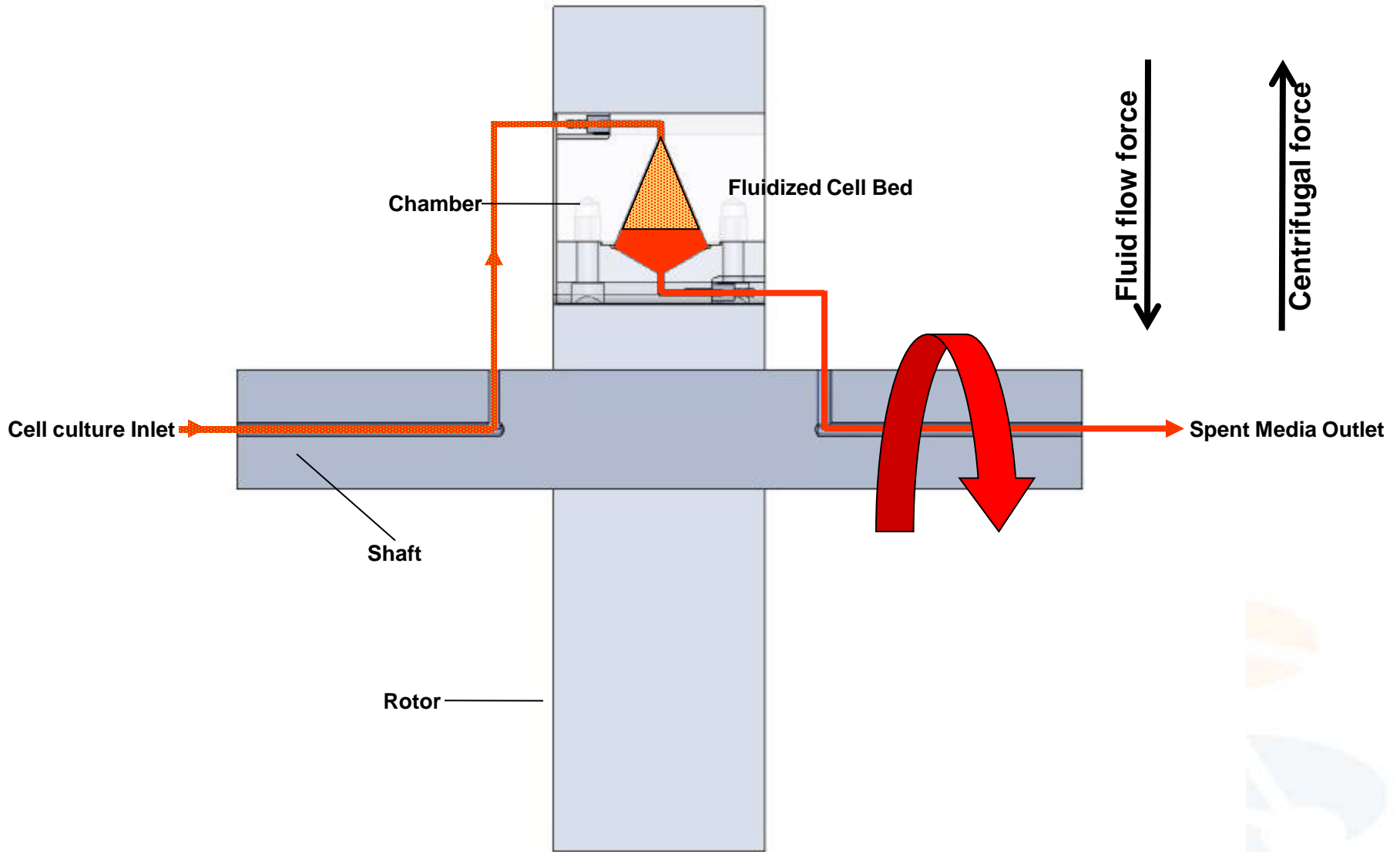
KBI has developed its proprietary kSep[®] technology to solve a wide range of significant bioprocessing problems. We have now successfully completed several client-funded proof of concept programs, resulting in ongoing implementations at these large pharma clients.



Current Issues in Cell Therapy Manufacturing

- Processes used in cell therapy manufacturing are challenging (not simple, scalable, or robust).
- Existing bioprocessing technologies are not applicable to cell therapy manufacturing.
 - Cells are discarded during protein therapeutics manufacturing
 - Cannot use 0.2um filtration
- kSep[®] technology has multiple allogeneic and autologous applications.
 - Cell concentration, washing, harvest, cell fractionation, encapsulation, formulation etc.

Schematic of an Early kSep[®] Prototype



Principle of kSep[®]

- Counteraction of Centrifugal force and fluid flow force
 - Creates fluidized bed of cells
 - Cells remain in suspension
 - Very low shear
 - Constant oxygen and nutrient supply
- Rotation along horizontal axis
 - No gravitational effect , therefore no slant effect
 - Stable fluidized bed even at much larger scales
- Continuous operation
 - Reversal of flow direction empties the chamber
 - System does not stop rotating
- 12 US and international patents granted; 14 pending

Operation of kSep[®]

[Click here](#)



Performance Issues of Traditional Cell Retention Systems

- Centrifugation based (e.g. cont. centrifuge)
 - High shear stress, nutrient deprivation
 - Cell clumping
 - No cell washing option
- Filtration based (e.g. spin filter, ATF, TFF)
 - High Shear stress
 - Clogging, retention and accumulation of cell debris and particulate matter
 - Diafiltration: Inefficient cell washing
- Cell sedimentation: Vertical/ Inclined
 - Scale-up issues
 - Performance issues
- Ultrasonic
 - Scale-up Issues
 - Heat Issues
- Hydrocyclones
 - High-pressure drop
 - Low retention efficiency

kSep[®] Key Advantages

- Advanced cell handling
 - Imparts low shear on cells and keeps the cells intact
 - Maintains healthy environment to sustain viability
 - Reduces intracellular protein contamination for harvest applications by keeping the cells intact
- Bioprocessing
 - Integrates and/or reduces processing steps and time
 - Improves recoveries
 - Provides option to selectively remove small particulate impurities
 - e.g. plastic generated
 - Potential to removes free virus
- cGMP manufacturing
 - Closed system with completely disposable fluid path
 - Simple, Robust, and Scalable
 - Clog-free and continuous operation

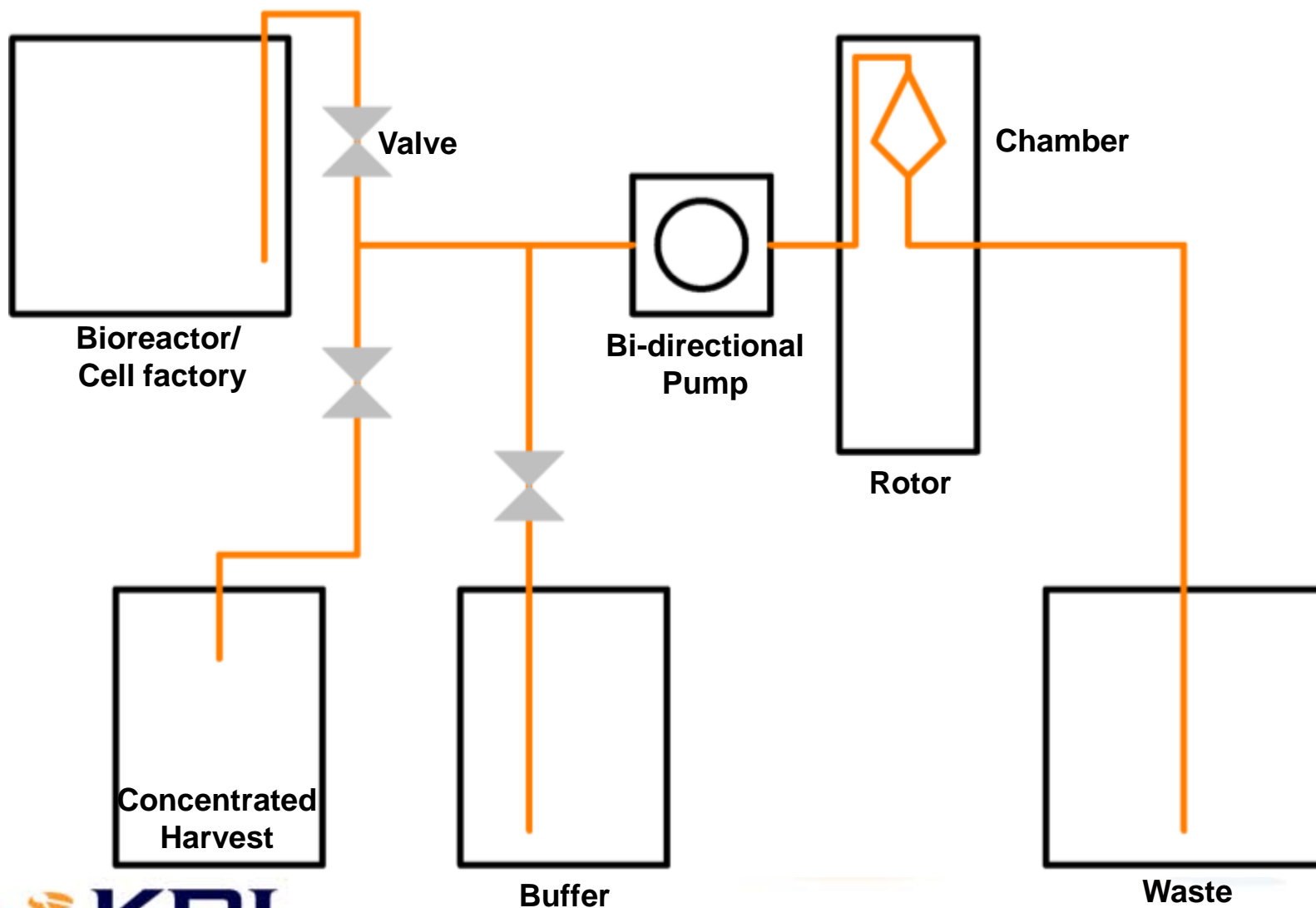
Selected kSep[®] Applications

- Bioprocessing
 - Stem cell manufacturing
 - Cell separation, concentration, washing, harvest
 - Cell banking
 - Cell concentration, washing, harvest
 - Perfusion
 - Cell retention
 - Vaccine production
 - Cell separation, concentration, washing, infection, transfection, harvest
 - Harvest clarification
 - Transfection / Infection
- Medical applications
 - Stem cell isolation and processing
 - Blood processing

kSep[®] Evaluation for Concentration-Wash-Harvest

- Client evaluated kSep[®] for concentration, wash, and harvest of cells prior to transfection
- TFF : Poor recovery, low density, cell death, scale-up
- Goal to maintain $\sim 100 \times 10^6$ cells/mL density after wash
- Goal to have similar transfection efficiency with kSep[®] as the research process (centrifugation-resuspension-centrifugation)
- Client provided the data to KBI

Concentration-Wash-Harvest by kSep[®]



Performance Post-Concentration and Wash

	Volume (mL)	Viable Count/mL	Total Viable Cells	% Recovery	Viability	Size (uM)	Total Cells	% Recovery
Original Cells, Pre-processing	160	1.60E+07	2.50E+09		98.8	17	2.50E+09	
Control Cells	3.5	9.80E+07	3.40E+08		97.2	17	3.50E+08	
kSep® Concentrate 1	22	9.60E+07	2.10E+09	84.60%	96.4	16	2.20E+09	86.70%
kSep® Concentrate 2	25	1.60E+07	4.00E+08	16.00%	97.8	16	4.10E+08	16.20%
kSep® Total			2.50E+09	100.00%	97.1	16	2.57E+09	102.99%

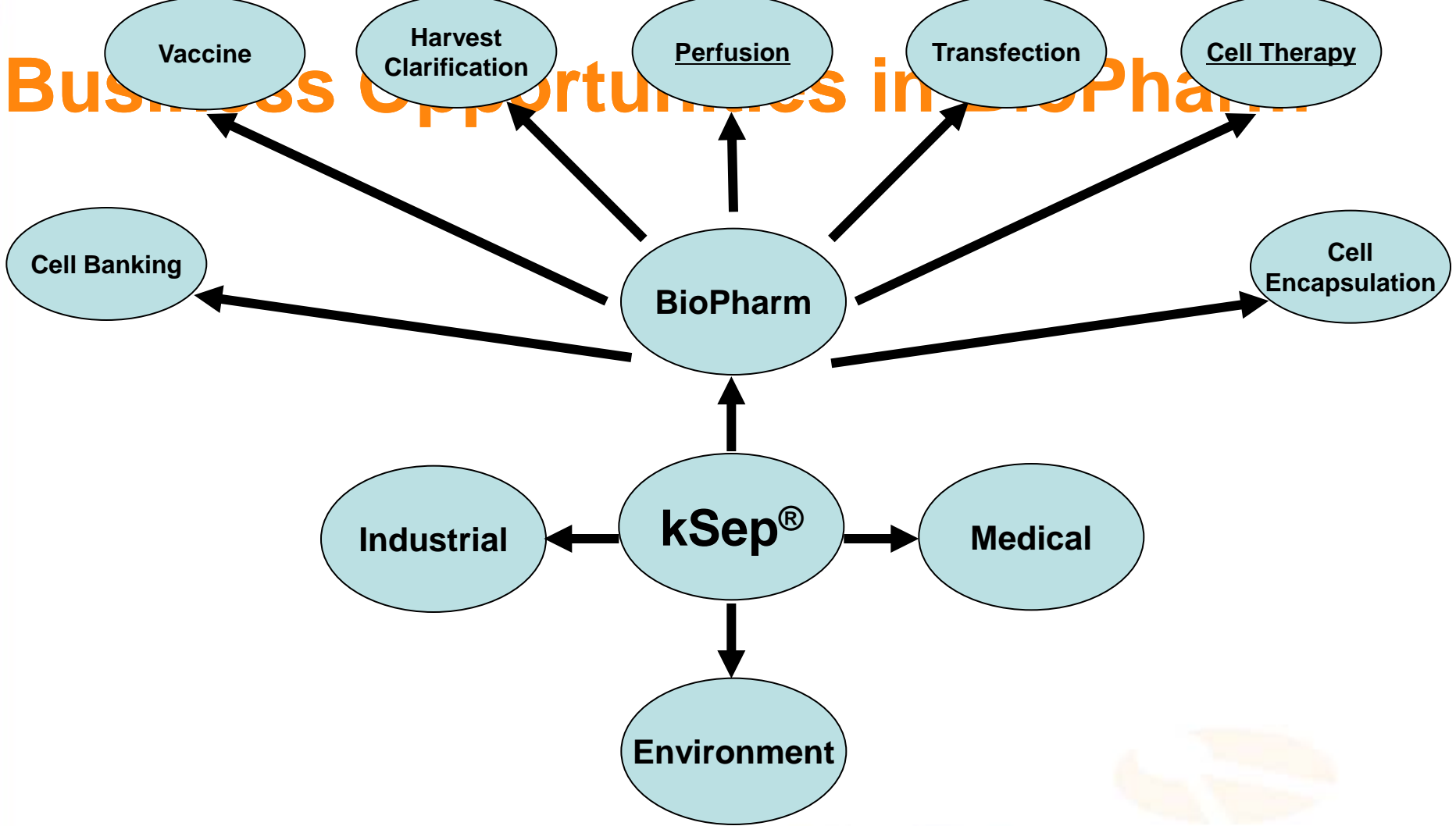
- 100% recovery
- Unchanged viability
- Fast and integrated processing

Transfection of kSep[®]-Processed Cells

Virus productivity of kSep[®] processed cells



Business Opportunities in BioPharma



kSep[®] Design Development

- Designed with Invetech, a leading global equipment engineering and product development firm
- Large pharma clients involved in next generation design
- Modular (Mechanical & Control)
- Two different scale platforms, each capable of processing a range of volumes
- Completely disposable fluid path
- cGMP closed system operational design



Process-scale kSep[®] System



Process-scale kSep[®] System

- Seal-less single-use design using class VI materials
- Automated processing for cell concentration-wash-harvest
- 4 L chamber volume
 - 400-800 billion cell capacity per cycle
- 4L/min flowrate
- cGMP closed system



Disposables Loading



Disposables Loading



Control Panel Menu

KBI BIOPHARMA

Invetech Main Screen

Recipes - Concentrate, Wash & Harvest

Current Selection: s..s (s..s)
Estimated Processing Time (# vessels): ##### #m

Recipe Name:

Active Vessels: **A** B C D

Parameters

Current Recipe

Application Type:

Recipe Name:

Bioreactor Volume: (l)

Vessel Size: (ml)

Wash Volume: (No. of Changes)

Harvest Flow Rate: (ml/min)

Harvest Initial Dump Volume: (ml/vessel)

Harvest Collection Volume: (ml/vessel)

Outlet Waste Tube ID: (in)

Outlet Waste Tube Length: (ft)

Outlet Media Tube ID: (in)

Outlet Media Tube Length: (ft)

Cell Harvest Tube ID: (in)

Cell Harvest Tube Length: (ft)

Centrifuge Speed: (g)

Normal Flow Rate: (ml/min)

Starting Flow Rate: (ml/min)

Time to Establish Bed: (min)

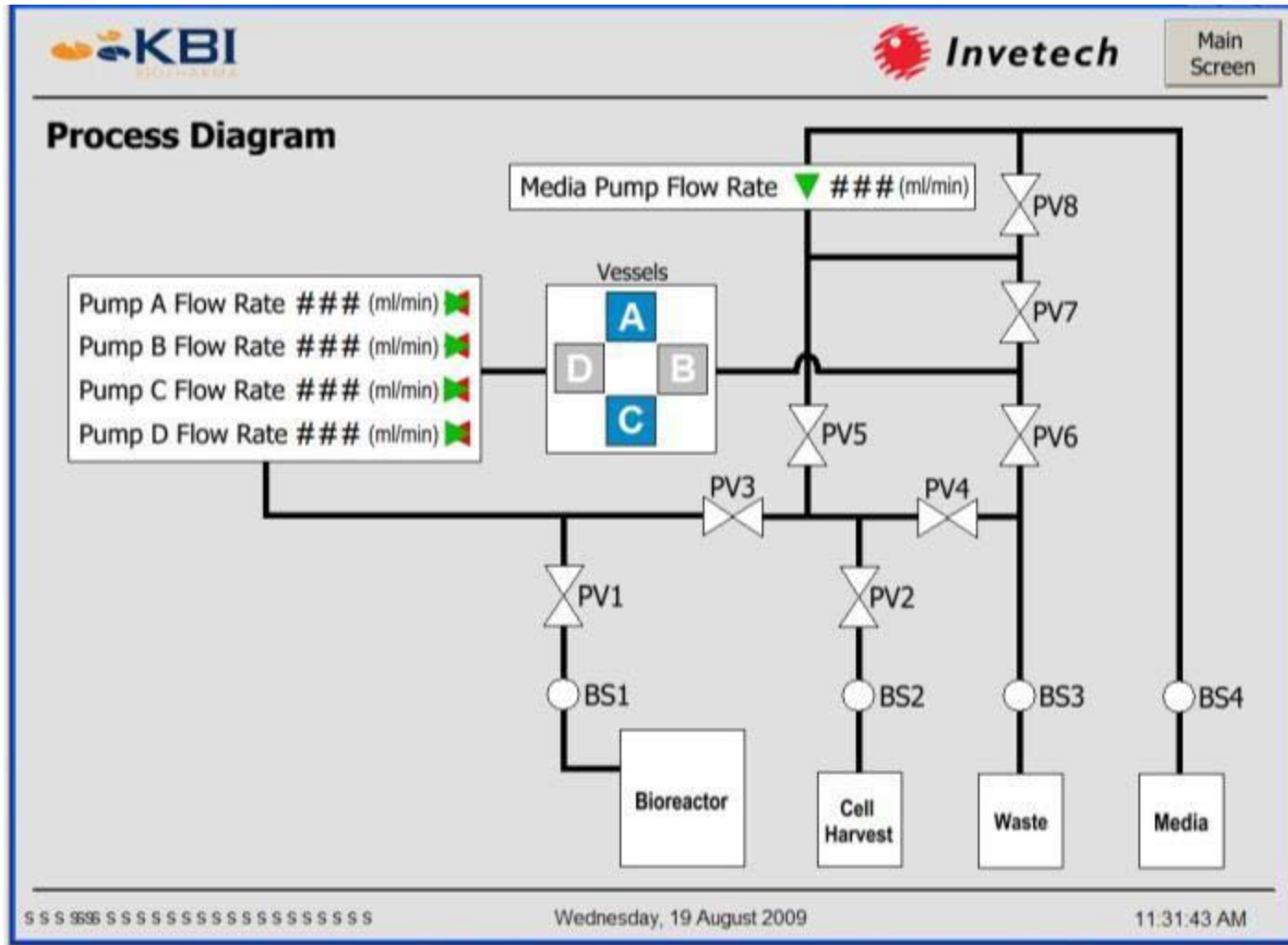
Flow Rate Ramp-Up Time: (min)

Download to Controller

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- Allen Bradley Display
- Built in PC
- 15" touch screen
- Solid state drive.

Control Panel Menu

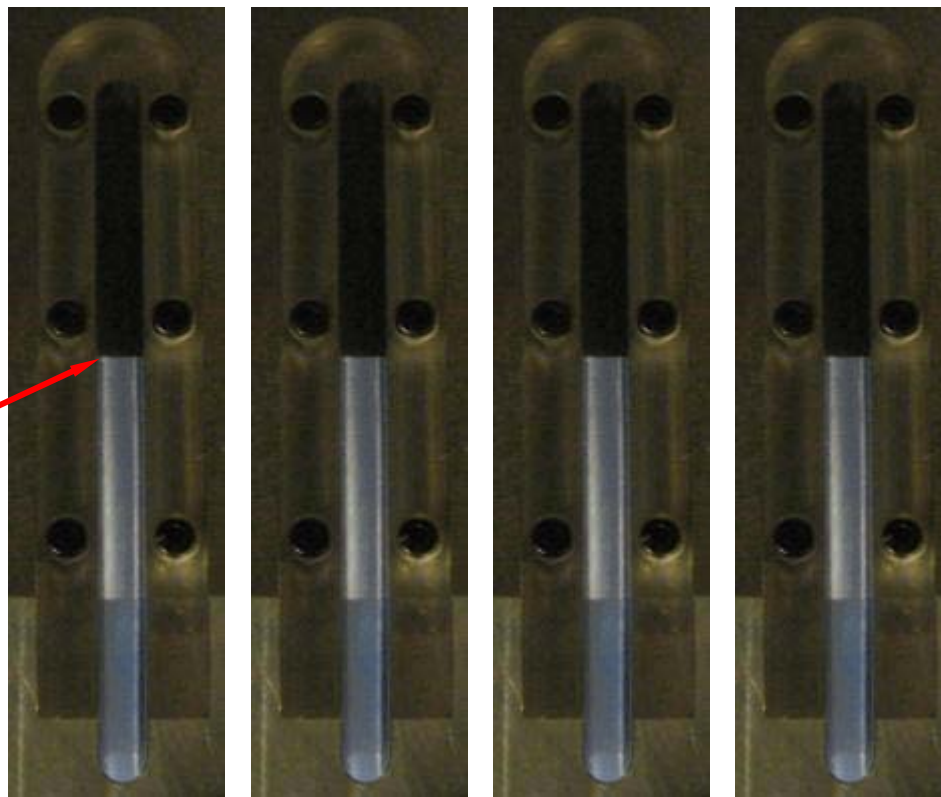


Cell Bed Visualization

Display plan:

Vessel Vessel Vessel Vessel

Cell bed height



Small-Scale kSep[®] System

- Seal-less single-use design using class VI materials
- Automatic cycle for cell concentration-wash-harvest
- 400 mL chamber volume
 - 40-80 billion cell capacity per cycle
- Upto 1000 mL/min flowrate
- cGMP closed system





The Science to Succeed.

Thank You



THE SCIENCE TO SUCCEED.