

WAVE Bioreactor™ 2/10 and 20/50 systems

WAVE Bioreactor 2/10 and 20/50 systems (Fig 1) are part of GE Healthcare Life Sciences' ReadyToProcess platform of ready-to-use products. The system is a cell culture instrument for the production of recombinant proteins in mammalian and insect cell lines in batch, fed-batch, and perfusion culture. Culture medium and cells are loaded into the Cellbag™ bioreactor, which is a single-use, presterilized bag. The Cellbag bioreactor is placed on a rocking base. The rocking motion induces waves in the cell culture fluid within the Cellbag bioreactor to provide efficient mixing and gas transfer (Fig 2). The resulting environment within the Cellbag bioreactor can easily support 1×10^7 cells/mL. The Cellbag bioreactor requires no cleaning or sterilization, providing easy operation and protection against cross-contamination.

As part of ReadyToProcess platform, WAVE Bioreactor brings flexibility and speed to upstream processing of biologicals. ReadyToProcess platform comprises WAVE Bioreactor systems, WAVE Mixer™, tubing sealers and welders, hollow fiber and normal flow filters, prepacked chromatography columns, and ÄKTA™ ready chromatography system with a disposable flow path, as well as the assemblies and connections in between. The platform is scalable from the lab bench to manufacturing.

WAVE Bioreactor 2/10 and 20/50 systems deliver:

- Convenience: Presterilized, single-use Cellbag bioreactors protect against the risk of cross-contamination, require no cleaning, and involve minimal validation and they are supplied in a ready-to-use format
- Reliability: Cellbag bioreactors, including all fittings and filters, are supplied sterile and ready for use. They are suitable for cGMP commercial production and a biosafety cabinet is not required for inoculation or sampling



Fig 1. WAVE Bioreactor 20/50 system with WAVEPOD™II Integrated Controller.

- Flexibility: Multiple instrument configurations for suspension, microcarrier, batch, fed-batch, or perfusion culture
- Versatility: The systems are capable of handling culture volumes from 100 mL to 25 L

Principles of operation

Cellbag bioreactor

The Cellbag bioreactor is a presterilized inflatable plastic bag that forms a disposable cell cultivation chamber. The bioreactor is available in different sizes, in both standard and customized configurations. The Cellbag bioreactor is used together with the electrically driven rocking base.

Rocking base

The rocking base is electrically heated and it is designed to inflate and rock the bioreactor for rapid gas transfer and mixing. The wave action sweeps up cells and prevents settling in the bioreactor. The gentle wave action limits shear force effects on the cells.

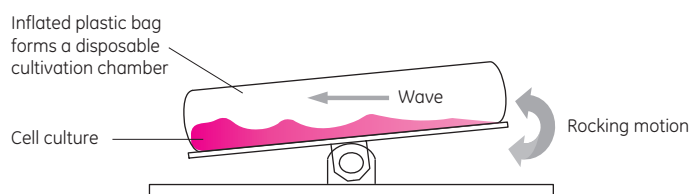


Fig 2. Principle of operation of the rocking base.



System specifications and selection

To select the correct WAVE Bioreactor system for your application, first determine the Cellbag bioreactor size you need by estimating the culture volume you require and then select the appropriate instrumentation and options (Table 1).

Table 1. Specifications for WAVE Bioreactor 2/10 and 20/50 systems

	BASE 2/10EH	BASE 20/50EHT
Working volume (L)	0.1 to 5	0.1 to 25
Integral features	Speed and angle control Temperature control Aeration	Speed and angle control Temperature control Aeration
Options	CO2/Air Mix controller O2/Air Mix controller Dissolved oxygen Optical monitor Perfusion controller	WAVEPOD II controller with CO2/Air Mix, O2/Air Mix, dissolved oxygen optical monitor, optical pH sensor Perfusion control with Loadcell Air and temperature dual control KIT20EHTD KIT50EHTD
Weight (kg)	4.2	15.5
Dimensions of base (mm)	230 × 330 × 200	573 × 465 × 179
Base dimensions with Cell Holder Kits (mm)	KIT2EH: 489 × 330 × 200	KIT20EHT: 711 × 575 × 254 KIT50EHT: 775 × 700 × 254
Utilities	110/220 VAC	100/240 VAC 6/3 A 50/60 Hz

Note: "EHTD" stands for Electrically Heated with Touch panel in Dual configuration.

System options

WAVE Bioreactor 2/10 system

The WAVE Bioreactor 2/10 system (Fig 3) is a compact unit fitted with integral features such as an air pump with a mass flow meter and a temperature control with a heater and sensor. Options include weight controllers for perfusion culture and dissolved oxygen amplifiers. Multifunction control enables adjustment of rocking angle, speed, and aeration rate.



Fig 3. WAVE Bioreactor 2/10 system can be used with the following Cellbag volumes: 500 mL, 1, 2, and 10 L.

WAVE Bioreactor 20/50 system

The WAVE Bioreactor 20/50 system (Fig 4) is modular, consisting of an electrically powered base unit (BASE20/50EHT) and a choice of kits for holding the Cellbag bioreactor. The Cellbag Holder Kit is available in two sizes: the KIT20EHT is suitable for culture volumes of up to 10 L and the KIT50EHT is suitable for culture volumes of up to 25 L. Other options for the WAVE Bioreactor 20/50 system include weight controllers for perfusion culture and dissolved oxygen monitor. The WAVE Bioreactor 20/50 system can be used with the WAVEPOD II controller, which provides simplified control of all culture parameters including oxygen, pH, and CO₂/O₂ gas mixing in a single module. The WAVE Bioreactor 20/50 system can also be configured to allow independent control of two individual cultures using a single base unit.



Fig 4. WAVE Bioreactor 20/50 system accommodates combinations of Cellbag volumes: 2, 10, 20, 22, and 50 L depending on which Cellbag Holder Kit is used.

Cabinet

The cabinet (Fig 5) provides a space saving unit for up to three base units of the WAVE Bioreactor 20/50 system. Slide-out shelves provide easy access to instrumentation and the cabinet is mounted on casters for portability.



Fig 5. The cabinet fits through standard doorways and it is mounted on casters for mobility. It can accommodate up to four 19" instrument racks on the top shelf and up to three BASE20/50EH series bioreactors on slide-out shelves. In addition, the cabinet has CO₂/O₂ manifold for gas distribution, removable stainless-steel door and sides.

WAVEPOD II

WAVEPOD II (Fig 6) is an integrated controller for CO₂/O₂/pH and dissolved oxygen. Multiple configurations (Table 2) are available for insect cell, mammalian cell, perfusion or cell therapy applications.



Fig 6. WAVEPOD II combines the four key components (WAVE Bioreactor 20/50, dissolved oxygen, pH, and CO₂/O₂ gas mixing controls), into a single compact device, which connects via a digital link to the WAVE Bioreactor base.

Table 2. WAVEPOD II options

Module	Description
CO ₂ /Air Mix controller	Integrated CO ₂ sensor and controller aeration system provides a continuous supply of CO ₂ conditioned air to the Cellbag bioreactor Control range of 0% to 15% CO ₂
O ₂ /Air Mix controller	Provides continuous supply of O ₂ enriched gas to the Cellbag bioreactor for insect cell, virus, and high cell density applications Maintains low oxygen environment for near anaerobic applications Control range of 0% to 50% O ₂
Dissolved Oxygen Optical Monitor	Monitor with miniature fiber-optic microprobes enabling real-time measurement of dissolved oxygen Reusable DOOPT probe purchased separately
Optical pH Controller	Enables pH measurement and control using CO ₂ and/or acid/base addition Optical pH probe is for single-use and it is available preinstalled in Cellbag bioreactors pH control range 6 to 8 Measurement range 4.5 to 8.5

Technology

Digital speed and temperature controls

Digital electronic PID controller (Fig 7) maintains precise control of temperature, speed, and angle. These industry-standard units do not require user programming and considerably ease the burden of equipment validation. Outputs can be analog for recorders or digital (MODBUS) for data acquisition systems.



Fig 7. Touch-screen for system control.

Servo electric motor

A geared brushless DC servo motor is used to maintain efficient wave action within the Cellbag bioreactor by controlling the speed and angle of the rocking platform. This motor is programmed to follow a precise speed and acceleration profile that has been determined to be optimal for cell culture and can be adjusted to precisely match the needs of different cell types. Safety switches will shut the rocker off in the event of over-torque, over-temperature, or if the rocking platform becomes obstructed.

UNICORN™ DAQ

UNICORN DAQ 1.0 software facilitates real-time data acquisition for the management and evaluation of results from cell cultures performed using up to four different WAVE Bioreactor systems connected to a single PC. The WAVE Bioreactor system can be connected directly or networked to the software providing a common platform and user interface for monitoring and storing result data. A dynamic graphical user interface informs you about the real-time status of the run being monitored. During a run, data is automatically saved to a local hard drive or server in a secure and unalterable result file for added security.

Loadcell

Loadcells can be mounted under the holder tray to measure the Cellbag bioreactor weight during rocking. A built-in pump controller can be used for feeding, harvesting, and perfusion operations.

Heater Pad and surface RTD temperature sensor

A Heater Pad (Fig 8) is included in the Cellbag Holder Kit, which is linked to a surface temperature sensor for accurate temperature control (Fig 9).

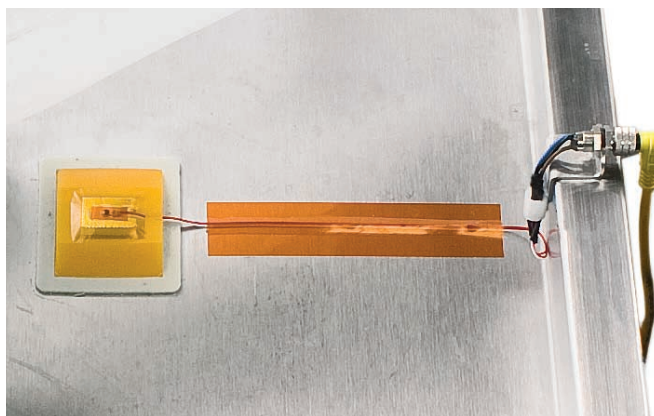


Fig 8. Heater Pad is located on the tray, under the Cellbag bioreactor.

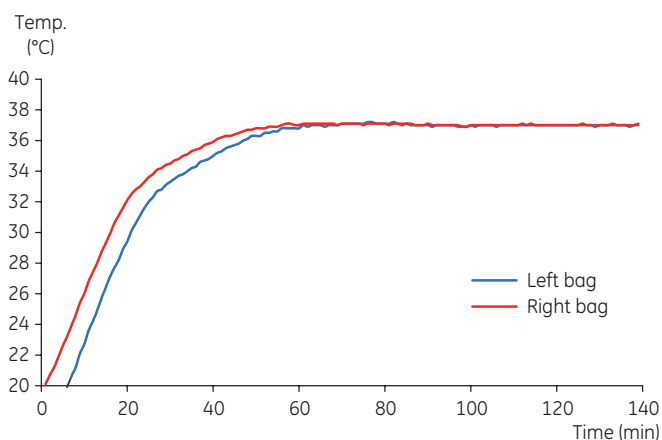


Fig 9. Accurate temperature control for the dual Cellbag bioreactor.

Quick-release holder trays

Holder trays (Fig 10) have two cam-locks to quickly and securely lock the Cellbag bioreactor in place. This mechanism allows the Cellbag bioreactors to be installed correctly and changed rapidly.



Fig 10. Holder trays are an integral part of the KIT20 and KIT50 units. The tray is made of stainless steel and aluminum and it can be autoclaved if needed.

Analog output and alarms

Process parameters such as speed and temperature can be supplied as an analog output from the mini-din jack on the back of the unit. In addition, we provide a dry contact that can interface with your system to alert you when an alarm goes off.

Cellbag bioreactors

Cellbag bioreactors (Fig 11) are made of USP Class VI plastics typically used for biological fluid handling; the cell contact surface is an approved ethylene vinyl acetate (EVA)/low density polyethylene copolymer of the type routinely used for blood collection and handling of biological fluids. The outer layers are made of proprietary composites that provide flexibility, strength, and extremely low gas permeability. Data is available to demonstrate biocompatibility. However, we recommend validation for specific applications.

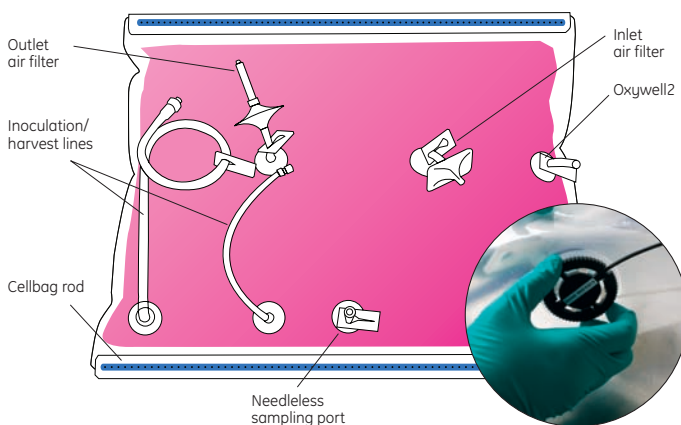


Fig 11. The pHOPT sensor allows you to continuously measure and control pH using CO₂ or acid/base addition. The sensor is embedded in the Cellbag bioreactor.

Standard format Cellbag bioreactors have air inlet and outlet filters, a needleless sampling port, an Oxywell™2 dissolved oxygen probe insertion port, and a fill/harvest port although Cellbag bioreactors can be easily customized to suit your specific cell culture process needs. Our product specialists will work with you to create the optimal cell culture bag (Table 3) for your WAVE Bioreactor system.

Table 3. Cellbag bioreactor selection guide for WAVE Bioreactor 2/10 and 20/50 systems

Culture volume	Cellbag bioreactor	Systems
100 to 250 mL	Cellbag 500 mL	2/10
100 to 500 mL	Cellbag 1 L	2/10
100 mL to 1 L	Cellbag 2 L	2/10, 20/50 + KIT20
500 mL to 5 L	Cellbag 10 L	2/10, 20/50 + KIT20
1 to 10 L	Cellbag 20 L	20/50 + KIT20
1 to 10 L	Cellbag 22 L	20/50 + KIT50
5 to 25 L	Cellbag 50 L	20/50 + KIT50

Key applications

Monoclonal antibodies

The WAVE Bioreactor system has been used extensively for monoclonal antibody production. Culture can be started at low volume and then fresh media added whenever the cell count is sufficiently high. This enables inoculum scale up without transfers. Batches ranging from 100 mL to 580 L were run with cell densities over 10×10^6 cells/mL, resulting in productivity and product quality that is comparable to that of stirred tank bioreactors. Dissolved oxygen concentrations are typically not limiting and remain above 50% saturation.

Anchorage-dependent cells

Agitation in the WAVE Bioreactor system is powerful enough to mix and aerate the culture, yet it is gentle enough to cultivate anchorage-dependent cells on various microcarriers. The wave motion prevents settling and provides oxygenation without sparged bubbles.

Virus production

The WAVE Bioreactor system provides a closed system that is suitable for virus production. In a gene therapy application, human 293 cells were grown in suspension and then infected with recombinant adenovirus. Cells grew to 4×10^6 cells/mL and virus production was 1×10^5 virus particles/cell. The WAVE Bioreactor system produces viruses under complete containment without the need for a biosafety cabinet.

cGMP production

WAVE Bioreactor systems are in use in cGMP applications to produce inoculum for large conventional bioreactors, and also for clinical and commercial production of human therapeutics. Reduced cleaning and validation requirements make this a suitable system for cGMP applications.

Insect cell/Baculovirus

The high oxygen supply capability of the WAVE Bioreactor system makes it suitable for insect cell culture. Cell densities over 9×10^6 cells/mL are routinely achieved. The WAVE Bioreactor system is easy to operate and inoculum scale-up and infection can be done inside the bioreactor, reducing the need for transfers.

Ordering information

Product Bioreactors	Code no.
BASE2/10EH	28-4115-00
BASE20/50EHT 100-120V	28-9413-41
BASE20/50EHT 220-240V	28-9413-42
BASE20/50EHT-L 100-120V	28-9413-43
BASE20/50EHT-L 220-240V	28-9413-44
BASE20/50EHTD 100-120V	28-9413-45
BASE20/50EHTD 220-240V	28-9413-46
BASE20/50EHTD-L 100-120V	28-9413-47
BASE20/50EHTD-L 220-240V	28-9413-48
BASE20/50EHT-CO2 100-120V	28-9413-49
BASE20/50EHT-CO2 220-240V	28-9413-50
BASE20/50EHT-CO2-L 100-120V	28-9413-51
BASE20/50EHT-CO2-L 220-240V	28-9413-52
BASE20/50EHT-O2 100-120V	28-9413-53
BASE20/50EHT-O2 220-240V	28-9413-54
BASE20/50EHT-O2-L 100-120V	28-9413-55
BASE20/50EHT-O2-L 220-240V	28-9413-56
KIT20EHT 110-120V	28-4115-26
KIT20EHT 220-240V	28-9416-44
KIT20EHTD 110-120V	28-4115-27
KIT20EHTD 220-240V	28-9416-45
KIT50EHT 110-120V	28-4115-28
KIT50EHT 220-240V	28-9416-46
KIT50EHTD 110-120V	28-4115-30
KIT50EHTD 220-240V	28-9416-47
LID2/10W - Opaque	28-4115-33
LID20 Clear	28-4115-34
LID20W - White	28-4115-35
LID50 - Clear	28-4115-37
LID50W - White	28-4115-38

WAVEPOD II

WAVEPOD II CO2 O2 pHOPT DOOPT	28-9847-40
WAVEPOD II CO2 pHOPT	28-9847-41
WAVEPOD II O2 DOOPT	28-9847-42

Stand-alone instrument

DOOPT20	28-4129-52
CO2MIX20	28-4129-47
CO2MIX20-R	28-4129-48
O2MIX20-R	28-4129-50
O2MIX20	28-4129-49
PUMP20-L	28-4116-31
PUMP20-R	28-4116-33

Related products	Code no.	Related products	Code no.
Accessories		Other ReadyToProcess products	
Bag sensor adaptor 2.5 m assembly	28-9841-89	Hot Lips Tube Sealer™	28-4117-04
PERFCONT2E	28-4116-35	HLTS-II-CALKIT	28-4117-07
ETHERNET485	28-4116-38	MIXER 20/50EHT 110-120V	28-9515-84
FLTHTR2	28-4116-39	MIXER 20/50EHT 220-240V	28-9515-12
CABINET 110-120V	28-4116-43	MIXER 20/50EHTL 110-120V	28-9515-85
CABINET 220-240V	28-4116-44	MIXER 20/50EHTL 220-240V	28-9515-32
RTDPROBE	28-4116-67	MIXKIT20	28-4115-73
DOOPTPROBE	28-4116-72	MIXKIT20EH 110-120V	28-9514-79
UNICORN DAQ 1.0	28-9848-23	MIXKIT20EH 220-240V	28-9526-27
Converter 100	28-9770-48	MIXKIT50	28-4115-76
Other ReadyToProcess products		MIXKIT50EH 110-120V	28-9514-80
Sterile Tube Fuser	28-4116-77	MIXKIT50EH 220-240V	28-9526-28
Tube Holder 5/8in	28-4116-81	MIXHOLDER20	28-4115-72
Tube Holder 3/4in	28-4116-82	MIXHOLDER50	28-4115-75
Tube Holder 7/16in	28-4116-83	MIXLID20	28-4115-71
Tube Holder 1/4in	28-4116-84		
Tube Holder 5/16in	28-4116-85		
Tube Holder 3/8in	28-4116-86		
Tube Holder 1/2in	28-4116-87		
Tube Holder 7/8in	28-4116-88		
STF-IRc-CALKIT	28-4116-98		
BLADES-IR/50	28-4117-01		

Related literature

WAVE Bioreactor 200 and 500/1000 systems, Data file	28-9606-53
WAVEPOD II Integrated Controller, Data file	28-9606-57
UNICORN DAQ 1.0, Data file	28-9778-46

For local office contact information, visit

www.gelifesciences.com/contact

www.gelifesciences.com/wave

www.gelifesciences.com/ReadyToProcess

GE Healthcare Bio-Sciences AB

Björkgatan 30

751 84 Uppsala

Sweden



imagination at work

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GE Healthcare UK Limited
Amersham Place
Little Chalfont
Buckinghamshire, HP7 9NA
UK

GE Healthcare Europe, GmbH
Munzinger Strasse 5
D-79111 Freiburg
Germany

GE Healthcare Bio-Sciences Corp.
800 Centennial Avenue, P.O. Box 1327
Piscataway, NJ 08855-1327
USA

GE Healthcare Japan Corporation
Sanken Bldg., 3-25-1, Hyakunincho
Shinjuku-ku, Tokyo 169-0073
Japan