Leaders in

Scalable Ultracentrifugation Solutions

ALFA WASSERMANN
SEPARATION TECHNOLOGIES

AWST.COM

ALFA WASSERMANN

SEPARATION TECHNOLOGIES

Leaders in Scalable Ultracentrifugation Solutions

Alfa Wassermann Separation Technologies (AWST), a subsidiary of Alfa Wassermann Inc., for over 60 years the supplier whose singular purpose has been the support of bioprocess and pharmaceutical industries by providing expertise in continuous flow ultracentrifugation separation applications, fluid management solutions, and process monitoring.

AWST systems are designed, manufactured, serviced, and supported to the highest level of quality to:

- Maximize product yield
- Standardize bio-manufacturing processes
- Minimize costs

AWST's continuous flow ultracentrifuges efficiently and reliably separate viruses, virus like particles and viral vectors for the development and manufacture of vaccines, gene therapies, and other bio-products. With the addition of the AWST Automated Fluid Handling (AFH), customers now have a system that fully automates and standardizes critical bio-manufacturing processes.

Products Overview

Continuous flow ultracentrifugation

Promatix 1000®

Research & Development

Develop protocols for the separation, fractionation and concentration of AAV, viral vectors, virus-like particles, viruses, viral and bacterial vaccines, macromolecules and cellular organelles.

PKII

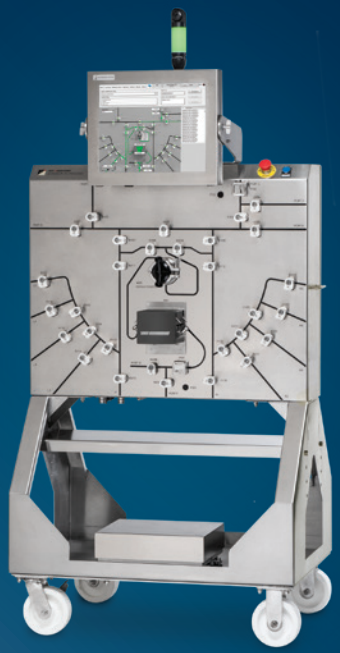
Pilot Scale-up

Sized for scale up process development and pilot scale production, suitable for use in cGMP manufacturing.

KII

Production Scale

The KII Ultracentrifuge system is designed for industrial scale production suitable for use in cGMP manufacturing.



AFH

Automated Fluid Handling

Fully automated, customizable fluid handling system in a self-contained, mobile work station that supports fluid filling and fractionation.

KII Ultracentrifuge

cGMP Production Scale Manufacturing

The KII system is designed to expertly perform in FDA approved processes for the manufacture of viral vaccines, particulate proteins, gene therapies and nanostructures.

The KII Ultracentrifuge is the global standard for vaccine manufacturing. This unit is selected more than any other manufacturer's system because of its reliability, funtionality and cost effective operation.

Alfa Wassermann's extensive experience in the design, manufacture, service and support of continuous flow ultracentrifuges in the vaccine manufacturing industry is demonstrated in the KII ultracentrifuge. The KII's control system has all the features expected from modern bioprocess equipment. The large rotor volumes yield high process volumes when manufacturing vaccines and other bio-products.

Highly regarded for its versatility, reliability and ease of operation, the KII is the benchmark for quality in the large scale commercial preparation and production of bioprocess materials.

Density gradient ultracentrifugation allows concentration and purification in a single step which reduces process time while increasing overall yield and production capacity. Our range of linear scalable rotor cores enables scale up and scale down of process parameters*. The simple fluid path design of KII ultracentrifuge rotors create a low shear environment for maximum viability of virus particles during downstream processing.

* Patent Pending

Features include:

- Up to 200 L production capacity per batch
- Multiple rotor configurations in air turbine or electric motor drive
- Throughput — up to 60 L/h
- Rotor capacity — up to 8.4 L
- Speed — 40,500 rpm
- Centrifugal force — 121,000 xg

PKII Ultracentrifuge

cGMP Pilot Scale Manufacturing

The PKII Ultracentrifuge retains all the cGMP capabilities of the KII ultracentrifuge and features scalable rotor design for process development studies or production scale output with one rotor system.

This technology platform is designed for efficient, linear scale-up unique to AWST ultracentrifuges. In addition to widespread use for purification, the PKII can be used for large scale clarification applications.

The PKII is manufactured to meet specific customer needs from pilot to small scale production. With a range of linear scale cores, the rotor capacity can be adjusted from 400 mL to 1,600 mL while retaining the same separation parameters as the KII and Promatix 1000 ultracentrifuges.

Features include:

- Up to 100 L production capacity per batch
- Multiple rotor configurations in air turbine or electric motor drive
- Throughput — up to 60 L/h
- Rotor capacity — up to 4 L
- Speed — 40,500 rpm
- Centrifugal Force — 121,000 xg

AW Promatix 1000

Research and Development with Linear Scalability

The Promatix 1000 is designed to develop protocols for the separation, fractionation and concentration of viral vectors, virus-like particles, viruses, viral and bacterial vaccines, macromolecules and cellular organelles.

Fully programmable to run user defined applications. Fully automated for gradient and product loading, continuous flow separation, fraction collection and cleaning. The system provides operators with easy to read continuous displays of operational steps, critical run data and subsystem status.

Scalable cores available with the Promatix 1000 enable researchers to utilize continuous flow methodologies with research scale process volumes and eliminate traditional small scale, batch-type processes. The AWST patented core technology allows for linear scalability to full manufacturing scale with no revalidation or compromise of yield and purity.

Features include:

- Process volumes from 500 mL to 10 L
- Electric motor drive
- Linear scale down or scale up capability
- Rotor capacities 55 mL, 120 mL, 230 mL
- Speed 35,000 rpm
- Centrifugal force 90,500 xg

AFH

Automated Fluid Handling System

Alfa Wassermann's fluid handling system fully automates and standardizes the critical process of fluid filling and fractionation in a self-contained mobile work station.

System design includes:

- Fluid routing pinch valves
- Flow rate and direction control pump
- Flow, pressure, and temperature product sensors

AFH software comes pre-loaded with standard fluid handing protocols. Custom protocols that include sanitation, rinsing, filling, fractionation and other methods can be programed on site by the user. Network integration is available to utilize upstream/downstream inputs and outputs via open platform communication (OPC).

- Fully automated filling and fractionation of ultracentrifuge density gradient process
- Operator programmable standard and customized process steps
- Real time display and stored reporting of critical process parameters
- Compact, mobile and self-contained with reservoir and process bag storage shelf

Benefits of Automated Fluid Management

Features	Benefits
Standard and customizable processes	• Model existing SOP's • Repeatable sequences without variation result in more consistent batches • Simplifies operator training • Reduces procedural errors that can result in rejected batches
Domain authentication of system operators	• Eliminate the need for special operator databases and database maintenance by integrating with existing facility security policies
SQL Server database stores all methods, batch data and audit logs	• All information is stored locally in a 21 CFR Part 11 compliant database • Access to all data is provided to the facility system administrator
Storage and real time monitoring of critical parameters: pressure, flowrate, temperature, weight, Brix value and density	• Warns operator of out of limit conditions potentially saving costly batch loss • Stored databases for easy access to previous batch parameters
Integrated OPC Server	• Network integration allows the AFH to react with and respond to other facility equipment • Batch records integrated with facility data history
IP65 enclosures, non-contact pump, pressure transducers and temperature monitors	• System can be cleaned without special preparation • Disposable Class VI refractometer flow cell (PES material) reduces cost • Optional stainless steel 316 flow cell for easy cleaning
Expandable	• Specific customer instrumentation can be integrated into the fluid handling system

Linear Scalability

Linear scalability delivers operational efficiency and cost savings in the product development race.

Only Alfa Wassermann uniquely designed ultracentrifuges are linear scalable. Data analysis of product peaks for each run confirm similar peak height and width in both the KII large-scale, PKII Pilot-scale and the Promatix 1000 research scale ultracentrifuge systems. The peak densities are similar in all centrifuge runs.

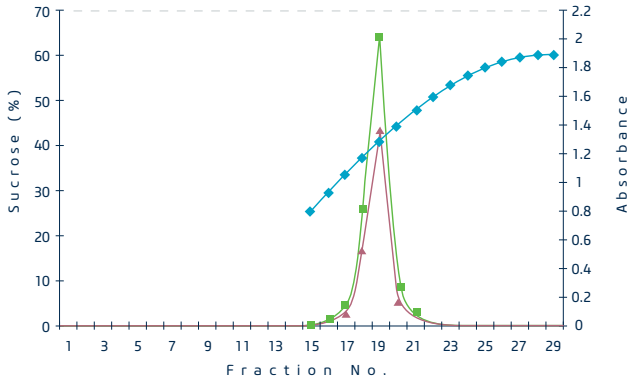
The figures on page 13 describe a similar gradient shape across the Alfa Wassermann range of ultracentrifuges. From the figures both scalability and linearity of the particle separations are achieved.

Scalability is demonstrated because the run parameters remained the same with the only variation being rotor volume.

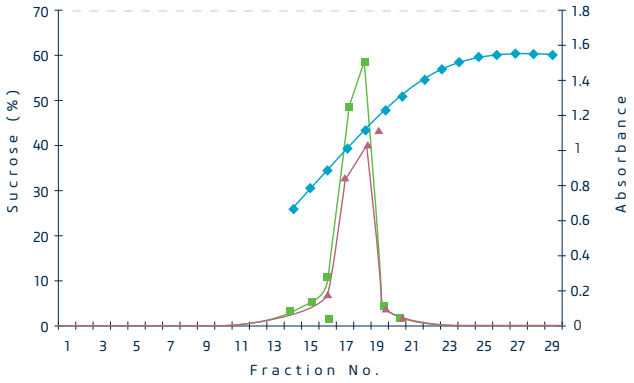
Linearity is confirmed: equivalent product separation and gradient formation are achieved in the KII large-scale, PKII pilot-scale and the Promatix 1000 research scale. Throughout each run, product separation at the iso-dense layer and equivalent product peak shape in the gradient for each scale rotor assembly are achieved.

In operational runs where the sucrose gradient remains identical and only volumetric differences vary between each separation, Alfa Wassermann ultracentrifuges deliver the same separation parameters in processes where the product volume is to be scaled up or down.

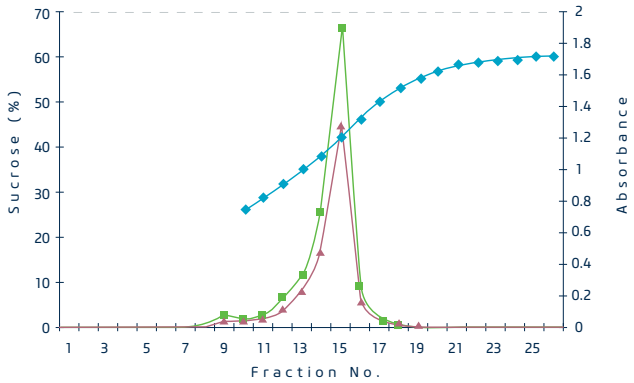
KII with K3 Core 3200 mL



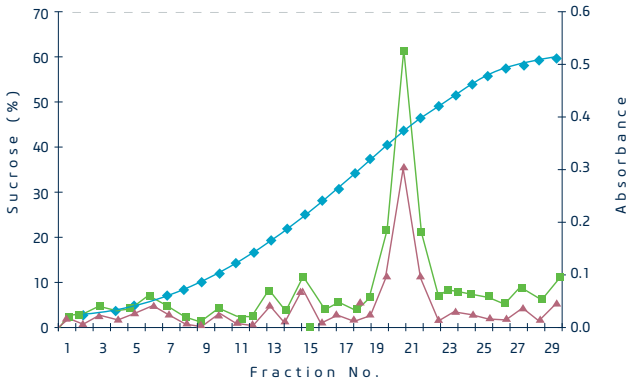
PKII with PK3 Core 1600 mL



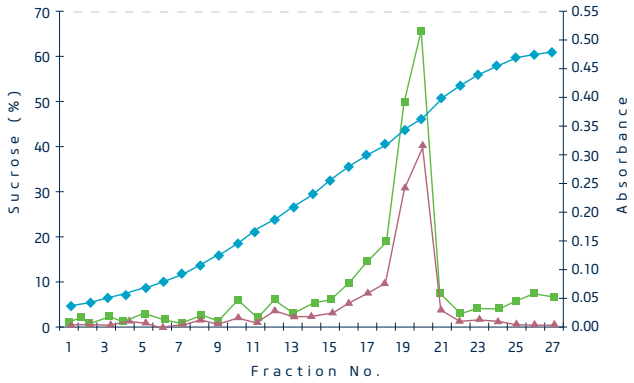
PKII with PK3 Core 800 mL



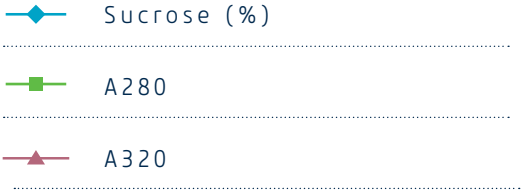
PKII with PK3 Core 400 mL



Promatix 1000 with PX3 Core 230 mL

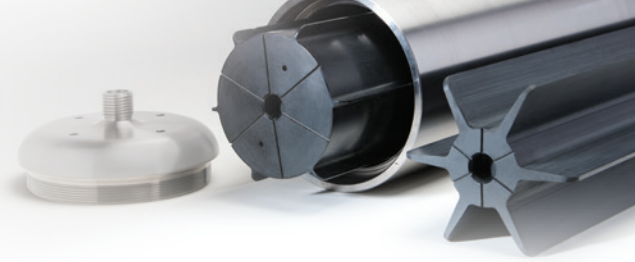


Legend



Core	Flow Rate	Time to Sediment	Speed of Operation	K Factor	Centrifugal Force Max	Centrifugal Force Min
3200 mL*	28 L/h	2.5 min	40,500 rpm	29.7	121,200 xg	100,000 xg
1600 mL*	14 L/h	2.5 min	40,500 rpm	29.7	121,200 xg	100,000 xg
800 mL*	7 L/h	2.5 min	40,500 rpm	29.7	121,200 xg	100,000 xg
400 mL*	3.5 L/h	2.5 min	40,500 rpm	29.7	121,200 xg	100,000 xg
230 mL*	1.5 L/h	3.4 min	35,000 rpm	40	90,500 xg	74,600 xg

*See U.S Patent : 9,050,609



Rotor Specifications and Applications

Alfa Wassermann offers a broad range of rotors each uniquely suited to specific particle applications and desired volumes. Rotor volumes range from as little as 0.19 L to 8.4 L for batch or continuous flow operations. Common applications include Influenza, AAV, Adenovirus, Hepatitis B, Rabies, and more.

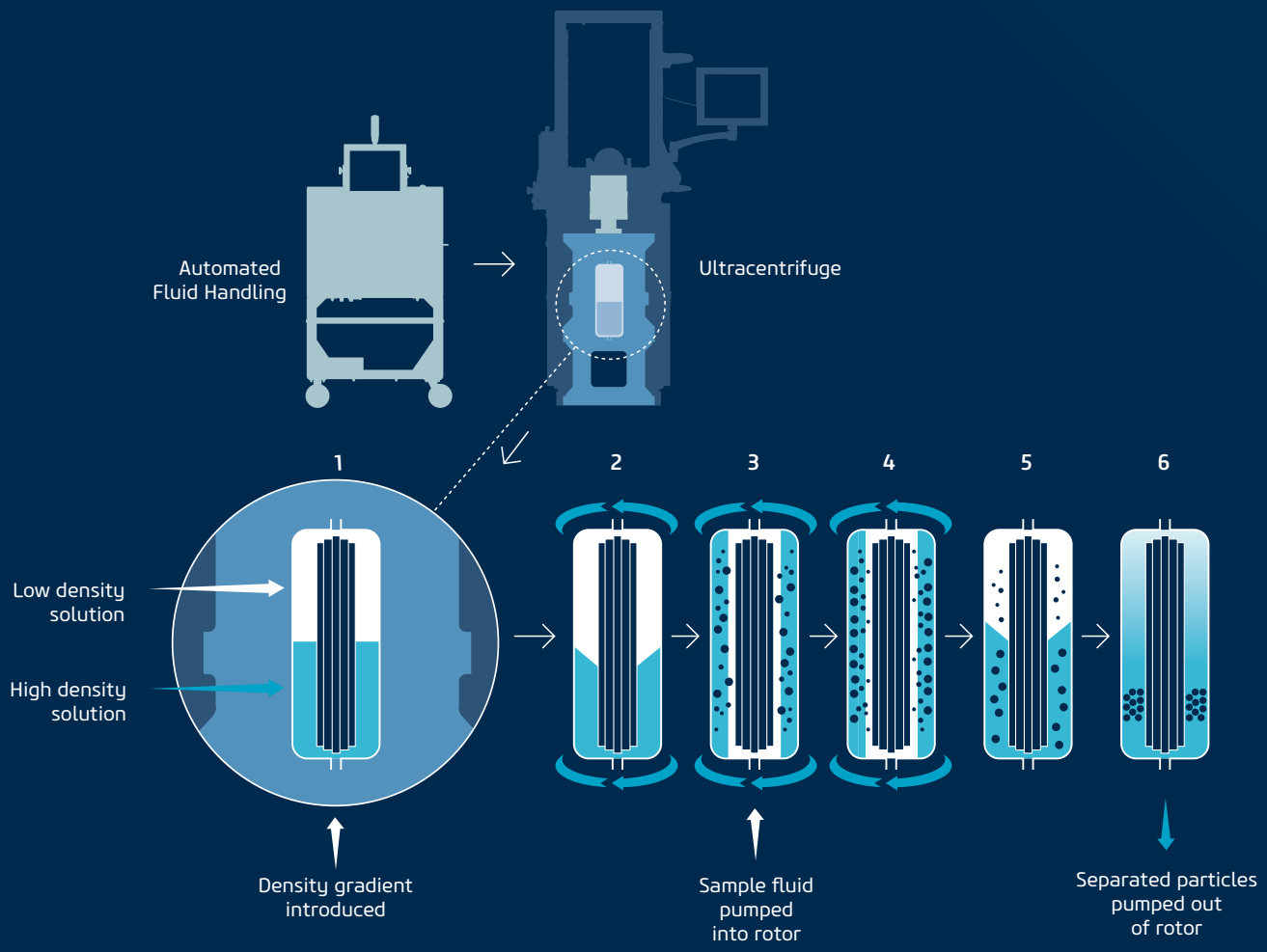
Each rotor assembly is composed of a tubular bowl and two end caps which are made of titanium alloy. Contained within the titanium bowl is the Noryl® rotor core. This assembly forms flow channels down which process material flows during operation.

Maximum Speed and Centrifugal Force	**40,500 rpm, 121,000 xg**
Flow Rate Range	**0 L/h (batch) up to 60 L/h**
Process Volume	**500 mL to 200 L continuous flow**

Rotor Type	Application	Max. Force	Capacity with Core	Dimensions
 K3 PKII PK3	Continuous flow Isopycnic banding	At 40,500 rpm **Rmax:** 121,200 xg **Rmin:** 100,000 xg **K factor** 29.7	3.2 L 1.6 L 0.8 L 0.4 L	**Diameter:** **Max:** 130 mm **Min:** 110 mm **Path Length:** 11 mm
 K5	Rate zonal separations	At 40,500 rpm **Rmax:** 121,200 xg **Rmin:** 38,500 xg **K factor** 177	8.4 L	**Diameter:** **Max:** 130 mm **Min:** 42 mm **Path Length:** 45 mm
 K5	Continuous flow isopycnic banding with pre-clarifier	At 40,500 rpm **Rmax:** 121,200 xg **Rmin:** 100,000 xg **K factor** 29.7 **Pre-clarifier:** **Rmax:** 53,900 xg **Rmin:** 49,000 xg	3.2 L **Pre-clarifier:** 0.17 L	**Diameter:** **Max:** 130 mm **Min:** 110 mm **Path Length:** 11 mm **Pre-clarifier Diameter:** **Rmax:** 58 mm **Rmin:** 23 mm
 K10 PK10	Isopycnic banding separation	At 40,500 rpm **Rmax:** 121,200 xg **Rmin:** 38,500 xg **K factor** 140	8.0 L 4.0 L	**Diameter:** **Max:** 130 mm **Min:** 53 mm **Path Length:** 39 mm

Particles are separated by buoyant density using a reorienting gradient

Step	Process
1	While at rest the rotor is filled, using a pump, with density gradient material.
2	During rotor acceleration the density gradient reorients vertically inside the rotor.
3	Once at operating speed, product fluid containing the vector particles is pumped into the rotor.
4	Vector particles begin to sediment radially and band isopycnically in the gradient. Waste material flows out of the rotor.
5	After the product fluid is processed, the rotor is decelerated and brought to a stop. The gradient reorients horizontally while retaining particle separation.
6	With the rotor now at rest, the desired separated particles are now ready to be collected.



Applications

	Influenza Vaccine	Rabies Vaccine	Hepatitis B Vaccine	Adenovirus Vector	AAV
System	KII	KII	KII	PKII	Promatix 1000
Rotor	K3 3.2 L	K3 3.2 L	K5 8.4 L	PK3 1.6 L	PX3
Flow Rate	20 L/h	16 L/h	Batch Operation	10 L/h	10 mL/m
Gradient	0-55% (w/w) sucrose	0-65% (w/w) sucrose	0-55% (w/w) sucrose	0-40% (w/w) Nycodenz®	1-50% (w/w) Iodixanol
Volume	150 L	40 L	5 L	20 L	100 mL
Capture	95%	95%	100%	95%	99%
Recovery	70%	90%	80%	70%	80%
Purification factor	x 50	x 90	x 10	x 20	x 10

Service and Technical Support

Alfa Wassermann has a rich history of product innovation and unsurpassed commitment to customer care. With service and support tailored to the unique needs of each customer, no other company can match our breadth of experience and technical expertise in ultracentrifugation solutions for the biopharmaceutical industry.

Service for all AWST systems is performed only by our expertly trained service engineers. AWST engineers are skilled in the use of our products which result in maximizing operational uptimes and efficiencies that meet customer needs.

To meet the needs of biopharmaceutical manufacturing and customer specific design requirements, AWST provides a design qualification pipeline to generate user specific hardware and software interfaces.

With AWST as your separation and fluid handling solutions provider comes the peace of mind you get from having:

- Dedicated Service Engineers
- Flexible maintenance tailored to your specific needs
- Expertise in process and method development
- Complete validation packages
- Installation support and on-site training
- Software customization to specific customer requirements

System Control

A PLC or PC based control runs the proprietary AWST control interface. Critical speed control and lubrication systems are built in with alarms configured to protect the product and machine.

Control Interface

A Windows® based HMI allows for easy operator interaction. Input of data is via keyboard and touch screen. On-screen visual and audible alarms enable unattended operation.

Monitoring Data

- Speed
- Vacuum
- Lubrication Flow
- Coolant Flow
- Lubrication Level
- Coolant Level
- User ID
- Password
- Batch ID
- Rotor ID
- Batch Time
- System Run Time
- Rotor Run Time

System Technical Data

Parameter	Specification
Rotor Material	Titanium Alloy
Core Material	Noryl®, PEEK or Titanium
Drive Technology	Electric Motor or Air Drive
Process Flow Rates & Pressures	Up to 60 L/h @ 1 bar max.
Process Temperatures	4 to 30°C +/- 2°C
Process Volumes	Up to 200 L per run
Maximum Speed	40,500 rpm +/- 100 rpm
Maximum Centrifugal Force	121,200 xg
Process Connections	3A Sanitary Fittings
Material (process wetted)	316 SS, Titanium, Noryl®, Teflon®, 440C SS, Vespel, Viton, Class VI Rulon face seals and Parafluor O-rings
Lubricants	General and H1 food grade hydraulic oil
Noise emissions	Compliant with CE; suitable for use in laboratory environments
Control Panel Specifications	IP65 HMI with touch screen
Interface Language	English, French, German, Italian, Russian, Dutch
Regulatory Compliances	Hybrid 21 CFR part 11, GAMP
Manufacturing Compliances	CE, ISO 13485 Registered Company
Warranty	1 year including rotor

Installations Requirements

	e-drive	Air Drive
Models Available	eKII ePKII Promatix 1000	KII PKII
Process Air	N/A	2.83 m^3/min at 6.9 bar
Process Cooling	Integrated	4.5° C, 4 L/min
Electrical Supply	32 A 1ph 230 V 50-60 Hz	15 A 1ph 230 V 50-60 Hz
Environmental Conditions	0-40° C, RH 85%	0-40° C, RH 85%
Clean Room Classifications	Class B,C,D	Class B,C,D
Bio-containment	Up to BL3	Up to BL3
Dimensions	eKII: 84 cm W x 67 cm D x 288 cm H ePKII: 84 cm W x 67 cm D x 222 cm H Promatix 1000: 129 cm W x 84 cm D x 156 cm H	KII: 206 cm W x 180 cm D x 288 cm H PKII: 206 cm W x 180 cm D x 222 cm H
Minimum Height Requirements	eKII: 300 cm ePKII: 250 cm Promatix 1000: 190 cm	KII: 300 cm PKII: 250 cm
System Weight	epKII: 1050 kg eKII: 1140 kg Promatix 1000: 480 kg	pKII: 1200 kg KII: 1270 kg

	AFH
System Weight	180 kg
Electric	100-240 V 16 A 50/60 Hz
Dimensions	91 cm W x 66 cm D x 214 cm H

Please note: Installation requirements and technical data can vary by system. Contact your sales representative for further details.

ALFA WASSERMANN

Alfa Wassermann, Inc.
4 Henderson Drive . West Caldwell, NJ 07006 . USA
T 1-800-220-4488 F 1-973-276-0383
E info@awst.com

Alfa Wassermann B.V.
Lorentzlaan 5 . 3401 MX IJsselstein . The Netherlands
T +31 348 487 300 F +31 348 433 000
E office@AlfaWassermann.nl

SEPARATION TECHNOLOGIES | AWST.COM