

# ATMI LifeSciences

Giving life to innovative disposable technologies

Open Architecture Enables  
Integrated Disposable Processes Trains

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IBC Single-Use Conference

June 1-3, 2009

# Agenda

- › Set Stage for Panel Discussion on Interchangeability
  - › SUT Market Overview
  - › Mixing Systems with Open Architecture
    - › Specifications & Data
  - › Outlook for SUTs
- › Transition: DSP Overview & Interchangeability Panel



# Single-Use Technology Outlook

- › Globalization of markets, cost of goods & time to market pressures, rise of biosimilars and threat of epidemics are driving the use of single-use technologies (SUTs) in bioprocessing
- › Single-use bioprocessing technology development will mirror other mature high tech businesses (like microelectronics)
- › SUTs are technically proven and demonstrate compelling economic and operational advantages
  - › SUTs are evolving from components to units of operation to integrated bioprocessing platforms
  - › “Open architecture” provides end-users the best technologies for the best integrated processes
- › SUT innovation will include harmonization of specifications, upgraded product integrity, optimized surface chemistry and “smart” bags and processes
- › End-users and regulators are seeking clarity & harmonization of leachable & extractable specs

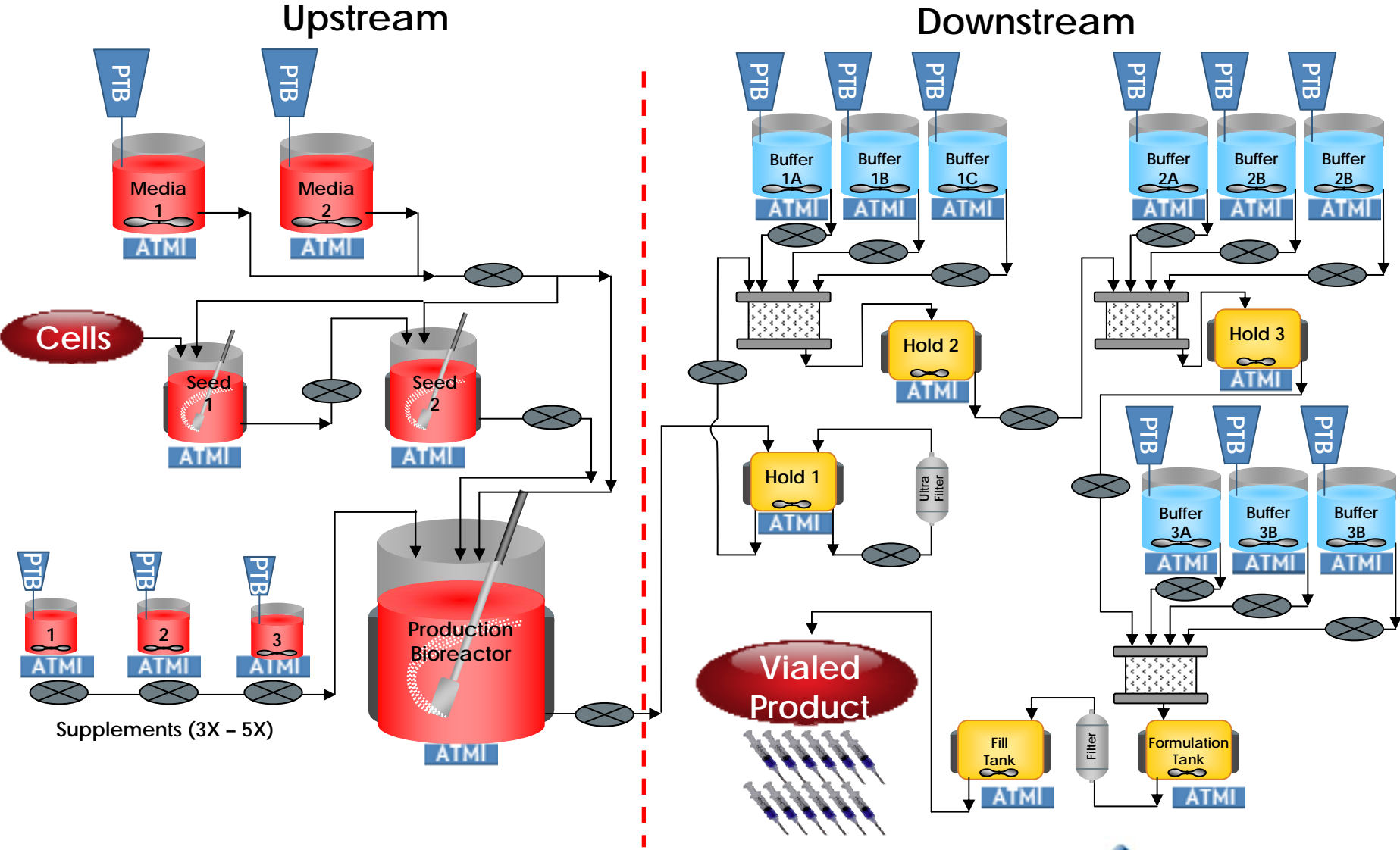


# ATMI Voice of the Customer 2009

- › Drivers
  - › Decrease capital and operating costs
  - › Eliminate cleaning and sterilization of stainless steel vessels
  - › Improve process safety (Reducing risk of cross-contamination and microbial contamination)
  - › Decrease build out time & time-to-market
  - › Flexibility in design
  
- › Current concerns
  - › Unclear leachable & extractable guidelines
  - › Risk of leakage
  - › Delivery time
  - › Vendor dependency
  - › Supply chain reliability
  - › Sustainability



# There are Multiple Mixing Steps in a Typical Train



# Selecting Best Mixing Technology Requires “Open Architecture”

**Table 1.** Typical mixing applications and disposable technology options for cell culture

		Bioreaction	Mixing media	Mixing buffers	pH adjustment	Blending (i.e., ultra-filtration)	Reaction	Formulation
<b>Typical process integrity</b>	Sterile	X					O	X
	Bioburden control				X	X	X	
	Nonsterile (contained)		X	X				
	Nonsterile (open)			X				
<b>Duties (primary)</b>	Gas liquid	X						
	Heat transfer	X	O	O				
	Solid-liquid		X	X				
	Liquid-liquid equivalent volumes					X	X	X
	Liquid-liquid small to large volumes				X		X	
<b>Mixing technologies</b>	Agitator mechanical	A	A	A	A	A	A	
	Agitator magnetic coupled	P	Op	Op	A	A	A	A
	Paddle	A	A	A	A	A	A	
	Recirculation				A	A	A	A

X: primary requirement; A: used and should be actively considered; O: required in some applications; Op: an option that might require testing for a particular application

Source: Andrew Sinclair, BioPharm Services, 2009.




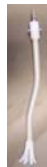
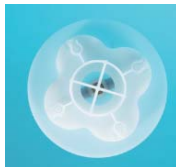


# Other Considerations for Best Mixing System

- › Scale & Scalability
- › Particle generation
- › Shear / grinding sensitivity
- › Footprint & height
- › Portability
- › Ease of Storing Process Intermediates
- › Interchangeability / Flexibility (Vessel Size, Application)
- › Continuity of supply
- › Support & service
- › Intellectual property

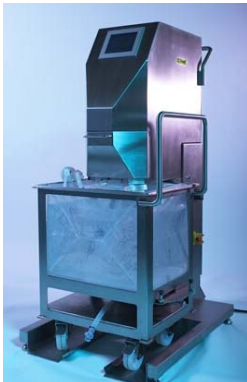


# Mixing Systems: Product Segmentation

	Pad-Drive	LevMixer	Magnetic Mixer	WandMixer	Jet-Drive
Mixer/ Segmentation					
Positioning	All Applications, High-end Controls & Abilities	Versatile Mixing, Universal Drive Machine	Industrious Buffer and Media Machine	Small Scale Mixing	Stackable & Portable Homogenization
Primary Advantage	Comprehensive Application Range	Universal Drive (one drive unit services all bag volumes)	Robust Mixing	Economy with Ability	Stackable Tanks
General Applications	Ultra-Clean All Powder to Liquid All Liquid to Liquid	Ultra-Clean Most Powder to Liquid Most Liquid to Liquid	Clean All Powder to Liquid All Liquid to Liquid	Clean Most Powder to Liquid Most Liquid to Liquid	Clean Most Liquid to Liquid
Standard Container Volumes (L)	25, 50, 200, 500, 1000	30, 50, 100, 200, 350, 500, 1000	50, 100, 200, 350, 500, 1000, 2000	5, 10, 20, 50, 100, 200	50, 200
Focused Applications	Purification Suspension/Re- suspension Final Formulation, Fill Harvesting Media, Buffer Preparation	Purification Suspension/Re- suspension Final Formulation, Fill Harvesting Media, Buffer Preparation	Buffer Preparation Media Preparation Formulation High Viscosity Mixing Heavy Powder Loads	Media, Buffer Preparation Purification Suspension/Re- suspension Final Formulation, Fill Harvesting	Homogenization Re-Homogenization Harvesting Storage & Transport

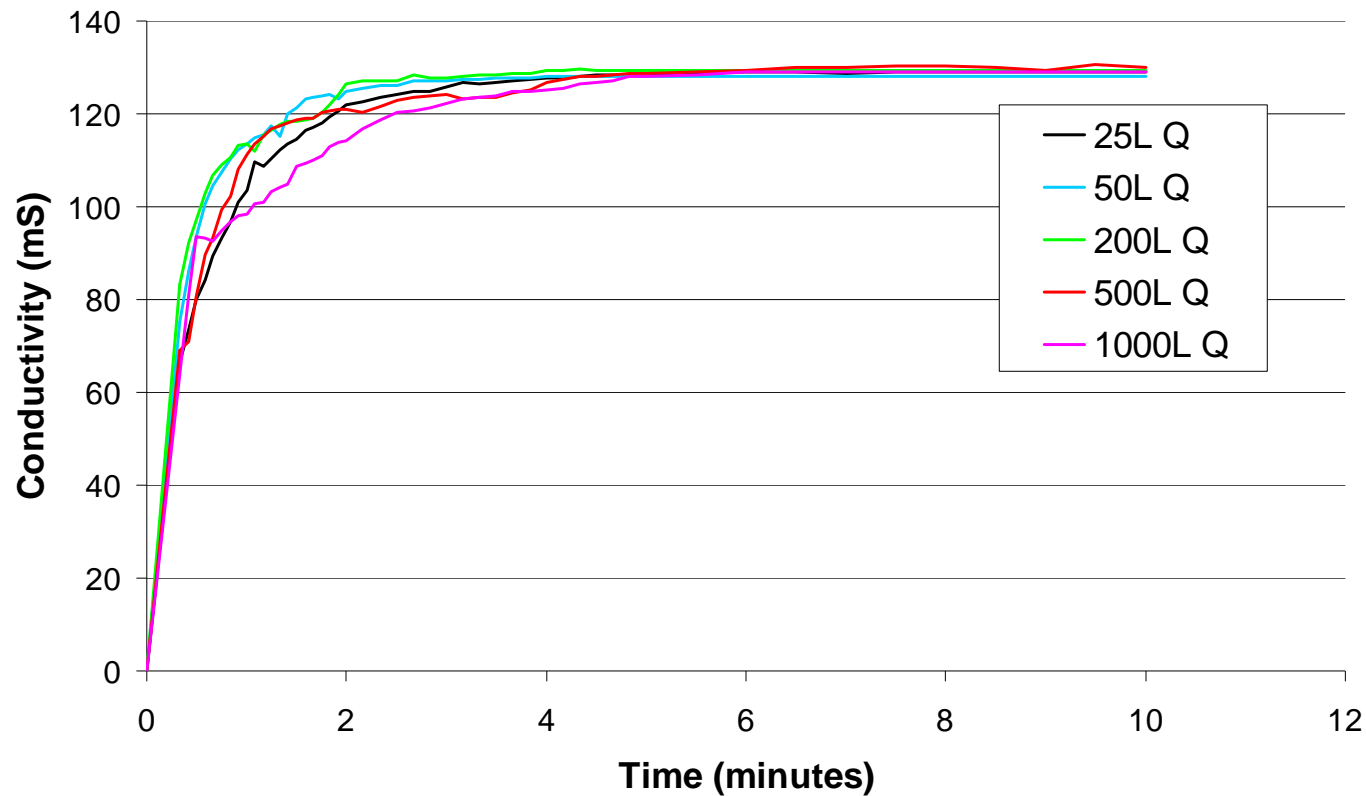
# Pad-Drive™ System

- › Accommodates scaling from 5L up to 1000L
- › Comprehensive application range
- › Ultra-clean; one product contact material
- › Inflating system to assure the perfect shape of the mixing bag
- › Height adjustable for different container/bag sizes
- › Alternating mixing direction to increase mixing efficiency
- › Optional jacketed containers for cooling and heating processes
- › Adjustable rotation angle of stir rod fo different bag volumes



# Pad-Drive™: Performance (Powder)

Scale-ability PAD-Drive: mixing performance at fixed RPM (70) and fixed angle (15°). Mixing of 10% salt in water.



Mix Times = <5 min

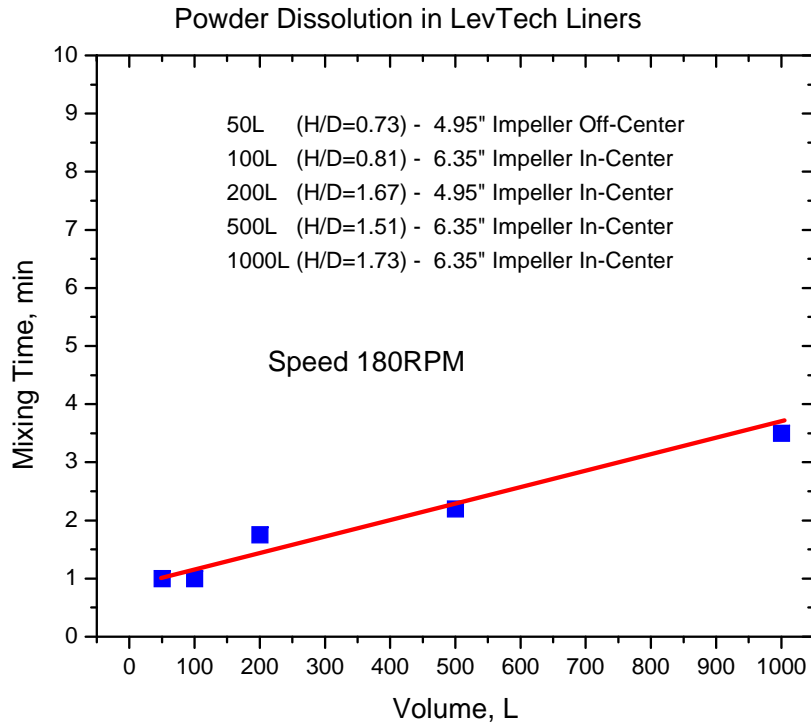


# LevMixer® System

- › Accommodates scaling from 5 to 2000L
- › Universal drive (one drive unit services all bag volumes)
- › Ultra-clean; no shafts, seals or bearings inside the mixing bag
- › Portable, ergonomic hardware
- › Simple and quick bag installation
- › Hardware is easy to set-up and operate/control
- › Integration of floor scales or load cells
- › Jacketed containers enable cooling and heating processes

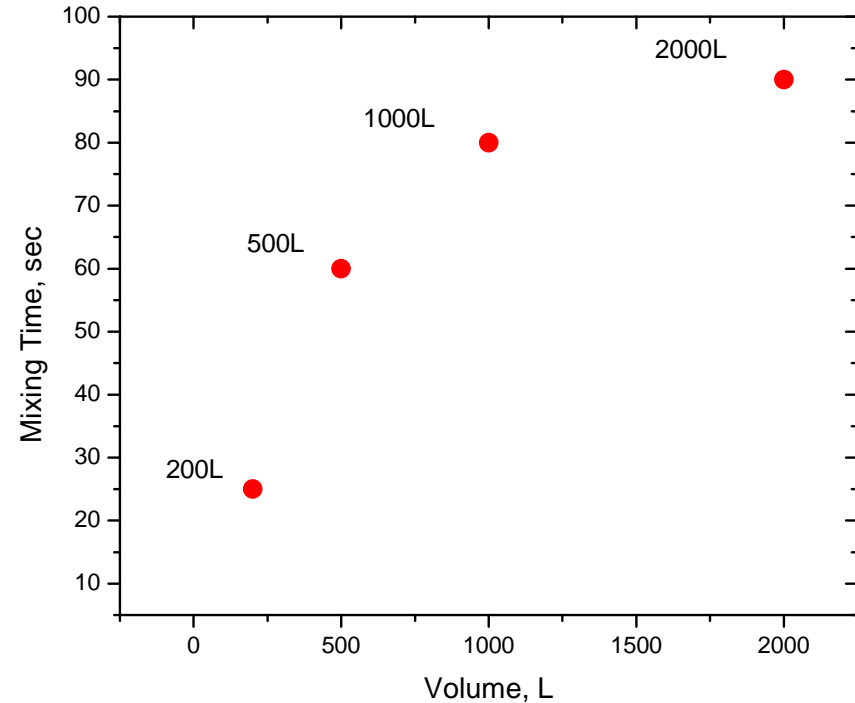


# LevMixer<sup>®</sup>: Performance (Powder & Liquid)



Mixing time of powder NaCl to 0.15M in 50L, 100L, 200L, 500L and 1000L LevMixer

**Mix Times = 1 to 3.5 min**



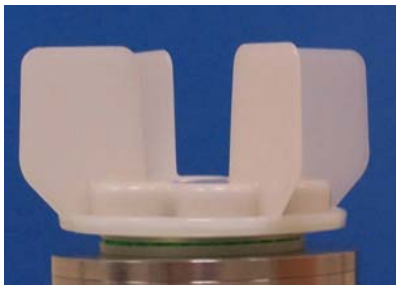
Fluid-In-Fluid Mixing in 200-2,000L liners with Levitated impeller (3L NaCl Solution, ~250g/L)

**Mix Times = 25-90 sec.**

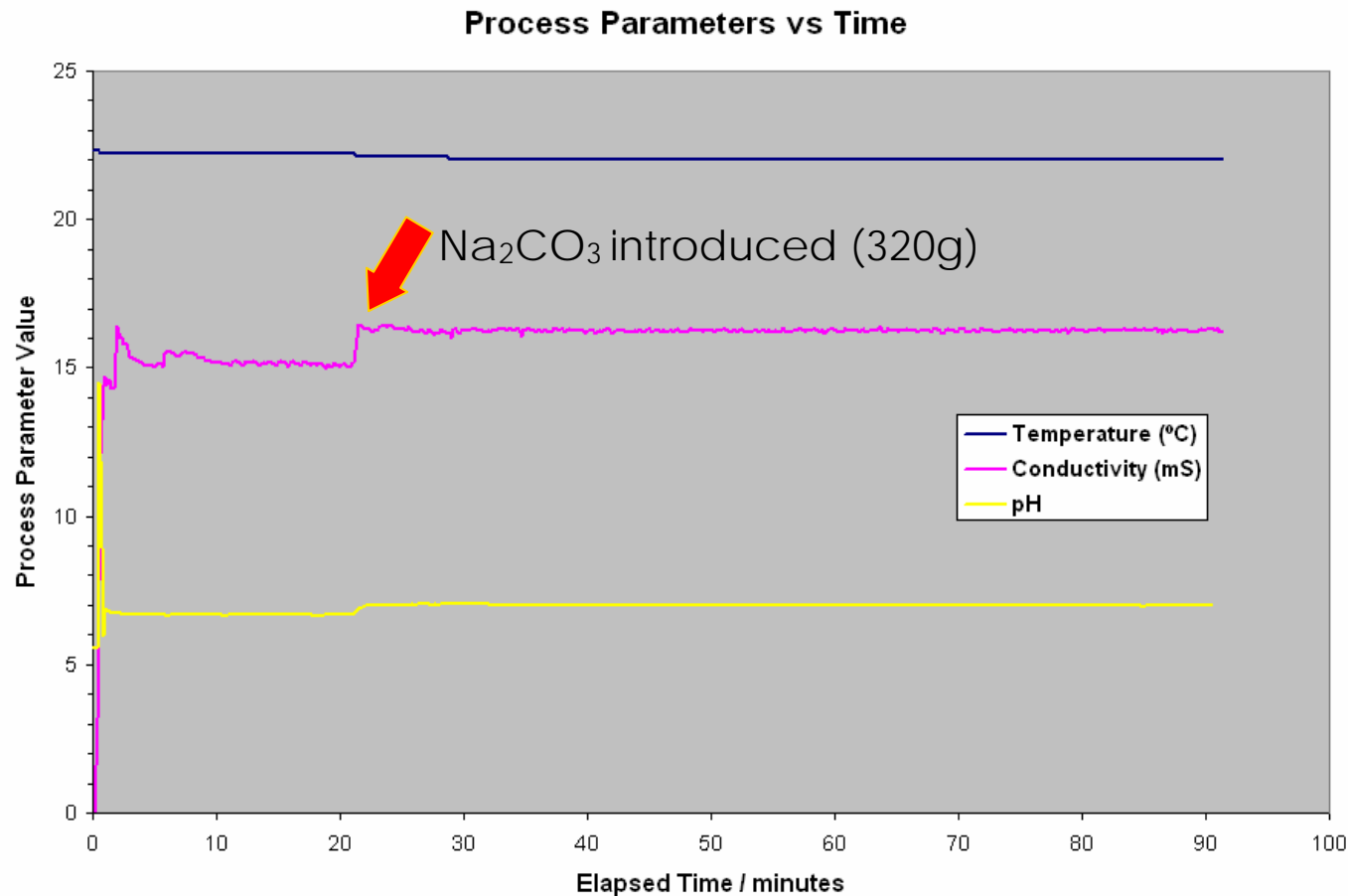


# Magnetic Mixer System

- › Accommodates scaling from 5L up to 2000L
- › Robust mixing. Aggressive power for industrial applications
- › Universal drive (one drive unit services all vessel volumes)
- › Portable, ergonomic hardware
- › Simple and quick bag installation
- › Hardware is easy to set-up and operate/control
- › Optional floor scales or tanks with integrated load cells
- › Optional jacketed containers for cooling and heating processes
- › Designed to resist shedding of particles



# Magnetic Mixer: Performance (Powder Media)



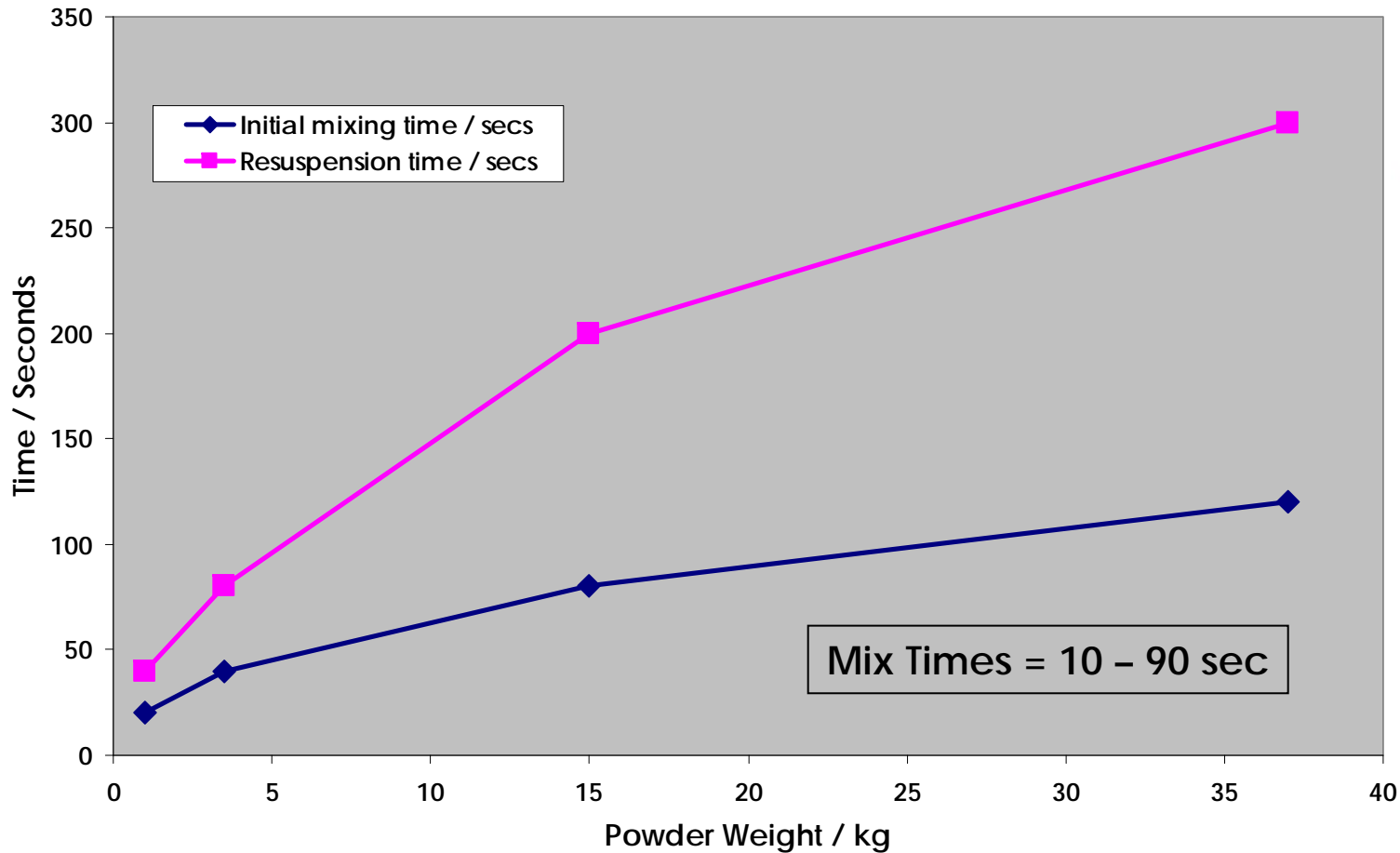
- Hydrating Media Powder at the 180L Scale using a Magnetic Mixer with 200L vessel
- SAFC Ex-Cell 302 Serum-Free CHO; Dry Powder Media (4,242g from NewSafe powder transfer bag)
- Impeller = 6.35" in center location, 300rpm

Mix Times = 10 & 8 min



# Magnetic Mixer: Performance (Colloidal)

Mixing and Re-Suspension Times vs. Powder Weight



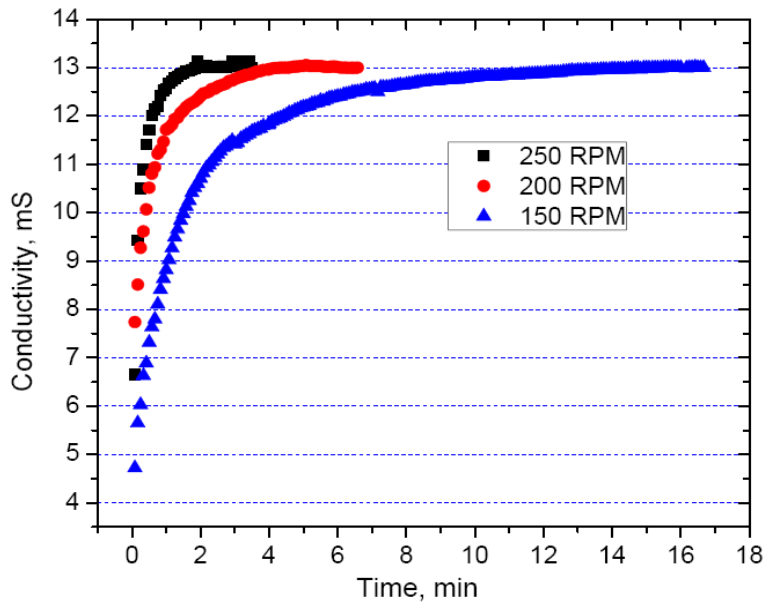
- Diatomaceous earth powder ( $d=0.22\text{kg/L}$ ) up to a cumulative weight of 37kg
- 37kg was suspended within 1.5 minutes. (6.35' Impeller/300rpm)
- After allowing the powder to settle & completely cover the magnetic impeller, the mixer was able to fully re-suspend the powder in less than 5 minutes.
- At no time did the impeller stall or hesitate.

# WandMixer® System

- Scalable; Bench-top (1L to 20L), floor-based (10L to 200L)
- System provides economy with ability
- Flexible hardware accommodates multiple tank sizes
- Simple and quick bag installation
- Hardware is easy to set-up and operate/control
- Optional floor scales or integrated load cells
- Optional jacketed containers for cooling and heating processes

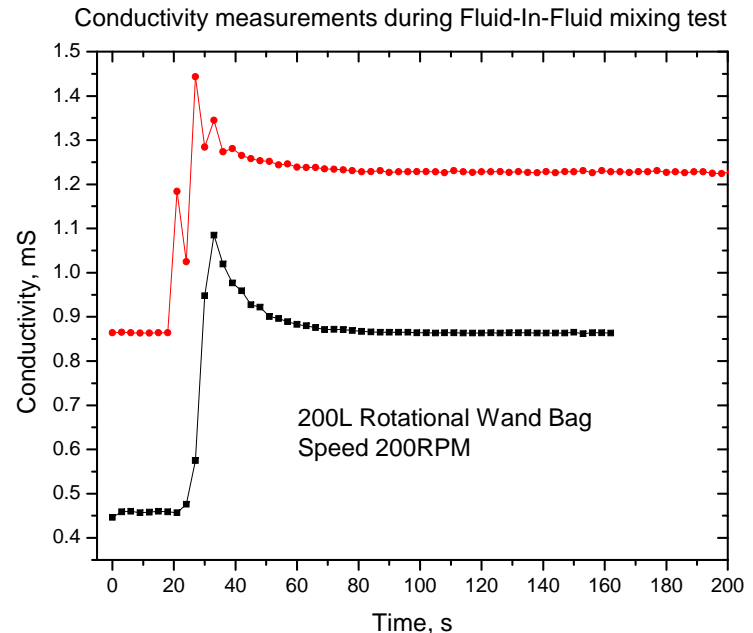


# WandMixer<sup>®</sup>: Performance (Powder & Liquid)



WandMixer NaCl Powder Mixing Time (15L)

Mix Times = 1 - 10 min



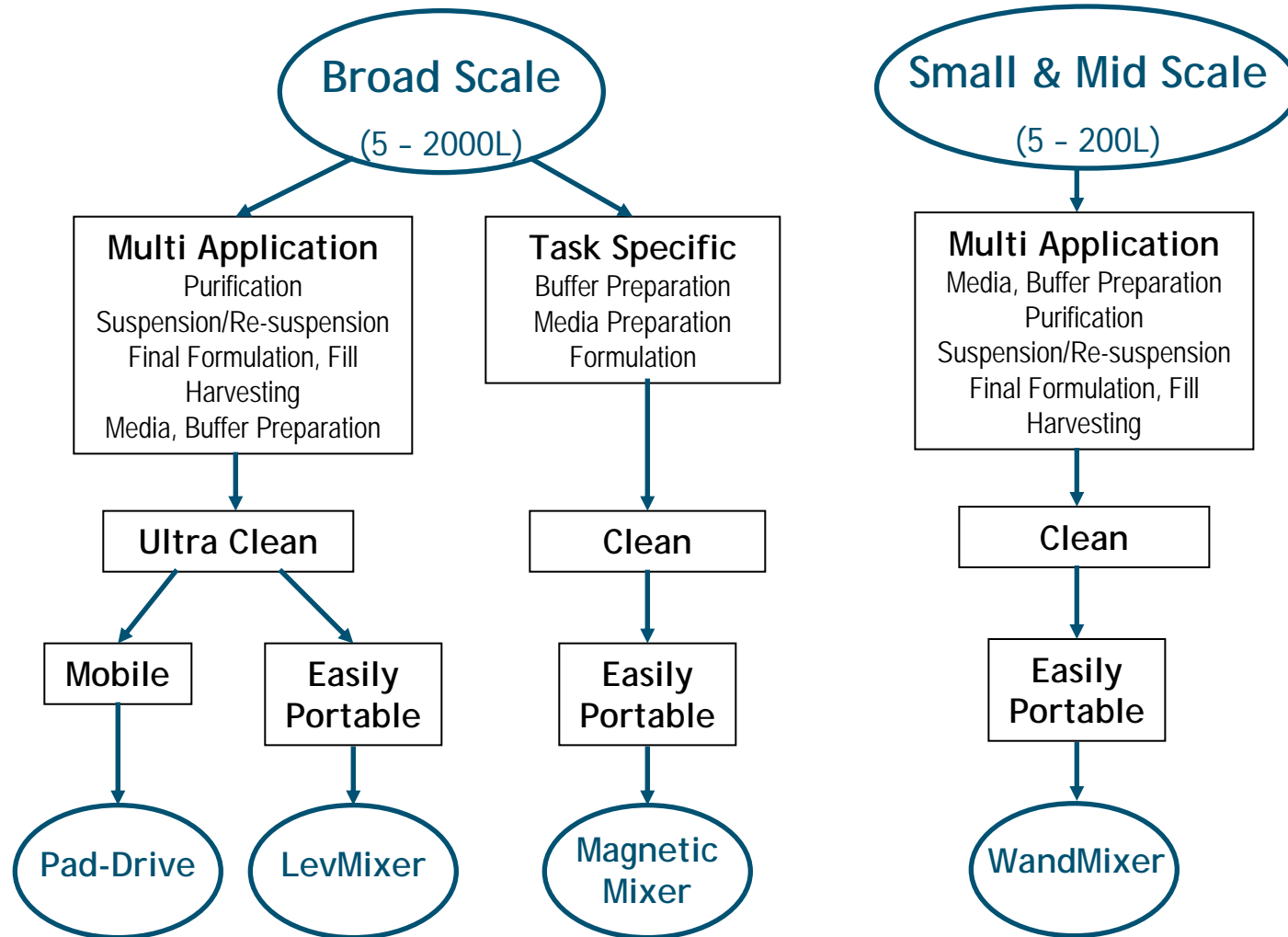
Conductivity measurements during Fluid-In-Fluid mixing test

WandMixer Liquid Mixing Time (200L)

Mix Times = 70 sec

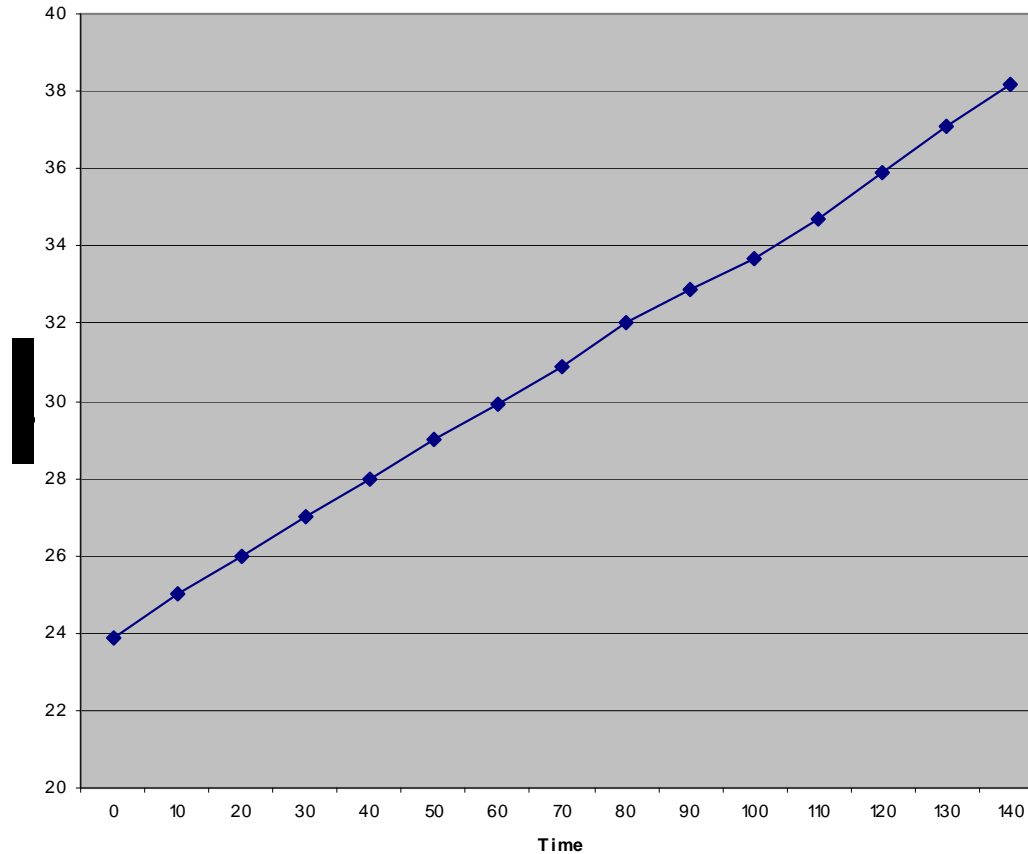


# ATMI Mixing System Segmentation



# Mixing Vessel Temperature is Controllable

## LevMixer®; 200L; 24C to 38C

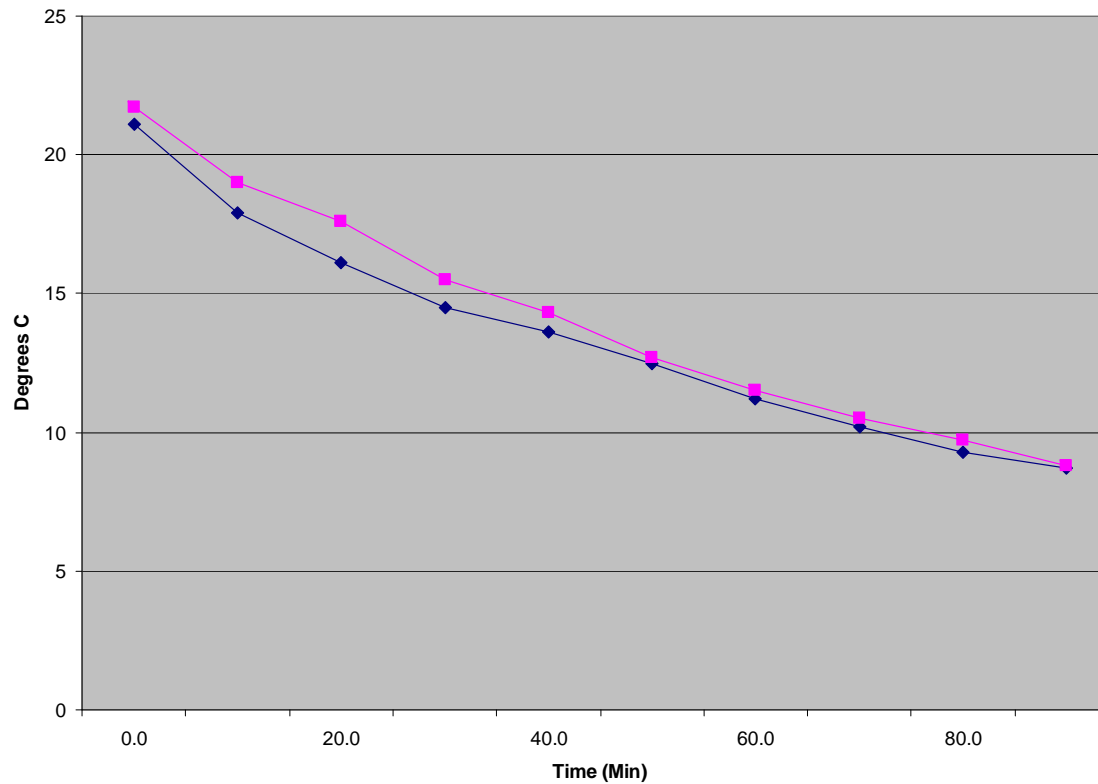


Time vs. temperature in a 200L LevTech disposable mixing bag, retained in a 200L stainless steel jacketed tank. Heating performed by Polyscience laboratory-scale recirculating heater. Heater: 2200W. Flow Rate: 13L/min. Impeller speed: 180RPM. *Study performed by LevTech.*



# Mixing Vessel Temperature is Controllable

## LevMixer®; 100L; 22C – 9C

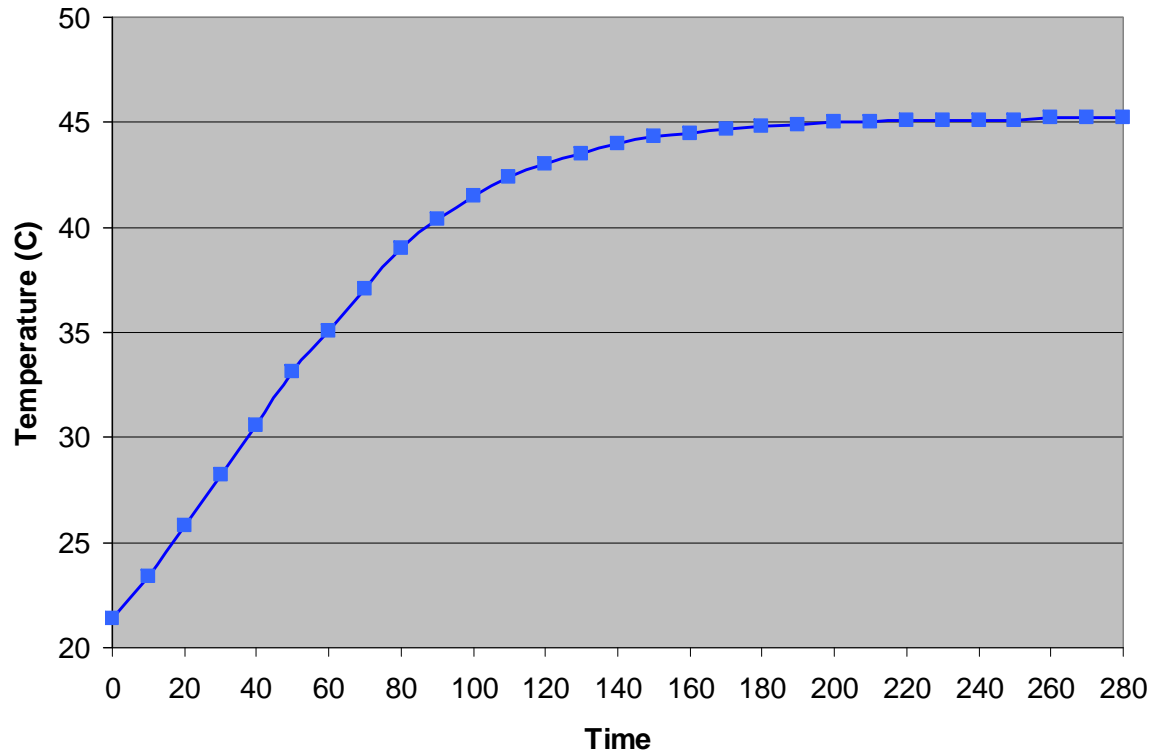


Time vs. temperature in a 100L LevTech disposable bag retained in a 100L stainless steel jacketed tank. Cooling performed by Lada chiller. Impeller speed: ~170RPM. Study performed by LevTech customer.



# Mixing Vessel Temperature is Sustainable

LevMixer®; 100L; 20C - 45C



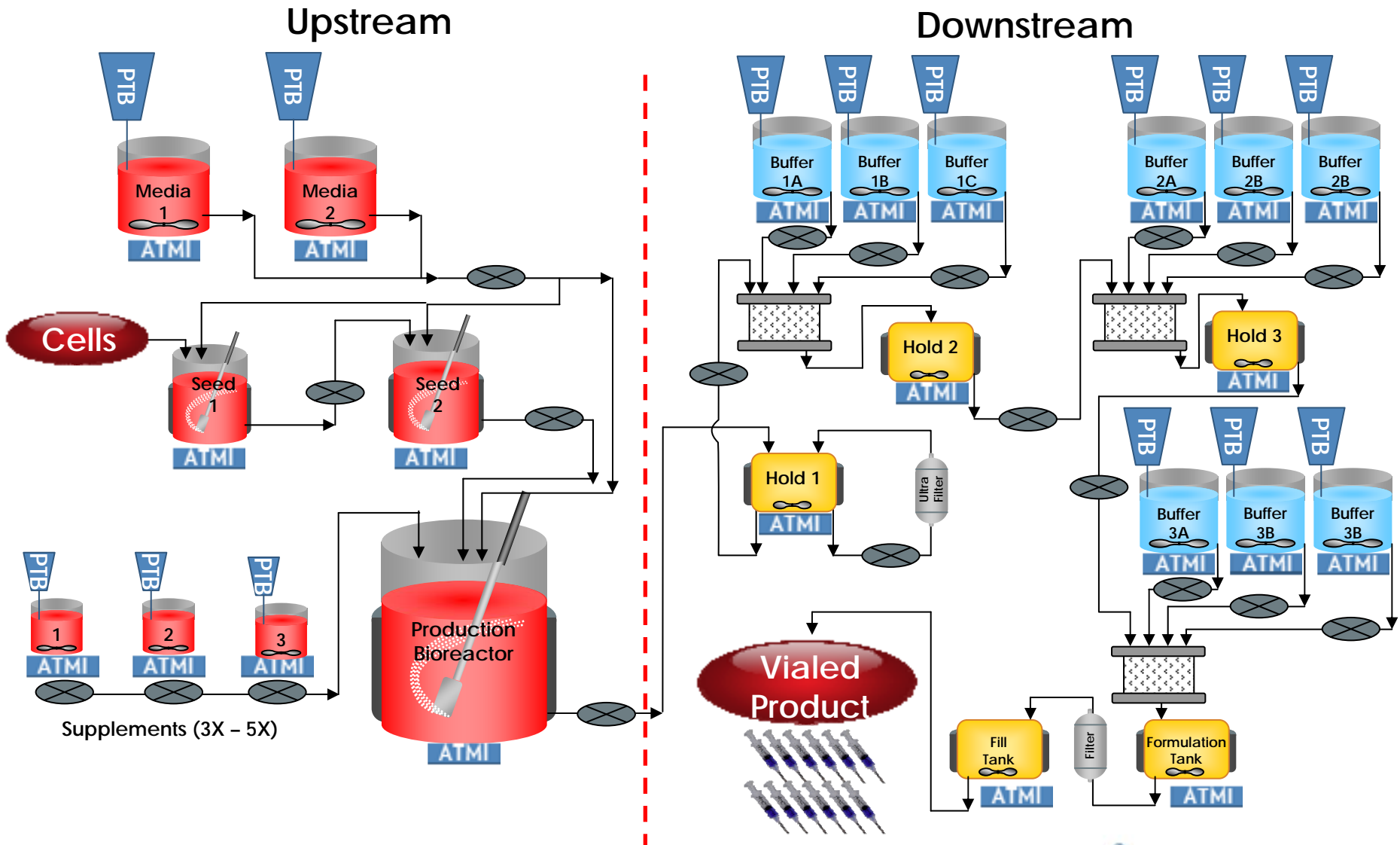
Time vs. temperature in a 100L LevTech disposable mixing bag, retained in a 100L stainless steel jacketed tank. Heating performed by Polyscience laboratory-scale recirculating heater. Heater: 2200W. Flow Rate: 13L/min. Impeller speed: 180RPM. *Study performed by LevTech.*



# Integrated ATMI Systems



# Open Architecture Provides Best Mixer for Each Operation



# Conclusions/Outlook

- › SUTs are evolving from components to units of operation to integrated bioprocessing platforms
- › “Open architecture” provides end-users the best technologies for the best integrated processes
- › End-users and regulators are seeking clarity & harmonization of leachable & extractable specs (**End users MUST participate in drafting of these standards.**)
- › There are unmet needs to be addressed in the area of downstream processing





**Thank You**

**Back-up Slides**

# Microelectronics versus BioPharm

Industrialization of microelectronics brings valuable perspective to the biopharmaceutical industry

- › Exacting quality requirements
- › Breakthrough processing innovation drives industry
- › Robust growth of market
- › Globalization of markets
- › COGS and time to market pressure
- › Consolidation of businesses = vertical integration of technologies
- › Movement of manufacturing to Asia
- › Need for continuous improvement to process & cost efficiency
- › Need for best tools per unit operation (Open Platform)

Single-use bioprocessing market is about a decade behind semiconductor manufacturing market

