

BelloCell[®] Cell Culture Systems GlucCell[®] Glucose Monitoring System

2019



BelloCell[®]

*Disposable High-Yield
Cell Culture Systems*

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

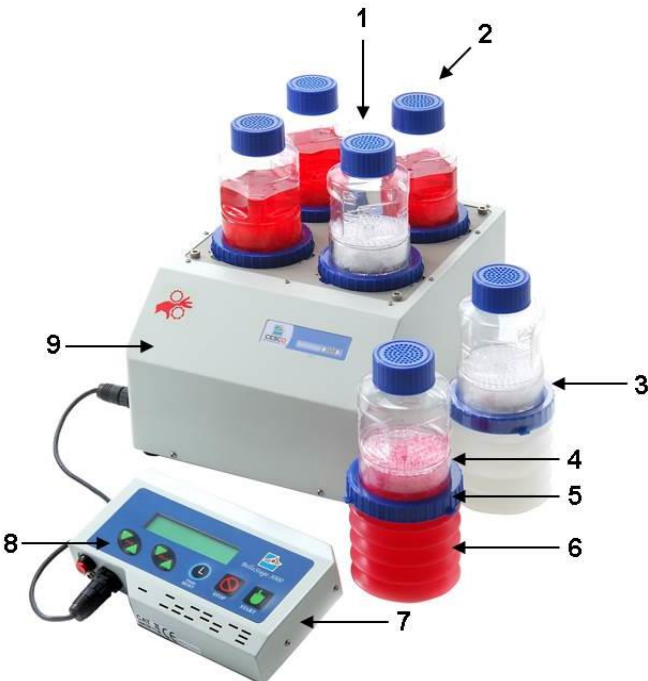
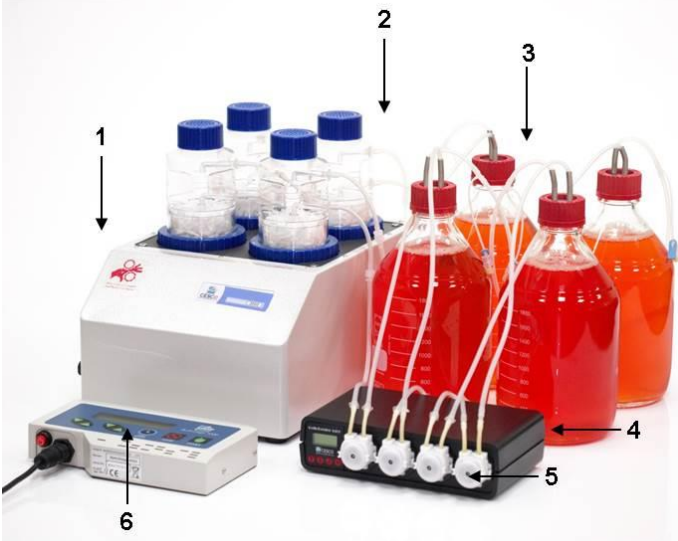


BelloCell®

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.

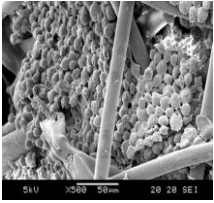
No steam or water lines, autoclave or utilities required, just a power outlet and a CO₂ incubator.

 <p>The image shows the BelloCell High Density Cell Culture System. It consists of a white BelloStage console with a digital display and control buttons. Four disposable bottles are mounted on the console. A separate controller unit is connected to the console. Numbered callouts (1-9) point to various components: 1) bottle cap, 2) ventilation filter, 3) BioNOC matrix bed, 4) sampling port, 5) retaining ring, 6) collapsible bellows, 7) magnetized controller, 8) main controller, and 9) BelloStage console.</p>	<p>BelloCell High Density Cell Culture System</p> <ol style="list-style-type: none">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 BioNOC™ II matrix bed simplifying media replacement and product harvesting.4) Sampling Port enables aseptic removal of BioNOC™ II carriers 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.
 <p>The image shows the BelloCell Continuous Cell Culture System Complete. It features a BelloStage console with four bottles. A BelloFeeder unit with four independent pumps is connected to the bottles via tubing. A separate controller unit is also shown. Numbered callouts (1-6) point to: 1) BelloStage console, 2) BelloFeeder unit, 3) tubing set, 4) BelloFeeder unit, 5) BelloFeeder unit, and 6) controller unit.</p>	<p>BelloCell <u>Continuous</u> Cell Culture System Complete</p> <ol style="list-style-type: none">1) Extremely compact system fits in most standard CO₂ incubators.2) Useful for continuous operation/media recirculation, where process components are easily traceable.3) Tubing set with peristaltic pump head enable recirculation and continuous feeding of nutrient.4) BelloFeeder enables 4 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, 10¹¹ to 10¹² pfu* viruses, whole cell or cell components, eliminating the need to maintain numerous spinners, dozens of roller bottles, and hundreds of T-flasks.

* pfu = plaque forming units

BelloCell® Principle



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

BelloCell® is designed based on the concept of bellow-induced alternation flow of media 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 media and inoculated with cells.

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

Because of its high efficiency in nutrient and oxygen transfer, one BelloCell® bottle, with a specific surface area of 15,600 cm², is capable of producing cell mass comparable to 20 to 30 roller bottles.

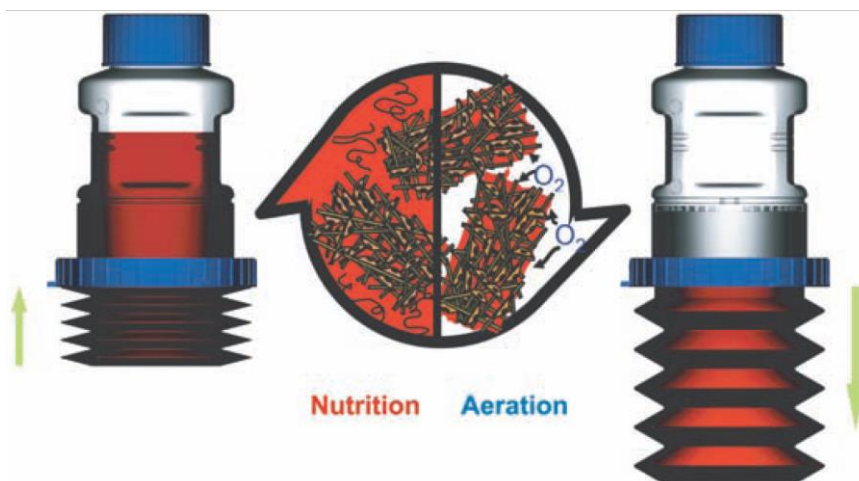
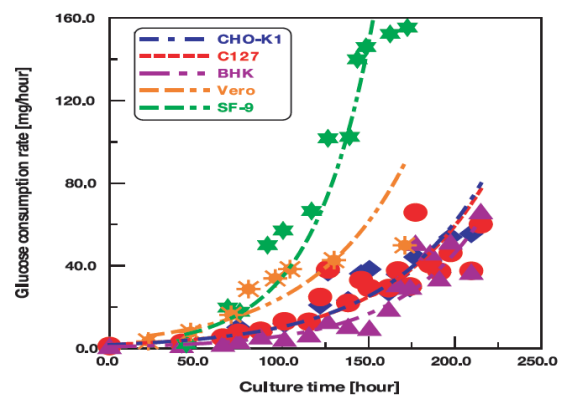
Since the matrix surface is specially treated, BelloCell® can grow many anchorage-dependent cells and allow easy harvest of whole cells, cell components or secreted proteins.

Features and Advantages

- Sterile, ready-to-use, disposable
- Low shear stress, foam-free, no O₂ limitation
- Large surface area for high density cell culture (comparable to 20 to 30 roller bottles)
- Compatible with most serum free media
- Able to collect whole cells or cell components

Applications

- Mammalian and insect cell culture
- Protein and virus production
- Monoclonal antibody production
- Proteome research
- Drug discovery
- Pharmacokinetics study
- Gene and cell therapy



Cells remain entrapped in the disk bed, as the BelloCell® bottle is compressed. The media is forced up through the disk bed, supplying the cells with nutrients and facilitating removal of metabolic waste.

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

Cells are protected by the disk without interference by the media flow. There are no oxygen limitations, foaming problems and low shear stress.

BioNOC™ II Cell Culture Microcarriers

BioNOC™ II are carriers for the growth of animal, mammalian and insect cells. Most anchorage-dependent cells have been successfully grown in BioNOC™ II carriers in both serum-containing and serum-free medium.

BioNOC™ II is made by 100 % pure polyester (PET) non-woven fabrics according to cGMP guidelines. The fabrics are specially surface-treated to make it hydrophilic and biocompatible. It is then processed through a cutting procedure to form a 5 mm wide and 10 mm long strip.

BioNOC™ II enables cells to grow in 2D monolayer, or even in 3D mode.

Features

Pure

- 100 % pure PET non-woven fabrics
- Non-pyrogenic
- Non-cytotoxic

Light

- High cell density (up to 1×10^9 cells/g)

High

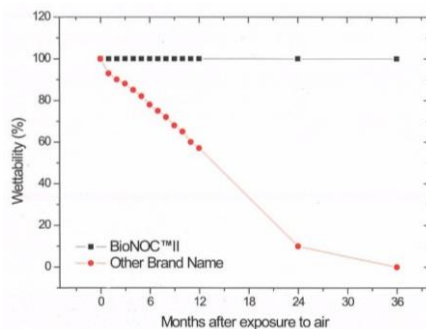
- High surface area to volume ratio (approx. 160 cm^{-1})
- High specific surface area ($2,400 \text{ cm}^2/\text{g}$)

Consistent

- Novel surface treatment technology with no decay of hydrophilicity and high biocompatibility
- All materials are manufactured according to cGMP guidelines



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



Long term monitoring for hydrophilicity stability test indicating zero decay of wettability in BioNOC™ II carriers for over 36 months, compared with the decay profile in other matrices

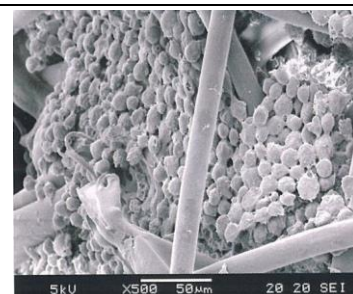


BioNOC™ II is made from 100 % PET fabrics

BioNoc™ II Specifications

Material	100 % PET
Dimension	5 mm x 10 mm strip
Pore Size	50 - 200 μm
Porosity	90 - 94 % in packed bed
Specific Surface Area	$2,400 \text{ cm}^2/\text{g}$
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>,<83>, ISO 10993-5
Storage / Shelf Life	Room temperature, dark / 2 years
Cell Lines	CHO, CHO-K1, rCHO-hlgO, 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 Cell Culture System Complete (Cat. No. BCS04000)



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

It is designed to support four BelloCell® culture bottles and with its 264 mm x 359 mm foot-print it fits inside a standard CO₂ 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, and a GlucCell Glucose Monitoring Kit.
- Extremely compact system fits in most standard CO₂ 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 antibodies production applications

BelloCell® Continuous 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 tubing complete sets to provide continuous media exchange in the BelloCell®-500P or -500AP bottles. Includes a GlucCell Glucose Monitoring Kit (GC001000).

Each BelloCell®-500P and -500AP bottle has additional inlet and outlet lines for media recirculation.

Each bottle can link to an extra glass media vessel (not included) and provide continuous exchange of nutrient, eliminating the need for media exchange and avoiding possible shock to the cells during culture.

- Each bottle connects with an independent media 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.

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

- Includes a magnetized controller, which can be conveniently mounted and accessed from the outside of the 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®-1400 Pump Module (Cat. No. BCA01400)



BelloFeeder®-1400 pump is a microprocessor-controlled peristaltic pump to achieve the re-circulation and perfusion processes for BelloCell® continuous cell culture system

- Control four 500P/AP bottles individually
- Feeding rate of each pump: 1 - 1,999 ml/day
- Feeding Frequency: 1 - 24 times
- Environment: Ambient to 45 °C, 0 to 95 % Relative Humidity

Disposable BelloCell® Bottles

Dimensions:	Height 243 mm x Diameter 100 mm
Vent Filter type:	0.22 µm PTFE membrane with PP support
Working Volume:	500 ml
Carriers Volume:	Approx. 5.5 g, 865 pcs. +/- 5 %
Carrier type:	BioNOC™ II PET macroporous carriers
Material:	Bottle: PETG, LDPE/EVA and PP; Tubings: Silicone



BelloCell®-500 Cell Culture Bottle (Cat. No. BCB00500)

BelloCell®-500 was the first 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 BelloCell®-500 provides unlimited oxygen during culture with relatively gentle movement of the culture medium. Porous carriers are packed in the bottle that provides 15,600 cm² surface area for cell growth. Its space and labour savings are the most notable features.

Features:

- High cell density (1 x 10⁹ cells/bottle)
- 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
- Super low shear stress, foam-free, no oxygen limitation
- Pre-sterilized, ready-to-use, disposable



BelloCell®-500A Cell Culture Bottle (Cat. No. BCA00500)

BelloCell®-500A is designed without the lid on the matrix basket allowing for easier collection of the carriers. Inverting the bottle, carriers fall into the cap to improve cell seeding, virus infection, transfection, transduction, and cell harvest. (Solid screw cap is provided for this purpose). This is particularly ideal for extracting cellular protein or viruses directly from the carriers.

Features: Please see BelloCell®-500 Cell Culture Bottle

- No lid on the matrix basket
- Including 1 cell strainer per case of 4 cell culture bottles
- Additional solid cap



BelloCell®-500P Cell Culture Bottle (Cat. No. BCB01000)

BelloCell®-500P is an alternative choice with automatic medium recirculation that does not require manual culture media exchange. It reduces chances of contamination, and maximizes stability by supplying sufficient culture medium.

With the aid of the BelloFeeder® pump, the inlet and outlet ports allow media to flow from and to the associated medium reservoir that provides sufficient nutrient and stable pH during culture.

Features: Please see BelloCell®-500 Cell Culture Bottle

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



BelloCell®-500AP Cell Culture Bottle (Cat. No. BCA01000)




BelloCell®-500AP is designed without the lid on the matrix basket allowing for easier collection of the carriers by inverting the bottle (please see BelloCell®-500A). Additionally, this bottle allows the automatic medium recirculation that does not require manual culture media exchange (please see BelloCell®-500P).

Features: Please see BelloCell®-500A and -500P Cell Culture Bottles


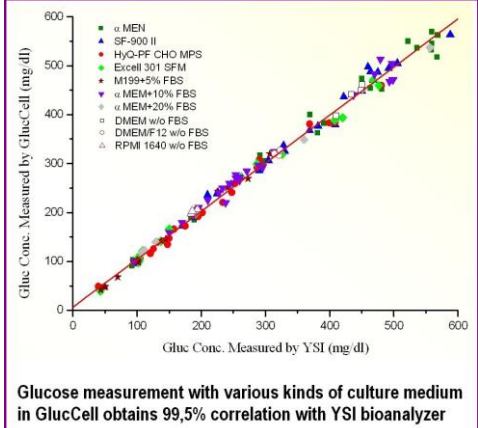
Selection Guide:

Application/Bottle	Secreted Protein and Viruses (adherent cells)	Cell Harvest (for non-secreted proteins, viruses, cells)	Carrier Harvest (for protein extraction or reuse of carriers)	Suspension Cells
BelloCell®-500	Best application	Applicable / not optimal	Not applicable	Not applicable
BelloCell®-500P	Best application	Applicable / not optimal	Not applicable	Not applicable
BelloCell®-500A	Applicable / not optimal	Best application	Best application	Not applicable
BelloCell®-500AP	Applicable / not optimal	Best application	Best application	Not applicable

BelloCell® System Accessories

	<p>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 the 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.</p>
	<p>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.</p>
	<p>Mini-TideCell (Cat. No. BAG001AA) One Mini-TideCell contains two BioNOC™ II microcarriers (equivalent to two 25 cm² 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.</p>

GlucCell® Glucose Monitoring System

<p>GlucCell® Glucose Monitoring System (Cat. No. GC001000)</p>	
<p>With the GlucCell® Glucose Monitoring System your glucose measurement during cell culture is faster and simplified. It is mainly designed for measuring the glucose metabolites during animal cell culture, but also for fungal cell culture, while general diabetes glucose meter on the market are normally not suitable for these cell culture applications.</p>	
<p>The GlucCell® System includes a portable, palm-size glucose meter and pre-calibrated, disposable test strips, specially designed for measuring the glucose concentration during mammalian cell and insect cell culture.</p>	
<p>Principle:</p>	
<p>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 your needs: calibration and maintenance-free, fast, disposable, portable and with high accuracy. The measurement is based on the oxidation of glucose by glucose oxidase.</p>	
<p>GlucCell® Features</p>	
<ul style="list-style-type: none"> • 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 for 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 	
	
<p>GlucCell™ Specifications</p>	
<p>Assay Method Test Sample Test Result Sample Size Measure range Accurate range Test result time Dimension/Weight Power source Battery life Display Memory Environment Strip Size</p>	<p>Electrochemical biosensor Cell culture medium or equivalent solution Glucose concentration (mg/dl or mmol/l) 1.5 µl 20 - 600 mg/dl (1.1 – 33.3 mmol/l) 30 - 500 mg/dl (1.67 - 27.78 mmol/l) Less than 15 seconds 96 x 60 x 18.5 mm, 70 g incl. battery CR2032 3V Lithium coin battery Approximately 1000 tests Large LCD 180 test results 10 - 40 °C, 20 % - 80 % relative humidity 45 mm x 6 mm x 0.6 mm</p>
 <p>Glucose measurement with various kinds of culture medium in GlucCell obtains 99,5% correlation with YSI bioanalyzer</p>	

Order information

Cat. No.	Description	Case
BCS03000	BelloStage [®] -3000 Compressor (without Bottles): <ul style="list-style-type: none"> - 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 Cell Culture System Complete (without Bottles): <ul style="list-style-type: none"> - 1 BelloStage[®]-3000 Compressor (BCS03000) - 1 GlucCell Glucose Monitoring Kit (GC001000) 	1
BCS07000	BelloCell [®] Continuous Cell Culture System Complete (without Bottles): <ul style="list-style-type: none"> - 1 BelloStage[®]-3000 Compressor (BCS03000) - 1 Bello Feeder[®]-1400 Pump Module (BCA01400) - 2 Tubing Complete Sets (BCA01301) (One set per bottle needed) - 1 GlucCell Glucose Monitoring Kit (GC001000) 	1
BCA01400	BelloFeeder [®] -1400 Pump Module	1
BCA01301	Tubing Complete Set: <ul style="list-style-type: none"> - Silicone Tubing Set - Polypropylene Pump Head - GL45 Stainless Steel Head plate 	1 1 1
BCA01302	Disposable Tubing Accessory Set: <ul style="list-style-type: none"> - Silicone Tubing Set 	5
BCA01303	Disposable Tubing Set and Pump Head: <ul style="list-style-type: none"> - Silicone Tubing Set - Polypropylene Pump Head 	1 1
	BelloCell[®] 500 ml Culture Bottles: Pre-sterilized, irradiated, ready-to-use, disposable, filled with BioNOC™ II PET macroporous carriers	
BCB00500	BelloCell-500: carrier volume 865 pcs. +/- 5 %	4
BCA00500	BelloCell-500A: designed to remove the lid on the matrix basket, carrier volume 865 pcs. +/- 5 %, including 1 cell strainer per case of 4 bottles	4
BCB01000	BelloCell-500P: for continuous culture with automatic medium recirculation, carrier vol.: 865 pcs. +/- 5 %	4
BCA01000	BelloCell-500AP: for continuous culture with automatic medium recirculation, designed to remove the lid on the matrix basket, carrier volume 865 pcs. +/- 5 %, including 1 cell strainer per case of 4 bottles	4
	BioNOC™ II Cell Culture Microcarriers	
BNC00050	BioNOC™ II (50 g)	1
BNC00250	BioNOC™ II (250 g)	1
BNC01100	BioNOC™ II (2 x 550 g)	2
	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

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