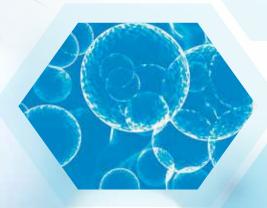


CelCradleTM Cradle for High Density Cells

VACCINCELL FSCO CELCRADLE



The Cradle for Your Cells

The CelCradle™ is a cost-effective, single-use, benchtop bioreactor system capable of supporting high density culture of anchorage-dependent or adherent cells. It is a single-use packed-bed bioreactor system that has linear scalability from laboratory scale to production scale, complete with automated cell harvesting.

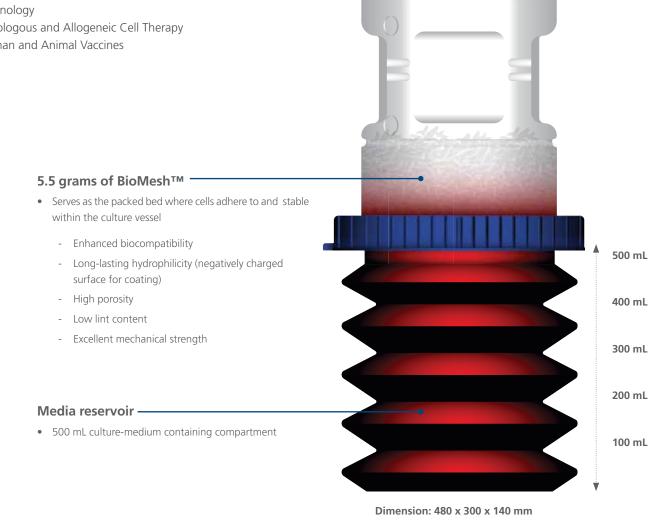
The CelCradle[™] operates through the Tide Motion principle wherein cells, attached to BioMesh[™] carriers, are alternately exposed to aeration and nutrition via the decompression and compression of the bellows holding the culture medium. The gentle vertical oscillation of the culture medium creates a dynamic interface between air and culture medium on the surface of the cells, providing the cells with an environment that is of low shear stress, high aeration and nutrition levels, zero foaming, and no O₂ limitation. This efficient nutrient and oxygen transfer allows the CelCradleTM system to produce high density cell yield.

Applications

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The CelCradle[™] can be used in many different applications, as exhibited by journal articles (see literature support). These include the following applications:

- Culture of anchorage-dependent or adherent cells
- Conversion from Roller Bottles to single use, closed system
- Overcome limitations of microcarrier-stirred tank bioreactor technology
- Autologous and Allogeneic Cell Therapy
- Human and Animal Vaccines



Weight: 2 kg

CelCradle[™] • Cradle for High Density Cells

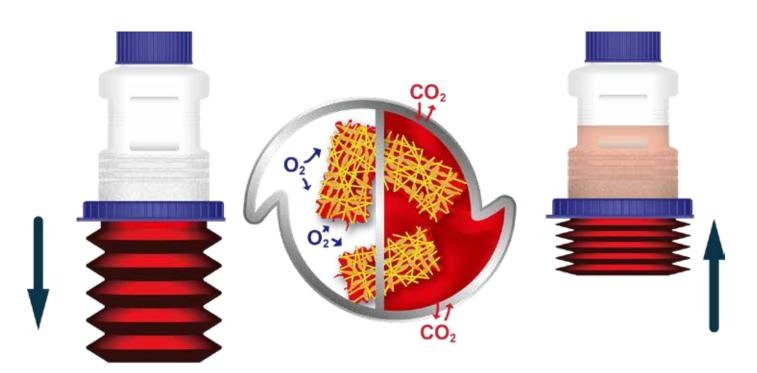


Established Cell Lines

≤	VERO	≤	MSC
≤	MDCK	⊴	СНО
	MDBK	≤	XC-18
≤	Sf-9	≤	ST
≤	HEK-293	⊴	CEF
≤	HEK-293T	≤	GL 37
≤	BHK 21	≤	Marc 145



The Tide Motion Principle



Aeration

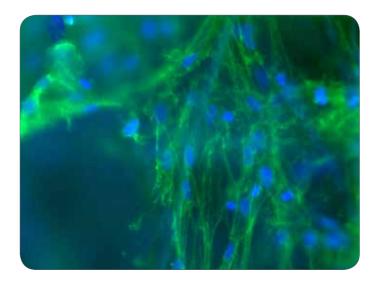
Bellows are released exposing the carriers to carbon dioxide. The cells attached to the carriers will take in aeration.

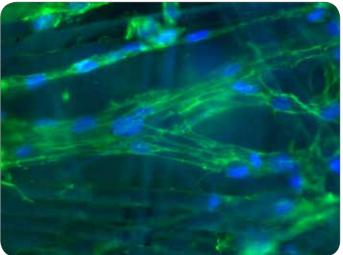
Nutrition

Bellows are pushed up submerging the carriers in the culture medium. The cells attached to the carriers will take in nutrition from the culture medium

Anchorage-dependent cell culture

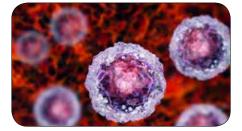
• One CelCradle[™] bottle consists of 5.5 grams of BioMesh[™] providing up to 2,400 cm²/g of surface area for cell attachment and growth. The carriers are proven to have enhanced biocompatibility, long-lasting hydrophilicity, low lint content, and excellent mechanical strength.





FDA and Hoescht 33342-stained cells attached to the BioMesh™ carriers

Autologous and Allogeneic Cell Therapy



Cell Therapy is the use of live whole cells for the treatment of diseases and involves cultivation of cells to a certain density prior to administration. A commonly used cell type in cell therapy is mesenchymal stem cells, which are anchorage-dependent. Currently, cultivation of cells for cell therapy is done using T-flasks; however this method is quite laborious, time and space consuming. T-flasks have limited surface area for growth and thus, require handling of several hundred T-flasks and multiple passaging. The CelCradle™ system's large surface area and compact design help solve these problems, with a single CelCradle™ bottle equalling the productivity of several hundred T-flasks.

Human and animal vaccine

Cell culture-based vaccine production is the current trend in vaccine production as it offers several advantages over traditional vaccine production technologies including simpler mass production, rapid manufacturing, independent of SPF animal, controllable quality, and hypoallergenic products.

The CelCradle[™] is an ideal system for laboratory-scale, cell-culture based vaccine production as it is capable of supporting high density cell culture, production of high viral titer, and linear scalability to production level. VacciXcell's Tide Motion bioreactor system has been used for the research and development, and production of vaccines for several indications including:

- Influenza
- JEV
- Rabies

- Hog Cholera
- Hepatitis A
- EV71



- Rabies
- IBDV

Apart from these, the CelCradle[™] has also been used for other applications including recombinant protein production, pharmacokinetic studies, and cellular component production. Details of these applications can be found from literature support.

Literature Support

The following are some of the available literature support online for the various applications of the CelCradle™ system.

- [1] Asaoka, Y., Tanaka, T., Tsumoto, K., Tomita, M., & Ide, T. (n.d.). Efficient expression of recombinant soluble human FcyRI in mammalian cells and its characterization. Protein Expression and Purification, 155-161.
- [2] Brown, A., Singer, D., Mcsharry, J., Barnard, R., Hazuda, D., & Drusano, G. (n.d.). In Vitro Dose Ranging Studies for Serine Protease Inhibitor, MK-4519, Against a Hepatitis C Virus (HCV) Replicon using the Bellocell System. Antiviral Research.
- [3] Chen, Y., Wu, J., Wang, K., Chiang, Y., Lai, C., Chung, Y., & Hu, Y. (n.d.). Baculovirus-mediated production of HDV-like particles in BHK cells using a novel oscillating bioreactor. Journal of Biotechnology, 135-147.
- [4] Drugmand, J., J.-F., J., Agathos, S., & Schneider, Y. (n.d.). Growth of Mammalian and Lepidopteran Cells on BioNOC® II Disks, a Novel Macroporous Microcarrier. Cell Technology for Cell Products, 781-784.
- [5] Hammonds, J., Chen, X., Zhang, X., Lee, F., & Spearman, P. (n.d.). Advances in methods for the production, purification, and characterization of HIV-1 Gag–Env pseudovirion vaccines. Vaccine, 8036-8048.
- [6] Ho, L., Greene, C., Schmidt, A., & Huang, L. (n.d.). Cultivation of HEK 293 cell line and production of a member of the superfamily of G-protein coupled receptors for drug discovery applications using a highly efficient novel bioreactor. Cytotechnology, 117-123.
- [7] Hu, Y., Lu, J., & Chung, Y. (n.d.). High-density cultivation of insect cells and production of recombinant baculovirus using a novel oscillating bioreactor. Cytotechnology, 145-153.
- [8] Huang, K., Lo, W., Chung, Y., Lai, Y., Chen, C., Chou, S., & Hu, Y. (n.d.). Combination of Baculovirus-Mediated Gene Delivery and Packed-Bed Reactor for Scalable Production of Adeno-Associated Virus. Human Gene Therapy, 1161-1170.
- [9] Lu, J., Chung, Y., Chan, Z., & Hu, Y. (n.d.). A Novel Oscillating Bioreactor BelloCell: Implications for Insect Cell Culture and Recombinant Protein Production. Biotechnology Letters Biotechnol Lett, 1059-1065.
- [10] Mcsharry, J., Singer, D., Kulawy, R., Brown, A., & Drusano, G. (n.d.). Use of the BelloCell System to Determine the Optimal Dose of Ribavirin to Inhibit the Expression of an HCV Replicon in 2209-23 Cells. Antiviral Research.
- [11] Toriniwa, H., & Komiya, T. (n.d.). Japanese encephalitis virus production in Vero cells with serum-free medium using a novel oscillating bioreactor. Biologicals, 221-226.



Conversion from roller bottle to single-use, closed system cell culture

The roller bottle system plays a major role in cell culture-based vaccine production as it is low cost and easy to operate, has a simple scale-up method, observable cell growth and CPE, and limited contamination ; however, the system has many limitations including intensive labor, large space requirement, high running costs, and low efficiency of culture medium utilization.

In principle, the roller bottle system is very similar to CelCradle[™] system. In both systems, cells are alternately exposed to aeration and nutrition. The CelCradle™, however, can overcome the limitations of the roller system while improving output. The advantages of the CelCradle™ system over the roller bottle include:

- One CelCradle[™] system is equivalent to eighty roller bottles •
- Reduced labor and space requirements
- More controllable
- Reduced contamination risks
- Cell harvest in a closed system
- More efficient use of culture medium
- Higher cell density and viral titer •

x80 es (5.5g) Bio 1 CelCradle™ Stage accommodates 4 CelCradle™ bottles Roller Bottles

850 cm²

CelCradle™ System Complete

Simple to operate and virtually no learning curve. CelCradle™ 500 and 500A bottles are placed in the CelCradle[™] unit stage for batch and semi-batch operation where process components are easily traceable.

Filtered Cap

0.22µm ventilation filter provided in the cap



CelCradle™ Stage Stainless Steel 316 L Carcass that can hold up to 4 CelCradle[™] bottles.

Controller

Magnetized back for convenient positioning on the side or on the front of a CO₂ Incubator.

> Place inside a 170 L or 6 ft³ CO, incubator

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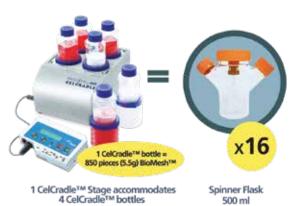
CelCradle™ ● Cradle for High Density Cells

Overcome limitations of microcarrier-stirred tank bioreactor technology

Another technology used for the culture of adherent cells is the use of microcarriers, specially-treated micro-beads where cells attach to and grow on. The microcarriers are suspended in culture medium in stirred tank bioreactors where the medium is continuously agitated and parameters are automatically

monitored and controlled. The microcarrier technology, however, has several disadvantages including reduced cell attachment efficiency, shear stress, foaming, and lack of linear scalability, all of which the CelCradle[™] system are able to overcome. The CelCradle[™] system also has improved features compared to the microcarrier system in terms of the following:

- Viral titer and cell density
- Cell harvest efficiency
- Culture medium usage efficiency
- Harvest purity



BioMesh[™] (packed bed) Cells remain entrapped in the carriers simplifying media replacement and product harvesting VACCINCELL ESCO CELCRADLE **Compressible Bellows** Compresses for nutrition and decompresses for aeration



CelCradle™ Continuous System Complete

Same CelCradle[™] unit stage but utilizes CelCradle[™] 500P and 500AP bottles for recirculation/continuous processes.

Each CelCradle[™] System accomodates up to four single-use bottles, making this an ideal screening device to test varying medium formulations or cell lines.

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

Fits in a 240 L or 8 ft³ CO₂ incubator



CelCradle™ Stage

Stainless Steel 316 L Carcass that can hold up to 4 CelCradle™ bottles.

CelFeeder Enables four-pump operation with individual programming setting.

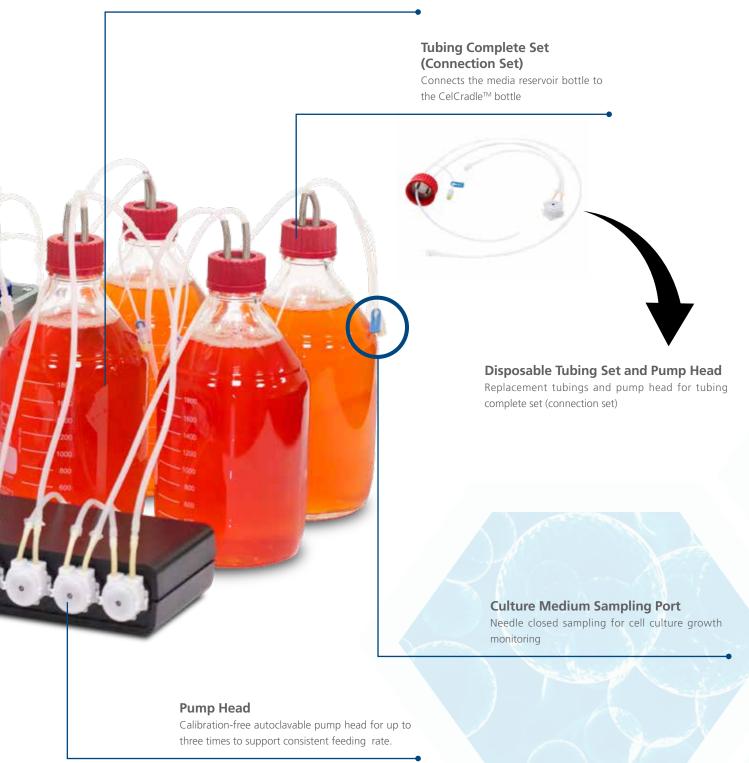
VACCIXCELLESCO CELCRADLE

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CelCradle[™] • Cradle for High Density Cells

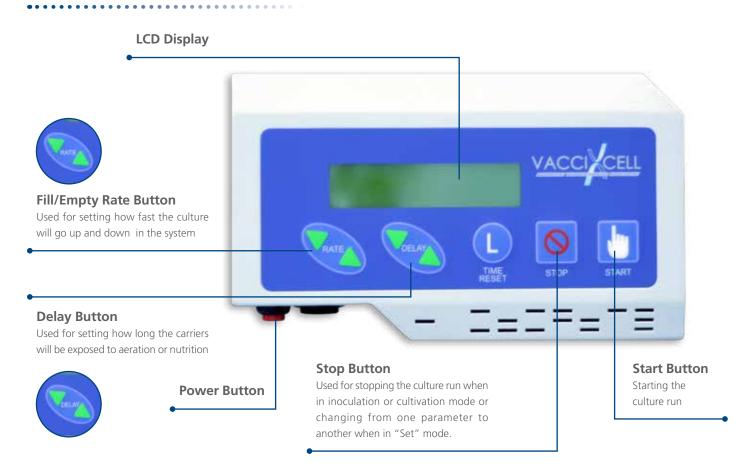
Media Reservoir

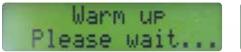
Fresh culture medium bottle in either 1 L or 2 L volume

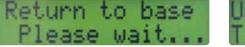


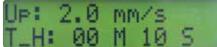


The Main Controller









Message displayed on screen once controller is turned on

Message that will be displayed when stage is rendered on top before opening

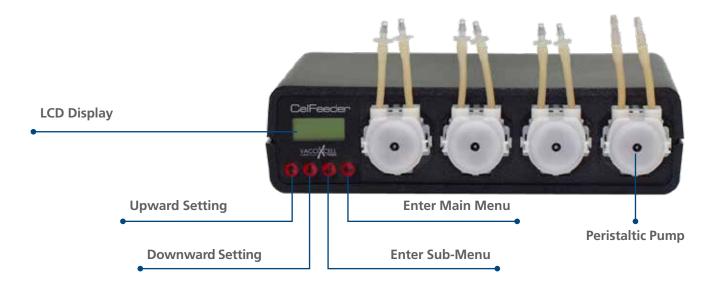
Display message after system has warmed up



The CelFeeder

CelFeeder is a microprocessor-controlled pumping unit of the CelCradle™ Continuous Complete or other cell culture systems.

The CelFeeder is designed to simplify user's operation such that daily feeding volume and frequency of the feeding are the only two parameters required. It simplifies setup work by avoiding calibration and calculation as usually needed in conventional peristaltic pumps.



- Controls four (4) peristaltic pumps individually
- Controls four (4) recirculation process of CelCradle™ 500P/AP bottles at a time
- Daily feeding rate ranges from 1 1999 mL/day
- Feeding frequency of 1-24 times
- Pump calibration made possible to improve accuracy

Dimension	230 (W) x 131 (D) x 61 (H) mm, (5.2 x 9.1 x 2.4 inches)				
Weight	0.645 kg (1.42 lb)				
Power	85~240 Volts AC, 50/60 Hz (Input); ~180 mA				
Environment	Ambient to 45°C, ~95% Relative Humidity				

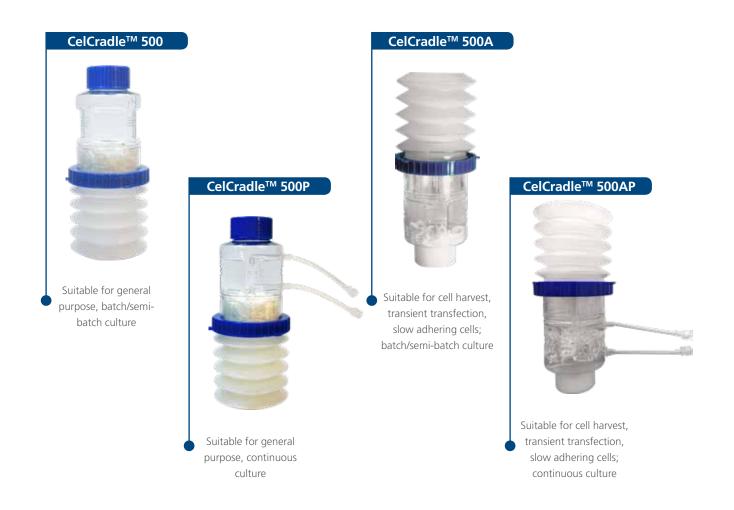




Single-Use and Ready-to-Use CelCradle[™] Bottles

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CelCradle[™] bottles are sterilized through gamma irradiation and comes pre-packed with 5.5 grams of carriers as standard. Different models of bottles cover a specific application in cell culture.



Application/ Bottle	Item Code	Secreted Protein, Viruses	Cell Harvest (for non-secreted proteins, viruses or cells)	Carrier Harvest (for protein extraction or reuse of carriers)
CelCradle [™] 500	1400001	Best application	Applicable, but not optimal	Applicable, but not optimal
CelCradle™ 500A	1400003	Applicable, but not optimal	Best application	Best application
CelCradle™ 500P	1400002	Best application	Applicable, but not optimal	Applicable, but not optimal
CelCradle [™] 500AP	1400004	Applicable, but not optimal	Best application	Best application

CelCradle[™] • Cradle for High Density Cells

> Carrier Sampling

500/500P Bottles

500A/500AP Bottles

> Cell Monitoring



A portable, easy-to-use glucose monitoring system for cell culture. Get results in just 15 seconds. Measurement ranges from 30-500 mg/dL

Crystal Violet Dye

A simple tool for the quantification of cells based on the number of nuclei dyed. The CVD kit contains reagents that disrupt the cells, thereby releasing the nuclei, which are subsequently dyed.



Inoculation Phase pH Control

OPTION 1

If using a pre-mixed media with fixed amount of sodium bicarbonate ($NaCO_3$), readjusting before culture may be difficult. Alternatively, users can opt to:

For Upright Seeding

Seed at a lower CO₂ concentration



For Inverted Seeding

Adjust pH with HCl to pH 6.8 as a starting point



OPTION 2

Use 500AP bottle and connect one tubing with air filter and the other leaving tightly closed.



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OPTION 3

Compress the bellows before closing the bottles with a non-vented cap (white cap). This method lessens excessive air in the CelCradleTM bottle which may affect the pH value of the culture medium. This can be attributed to the decrease of CO_2 concentration in the liquid rendering it basic.















Ordering Information

Product Name	Item Code	Dimension	Weight	Package
CelCradle [™] System Complete	2230006	590 x 380 x 420 mm	14 kg	1 x CelCradle™ Stage 1 x GlucCell® Glucose Monitoring System
CelCradle™ Continuous System Complete	2230007	590 x 380 x 420 mm	15 kg	1 x CelCradle™ Stage 1 x CelFeeder Pump 2 x Tubing Complete Set
CelCradle™ Stage	2230005	360 x 265 x 170 mm	9.88 kg	1x Main Console 1x Control Box 1x 100-240 V power adapter 1x Signal Cable 1x Manual CD 2x Forceps 1x Crystal Violet Dye Nucleus Count Kit
CelFeeder Pump	1400067	290 x 210 x 80 mm	1 kg	1 x CelFeeder Pump
Tubing Complete Set	1400011	370 x 150 x 75 mm	0.5 kg	1x Disposable Tubing Accessory 1x Pump Head
Disposable Tubing Set & Pump Head	1400012	370 x 150 x 75 mm	0.5 kg	1x Tubing Set 1x Pump Head
Disposable Tubing Accessory	1400013	370 x 150 x 75 mm	0.5 kg	5x Disposable Tubing Accessory
GlucCell [®] Glucose Monitoring System	1400009	96 x 60 x 18.5 mm	0.5 kg	1 x GlucCell [®] Glucose meter 2 bottles of Glucose Test Strip (1bt = 25 test strips)
GlucCell [®] Glucose Test Strip	1400010	80 x 70 x 35 mm	0.05 kg	2 x Glucose Test Strip bts (2 x 25pcs)
Crystal Violet Dye Nucleus Count Kit	1400014	50 x 50 x 105 mm	0.5 kg	1 x CVD Bottle (100ml/bt)
Filtered Cap	1400015	370 x 150 x 75 mm	0.5 kg	Cap for CelCradle™ Bottle
Non-Vented Cap	1400016	370 x 150 x 75 mm	0.5 kg	Cap for CelCradle™ Bottle
Forceps	1400017	250 x 15 x 10 mm	0.1 kg	Used for sampling of BioMesh™ carriers
CelCradle™ 500A/500AP Strainer	1400021	370 x 150 x 75 mm	0.5 kg	Single-use Strainer (Pack of 10)

CelCulture® CO₂ Incubator

Sleek, reliable, and intuitive, Esco CelCulture[®] CO₂ incubators provide all-rounded sample protection that brings your scientific dreams one step closer to reality.

Features:

- HPA-validated 90°C overnight moist heat decontamination cycle
- ISO Class 5 cleanliness via ULPA Filter System
- Direct heat, air jacketed system for fast and uniform heating and rapid recovery without overshoot
- Rounded corners and seamless design for easy cleaning

CelCradle™ ● Cradle for High Density Cells

- Constructed using electrogalvanized with ISOCIDE™ powder-coating to eliminate 99.9% of surface bacteria within 24 hours of exposure
- With optional copper interiors for added antimicrobial protection
- Available in 50 L, 170 L, and 240 L sizes
- ULPA Filter
 - 99.999% efficient, superior to conventional HEPA filters
 - Filters air continuously
 - Chamber returns to ISO Class 5 cleanliness in 11 minutes upon door closing to prevent contamination
- Direct Heat & Air Jacket
 - Fast and uniform heating
 - Rapid temperature recovery without overshoot
 - Air jacket improves chamber stability
- O₂ Sensor
 - Long life
 - Stable output signal
 - No influence from CO₂



- CO₂ Sensor
 - CelCradleTM and CO_2 Incubator Combination
 - Single-beam, dual-wavelength IR sensor is drift-free
 - Auto-zeroing
- SmartSense[™] Microcontroller Interface
 - Intuitive, fully equipped control and monitoring system

	CelCulture [®] CO ₂ Incubators IR Sensor Model with Stainless Steel Chamber					
230 VAC, 50/60 Hz 115 VAC, 50		50/60 Hz	Description			
Item Code	Model	Item Code Model		Description		
2170034	CCL-050B-8	2170054	CCL-050B-9	CelCulture [®] Incubator, 50 L, IR sensor, CO ₂ Control, Moist Heat Decon		
2170002	CCL-170B-8	2170004	CCL-170B-9	CelCulture [®] Incubator, 170 L, IR sensor, CO ₂ Control, ULPA, Moist Heat Decon		
2170068	CCL-170B-8-NF	2170075	CCL-170B-9-NF	CelCulture [®] Incubator, 170 L, IR sensor, CO ₂ Control, Moist Heat Decon (No ULPA Filter)		
2170058	CCL-240B-8	2170060	CCL-240B-9	CelCulture [®] Incubator, 240 L, IR sensor, CO ₂ Control, ULPA, Moist Heat Decon		
2170069	CCL-240B-8-NF	2170079	CCL-240B-9-NF	CelCulture [®] Incubator, 240 L, IR sensor, CO ₂ Control, Moist Heat Decon (No ULPA Filter)		

	CelCulture [®] CO ₂ Incubators Suppressed O ₂ Models with Stainless Steel Chamber						
230 VAC, 50/60 Hz		115 VAC, 50/60 Hz					
Item Code	Model	Item Code	Model	Description			
2170055	CCL-050T-8	2170056	CCL-050T-9	CelCulture [®] Incubator, 50 L, IR sensor, CO ₂ & O ₂ Control, Moist Heat Decon			
2170047	CCL-170T-8	2170048	CCL-170T-9	CelCulture [®] Incubator, 170 L, IR sensor, CO ₂ & O ₂ Control, ULPA, Moist Heat Decon			
2170070	CCL-170T-8-NF	2170076	CCL-170T-9-NF	CelCulture [®] Incubator, 170 L, IR sensor, CO ₂ & O ₂ Control, Moist Heat Decon (No ULPA Filter)			
2170061	CCL-240T-8	2170062	CCL-240T-9	CelCulture [®] Incubator, 240 L, IR sensor, CO ₂ & O ₂ Control, ULPA, Moist Heat Decon			
2170071	CCL-240T-8-NF	2170080	CCL-240T-9-NF	CelCulture [®] Incubator, 240 L, IR sensor, CO ₂ & O ₂ Control, Moist Heat Decon (No ULPA Filter)			



CelCradle[™] • Cradle for High Density Cells

CelCradle™ and Esco CO₂ Incubator

The Perfect Combination for High Density Adherent Culture

The CelCradleTM system can be incorporated into an existing CO₂ incubator or can be purchased with an Esco CO₂ incubator. Esco offers a wide range of CO, incubators that suit clients' different requirements, provide superior performance and cell protection.

CelCulture® Stainless Steel CO₂ Incubator

The Esco CelCulture® CO, incubator is also available with stainless steel exterior with the same superior features.

Features:

- Corrosion Resistant Surface
- Meets Pharmaceutical and Clinical Laboratory Requirements HPA-validated 90°C overnight moist heat decontamination cycle
- ISO Class 5 cleanliness via ULPA Filter System
- Available in 50 L, 170 L and 240 L sizes

Ordering Information

IR SENSOR MODEL WITH STAINLESS STEEL EXTERIOR CABINET				
Models Item Code		Description		
CCL-050B-8-SS	2170128	CelCulture [®] Incubator 50 L, IR Sensor, CO_2 Control, Moist Heat Decon, SS Cabinet, 230 VAC, 50/60 Hz (Without Decon Pump)		
CCL-170B-8-SS	2170065	CelCulture [®] Incubator 170 L, IR Sensor, CO_2 Control, ULPA, Moist Heat Decon, SS Cabinet, 230 VAC, 50/60 Hz		
CCL-240B-8-SS 2170137		CelCulture [®] Incubator 240 L, IR Sensor, CO_2 Control, ULPA, Moist Heat Decon, SS Cabinet, 230 VAC, 50/60 Hz		

SUPPRESSED O ₂ MODEL WITH STAINLESS STEEL EXTERIOR CABINET				
Models Item Code		Description		
CCL-050T-8-SS	2170171	CelCulture [®] Incubator 50 L, IR Sensor, $CO_2 & O_2$ Control, Moist Heat Decon, SS Cabinet, 230 VAC, 50/60 Hz (Without Decon Pump)		
CCL-170T-8-SS	2170129	CelCulture [®] Incubator 170 L IR Sensor, $CO_2 \& O_2$ Control, ULPA, Moist Heat Decon, SS Cabinet, 230 VAC, 50/60 Hz		
CCL-240T-8-SS	2170138	CelCulture [®] Incubator 240 L, IR Sensor, CO ₂ & O ₂ Control, ULPA, Moist Heat Decon, SS Cabinet, 230 VAC, 50/60 Hz		



CelCulture® CO₂ Incubator with Cooling System

Esco CelCulture[®] CO₂ Incubator with Integrated Cooling System provides solution for highly specialized application. The integrated cooling system allows studies of samples that requires temperature at/or below ambient temperature.

Features:

- Wider temperature range of 12°C below ambient to 60°C above ambient
- Highly efficient, environment friendly Peltier Cooling System
- Constructed using electrogalvanized with ISOCIDE™ powder-coating to eliminate 99.9% of surface bacteria within 24 hours of exposure
- Complete contamination control methods
 - 90°C Validated Moist Heat Decontamination Cycle
 - ULPA Filter
 - 0.2 micron inlet filter
- Available in 170 L and 240 L sizes



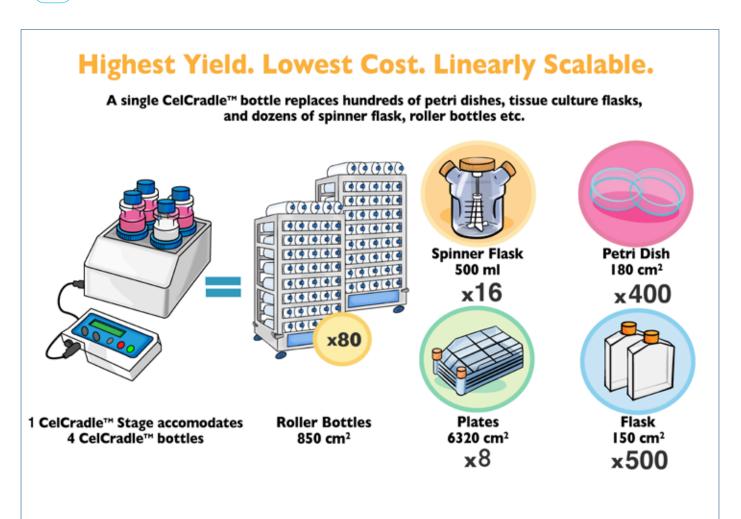
GUIDE TO MODELS, CelCulture [®] CO ₂ Incubators with Cooling System							
IR Sensor Model With Stainless Steel Chamber							
230 VAC, 50/60 Hz 115 VAC, 50/60 Hz		50/60 Hz					
Item Code	Model	Item Code	Model	Description			
2170101 CCL-170B-8-P 2170115 CCL-170B-9-P		CCL-170B-9-P	CelCulture [®] Incubator, 170 L, IR sensor, CO ₂ control, Moist Heat Decon, Peltier System				

2170116 | CCL-240B-8- | 2170266 | CCL-240B-9-P | CelCulture® Incubator 240 L, IR Sensor, CO2 Control, Moist Heat Decon, Peltier System

	Suppressed O ₂ Models with Stainless Steel Chamber						
230 VAC, 50/60 Hz 115 VAC, 50/60 Hz		50/60 Hz	Description				
Item Code	Model	Item Code	Model	Description			
2170112	CCL-170T-8-P	2170153	CCL-170T-9-P	CelCulture [®] Incubator, 170L, IR sensor, CO ₂ control, O ₂ control, Moist Heat Decon, Peltier System			

2170267 | CCL-240T-8-P | 2170268 | CCL-240T-9-P | CelCulture® Incubator 240 L, IR Sensor, CO2 & O2 Control, Moist Heat Decon, Peltier System





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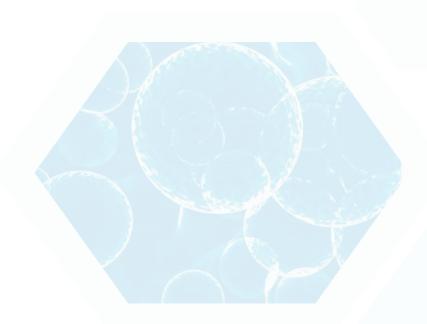
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