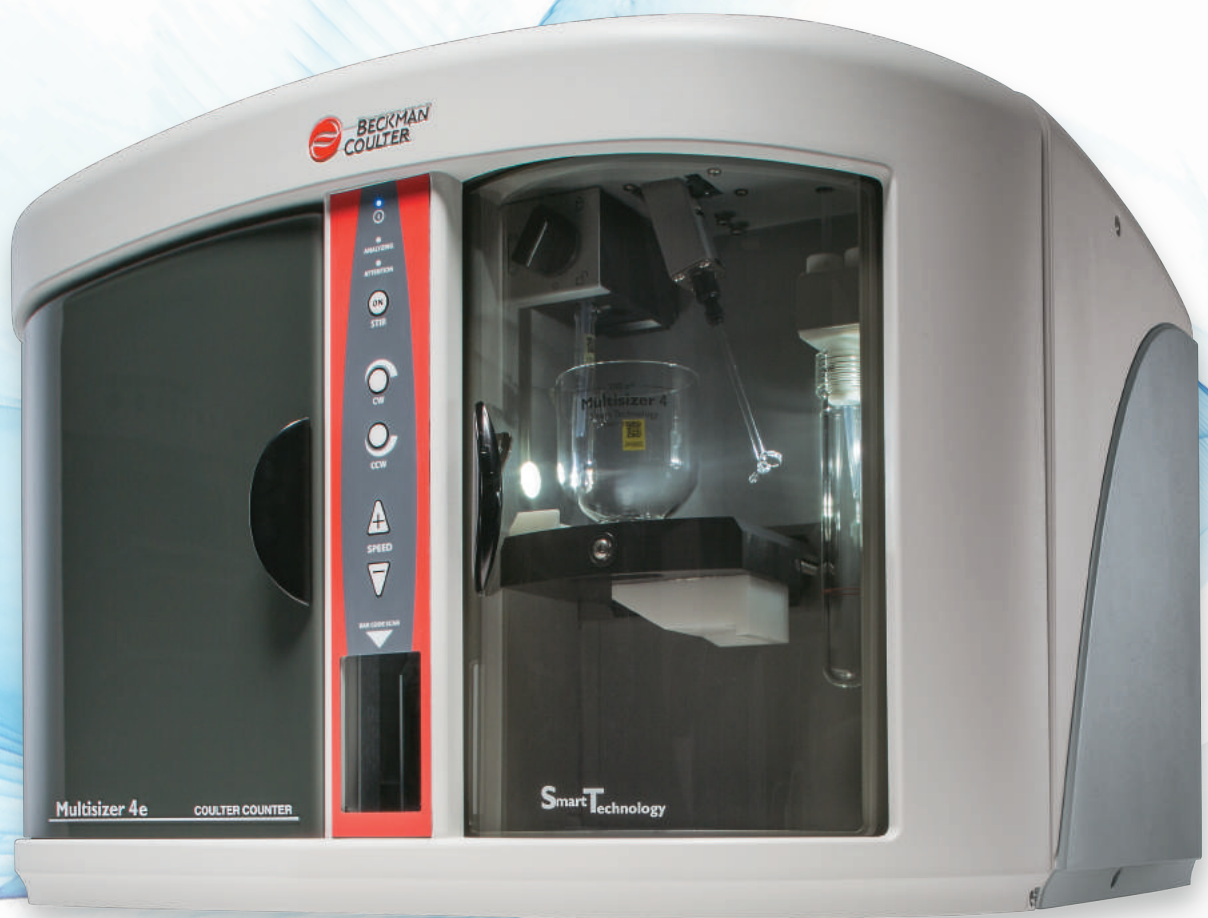




# MULTISIZER 4E COULTER COUNTER

THE UTMOST PRECISION IN  
PARTICLE SIZING AND COUNTING



CHARACTERIZED  
*by ingenuity.*

 **BECKMAN  
COULTER**  
*Life Sciences*



AUTOMATED MULTI-PARAMETRIC  
ANALYSIS ACCURATE CONSISTENT  
THE COULTER PRINCIPLE

TYPE APPROVAL CERTIFICATE  
US.C.27.001.A №51632

RECOMMENDED IN THE XIII EDITION OF  
THE RUSSIAN PHARMACOPEIA



- 1953** : *Patented Coulter Principle*
- 1956** : ***The First Coulter Counter - "Model A"***
- 1999** : *Patent on digital signal processing technology*
- 2014** : *Release of Multisizer 4e*



## **WE CREATED THE COULTER METHOD AND CONTINUE ITS DEVELOPMENT**

Since the invention of the microscope, laboratory workers have spent hours estimating cell counts. The results depend to a large degree on the user, and the process is excruciatingly slow.

In 1953, the brothers Joseph and Wallace Coulter developed a conductometric method for counting cells, also known as the Electrical Sensing Zone method. The method is based on analysis of voltage pulses generated when suspended particles pass through a microscopic opening (aperture), under an electrical current. The amplitude of this pulse is proportional to the volume of the particle. This made it possible for the first time to determine the size and number of several thousand microscopic particles a second!

This ingenious invention led to creation of an entire field of particle analysis and opened new doors for research.

The first Coulter counter model (model A) was offered for sale in 1956 and was used to count blood cells.

Today, the Coulter method is the standard for blood tests and is used in 98% of blood analyzers.

The electrical sensing zone method (Coulter method) is recommended in the XIII edition of the Russian Pharmacopeia to monitor invisible particulate matter in parenteral solutions (OFS 1.4.2.0006.15) and to determine concentration of microbial cells (OFS 1.7.2.0008.15).

The method is also widely used in various industries for quality control of starting materials and finished products. The Coulter principle has been used as the basis of guideline documents ASTM and ISO 13319 (Determination of particle size distributions).

Current Company Portfolio Beckman Coulter Life Sciences offers counters and particle analyzers that can be used for thousands of different applications working with suspensions, emulsions, or powders.



We are constantly striving to improve our instruments: in the over 60 years since the invention of the first Coulter counter model in 1956 we have produced more than 40 instrument models for scientific and piratical tasks and medical blood tests.

The Coulter principle is used to analyze thousands of various biological specimen types. This method determines the number of cells and changes in their size for research on cell cycles and cell-mediate responses in pathological processes, apoptosis, stem cells, and cryobiology, marine

## NEW MULTISIZER 4E NEW OPPORTUNITIES

The Multisizer 4e is the newest particle sizing and counting system in the Beckman Coulter Life Sciences Coulter Counter line. It is the most accurate and flexible particle characterization device available, boasting an unparalleled sizing range of 0.2 - 1600  $\mu\text{m}$ . The new 10  $\mu\text{m}$  Aperture allows users to study sub-cellular and micro-particles as small as 200 nm, while the advanced noise reduction system for small apertures improves measurement accuracy.

Generated data are processed using patented digital pulse processing technology and can be saved and later re-analyzed. This technology provides ultra high resolution and accuracy unattainable through any other technologies: detection of 1 particle in 1 ml of a sample with the optimal instrument configuration. Analysis results are not dependent on particle shape, structure, or optical properties.

New protocol and data processing options have been added to the software. Particle size dynamics can now be monitored in real time, making it possible to analyse cell mediated response time, solutions, aggregates, or particle dissociation.



biology, ecology, and many other fields. Today the Multisizer is mentioned in more than 7,000 articles, and the Coulter counter in more than 115,000.

A large selection of apertures allows the user to select the optimal configuration for a broad range of industrial applications requiring particle counts and sizing, control of particle size uniformity, identifying particulate matter, evaluating sample filtration efficiency, and pre- and final analyzes of various materials and liquids. The electrical sensing zone (Coulter) method was recommended in the XIII edition of the Russian Pharmacopeia.

## 1 Apertures

A wide range of apertures is available with diameters from 10 to 2,000  $\mu\text{m}$ .

The extended measurement range (2 - 80% of aperture diameter) means the aperture doesn't need to be changed as often, giving more options for analysis.

The instrument automatically detects and cleans up any blockage of the aperture.

## 2 Code Scanner

The bar code is used to quickly enter information on samples, electrolytes, aperture size, and sample beaker.

This information is automatically output.

## 3 Fluid Levels Monitoring

The EZAccess system monitors tank fluid levels and displays warnings when electrolytes need to be added or containers are filled with waste.

## 4 Stirrer

Users can select stirrer speed and direction for an even particle distribution in suspensions.

Position and speed memorized in SOM for consistent future analysis.

## 5 Dependable Protection Against External Dirt and Dust

The new instrument design ensures maximum sample protection against dust and dirty from the environment.



## Nalgene Vial Adapter

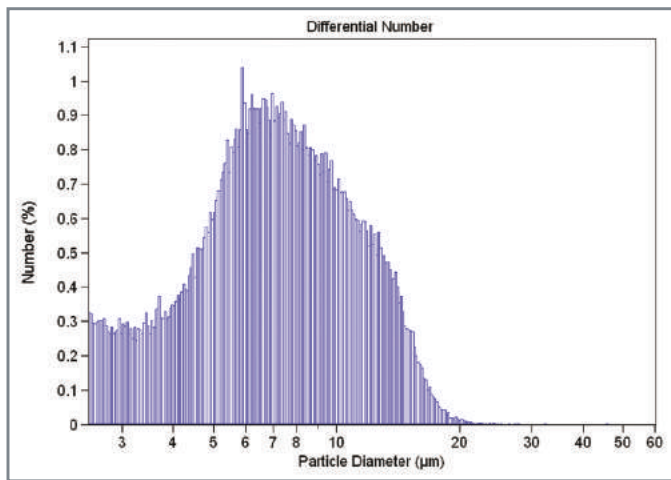
Depending on sample type and aperture size, samples can be analyzed in 100 - 400 ml beakers, or in vials (5 or 25 ml).

Beckman Coulter Life Sciences offers 25 ml Acuvette vials and adapters for using 5 ml Nalgene vials, which is crucial for precious samples or where there is very little sample material.

# ADVANCED SOFTWARE

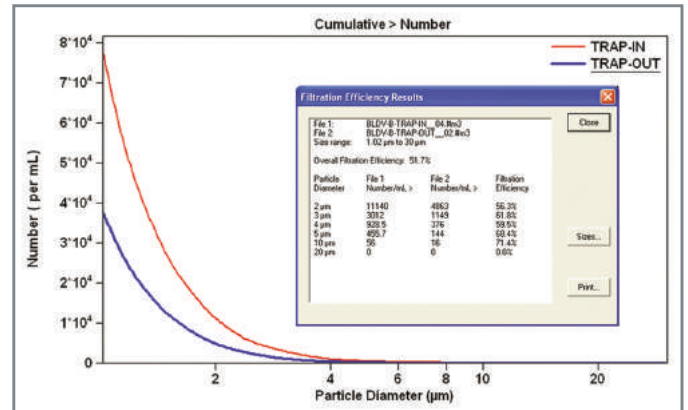
The instrument is unbelievably simple to use: operation is completely computer controlled. Incremental templates and a settings menu wizards allow quick configuration of parameters.

The flexible and intuitive Multisizer 4e software allows the user to access various formats for display of particle size distribution information, in either differential or cumulative form: number, volume, mass, and surface area graphs or comparative tables with particle number, volume, mass, surface area, and size.

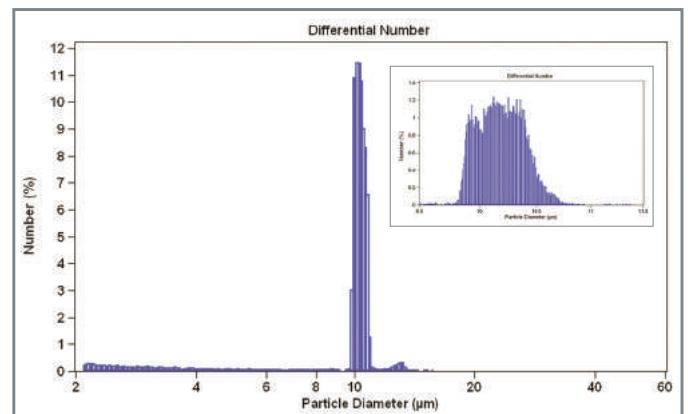


In multiple-aperture mode the software combines data from multiple series of analyzes using progressively smaller diameter apertures.

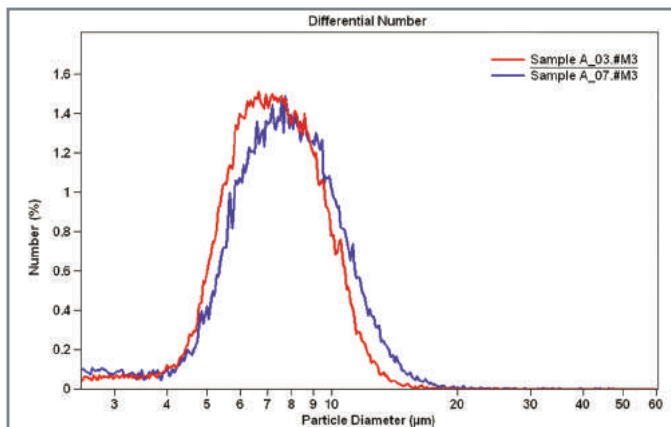
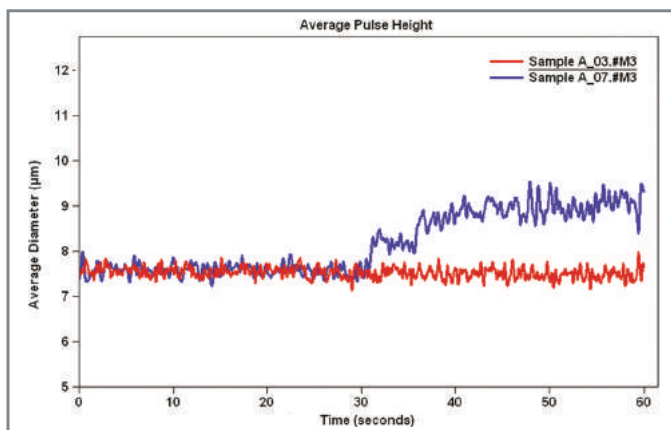
A wide range of statistics, filtration efficiency, and degree of aggregation



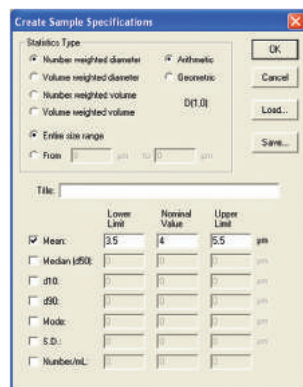
The Multisizer 4e control station memory stores complete information on pulses registered during an experiment. This allows the data to be reanalyzed after an experiment with different particle size range settings to obtain more detailed information on particle size distribution. The instrument not only increases the distribution fragment, but processes and re-analyzes pulses recorded for a given range.



Changes in particle size can be measured in real time thanks to patented digital pulse processing technology. This allows the speed of cell-mediated responses, solutions, aggregates, and dissociation of particles to be analyzed.

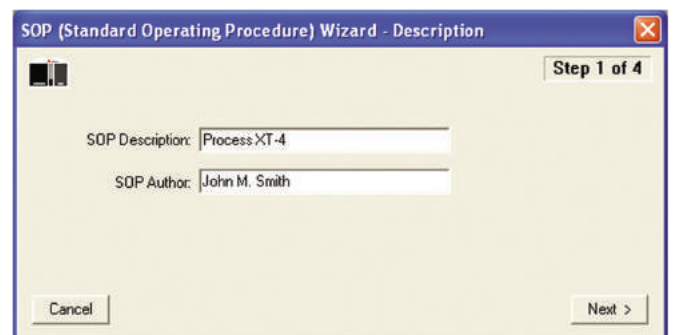


The new “Create Sample Specifications” function is a quality control feature that allows the user to preset specifications that samples must meet.



After analysis, the software will automatically highlight results that differ from presets Spec's.

Simplified SOP (Standard Operating Procedure) Creation



The automatic aperture monitoring function makes it possible to detect any blockage during an experiment. The Multisizer 4e will clean apertures without interrupting a process run and continue sample analysis.

The automatic calibration and calibration verification functions guarantee accurate results.

21CFRPart11Securitycomplianceensures that all parameters can be configured according to the US Food and Drug Administration (FDA) regulations on electronic records and electronic signatures.

All results are printed in a report whose format the user can configure according to need for biological, research, or industrial applications.

# MULTISIZER 4E FOR BIOLOGICAL RESEARCH

Cell size is a key parameter in research on cell cycle, osmotic regulation, cell death, pathogenesis, phagocytosis, species diversity, and other biological research. The Multisizer 4e can detect changes in size in real time. Data comparison and graphic summary features make studying processes over time easier.

Cell concentration in a medium is important to determine precisely and quickly to select the optimal parameters for cell culture growth and study the proliferation and effect of a target substance on a culture.

The 10 micrometer diameter aperture can detect sub-cellular particles as small as 200 nm, opening up new possibilities for study of mitochondria and liposomes.

## Application:

- Cellular Biology
- Microbiology
- Marine Biology

## Key Specifications:

- detection of particles from 200 nm to 1,600  $\mu\text{m}$
- accurate determination of sample cell number, size, and concentration
- the Coulter method is the only “direct” method for studying particle volume
- analysis of a single cell per unit of time
- real time detection of changes in the average cell size
- detection of individual particles that deviate significantly from the average sample particle size (determination of cell aggregates)





# MULTISIZER 4E FOR INDUSTRIAL QUALITY CONTROL



The Multisizer 4e detects and analyzes each particle individually without using optical methods, which guarantees an accurate result even with intensely colored samples or transparent particles.

The instrument can detect particles from 200 nm to 1,600  $\mu\text{m}$ . Using a single aperture, it can analyze samples where particles have a size differential of up to 40 times, which is important in quality control of filtration, product homogeneity, and particulate matter detection.

## Application:

- Biopharmaceutical and Pharmaceuticals
- Food and Beverage Industry
- industry (petroleum, fuel, paints, varnishes, toners, abrasives, hydraulic and lubricant fluids, electronics, cosmetics, etc.)

## Key Specifications:

- ME register listed
- V-check program for IQ and OQ validation
- easy SOP creation
- configurable data output and display for industry-specific customization
- automated aperture calibration and calibration verification
- automated filtration efficiency monitoring
- method recommended in the XIII edition of the Russian Pharmacopeia
- included in ASTM and ISO 13319
- software compliant with 21 CFR part 11 rules on electronic records and electronic signatures

## SPECIFICATIONS

### MULTISIZER 4E TECHNICAL CHARACTERISTICS

Particle Sizing Range	Diameter: 0.2 – 1,600 $\mu\text{m}$ Volume: 0.004 – 2,145 x 10 <sup>9</sup> $\mu\text{m}^3$ (fl)
Aperture Size	10 – 2,000 $\mu\text{m}$ (nominal diameter)
Measurement range	Extended: 2 – 80% of aperture size Standard: 2 – 60% of aperture size
Measurement linearity:	Diameter: $\pm 1\%$ Volume: $\pm 3\%$
Dynamic range (accuracy)	Diameter: 1 : 40 (extended), 1 : 30 (standard) Volume: 1 : 64,000 (extended), 1 : 27,000 (standard)
Processor type	High speed signal digitalization processor
Number of pulses measured	Up to 525,000 per analysis
Resolution	User defined
Number of size classes	Up to 400 for display of any selected measurement range The number of classes and their width can be changed as needed
Pulse distribution data	X axis: time, registration sequence, pulse width Y axis: diameter, volume or voltage corresponding to pulse amplitude, pulse width, mean diameter, volume, or voltage corresponding to pulses amplitude, average pulse width, pulse distribution by width
Particle size distribution data	X axis: diameter, volume, surface area Y axis: absolute number, percent content (%), number per ml, absolute volume, volume percentage (%), volume per ml, absolute surface area, surface area (%), surface area per ml
Sample registration mode: total number of particles	50 – 500,000 counts
Sample registration mode: number of particles and measurement of parameters	10 – 100,000 counts
Sample registration mode: time	0.1 – 999 seconds with at 10 ms increments Standard registration time is 10 – 90 seconds
Sample registration mode: volume	50 – 2,000 $\mu\text{L}$
Dosage system	The dosing pump with even suspension flow across the aperture and volume measurement, error - less than 0.5%
Electrolyte type:	Aqueous and non-aqueous electrolyte solutions compatible with glass, fluoropolymers, fluoroelastomers and stainless steel.
Aperture current strength range:	30 – 6,000 $\mu\text{A}$ with 0.2 $\mu\text{A}$ increments
Aperture current stability:	$\pm 0.4\%$ of set value
Polarity error	Less than 0.5%
Compliance with standards	Software is 21 CFR part 11 compliant
Dimensions	64 x 61 x 51 cm, weight 45 kg
Power supply requirements	230 – 240 V $\pm 10\%$ , 47 – 63 Hz
Power consumption	Less than 55 Watts
Fuses	250 V, IEC (5x20 mm) with time delay, 2.0 A
Environmental requirements	The instrument is intended for work in enclosed spaces. Working temperature: 5 – 40°C Relative humidity: 30 – 85% without condensation

## STANDARD PACKAGE

### ORDERING INFORMATION

Part Number	Description
B23005	Multisizer 4e Coulter Counter with 100 µm aperture, 200 ml glass sample beaker, stirrer, and software v. 4.03
6602796	L10 calibration standard 10 µm (1 x 15 ml)
6602796	L20 calibration standard 20 µm (1 x 15 ml)
8448011	Isoton II electrolyte (20 L)
8546859	IsoFlow electrolyte (10 L)
8448222	Coulter Clenz cleaning solution (5 L)
A64620	V-Check validation program for Multisizer 4e

The control station for the Multisizer 4e must be purchased separately. Minimum requirements: Windows 7 or higher OS, 1 Ethernet port, 2 USB ports. OS language - English.

### V-Check Program

V-Check - is an integrated program used to install and verify the Multisizer 4e instrument (IQ, OQ)

The program is packaged with software, documentation, and calibration standards needed to calibrate and verify proper setup of the instrument.



## SAMPLE CONTAINERS

### ORDERING INFORMATION

Article	Description	Article	Description
A35595	100 ml glass beaker	A35473	Accuvette ST vials and caps (200 units x 25 ml)
A35596	200 ml glass beaker	A93166	Nalgene 5ml vial adapter
A35597	400 ml glass beaker	A35582	Stirrer

Depending on the selected aperture size, 1 - 2 ml to several tenths of a millimeter of sample may be required for analysis. Beckman Coulter Life Sciences offer various volume beakers. In addition, an adapter for samples in 5 ml Nalgene vials is available for order.

# SELECTING THE OPTIMAL APERTURE

The Multisizer 4e can measure particle size from 2% to 80% of aperture diameter. The standard measurement range is 2 - 60%, while the extended dynamic range (60 - 80%) is used to study rare events outside of the standard aperture range. A larger aperture must be used if a large number of particles are larger than 60% of the aperture diameter.

For small apertures (denoted by a † in the table) the measurement range largely depends on how clean the system is, solution conductivity, and electrical interference from the surrounding environment. The

upper measurement limit (†††) is dictated by solution viscosity and particle density. Apertures denoted by †† are also available in high resolution.

Apertures are marked with a bar code with size, serial number, and calibration constants for automatic configuration settings in the protocol.

When working with small apertures we recommend that you prefilter the electrolyte solution using a 0.2 micrometer filter. A 0.1 micrometer pore filter may also be used for further filtration.

MEASUREMENT RANGE						
Aperture diameter, $\mu\text{m}$	For size (diameter) $\mu\text{m}$			Volume $\mu\text{m}^3$ (fl)		
	2 - 80%	2 - 60%	60 - 80%	2 - 80%	2 - 60%	60 - 80%
10 <sup>†</sup>	0.2 - 8	0.2 - 6	6 - 8	$0.004 - 268 \times 10^3$	0.004 - 113	$113 - 268 \times 10^3$
20 <sup>†</sup>	0.4 - 16	0.4 - 12	12 - 16	$0.034 - 2.14 \times 10^3$	0.034 - 905	$905 - 2.14 \times 10^3$
30 <sup>†</sup>	0.6 - 24	0.6 - 18	18 - 24	$0.113 - 7.24 \times 10^3$	$0.113 - 3.05 \times 10^3$	$3.05 \times 10^3 - 7.24 \times 10^3$
50 <sup>††</sup>	1 - 40	1 - 30	30 - 40	$0.524 - 33.5 \times 10^3$	$0.524 - 14.1 \times 10^3$	$14.1 \times 10^3 - 33.5 \times 10^3$
70 <sup>††</sup>	1.4 - 56	1.4 - 42	42 - 56	$1.44 - 92 \times 10^3$	$1.44 - 38.8 \times 10^3$	$38.8 \times 10^3 - 92 \times 10^3$
100 <sup>††</sup>	2 - 80	2 - 60	60 - 80	$4.19 - 268 \times 10^3$	$4.19 - 113 \times 10^3$	$113 \times 10^3 - 268 \times 10^3$
140 <sup>††</sup>	2.8 - 112	2.8 - 84	84 - 112	$11.5 - 736 \times 10^3$	$11.5 - 310 \times 10^3$	$310 \times 10^3 - 736 \times 10^3$
200 <sup>††</sup>	4 - 160	4 - 120	120 - 160	$33.5 - 2.14 \times 10^6$	$33.5 - 905 \times 10^3$	$905 \times 10^3 - 2.14 \times 10^6$
280	5.6 - 224	5.6 - 168	168 - 224	$92 - 5.88 \times 10^6$	$92 - 2.48 \times 10^6$	$2.48 \times 10^6 - 5.88 \times 10^6$
400	8 - 320	8 - 240	240 - 320	$268 - 17.2 \times 10^6$	$268 - 7.24 \times 10^6$	$7.24 \times 10^6 - 17.2 \times 10^6$
560	11.2 - 448	11.2 - 336	336 - 448	$736 - 47.1 \times 10^6$	$736 - 19.9 \times 10^6$	$19.9 \times 10^6 - 47.1 \times 10^6$
800 <sup>†††</sup>	16 - 640	16 - 480	480 - 640	$2,145 - 137 \times 10^6$	$2,145 - 57.9 \times 10^6$	$57.9 \times 10^6 - 137 \times 10^6$
1,000 <sup>†††</sup>	20 - 800	20 - 600	600 - 800	$4,189 - 268 \times 10^6$	$4,189 - 113 \times 10^6$	$113 \times 10^6 - 268 \times 10^6$
2,000 <sup>†††</sup>	200* - 1,600	200* - 1,200	1,200 - 1,600	$4.19 \times 10^{6*} - 2.14 \times 10^9$	$4.19 \times 10^{6*} - 905 \times 10^6$	$905 \times 10^6 - 2.14 \times 10^9$

\* The standard dynamic range for the 2,000 micrometer aperture is 2 - 80%.

## ORDERING INFORMATION

Part Number	Description	Part Number	Description
B42812	10 µm aperture	A36395	140 µm aperture
A36390	20 µm aperture	A44584	high resolution 140 µm aperture
A36391	30 µm aperture	A36396	200 µm aperture
A36392	50 µm aperture	A44585	high resolution 200 µm aperture
A44581	high resolution 50 µm aperture	A36397	280 µm aperture
A36393	70 µm aperture	A36398	400 µm aperture
A44582	high resolution 70 µm aperture	A36399	560 µm aperture
A36394	100 µm aperture	A40889	800 µm aperture
A44583	high resolution 100 µm aperture	A36400	1,000 µm aperture
A35582	Stirrer	A36401	2,000 µm aperture

## CALIBRATION STANDARDS

We recommend calibrating the aperture using standard reference particles sized 10% - 20% of the aperture diameter (preferably 20%).

Standards are suspended latex particles sized according to the NIST (National Institute of Standards and Technology) standard. Standards are also certified in Russia (SSS type certified)

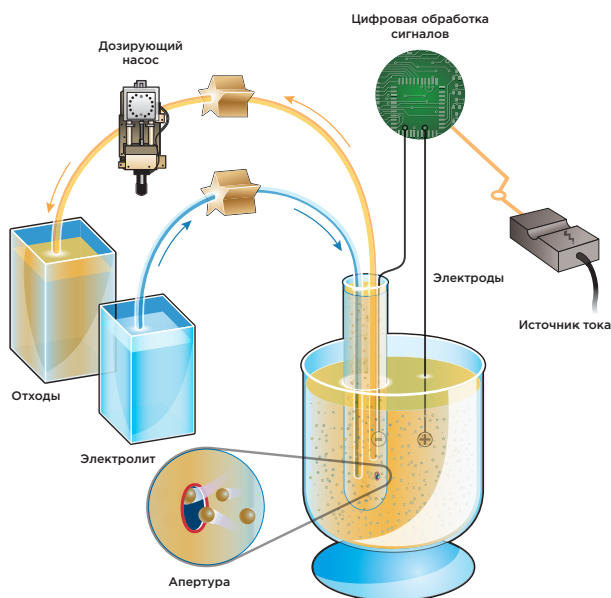


## ORDERING INFORMATION

Article	Description	Article	Description
6602792	L2 calibration standards 2 µm (1 x 15 ml)	6602799	L30 calibration standard 30 µm (1 x 15 ml)
6602793	L3 calibration standard 3 µm (1 x 15 ml)	6602800	L43 calibration standard 43 µm (1 x 15 ml)
6602794	L5 calibration standard 5 µm (1 x 15 ml)	6602801	L65 calibration standard 65 µm (1 x 15 ml)
6602796	L10 calibration standard 10 µm (1 x 15 ml)	6602802	L90 calibration standard 90 µm (1 x 15 ml)
6602797	L15 calibration standard 15 µm (1 x 15 ml)	383601	L200 calibration standard 300 µm (1 x 15 ml)
6602798	L20 calibration standard 20 µm (1 x 15 ml)	6601329	Calibration standard set: 2 µm, 5 µm, 10 µm, 20 µm, 43 µm (5 x 15 ml)

# COULTER COUNTERS ELECTRICAL SENSING ZONE

Particles suspended in a weak electrolyte pass through a small diameter opening (aperture). The aperture is set between two electrodes with an electric current. A “sensing zone” is created in the aperture, and when each particle/cell passes through the zone it displaces a certain amount of electrolyte, causing a jump in impedance.



This results in a small change in the voltage in the amplifier, which converts variance in current into a pulse. The height of the pulse is proportional to the particle size and sufficient to give a precise measurement of the particle.

Conversion of pulse amplitudes into volumetric units make it possible to generate data on particle size distribution. If a dosing/ metering device is used with the instrument

to release a known volume of suspension across the aperture, factoring the number of pulses and sample volume, we can determine the particular calculation.

The digital pulse processor was first installed in the Multisizer 3. High speed signal digitalization allows several parameters to be used at once for more accurate particle characterization.

In addition, the Multisizer 4e features dynamic particle size measurement. The instrument analyzes and saves measurement results from each particle in memory. Data can be saved and analyzed later without reanalyzing the same sample.

## Proven technology:

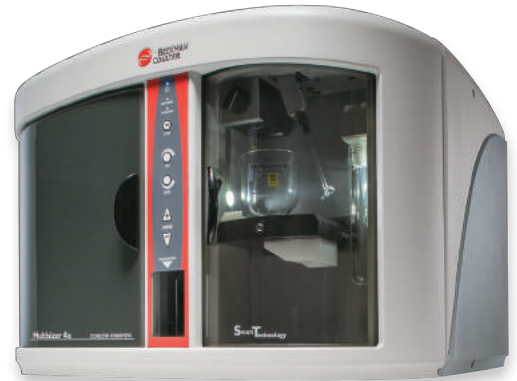
- over 60 years use in sizing and counting various particles and cells
- more than 115,000 bibliographic references to the Coulter principle
- instruments are included in the ME register
- technology defined under ISO 13319:2007
- more than 200 American Society for Testing and Materials (ASTM) standards
- particle size is determined based on direct measurement of particle volume - particle color and deflection coefficient do not affect the result

## Multisizer 4e

### Improved Analysis Ability

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- particle size range: 0.2 – 1,600  $\mu\text{m}$
- measurement range: 2 – 80% of aperture size
- dynamic range: 1 : 40 (diameter), 1 : 64,000 (volume)
- particle count and volume distribution
- digital processor
- real time detection of volume changes
- Software v 4.03 for instrument control and data analysis



## Multisizer 3

### Proven technology:

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- particle size range: 0.4 – 1,200  $\mu\text{m}$
- measurement range: 2 – 60% of aperture size
- dynamic range: 1 : 30 (diameter), 1 : 27,000 (volume)
- particle count and volume distribution
- digital processor
- Software v 3.53 for instrument control and data analysis



## Z-series

### Simple and Dependable Particle Counters

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- particle size range: 1 – 120  $\mu\text{m}$
- measurement range: 2 – 60% of aperture size
- dynamic range Z11 : 3 (diameter), 1 : 27 (volume), Z21 : 4 (diameter), 1 : 64 (volume)
- particle counting using two threshold values (Z1 and Z2)
- determination of volume and size distribution (Z2)
- analogue processor
- data analysis software v 3.01 (Z2)



## Handles any counting and particle characterization task

Since the invention of the first Coulter counter, we have continuously perfected particle sizing and characterization instruments. Beckman Coulter Life Sciences analyzers and particle counters are used in many quality control laboratories and research centers around the world. Today, the company's profile includes the following analyzers:

- laser diffraction particle size analyzer (LS 13 320)
- Coulter particle count and size analyzer (Multisizer, Z)
- molecular weight, zeta potential and particle size analyzer (DelsaMax)
- cell number and viability (Vi-Cell XR)
- fermentation process parameter analyzer (Vi-CELL MetaFLEX)
- pore area and size analyzer (SA 3100)
- aerosol particle counter (MET ONE)
- liquid particle counter (HIAC)
- general organic hydrocarbon analyzers (Anatel PAT 700, TOC 600, QbD 1200)

To inquire about package options and equipment demonstrations, contact the Beckman Coulter Life Sciences office in Russia and the CIS at +7 (495) 228-67-00 or by email at: [lcr-russia@beckman.com](mailto:lcr-russia@beckman.com)

More details at [beckman.com.ru](http://beckman.com.ru)

