

Xuri™ Cell Expansion System W25

CELL THERAPY SYSTEMS

The Xuri™ Cell Expansion System W25 provides a closely monitored and highly controlled environment for the growth of viable cells to densities suitable for cell therapy research, process development, and clinical manufacturing operations. The motion, speed, and angle of the rocking platform can be adjusted to suit different cell types and culture conditions while process parameters such as temperature, pH, gas transfer, and flow rates are monitored by a range of optical sensors and controlled via UNICORN™ software. With media perfusion, cell expansions reaching $> 10 \times 10^6$ cells/mL are possible in working volumes up to 25 L.

Functionally closed system

Cell expansion is performed in a choice of single-use, Cellbag™ Bioreactors with working volumes between 300 mL and 25 L. Manufactured from multilayer, laminated, clear USP class VI plastics, these bioreactors provide a functionally closed environment that minimizes the chance of contamination between different patient samples or with adventitious agents.

High cell densities with media perfusion

With perfusion, an entire therapeutic dose can be obtained in a single bioreactor eliminating the difficulties commonly associated with combining cultures in manual processes. High cell density and a reduced manufacturing footprint also allow you to maximize use of your manufacturing space.

Automated process monitoring and remote control

Process parameters such as rocking speed, dissolved oxygen (DO), pH, and perfusion rate are monitored and controlled by UNICORN™ software installed on a local or remote computer. Methods can be created, edited, and saved allowing you to optimize your cell culture protocol while alarms can be configured to alert you when pre-set conditions are met and report deviations from defined culture parameters.



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

Designed for use in a regulated environment

The Xuri™ Cell Expansion System W25 is designed to meet the demands and standards required in a regulated environment. The documentation includes material certificates, system specifications, installation and operational qualification (IQ/OQ) protocols, and a detailed user manual. UNICORN™ software supports compliance with 21 CFR Part 11 and Good Automated Manufacturing Practice (GAMP) 5.

Applications

The Xuri™ Cell Expansion System W25 can be used in a variety of cell culture applications including:

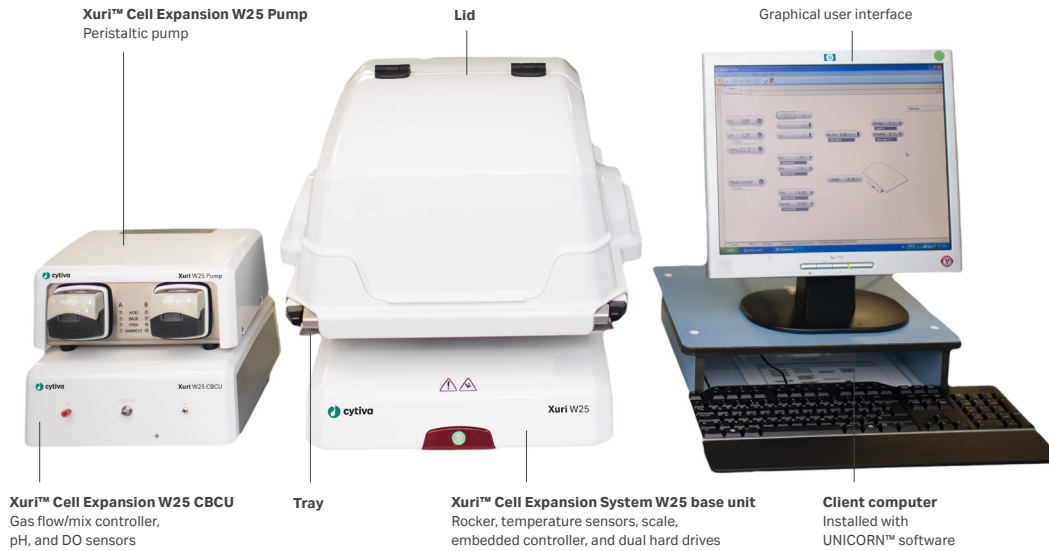
- Rapid production of clinical grade T-lymphocytes
- Perfusion culture of T-lymphocytes
- Perfusion culture of human natural killer cells

System overview

Components

The Xuri™ Cell Expansion System W25 consists of a base unit, an environmental control unit (CBCU), and a pump (Fig 2). Operations, control, and monitoring of the process are managed by UNICORN™ software installed on a client computer. The base unit is used in combination with a tray and a disposable Cellbag™ Bioreactor and has multiple functions including heating and culture mixing plus weight and temperature measurement.

The CBCU delivers gas of a defined composition to the culture and is used in conjunction with optical sensors fixed to the bioreactor for online control of culture pH and DO. The Xuri™ Cell Expansion W25 Pump delivers and removes media to and from the bioreactor. Flow rates can be adjusted for a range of processes including acid/base additions, delivering fresh medium for perfusion cultures, and harvesting.



System setup and integration of subunits

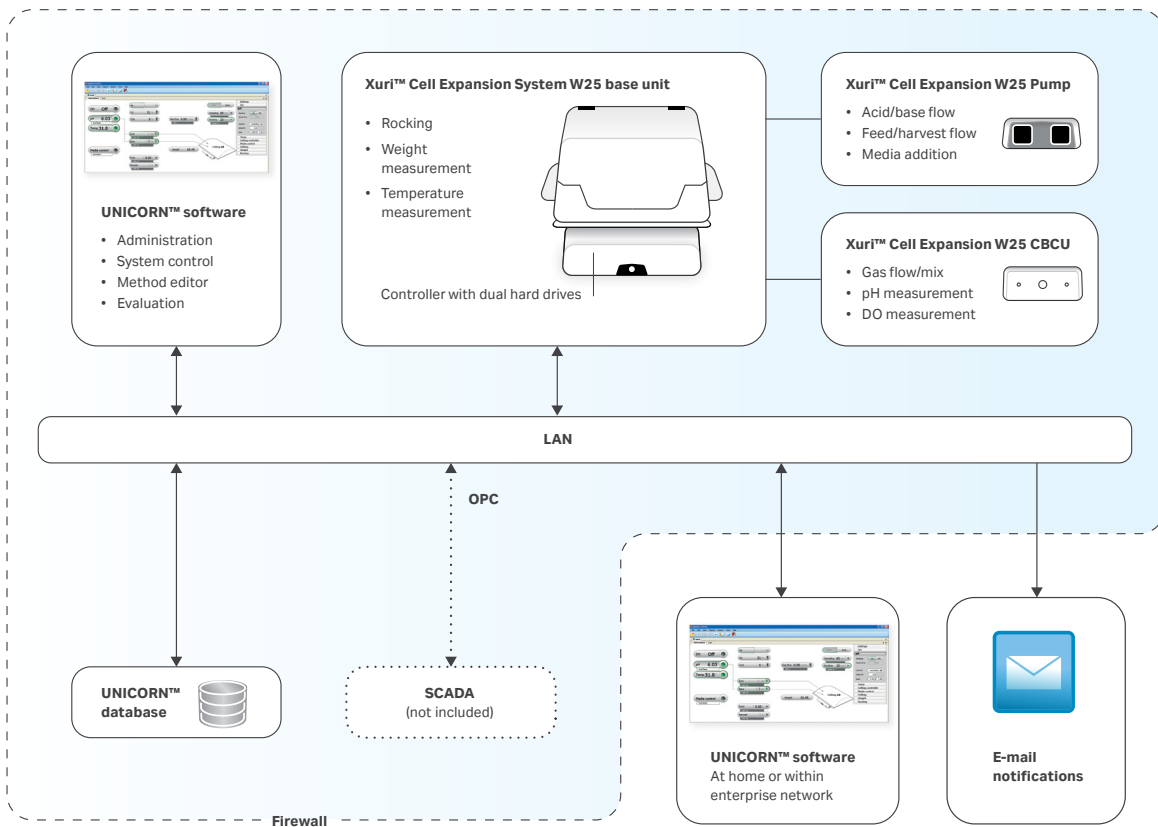


Fig 2. Xuri™ Cell Expansion System W25 overview. The system control module on the client computer is used to start and monitor the cultivation process. One UNICORN™ client can control up to three Xuri™ Cell Expansion W25 systems simultaneously. SCADA = supervisory control and data acquisition, OPC =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

Base unit

The base unit is the main hardware component of the system and provides mixing through rocking, reliable temperature measurement from integrated sensors, and accurate weight measurement using load cells. Designed to make handling convenient and easy, the bioreactor can be used in a tilt position for sampling and harvest operations (Fig 3) while the bench top footprint simplifies placement when space is limited.



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 culturing of up to 5, 10, and 25 L working volumes and can be attached to the base unit when in the tilt position. A snap lock mechanism ensures Cellbag™ Bioreactors are correctly installed and can be rapidly 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 locking mechanism for the secure attachment and rapid release of Cellbag™ Bioreactors.

Temperature control

Reliable, efficient, and evenly distributed heating is provided by the tray heater plate. Temperature measurement is managed by integrated sensors (Fig 5) and to minimize the risk of overheating, the heater plate 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.

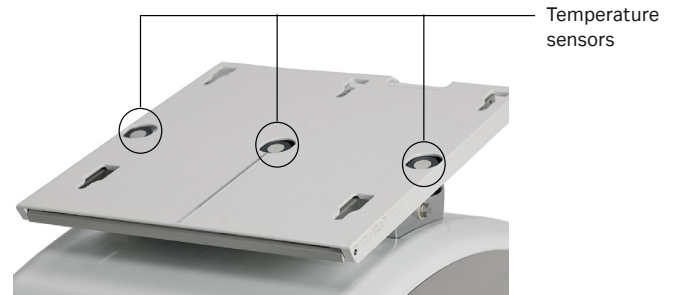


Fig 5. Integrated temperature sensors improve temperature control.

Mixing and gas transfer

The adjustable rocking parameters are speed, angle, and motion. Adjustment of these settings in combination with the cell culture volume affect the mixing and gas transfer rate in the Cellbag™ Bioreactor. The speed parameter determines the number of rocking cycles per minute, the angle relates to the tray's degree of tilting at the turning points, and the motion determines the acceleration profile. The lowest motion parameter setting is 15% and gives an almost constant speed throughout the rocking cycle, whereas the highest setting of 100% gives a faster 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 percent setting will result in a smoother wave suitable for more delicate applications, such as those required for the cultivation of adherent cells on microcarriers.

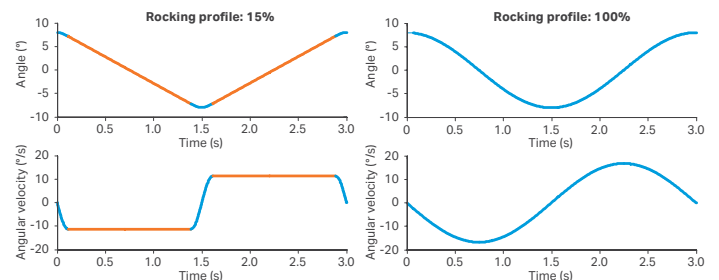


Fig 6. A user-defined rocking motion can be selected in UNICORN™ system control software. The wave can be aggressive or gentle, with a subsequent impact on mixing and gas transfer in the culture.

Weight measurement

Load cells in the base unit provide accurate and continuous weight measurement of the culture and eliminate the need for external scales. The load cells communicate with the system control function for smooth media handling and 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 even on non-level surfaces for increased precision.

Bioreactor

Cellbag™ Bioreactors are manufactured from multilayer, laminated, clear USP class VI plastics and require no sterilization or cleaning steps. They are single-use functionally closed bags that provide a suitable environment for the mixing of medium and the rapid expansion of cells during cultivation while minimizing the risk of cross contamination. Cellbag™ Bioreactors for the Xuri™ Cell Expansion System W25 are available in a range of working volumes from 300 mL to 25 L (Table 1).

Table 1. Working volumes for Xuri™ W25 Cellbag™ Bioreactors

Bioreactor	Working volume
Cellbag™ 2L	300 mL to 1 L
Cellbag™ 10L	500 mL to 5 L
Cellbag™ 20L	1 to 10 L
Cellbag™ 50L	5 to 25 L

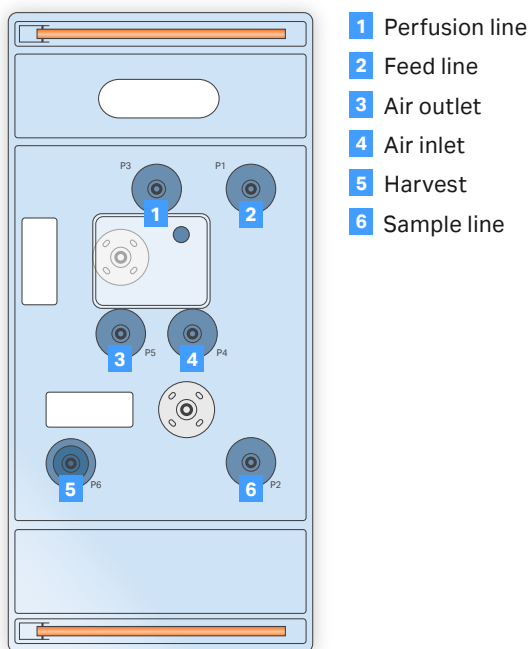


Fig 7. A range of fittings can be used with the Cellbag™ Bioreactor.

Data storage and communication

All run data and control parameters are stored on two independent, mirrored, solid-state drives integrated in the base unit. Thus, once cultivation 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 cultures to be run without losing any data even if only one drive is functional. After a run, data is stored in a UNICORN™ database on an external computer. To facilitate integration into a larger manufacturing operation, the base unit also contains software for enabling direct communication with the system via an open platform communication (OPC) link.

CBCU

The CBCU is a compact unit used primarily for providing gas to the culture and for monitoring pH and DO. It incorporates a mass flow controller, sensors for gas pressure, O₂ and CO₂ concentrations, and transmitters for pH and DO (Table 2).

Two configurations are available:

- CO₂, O₂, and pH
- CO₂, O₂, pH, and DO

The most suitable configuration will depend on the specific application.

Table 2. CBCU 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. Correct volumetric flow is achieved by compensation for CO ₂ concentration. Quick filling of gas into the Cellbag™ Bioreactor 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	pH is measured with optical pH sensors preinstalled in Cellbag™ Bioreactors. The sensor is connected to the CBCU via an optical fiber cable.
DO measurement	DO is measured with optical DO sensors preinstalled in Cellbag™ Bioreactors. The sensor is connected to the CBCU via an optical fiber cable.

Pump

The Xuri™ Cell Expansion W25 Pump is a peristaltic unit incorporating two roller pumps for feed, harvest, and pH control. Tubing sizes from 0.5 mm (1/50") to 4.8 mm (3/16") internal diameter can be installed by the user to support flow rates from 0.07 to 100 mL/min. Flow rate is regulated by weight feedback from the scale and is controlled by automatic adjustments of the pump speed. Manual adjustment of the flow rate is also possible.

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 in to the UNICORN™ database.

Automated pH control

To minimize fluctuations in pH during adjustments with CO₂/base or acid/base, the flow rate of the pumps needs to be rigorously monitored. The Xuri™ Cell Expansion System W25 uses combined information from the load cells, the current process pH value, the pump tubing diameter, and the acid/base molarity for calculation of the needed flow rate during the run.

UNICORN™ software

UNICORN™ system control software consists of four modules: **Administration**, **Method Editor**, **System Control**, and **Evaluation**. A comprehensive help tool is also included.

Administration

The **Administration** module is used to administer all functions of the UNICORN™ software. Available functions include user and email setup, controlling access to groups and network users, defining and editing system properties, database management, and logging records of usage and activity.

Method Editor

Instructions to control a bioreactor run can be defined in a method. The **Method Editor** module is used to create, edit, save, and work with methods. An existing method can be changed to simplify the editing process. Individual changes can be saved for later use on systems having the same instrument and component configuration.

System Control

The **System Control** module is used to connect to the system as well as to start, view, and control a run (Fig 8). Default parameter values for an instrument can be viewed and edited in the **System Settings** dialog before a run is started or during an ongoing run using manual instructions. It is also possible to connect to other systems.

The **Process Picture** pane enables manual interaction with the system and provides 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 user may customize which curves to display and the color and style of the displayed curves.

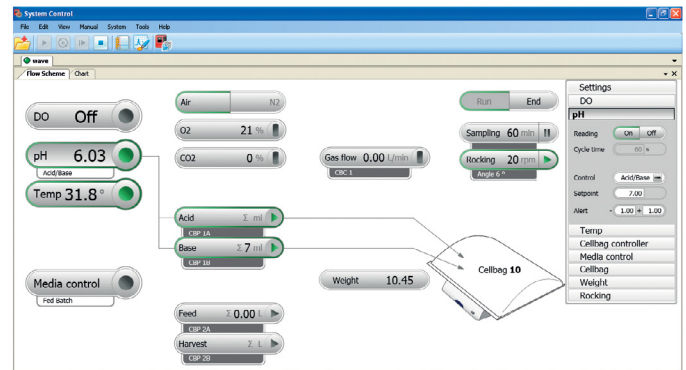


Fig 8. Monitoring and controlling all aspects of the culture is managed through the UNICORN™ graphical user interface.

Evaluation

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

Automation of process parameters in pH and DO control

The 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, either for optimization to reach a new set-point or to maintain a current set-point.

Alarms, notifications, and data logging

UNICORN™ software provides 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. Alarms can be configured to alert the user when certain conditions are met. Individual deviation alarms can be set for all essential parameters (e.g., heating, gas flow, CO₂, pH, and DO). Alarm sensitivity and delay is defined by the user. If an alarm condition is triggered, the source of the alarm is highlighted in the graphical user interface and information about the alarm, such as date and time of occurrence as well as a description of the cause and how to solve the problem are displayed in a dialog box. Alarms can also be configured to send email notifications of alarms and errors to an address of your choice.

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 user logons are password-protected. Active processes can be locked to enable unattended operations without the risk of unauthorized access. 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:

- A detailed description of the development model used for UNICORN™ software
- A 21 CFR Part 11 system assessment in checklist format
- An audit report and a 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 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. 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.

* Support and updates for Windows XP are no longer available. To protect your PC upgrade to Windows 7 as soon as possible.

System specifications

General system specifications

Control system	UNICORN™ 7.6 (or later version)	
<i>Dimensions (W × H × D) (mm)</i>		
Rocker	404 × 205 × 560	
Tray 10	475 × 60 × 430	
Tray 20	740 × 70 × 480	
Tray 50	800 × 70 × 610	
Lid 10	511 × 294 × 554	
Lid 20	823 × 308 × 557	
Lid 50	881 × 326 × 686	
CBCU	276 × 117 × 560	
Pump	275 × 115 × 280	
<i>Weight (kg)</i>		
Rocker	24.0	
Tray 10	4.5	
Tray 20	7.3	
Tray 50	9.5	
Lid 10	1.7	
Lid 20	3.0	
Lid 50	4.0	
CBCU	4.8	
Pump	3.8	
Power supply	100 to 240 V, ~ 50 to 60 Hz	
Power consumption	1500 VA	
Enclosure protective class	IP 21	
<i>Gas supply</i>	<i>Normal capacity</i>	<i>Fast-fill capacity</i>
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
Xuri™ Cell Expansion System W25, rocker		
Rocking speed control range [†]	2 to 40 rpm	
Rocking angle control range [†]	2° to 12°	
Rocking motion control range	15% to 100%	
Media weight control range	0.5 to 25 kg	
Scale, absolute accuracy	± (0.050 + 1% of load) kg	
Temperature sensor	Pt100 Class A	
Temperature measurement range	2°C to 50°C	
Temperature control range	(ambient temperature + 5°C) to 40°C	
Temperature control accuracy (excl. measurement error)	± 0.2°C	

[†] 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°, the rocking speed should not be set higher than 20 rpm.

CBCU

Gas flow control range	50 to 1000 mL/min
Total gas flow accuracy (reference flow – set-point)	± (10 + 3% of read value) mL/min
Fast-fill flow	~ 3 L/min
CO ₂ control range	0% to 15% CO ₂
CO ₂ measurement accuracy at 5% CO ₂	± 0.5% CO ₂ when mixed only with air/N ₂
CO ₂ control accuracy (versus set-point)	± 0.4% CO ₂
O ₂ control range	0% to 50% O ₂ when mixed with N ₂ , 21% to 50% O ₂ when mixed with air
O ₂ measurement accuracy	± (0.6% + 1% of read value) % O ₂ within 0% to 50% O ₂ when mixed only with air/N ₂
O ₂ control accuracy (versus set-point)	± 0.6% O ₂
pH measurement range	pH 4.5 to 8.5
pH control range	pH 6.0 to 8.0
pH measurement accuracy	± 0.05 pH within ± 0.25 pH from offset calibration pH ± 0.1 pH within 0.25 to 0.5 pH from offset calibration
pH control accuracy (versus set-point)	± 0.05 pH
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

Xuri™ Cell Expansion W25 Pump

Pump flow rate range	0.1 to 144 L/d (0.07 to 100 mL/min)
Pump flow accuracy	± (0.1 + 5% of read value) mL/min 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	Code number
Xuri™ Cell Expansion System W25 base unit	29064568
Xuri™ Cell Expansion System W25 Cellbag™ Control Unit Full	29064602
Xuri™ Cell Expansion System W25 Cellbag™ Control Unit pH	29064600
Xuri™ Cell Expansion System W25 Cellbag™ Control Unit DO	29064599
Xuri™ Cell Expansion System W25 Pump	29064571
Tray 10	29065231
Tray 20	29065232
Tray 50	29044474
Lid 10	29696647
Lid 20	29696648
Lid 50	29696649
Filter heater	29065252
Bag sensor adapter m assembly	28984189
UNICORN™ Workstation package, software and license	29046918
UNICORN™ Remote licence	29020351
UNICORN™ Dry licence	29020355
Xuri™ Cell Expansion System Cellbag™, 2 L, Basic	28937800
Xuri™ Cell Expansion System Cellbag™, 2 L, Basic	29105492
Xuri™ Cell Expansion System Cellbag™, 2 L, pH and DO	29105494
Xuri™ Cell Expansion System Cellbag™, 10 L, BC10, Basic	28937801
Xuri™ Cell Expansion System Cellbag™, 10 L, Basic	29105493
Xuri™ Cell Expansion System Cellbag™, 10 L, pH and DO	29105495
Xuri™ Cell Expansion System Cellbag™, 20 L, BC10, pH and DO	28937663
Xuri™ Cell Expansion System Cellbag™, 20 L, BC10, Basic	28937802
Xuri™ Cell Expansion System Cellbag™, 20 L, pH and DO	29105496
Xuri™ Cell Expansion System Cellbag™, 50 L, BC10, Basic	28937666
Xuri™ Cell Expansion System Cellbag™, 50 L, pH and DO	29105497
Xuri™ Cell Expansion System Cellbag™, 2 L, Perfusion and DO	28937652
Xuri™ Cell Expansion System Cellbag™, 2 L, Perfusion, pH and DO	29105498
Xuri™ Cell Expansion System Cellbag™, 2 L, Perfusion	29108442
Xuri™ Cell Expansion System Cellbag™, 10 L, Perfusion and DO	28937662
Xuri™ Cell Expansion System Cellbag™, 10 L, Perfusion, pH and DO	29105499
Xuri™ Cell Expansion System Cellbag™, 10 L, Perfusion	29108443
Xuri™ Cell Expansion System Cellbag™, 20 L, Perfusion, DO	28937664
Xuri™ Cell Expansion System Cellbag™, 20 L, Perfusion, pH and DO	29105500
Xuri™ Cell Expansion System Cellbag™, 2 L, Shot perfusion, pH and DO	29279162
Xuri™ Cell Expansion System Cellbag™, 2 L, Continuous perfusion, pH and DO	29279164
Xuri™ Cell Expansion System Cellbag™, 2 L, Shot perfusion	29279169
Xuri™ Cell Expansion System Cellbag™, 2 L, Continuous perfusion	29279170
Xuri™ Cell Expansion System Cellbag™, 10 L, Perfusion, pH and DO	29279165
Xuri™ Cell Expansion System Cellbag™, 10 L, Perfusion	29279171

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