GE Healthcare
Life Sciences

Xuri™ Cell Expansion System W25

Xuri Cell Expansion System W25 has been specifically designed for cell therapy manufacturing applications. This functionally closed system is based on the proven WAVE™ rocking technology, which provides mixing and aeration to the culture, resulting in high cell densities, whilst minimizing the risk of contamination. The system is enhanced by sensors to monitor your cell expansion, and is operated via UNICORN™ control software.

Xuri Cell Expansion System W25 offers the following benefits:

- Minimized risk of cell contamination
- Reach high cell densities with confidence
- Advanced control of cell expansion through process monitoring and remote operation
- Suitability for use in a regulated environment

The system delivers reliable and accurate performance across research, process development, and manufacturing environments.

Xuri Cell Expansion System W25 is intended for a variety of cell culture applications such as expansion of primary T-lymphocytes.

Fig 1. Xuri Cell Expansion System W25 is designed for cell therapy manufacturing applications.

System benefits

Minimized risk of cell contamination

The Xuri Cell Expansion System W25 is a functionally closed system, which minimizes the risk of contamination between different patient samples or with adventitious agents. The cells are grown in a single-use Cellbag™ bioreactor.

High cell densities and perfusion culture

The system is designed for both batch and perfusion culture. Perfusion culture in a single Cellbag bioreactor results in high cell density which is often needed for cell therapy purposes. This means that an entire dose of cells for a patient can be obtained in one functionally closed bioreactor system without the need to open the vessels to change the cell culture medium. This also eliminates the difficulties of combining culture vessels as is necessary with manual systems. High cell density, together with the small instrument footprint maximizes use of limited manufacturing space.

Advanced control with process monitoring and remote operation

Xuri Cell Expansion System W25 is equipped with sensors and automated controllers for key culture parameters—rocking speed, dissolved oxygen (DO), pH, and perfusion rate—which enable cell specific optimization of the cell expansion culture environment and production of high-quality and high-density cells.

Once a culture is underway, data is logged and recorded in the base unit as well as in the software. The system can be monitored and controlled remotely and it can send e-mail alerts if user-defined limits are exceeded. These features provide the monitoring and tracking necessary in a regulated environment.

Designed for use in a regulated environment

Xuri Cell Expansion System W25 is designed to meet the demands and standards required in a regulated environment. Documentation accompanying the system includes material certificates, system specifications, installation and operational qualification (IQ/OQ) protocols, and a detailed user manual. UNICORN software is suitable for use in a manner that complies with 21 CFR Part 11 and Good Automated Manufacturing Practice (GAMP) 5.

System overview

Xuri Cell Expansion System W25 components

Xuri Cell Expansion System W25 consists of a base unit, a gas mixer, and a pump, which are all operated by the UNICORN software installed on a client computer. The base unit is the main hardware unit, which is used with a tray and a disposable Cellbag bioreactor. The base unit has multiple functions, including heating, culture mixing, and weight measurement. The gas mixer delivers gas of a defined composition to the culture and is used for online control of culture pH and DO. Liquid is delivered accurately to the culture by the Xuri Cell Expansion W25 Pump Unit. The pump has a flow range covering multiple applications, from additions of acid and base to fresh medium for perfusion culture.

An overview of the Xuri Cell Expansion System W25 is shown in Figure 2. The individual components are described in the text.

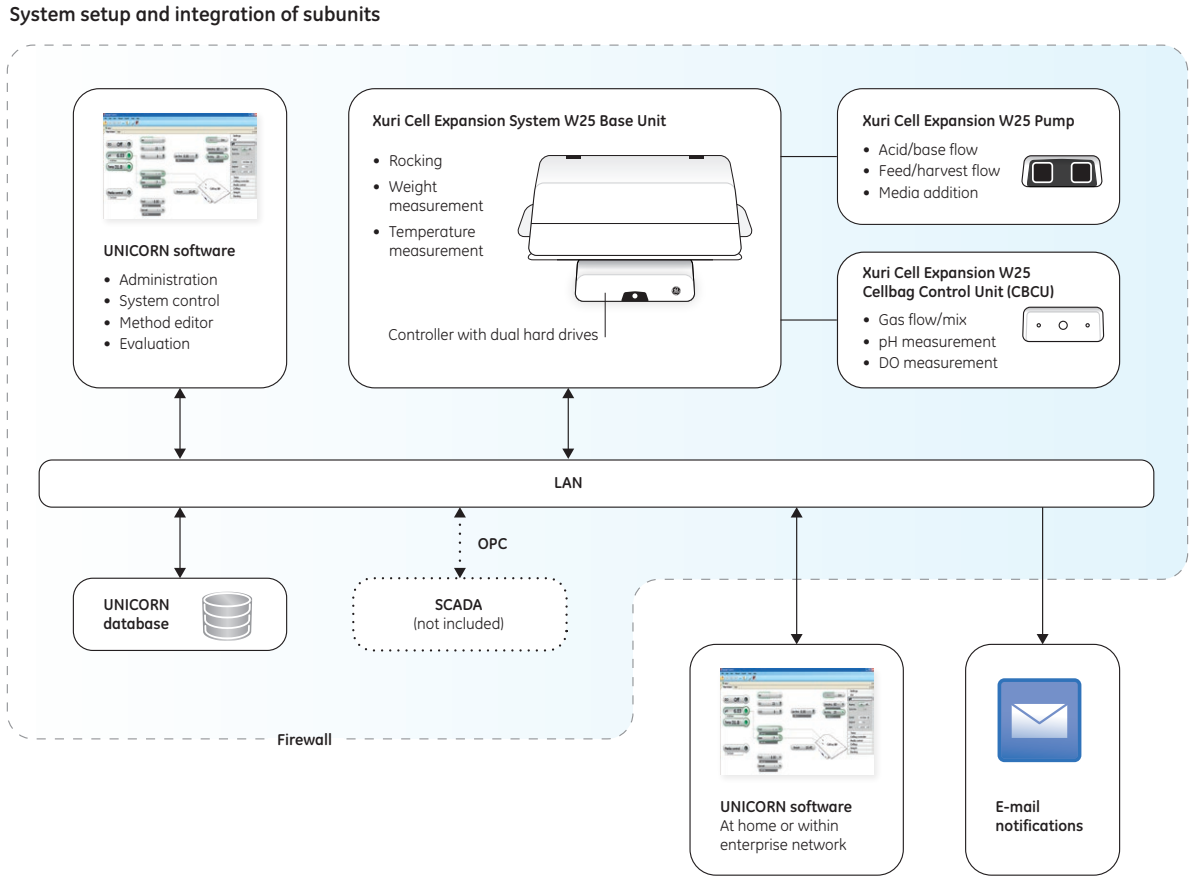

Fig 2. Xuri Cell Expansion System W25 overview. The System Control module on the client computer is used to start and monitor the cultivation process. One UNICORN client can control up to three Xuri Cell Expansion W25 systems simultaneously. SCADA = supervisory control and data acquisition, OPC = open platform communications, LAN = local area network.

Xuri Cell Expansion W25 Base Unit

The base unit is the main hardware unit, providing mixing of the culture through the rocking of the attached tray and Cellbag bioreactor, reliable temperature measurement from integrated sensors, and accurate weight measurement from integrated load cells. The ability to handle the bioreactor in a tilt position facilitates sampling and harvest (Fig 3). The small footprint is also advantageous when space is limited.

(A)

(B)

Fig 3. (A) Xuri Cell Expansion System W25 in tilt position. (B) The ergonomic design makes activities such as sampling and harvest convenient and easy.

Trays and lids

Trays are available in three different sizes for culture volumes of up to 5, 10, and 25 l. The trays attach easily to the base unit in the tilt position and a snap-lock mechanism ensures the Cellbag bioreactors are correctly installed and can be quickly changed (Fig 4). To protect light-sensitive components of the culture medium and to prolong the life of the optical sensors, lids are available for all tray sizes.

Fig 4. The tray has an easy-lock mechanism for convenient and proper attachment of Cellbag bioreactors.

Temperature control

Reliable, efficient, and evenly distributed heating is provided by the tray heater plate. The temperature measurement is managed by sensors integrated in the rocker base unit (Fig 5). To minimize the risk of overheating, heating is only enabled when the base unit is in motion. For accurate, stable, and fast temperature control, the heater power output is automatically adjusted based on the Cellbag bioreactor size and the media volume.

Fig 5. Integrated temperature sensors for convenient handling and reliable temperature control.

Mixing and gas transfer

The speed, angle, and motion of rocking are adjustable. These parameters, together with the cell culture volume, affect the mixing and rate of gas transfer in the Cellbag bioreactor.

The speed parameter determines the number of rocking cycles per minute, and the angle parameter relates to the tray's degree of tilting at the turning points.

The motion parameter determines the acceleration profile of the rocking motion. The lowest motion parameter setting, 15%, gives an almost constant speed throughout the rocking cycle, whereas the highest setting, 100%, gives a faster rocking speed in the middle of the cycle and slower at the turning points (Fig 6). A lower percent setting will give a more aggressive mixing with higher gas transfer rates. A higher setting will result in a smoother wave suitable for more delicate applications, such as adherent cultivation on microcarriers.

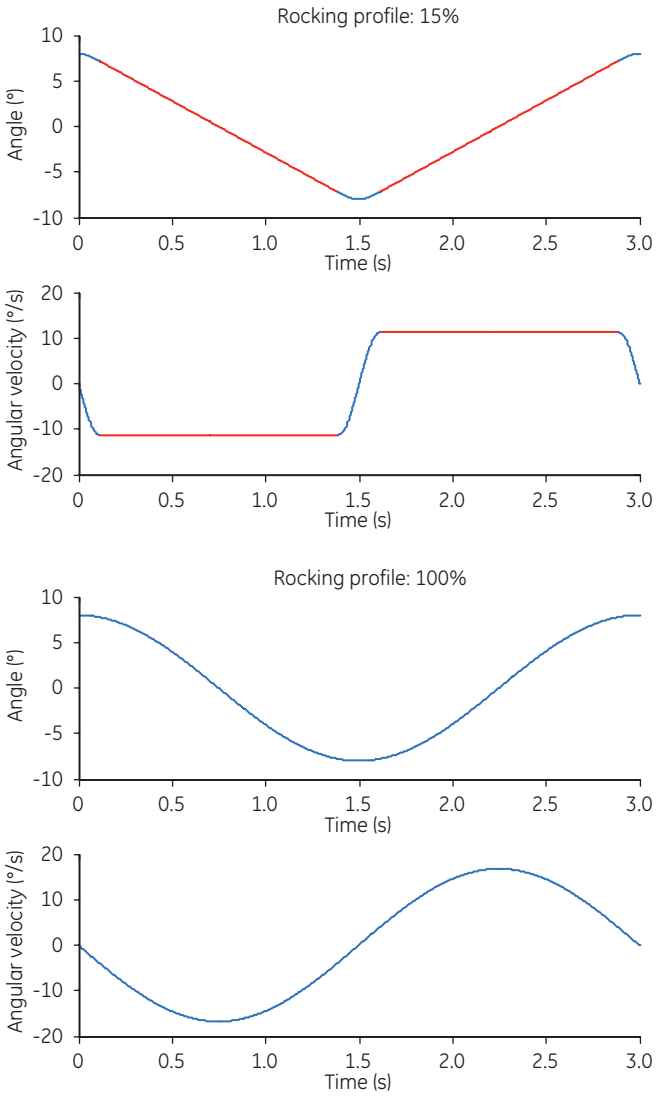

Fig 6. A user-defined rocking motion can be selected in UNICORN system control software. The wave can be aggressive or gentle, which can affect mixing and gas transfer.

Weight measurement

Load cells located in the base unit provide accurate and continuous measurement of the weight of the culture. The load cells communicate with the system control software for accurate medium handling and for tailored regulation of pH and temperature.

Weight measurement is also used for automatic calibration of the pump in perfusion cultures. Adjustable feet enable equal weight distribution between the load cells and accommodate uneven surfaces, making instrument setup easier.

Cellbag bioreactors

Cellbag bioreactors are single-use bags for the mixing of culture medium and cells during cultivation (Fig 7). Cellbag bioreactors require no sterilization or cleaning steps. The single-use, functionally closed bags provide a suitable environment for cell growth while minimizing the risk of cross-contamination. The bags are manufactured from multilayer, laminated, clear USP Class VI plastics and are easily connected to the full suite of Xuri cell expansion cell culture, purification, and fluid handling products. The selection of Cellbag bioreactors is listed in Table 1. For more information about Cellbag bioreactors, see Data file 28-9511-36.

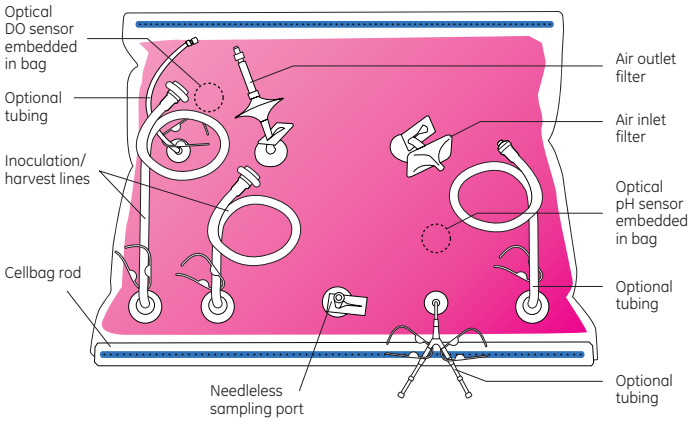

Fig 7. Cellbag bioreactor showing fittings.

Table 1. Selection of Cellbag bioreactor sizes

Cellbag bioreactor[1]	Working volume
Cellbag 2 l	300 ml[2] to 1 l
Cellbag 10 l	500 ml to 5 l
Cellbag 20 l	1 to 10 l
Cellbag 50 l	5 to 25 l

[1] All Cellbag bioreactor sizes are available with internal perfusion filter for perfusion cultures and/or can be equipped with single-use optical pH (pHOPT) and DO (DOOPT II) sensors.

[2] Cellbag bioreactors with optical sensors require 300 ml minimal working volume. Depending on application and configuration, it might be possible to cultivate below the recommended minimum volume. However, it is highly recommended to stay above this volume for applications that require high agitation and pH and DO control. The temperature, pH, and DO sensors need to be submerged in liquid throughout the complete rocking cycle to function correctly

Data storage and communication

Data and control parameters are stored on two independent, mirrored solid-state drives integrated in the base unit. Thus, once a culture has been started and data from the instrument modules have been collected, the run can continue without the need for a network connection. The use of two solid-state drives enables culturing without losing any data, even if only one drive is functional. Ensuring that data is not lost and traceability is maintained is required in a regulated environment. After a run, data is stored in a UNICORN database on an external computer. For integration into a manufacturing operation, the base unit contains software that enables direct communication with the system via an open platform communication (OPC) link.

Xuri Cellbag Control Unit

The Xuri Cellbag Control Unit provides gas to the culture and monitors pH and DO. The control unit contains a controller for mass flow, sensors for gas pressure as well as O_2 and CO_2 concentrations, and transmitters for pH and DO (Table 1).

Three Xuri Cellbag Control Unit configurations are available:

- CO_2, O_2, pH, and DO
- CO_2, O_2, and pH
- CO_2, O_2, and DO

The most suitable configuration will depend on the specific application.

Table 2. Xuri Cellbag Control Unit overview

Feature	Description
CO_2/O_2/air mix controller	Depending on the configuration, air is mixed with CO_2 and/or O_2 according to the set-points. Nitrogen may be used instead of air for maintaining a low oxygen environment for near-anaerobic applications.
Gas flow controller	The gas-mix flow is measured and controlled by a mass flow controller (MFC). A correct volumetric flow is achieved by compensation for CO_2 concentration. Quick filling of gas into the Cellbag bioreactor, enabled by the fast-fill function, significantly reduces start-up time. An alarm will inform the user if pressure sensors detect under- or overpressure at the gas inlets or within the Cellbag bioreactor.
pH measurement	The pH is measured with optical pH sensors preinstalled in Cellbag bioreactors of pHOPT type. The sensor is connected to the Xuri Cellbag Control Unit via a fiber optic cable.
DO measurement	The DO level is measured with optical DO sensors preinstalled in Cellbag bioreactors of DOOPT type. The sensor is connected to the Xuri Cellbag Control Unit via a fiber optic cable.

Xuri Cell Expansion W25 Pump

The Xuri Cell Expansion W25 Pump is a peristaltic unit incorporating two roller pumps for feed, waste, and pH control of the environment in the Cellbag bioreactor. Tubing installation is easy and tubing sizes from 0.5 mm (1/50") to 4.8 mm (3/16") internal diameter can be used to support flow rates from 0.07 to 100 ml/min. Flow rate is regulated by feedback from the load cells and automatic adjustments of the pump speed. Manual adjustment of the flow rate is also possible if required during process development.

Media handling and perfusion using calibrated pumps

Calibration of pumps can be performed manually or automatically during an ongoing perfusion process. Automatic calibration is possible for flow rates above 3.5 l/d and is easily managed by entering the tubing diameter.

UNICORN software

UNICORN system control software consists of four modules to ensure intuitive setup and operation: Administration; Method Editor; System Control; and Evaluation, supported by a comprehensive help tool.

Administration module

The Administration module administers all functions of the UNICORN software, such as user and e-mail setup, access control for groups, set up of network users, defining and editing system properties, database management, and logging of usage and activity.

Method Editor module

Instructions to control a bioreactor run are defined in a method. The Method Editor module is used to create, edit, save, and work with methods. Changes can be made to an existing method to simplify the editing process. To maximize reproducibility, individual changes can be saved for later use on systems having the same instrument and component configuration.

System Control module

The System Control module is used to connect the system and to start, view, and control a run (Fig 8). It is also possible to connect to other Xuri Cell Expansion Systems W25 when scaling up. Default parameter values for an instrument can be viewed and edited in the System Settings dialog before a run is started or during a run using manual instructions.

The Process Picture pane enables manual interaction with the system and displays the status of the run parameters. Data is shown in the process picture but can also be viewed as curves in the Charts tab and as numerical values in the Run Data pane. Curves and information about the run are saved in a database, which can be opened in the Evaluation module. The default view shows the most commonly used curves. The display, color, and style of curves can be customized.

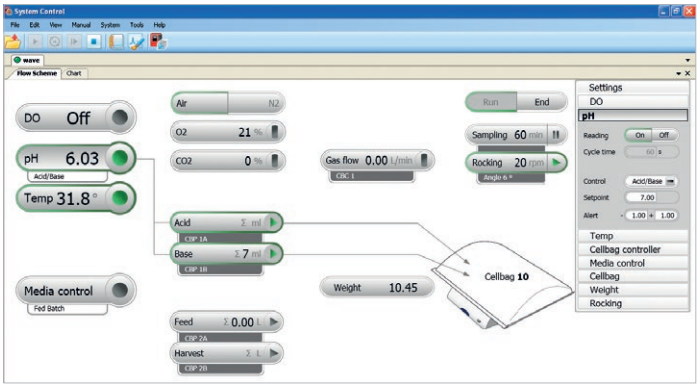

Fig 8. Monitoring and controlling all aspects of the culture is managed through the user-friendly interface

Evaluation module

In the Evaluation module, content of the result files can be viewed, analyzed, and compiled as reports. Reports can be customized, saved, and printed.

Automation of process parameters in pH and DO control

UNICORN software automatically sets the desired proportional-integral-derivative (PID) control parameters based on Cellbag bioreactor size and gas flow set-point. The system also adapts the parameters during the run, for optimization to reach a new set-point or to maintain a current set-point.

Alarms, notifications, and data logging

UNICORN software gives easy access to all operations, data, and alarm conditions. A dynamic, graphical user interface shows the real-time status of the run, while data are automatically saved. To minimize the risk of losing your sample, UNICORN software can configure the system to trigger an alarm when certain conditions are met. Individual deviation alarms can be set for all essential parameters (heating, gas flow, CO_2, pH, and DO). Alarm sensitivity and delay is defined by the user. If an alarm condition is triggered, the source is highlighted in the graphical user interface. A dialog displays information about the alarm, such as date and time of occurrence, as well as a help text describing the cause and solution. The system can be configured to send e-mail notifications of alarms and errors to trigger your prompt response.

Regulatory readiness

The Xuri Cell Expansion System W25 is suitable for biomanufacturing of regulated products under various Quality Management Systems. The use of UNICORN software in a 21 CFR Part 11 and GAMP 5 compliant manner enables use of the system in a regulated environment. Individual user access permissions can be set and individual users are password-protected. Active processes can be locked to enable unattended operations without the risk of unauthorized interference. All records are stored in a single, unalterable database, including results and extended run documentation. Additional validation support includes comprehensive documentation on control system validation as well as IQ/OQ services. Available validation support documentation includes:

- Detailed description of the development model used for UNICORN software
- 21 CFR Part 11 system assessment in checklist format
- Audit report and 21 CFR Part 11 conclusion on functionality by an external, independent expert

Networking capabilities

UNICORN software operates in Windows XP® and Windows® 7 environments and the network ability allows real-time control from a remote or local computer. Communication is Ethernet-based and each instrument is controlled by a dedicated instrument server. One database can be connected to 32 systems and up to three instruments can be controlled simultaneously from one UNICORN client. Results are saved locally, in the base unit, during the run and then stored on the database server. Because results and instructions are saved locally on the embedded drives, a run can continue even in the event of a network communication failure, minimizing the risk of losing your sample.

UNICORN software can be integrated in a supervisory control and data acquisition (SCADA) system such as the Emerson DeltaV™ control system using the UNICORN OPC server.

System specifications

System specifications are listed in Table 3.

Table 3. Xuri Cell Expansion System W25 specifications

General system specifications

Control system	UNICORN 6.3 or later version
Dimensions, W × H × D	
Base Unit	404 × 560 × 205 mm
Tray 10	475 × 430 × 60 mm
Tray 20	740 × 480 × 70 mm
Tray 50	800 × 610 × 70 mm
Lid 10	475 × 430 × 230 mm
Lid 20	740 × 480 × 245 mm
Lid 50	800 × 610 × 260 mm
Cellbag Control Unit	276 × 360 × 117 mm
Pump	275 × 280 × 115 mm
Weight	
Base Unit	24 kg
Tray 10	4.5 kg
Tray 20	7.3 kg
Tray 50	9.5 kg
Lid 10	1.7 kg
Lid 20	3.3 kg
Lid 50	3.9 kg
Cellbag Control Unit	4.8 kg
Pump	3.8 kg
Power supply	100 to 240 V, ~ 50 to 60 Hz
Power consumption	1500 VA
Enclosure protective class	IP 21

Gas supply	Normal capacity	Fast-fill capacity
External air supply, 1.0 to 1.5 bar	1.3 l/min	3.5 l/min
External CO_2 supply, 1.0 to 1.5 bar	0.2 l/min	0.5 l/min
External O_2 supply, 1.0 to 1.5 bar	0.7 l/min	1.7 l/min

Environmental aspects

Operating ambient temperature range	15°C to 32°C
Operating humidity range	20% to 80% (noncondensing)

Xuri Cell Expansion System W25 Base Unit

Rocking speed control range[1]	2 to 40 rpm
Rocking angle control range[1]	2° to 12°
Rocking motion control range	15% to 100%
Media weight control range	0.5 to 25 kg
Scale, absolute accuracy	± 0.050 kg + 1% of load kg
Temperature sensor	Pt100 Class A
Temperature measurement range	2°C to 50°C
Temperature control range	20°C (or ambient temperature + 5°C) to 40°C
Temperature control accuracy (incl. measurement error)	± 0.5°C

[1] When cultivating in a 50 l Cellbag bioreactor at maximum working volume of 25 l, rocking speed and angle multiplied should not exceed 240 rpm degrees. For example, if the rocking angle is set to 12 degrees, the rocking speed should not be set higher than 20 rpm.

Xuri Cellbag Control Unit

Gas flow control range	0 to 1000 ml/min
Gas flow total accuracy (process value to reference flow)	± 10 ml/min + 3% of read value
Fast-fill flow	~ 3 l/min
CO_2 control range	0% to 15%
CO_2 measurement accuracy	± 0.3% + 3% of read value when mixed only with air/N_2
Total CO_2 accuracy (process value to reference CO_2 content)	± 0.7% + 3% of read value
O_2 control range	0% to 50% when mixed with N_2, 21% to 50% when mixed with air
O_2 measurement accuracy	± 0.6% + 1% of read value within 0% to 50% when mixed only with air/N_2
Total O_2 accuracy	± 1.2% + 1% of read value
pH measurement range	4.5 to 8.5
pH measurement accuracy	± 0.05 for pH 6.75 to 7.25 ± 0.1 for pH 6.5 to 7.5
pH control range	6.0 to 8.0
Total pH accuracy (process value to reference pH)	± 0.1 for pH 6.75 to 7.25 ± 0.15 for pH 6.5 to 7.5
DO measurement range	0% to 250% air saturation
DO measurement accuracy	± 5% air saturation (excl. atmospheric pressure variations)
DO control range	0% to 100% air saturation
Total DO accuracy (process value to reference DO)	± 10% air saturation (excl. atmospheric pressure variations)

Xuri Cell Expansion W25 Pump

Pump flow-rate range	100 ml to 144 l/d (0.07 to 100 ml/min)
Pump flow accuracy	± 0.1 ml/min + 5% of read value after calibration
Accumulated pumped-volume accuracy	± 10% of measured volume
Supported tubing dimensions	i.d. 0.5 to 4.8 mm (1/50" to 3/16") wall thickness: 1.6 mm (1/16")

Ordering information

Product	Description	Code number
Xuri Cell Expansion System W25 Base Unit	Base unit	29-0645-68
Xuri Cell Expansion System W25 Cellbag Control Unit pH	Gas flow/mix and pH	29-0646-00
Xuri Cell Expansion System W25 Cellbag Control Unit Full	Gas flow/mix, pH, and DO	29-0646-02
Xuri Cell Expansion System W25 Pump		29-0645-71
Tray 10	For up to 5 l culture	29-0652-31
Tray 20	For up to 10 l culture	29-0652-32
Tray 50	For up to 25 l culture	29-0444-74
Lid 10	To fit Tray 10	29-0652-31
Lid 20	To fit Tray 20	29-0652-35
Lid 50	To fit Tray 50	29-0652-37
Filter heater		29-0652-52
Bag sensor adapter, 2.5 m assembly	Fiber cable for pH and DO control	28-9841-89
UNICORN 6.3.2 Workstation Package, software and license		29-0469-18
UNICORN 6.3 Remote license		29-0203-51
UNICORN 6.3 Dry license		29-0203-55

Related literature

Disposable Cellbag bioreactors for WAVE Bioreactor™ systems, Data file	28-9511-36
UNICORN 6.3, Manual package	29-0234-67
UNICORN 6 control software, Data file	28-9573-46
UNICORN 6.3, Validation support file	11-0029-94

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