ESCO LIFESCIENCES GROUP

Dunn Labortechnik

BelloCell® Cell Culture Systems
GlucCell® Glucose Monitoring System

Product Information

BelloCell®

Disposable High-Yield Cell Culture Systems

Cell Proliferation
Cell Mass
Cell Membrane Protein
Monoclonal Antibodies
Recombinant Protein
Virus Production

GlucCell®

Glucose Monitoring System

Glucose Measurement for Mammalian and Insect Cell Culture

Fast and easy-to-use

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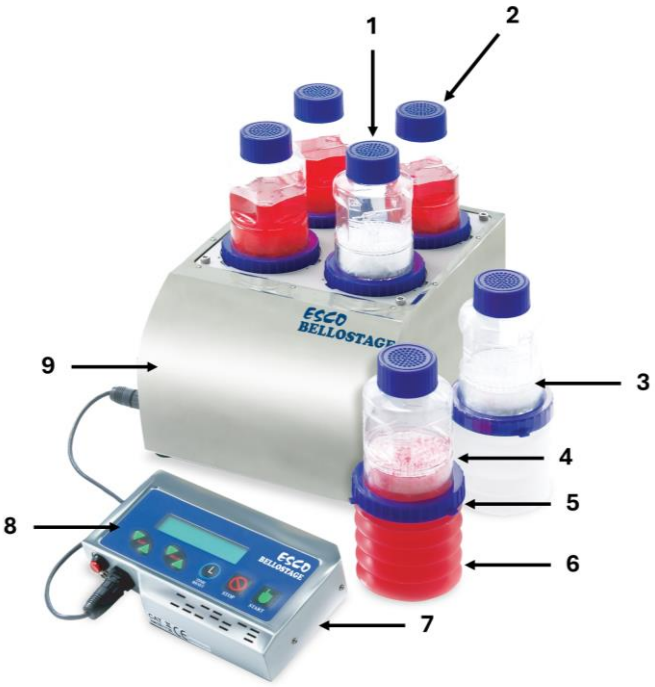
BelloCell®

Disposable High-Yield Cell Culture Systems

Each BelloStage® console accommodates up to four disposable bottles making this an ideal screening device to test various medium formulations or cell lines.

No steam or water lines, autoclave or utilities required,
just a power outlet and a CO_2 incubator.



BelloCell® High Density Cell Culture System

1) Useful for batch and semi-batch operation where process components are easily traceable.
2) 0.22 µm ventilation filter is provided in the cap.
3) Cells remain entrapped in the macrocarrier (BioNOC II® or BioMESH®) matrix bed simplifying media replacement and product harvesting.
4) Wide bottle neck for aseptic removal of carriers under the clean bench for cell counting.
5) Retaining ring locks bottles into place in the BelloStage® console.
6) Collapsible bellows.
7) Magnetized controller enables convenient positioning by attaching it to the outside of the incubator.
8) Controller - adjusts nutrient and gas exchange of the bottle.
9) Simple to operate - virtually no learning curve.

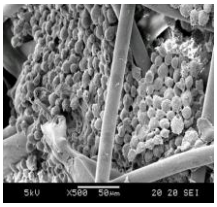
BelloCell® <u>Continuous</u> Cell Culture System (Complete)

1) Extremely compact system fits in most standard CO_2 incubators.
2) Useful for continuous operation/media recirculation, where process components are easily traceable.
3) Tubing set with peristaltic pump head enables recirculation and continuous feeding of nutrients.
4) BelloFeeder® enables four independent pump operations with individual programming.
5) Autoclavable pump head supports calibration free and consistent feeding.
6) Bright large display is easy to read.

Produce milligrams to grams of proteins, monoclonal antibodies, 10^{11} to 10^{12} pfu* viruses, whole cells or cell components, eliminating the need to maintain numerous spinners, dozens of roller bottles, and hundreds of T-flasks (example: standard bottles with BIONOC II® carriers).

* pfu = plaque forming units

BelloCell® Principle



BelloCell® is a disposable bioreactor capable of high-density cell culture for cell expansion, biomass production, protein expression, virus and monoclonal antibody production.

BelloCell® is designed based on the concept of bellow-induced alternation flow of medium and air through porous matrices, where cells reside and grow, providing a low shear, high aeration and foam free culture environment.

BelloCell® bioreactor consists of two components: a sterile, single-use culture BelloCell® bottle and a bellow compressor BelloStage®.

When in use, the BelloCell® bottle is partially filled with medium and inoculated with cells.

The medium is raised and lowered alternatively to submerge and expose the matrices, creating a dynamic interface between air and medium on cell surfaces to maximize nutrient uptake and oxygen transfer.

Because of its high efficiency in nutrient and oxygen transfer, one BelloCell® bottle with 5.5 g of BioNOC II® carriers, and a specific surface area of 15,600 cm^2, can produce cell mass comparable to 20 - 30 roller bottles.

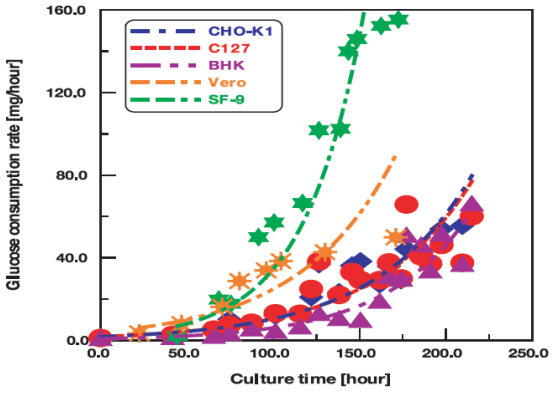
Since the BioNOC II® matrix surface is specially treated, BelloCell® can grow many anchorage-dependent cells and allow easy harvest of whole cells, cell components or secreted proteins.

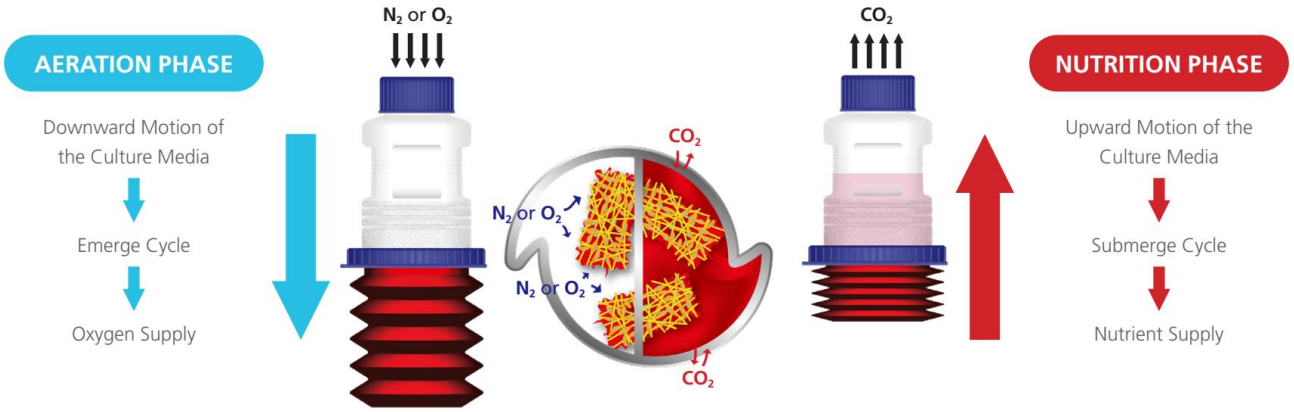
Features and Advantages

- Sterile, ready-to-use, disposable
- Low shear stress, foam-free, no O_2 limitation
- Large surface area for high density cell culture (e.g. 5.5 g (approx. 100 ml) BioNOC II® carriers are comparable to 20 - 30 roller bottles)
- Compatible with most serum free media
- Able to collect whole cells or cell components

Applications

- Animal, mammalian and insect cell culture
- Biomass and cell production
- Protein and virus production
- Monoclonal antibody production
- Proteome research
- Drug discovery
- Pharmacokinetic studies
- Gene and cell therapy





When the BelloStage® platform lowers, the bottle fully expands and medium recedes, exposing carriers to air to facilitate *aeration*.

Cells are protected by the carrier matrix without interference from the medium. There are no oxygen limitations, foaming problems and low shear stress.

Cells remain entrapped in the matrix bed, as the BelloCell® bottle is compressed.

Medium is forced up through the matrix bed, supplying the cells with nutrients and facilitating removal of metabolic waste.

BioNOC II® and BioMESH® Cell Culture Macrocarriers

BioNOC II® are carriers for the growth of animal, mammalian and insect cells. The carriers are recommended for production of secreted bioproducts and EVs/exosomes and can also be used for cell therapy and intracellular virus production applications. Most anchorage-dependent cells have been successfully grown in BioNOC II® carriers in both serum-containing and serum-free medium. BioNOC II® is made of 100 % pure polyester (PET) non-woven fabrics according to cGMP guidelines. The fabrics are specially surface-treated to make them hydrophilic and biocompatible.

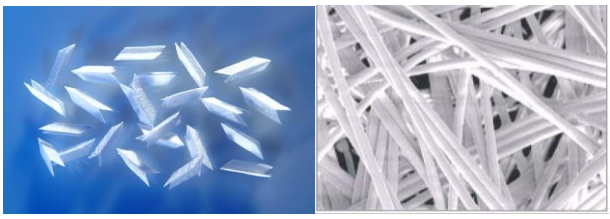
BioMESH® macrocarriers are the next generation grid-like PP/PET macroporous carriers with low-lint and low particulate contamination. BioMESH® carriers are specifically designed for high density cell harvesting and recommended for stem cell expansion, cell therapy applications, cultivated meat, as well as for production of EVs/exosomes and secreted bioproducts like viruses and proteins. BioMESH® carriers are used for cultivation of multipotent/pluripotent stem cells, epithelial cells, chondrocytes, fibroblasts and fibroblast-like cells (e.g. skin, cardiac fibroblasts).

Both BioNOC™ II and BioMESH® carriers enable adherent cells to grow in 3D mode.

Key Features

BioNOC II ®

- 100 % pure PET non-woven fabrics
- Non-pyrogenic and non-cytotoxic
- Safe to use and complies with USP Class VI USP <85>, <87>, <881>, ISO 10993-5
- High cell density (up to 2-8 x 10^9 cells in 5.5 g)
- High surface area to volume ratio (160 cm^{-1}), High specific surface area (2,400 cm^2/g)
- Surface treatment technology with no decay of hydrophilicity and high biocompatibility



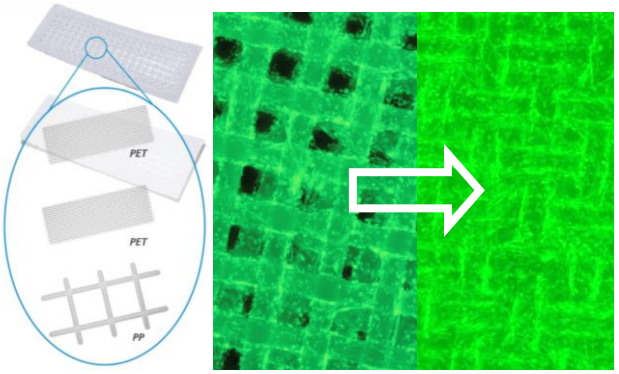
BioNOC™ II carriers are specially folded to enable sufficient nutrient transfer during cell culture

BioNOC™ II is made from 100 % PET fabrics

Key Features

BioMESH®

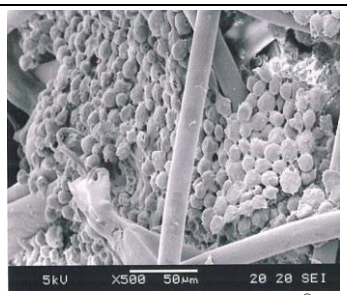
- High porosity, low-lint, low-particulate material: PP netting (670µm space between fibers) and PET mesh (200 µm space between fibers)
- Non-pyrogenic and non-cytotoxic
- Safe to use and complies to USP Class VI, USP <83>, <87>, <661.1>, <788>, ISO 10993-5, ISO 10993-6. ISO 10993-11, ISO 10993-18, ISO 10993-23
- High surface area for cell growth (up to 10.000 cm^2 per 0.1 L packed bed volume)
- Enhanced hydrophilicity, coating factors can be added



BioMESH® carriers consist of a PP and PET fiber mesh which enables cells to grow undisturbed in 3D

BioNOC II® specifications and tested cell lines

Material	100 % PET
Dimension	5 mm x 10 mm strip
Pore Size	50 - 200 µm
Porosity	90 - 94 % in packed bed
Specific Surface Area	2,400 cm^2/g
Packed Volume	15 ml/g
Autoclavable	OK (121 °C, 30 min in PBS)
Gamma Irradiation	OK (25 kGy)
Endotoxin Tested	Yes (< 0.25 EU/ml)
Bioburden Tested	Yes (< 1 CFU/g)
Cytotoxicity Tested	Yes, pyrogen-free
Quality Control	USP Class VI, USP<87>, <85>, ISO 10993-5
Storage / Shelf Life	Room temperature, dark / 2 years
Cell Lines	CHO, CHO-K1, rCHO-hIgO, rC-127-TPA, HEK-293, VERO, SF-9, Hi-5, BHK-21, rBHK-Factor VIII, HepG2, Hela, Huh 7, RK-13, ST, MDCK, MDBK, 3T3, MRC-5, CEF, human foreskin fibroblast, human muscle skeleton cell, human mesenchymal cell, human embryonic stem cell, etc.



SEM Figure of Sf-9 cells in BioNoc II® carriers

Lit.: "Growth of Mammalian and Lepidopteran Cells on BioNOC™ II carriers, a novel macroporous microcarrier", Drugmand J.-C., Michiels J.-F., Agathos S.N., Schneider Y.-J.; ESACT June 2005

BelloCell® System Components

BelloCell® High Density (Batch) Cell Culture System, Complete (Cat. No. BCS04000)

The BelloCell® Cell Culture System Complete contains all the necessary elements (except bottles) for users to start cell culture.

It is designed to support four BelloCell® culture bottles and with its 280 mm x 375 mm footprint it fits inside a standard CO_2 incubator.

It contains a BelloStage® console with a magnetized controller, which can be conveniently mounted and accessed from the outside of the incubator.

- Includes a BelloStage® compressor (BCS03000) and a GlucCell® Glucose Monitoring Kit (GC001000).
- Extremely compact system fits in most standard CO_2 incubators
- Controller with large bright display and large touch panel
- Easy to read and operate
- Suitable for batch or semi-batch operation
- Suitable for most protein and monoclonal antibody production applications

BelloCell® Continuous (Perfusion) Cell Culture System, Complete (Cat. No. BCS07000)

The BelloCell® Continuous Cell Culture System Complete provides similar features as the BelloCell® Cell High Density Cell Culture System. Complete but with additional BelloFeeder® pump and two complete tubing sets to provide continuous media exchange in BelloCell®-500AP, -500APH, -500APQ or -500AP BioMESH® bottles. Includes a GlucCell® Glucose Monitoring Kit (GC001000). Each BelloCell®-500APx bottle has additional inlet and outlet lines for recirculation of the medium.

Each culture bottle can be linked to an extra glass medium reservoir (not included) facilitating continuous exchange of nutrients, eliminating the need for periodic medium exchange and minimizing the risk of a metabolic shock during cell cultivation.

- Each bottle connects with an independent medium reservoir to eliminate cross-contamination.
- Programmable and ON/OFF pumping control simplifies the setting of recirculation rate for each bottle.
- One BelloFeeder® pump module operates up to 4 pump heads with individual micro-processor control.
- Suitable for cell mass production, cell component production, virus production, or protein expression.

BelloStage®-3000 Compressor (Cat. No. BCS03000)

BelloStage®-3000 is capable of operating 4 BelloCell® bottles at a time in a lab-scale 170 l (vol.) incubator (Note: Bottles must be purchased separately).

It is the most compact and user-friendly technology for the cell culture industry.

- Includes a magnetized controller **(1)** which can be conveniently mounted and accessed from the outside of an incubator.
- DC step motor with ball screw
- Micro-switch positioning sensor
- Up-Down Rate: 0.25 -2.0 mm/sec
- Holding Time: 0 - 99 min 59 sec

BelloFeeder®-1500 Pump Module (Cat. No. BCA01500)

BelloFeeder®-1500 pump is a microprocessor-controlled peristaltic pump with five pump heads to achieve the re-circulation and perfusion processes for the BelloCell® continuous cell culture system.

- Controls four BelloCell® bottles in a BelloStage® compressor individually
- Feeding rate of each pump: 1 - 2,999 ml/day
- Feeding frequency: 1 - 24 times
- Environment: ambient to 45 °C, 0 to 95 % relative humidity

Disposable Ready-to-Use BelloCell® Bottles

Dimensions:	Height 243 mm x Diameter 100 mm
Vent Filter type:	0.22 µm PTFE membrane with PP support (blue filter cap)
Working Volume:	500 ml
Carriers Volume:	1.4 g, 2.8 g or 5.5 g BioNOC II® or 18 g BioMESH® macrocarriers
Carrier type:	BioNOC II® PET or BioMESH® PP/PET macrocarriers
Material:	Bottle: PETG, LDPE/EVA and PP; Tubings: Silicone

BelloCell®-500 was the first 500 ml culture bottle available to the market introducing the new concept of tidal flow for high-density cell culture. The simple design combines multiple functions of a mixer, oxygenator, and a large growing surface to achieve a high density of cells.

The different types of pre-sterilized BelloCell®-500x bottles (see below) provide unlimited oxygen during culture with relatively gentle movement of the culture medium. Porous carriers are packed in the bottles that provide up to approximately 15,000 cm² surface area (per 0.1L carriers) for cell growth. Its space and labour savings are the most notable features.

BelloCell®-500A, -500AH and -500AQ (batch type) Cell Culture Bottles (Cat. No.s BCA00500, BCAH00500, BCAQ00500)

BelloCell®-500A, -500AH and -500AQ bottles (with 5.5 g, 2.8 g or 1.4 g **BioNOC II®** carriers) are for *batch or semi-batch cultivation* of adherent cells. The bottles have a blue filter cap and allow upright and inverted handling procedures due to a second solid (white) screw cap that is provided for this purpose. Inverting the bottle, carriers fall into the solid cap to improve cell seeding, virus infection, transfection, transduction, and cell harvest. This is particularly ideal for extracting cellular protein or viruses directly from the carriers.

Features:

- High cell density (up to 2-8 x 10^9 cells/bottle, depending on cell line)
- Capable of harvesting cells and cell components
- Ability to sample carriers for cell count
- Applicable for both serum-free and serum-containing media
- Applicable for most adherent cells
- Very low shear stress, foam-free, no oxygen limitation
- Available with carrier volumes: 100 ml (5.5 g), 50 ml (2.8 g) or 25 ml (1.4 g)

BelloCell®-500AP, -500APH and -500APQ (perfusion type) Cell Culture Bottles (Cat. No. BCA01000, AR2000063, AR2000064)

Perfusion type cell culture bottles BelloCell®-500AP, -500APH and -500APQ are available with three different carrier volumes (100, 50 or 25 ml **BioNOC II®** carriers) and allow automatic medium recirculation during continuos cell cultivation. With the aid of the BelloFeeder® pump, the inlet and outlet ports of the system allow medium to flow from and to the associated medium reservoir that provides sufficient nutrient and stable pH during cultivation.

Like batch type culture bottles they are provided with a solid lid allowing upright and inverted handling procedures (please see batch type bottles above for details).

Features: Please see BelloCell®-500 batch type Culture Bottle above

- Enable continuous medium recirculation or perfusion
- 10 cm silicon tubing with PP female (inlet) and male (outlet) luer connector

BelloCell®-500A BioMESH® (batch type) and
BelloCell®-500A BioMESH® (perfusion type)
Cell Culture Bottles (Cat. No.s BMA00500 and BCMAP100)

BelloCell®-500A BioMESH® Cell Culture bottles contain 100 ml (18 g) **BioMESH®** low-lint macrocarriers and are designed specifically for cell harvesting applications. The bottles are recommended especially for the cultivation of multipotent/pluripotent stem cells, skin and cardiac fibroblasts, epithelial cells and chondrocytes (see page 4 for more details)

Features: Please see BelloCell®-500 batch and perfusion type Cell Culture Bottle above

BelloCell® System Accessories

Tubing Complete Set (Cat. No. BCA01301)

Includes pre-assembled tubes, reusable polypropylene pump head and GL45 stainless steel head plate with a sampling port to support continuous culture in BelloCell® -500P and -500AP systems. It can be autoclaved at 121 °C for 30 minutes. One Tubing Complete Set per BelloCell culture bottle needed.

Crystal Violet Dye Nuclei Count Kit (Cat. No. BCA02001)

Crystal Violet Dye Nuclei Count Kit contains crystal violet dye, citric acid and detergent to disrupt cells and release cell nuclei for cell count. This provides an efficient reagent for cell count in a porous matrix.

Mini-TideCell (Cat. No. BAG001AA)

One Mini-TideCell contains two BioNOC II® microcarriers (equivalent to two 25 cm^2 T-flasks) in a culture plate for adding 10 ml medium. Developed to pre-test the BelloCell concept, especially cell growth, cell harvest and productivity. Individually packed, sterile, ready-to-use.

GlucCell® Glucose Monitoring System

GlucCell® Glucose Monitoring System (Cat. No. GC001000)

With the GlucCell® Glucose Monitoring System your glucose measurement during cell cultivation is fast and simple. The GlucCell® system is designed for measuring glucose *in animal cell culture media*, while general diabetes glucose meters on the market are normally not suitable for cell culture applications.

The GlucCell® System includes a palm-size, pre-calibrated glucose meter and disposable test strips.

Principle:

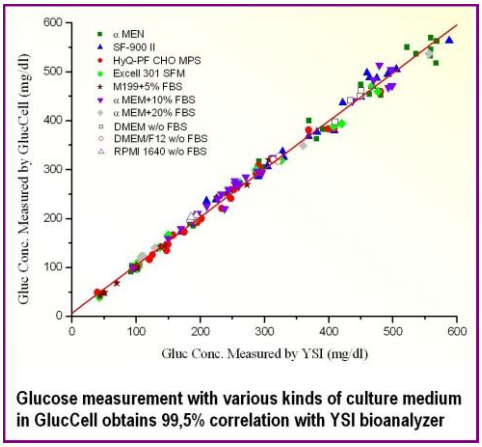
The GlucCell® Glucose Monitoring System is intended for use by laboratory researchers or bioreactor professionals to obtain a quantitative measurement of glucose in cell culture media. It is made to meet customer needs: calibration and maintenance-free, fast, portable and with high accuracy. The measurement is based on the oxidation of glucose by glucose oxidase.

GlucCell® Features

- Suitable for both serum and serum-free culture medium in mammalian and insect cell culture
- Portable, pre-calibrated, ready-to-use, disposable
- 99.5 % correlated with NOVA and YSI biochemical analyzer
- Precision: > 95 %, Accuracy > 90 %, Linearity = 0.9997
- Direct measurement without requirement to separate cells from culture medium
- User-programmable measurement unit display (mg/dl or mmol/l)
- A drop of 1.5 µl turns out an instant result in just 15 seconds
- Zero risk of contamination on the device and to the environment

GlucCell® Specifications

Assay Method	Electrochemical biosensor
Test Sample	Cell culture medium or equivalent solution
Test Result	Glucose concentration (mg/dl or mmol/l)
Sample Size	1.5 µl
Measure Range	20 - 600 mg/dl (1.1 - 33.3 mmol/l)
Accurate Range	30 - 500 mg/dl (1.67 - 27.78 mmol/l)
Test Result Time	Less than 15 seconds
Dimension/Weight	96 x 60 x 18.5 mm, 70 g incl. battery
Power Source	CR2032 3V Lithium coin battery
Battery Life	Approximately 1000 tests
Display	Large LCD
Memory	180 test results
Environment	10 - 40 °C, 20 % - 80 % relative humidity
Strip Size	45 mm x 6 mm x 0.6 mm



Glucose measurement with various kinds of culture medium in GlucCell obtains 99,5% correlation with YSI bioanalyzer

Order Information

Cat. No.	Description		Case
BCS03000	**BelloStage®-3000 Compressor (<u>without</u> Bottles):** – 1 Main Console, 1 Control Box – 1 100-240V Power Adapter, 1 Signal Cable – 2 Forceps, CD with Manual, 1 Crystal Violet Dye Nucleus Count Kit (50 ml)		1
BCS04000	**BelloCell® High Density (Batch) Cell Culture System Complete (<u>without</u> Bottles):** – 1 BelloStage®-3000 Compressor (BCS03000) – 1 GlucCell® Glucose Monitoring Kit (GC001000)		1
BCS07000	**BelloCell® Continuous (Perfusion) Cell Culture System Complete (<u>without</u> Bottles):** – 1 BelloStage®-3000 Compressor (BCS03000) – 1 Bello Feeder®-1500 Pump Module (BCA01500) – 2 Tubing Complete Sets (BCA01301) (one set per bottle needed) – 1 GlucCell Glucose Monitoring Kit (GC001000)		1
BCA01500	**BelloFeeder®-1500 Pump Module for continuous (perfusion culture) system**		1
BCA01301	**Tubing Complete Set:**		
	– 1 Silicone Tubing Set		1
	– 1 Polypropylene Pump Head		1
	– 1 GL45 Stainless Steel Head Plate		1
BCA01302	**Disposable Tubing Accessory Set:**		
	– Silicone Tubing Set		5
BCA01303	**Disposable Tubing Set and Pump Head:**		
	– Silicone Tubing Set		1
	– Polypropylene Pump Head		1
	BelloCell® 500 ml Bottles for batch culture (B) or continuous/perfusion (P) culture: Pre-sterilized, irradiated, ready-to-use, disposable, filled with macroporous carriers:		
BCA00500	BelloCell-500A: cell culture bottle with 100 mL (5.5 g) BioNOC II carriers	**(B)**	4
BCAH00500	BelloCell-500AH: cell culture bottle with 50 mL (2.8 g) BioNOC II carriers	**(B)**	4
BCAQ00500	BelloCell-500AQ: cell culture bottle with 25 mL (1.4 g) BioNOC II carriers	**(B)**	4
BCA01000	BelloCell-500AP: cell culture bottle with 100 mL (5.5 g) BioNOC II carriers	**(P)**	4
AR2000063	BelloCell-500APH: cell culture bottle with 50 mL (2.8 g) BioNOC II carriers	**(P)**	4
AR2000064	BelloCell-500APQ: cell culture bottle with 25 mL (1.4 g) BioNOC II carriers	**(P)**	4
BMA00500	BelloCell-500A **BioMESH®**: cell culture bottle with 100 mL (18 g) BioMESH® carrier	**(B)**	4
BCMAP100	BelloCell-500AP **BioMESH®:** cell culture bottle with 100 mL (18 g) BioMESH® carrier	**(P)**	4
	BioNOC II® and BioMESH® Cell Culture Macrocarriers		
BNC00050	BioNOC II®, non-sterile (50 g)		1
BNC00250	BioNOC II®, non-sterile (250 g)		1
BNC01000	BioNOC II®, non-sterile (1000 g)		1
AN100002	BioMESH®, non-sterile (50 g)		1
	BelloCell® Accessories		
BCA02001	Crystal Violet Dye Nuclei Count Kit, 100 ml bottle		1
BCA02003	Filtered Cap, sterile, irradiated		6
BCA02004	Non-vented Cap, sterile, irradiated		8
BCA02000	Forceps		1
BCA01206	BelloCell 500AP Strainer, sterile, irradiated		10
BAG001AA	Mini-TideCell, sterile, individually packed, 10 pcs. minimum order quantity		1
	GlucCell®		
GC001000	GlucCell® Glucose Monitoring Kit: Glucose Meter, Glucose Test Strips (Box / 2 x 25), Check Key, Case, and Quick Reference Sheet		1
GC001001*	Glucose Test Strips (Box / 2 x 25): calibration-free, single use, accuracy > 90 %, precision > 95 %		1

* <u>Note:</u> GlucCell® test strips with version number 0002 or higher are <u>not</u> compatible with GlucCell® glucose meters manufactured before March 2010.

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