

## OPERATIONAL PERFORMANCE

### LARGE-FOLD EXPANSION

The unique volume expansion roller of the SCINUS cabinet allows users to culture suspension cells from limited amounts to high cell numbers without the need for passaging. The system has shown to support the culture of an initial inoculum of 50 million T-cells to over 6 billion (DynaBead-activated) T-cells and even 17 billion (TransAct-activated) T-cells in a single culture (Figure 6). The system also leverages the unique phenomenon of bead-to-bead transfer observed in microcarrier culture. This phenomenon, coupled with the system's unique volume expansion, allows for culture of adherent cell types to clinically relevant cell numbers as well. The system has shown to support the culture of 25 mL bone marrow to 1.5 billion MSCs in a single culture (range 1.37-1.73 billion MSCs, Figure 7).

### REPRESENTATIVE SAMPLING

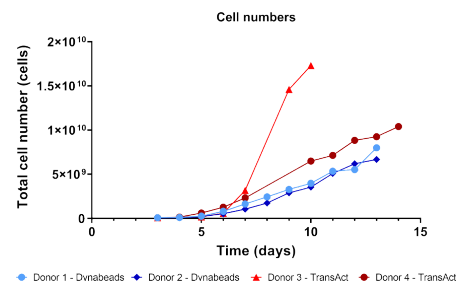
A major limitation of many automated cell culture systems is the lack of sampling capabilities. Cells that adhere to a fixed surface usually cannot be partially harvested for quality control. The SCINUS bioreactor, however, enables representative sampling of both cells and medium at any point during culture. These samples can then be used for quality control assays such as phenotyping and potency assays.

### CONTROLLED, HOMOGENEOUS ENVIRONMENT

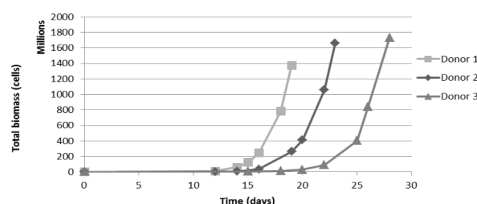
The system's unique agitation approach maintains a homogeneous environment through mixing of the culture bag. The gentle mode of agitation provides a fully homogeneous culture, but minimizes the shear that is usually associated with dynamic cultures (Figure 8). The integration of sensors for pH, oxygen and temperature at the cell culture site ensures that the cells experience an optimal environment.

### FLEXIBILITY

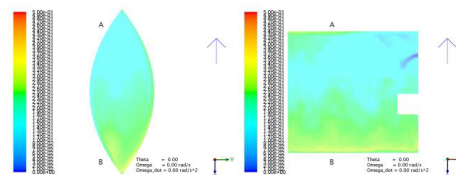
The SCINUS bioreactor is extremely flexible. Users can optimize the culture environment (medium, pH, oxygen, agitation etc.) to specific culture needs. In addition, for adherent cultures different microcarriers can be used depending on the specific substrate requirements of the cells. Therefore, the SCINUS bioreactor can be optimized for the culture of various cell types.



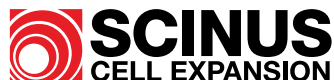
**FIGURE 6** Large-fold expansion of T-cells in the SCINUS bioreactor. DynaBeads activated T cells were expanded to up to more than 6 billion cells without passaging and Transact activated T cells were expanded up to more than 17 billion cells without passaging.



**FIGURE 7** Large-fold expansion of MSCs in the SCINUS bioreactor. 25 mL of bone marrow was expanded to up to 1.5 billion cells (range 1.37-1.73 billion) without passaging.



**FIGURE 8** Computational Flow Dynamics of the single-use SCINUS culture bag during operation reveal a highly homogenous culture environment.

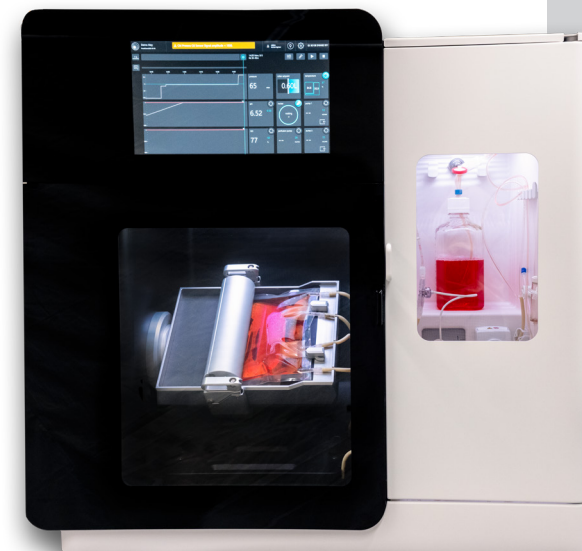


### SCINUS CELL EXPANSION NETHERLANDS B.V.

Professor Bronkhorstlaan 10, building 48  
3723 MB Biltoven  
The Netherlands  
Phone: +31850509300  
Email: info@scinus.com  
Web: www.scinus.com



## SCINUS BIOREACTOR



## FEATURES

- Closed, controlled single-use bioreactor platform for GMP cell therapy production
- Designed for large-fold expansion: the only bioreactor for cell expansion from biopsy to clinically relevant cell numbers using stepless volume expansion
- Unique agitation system superior to other microcarrier-based solutions
- Fully customizable to optimally suit your cell type, adherent or suspension
- Real-time monitoring and control of important cell culture parameters
- Reduce cost for operator involvement, medium use and clean rooms

## INTRODUCTION

Cell therapies typically require hundreds of millions of cells for one application. Initial cell numbers from source material are usually very low. Therefore, these cell numbers need to be increased significantly before they can be administered to the patient. Standard flask-based cell culture is highly inefficient for cell therapy production. Flasks require heavy operator involvement and expensive clean room infrastructure, while increasing risk of contamination and operator-related variability. Process automation using closed bioreactor technology can reduce costs and improve quality of cell therapy products. The SCINUS bioreactor is a closed system for reliable and efficient expansion of adherent, as well as suspension cells from minimal initial cell numbers to clinically relevant amounts. The system's unique volume-expansion capabilities make it possible to cultivate minimal cell numbers (e.g. biopsies) to clinically relevant cell numbers, without the need for passaging.

## SCINUS BIOREACTOR OVERVIEW

The SCINUS bioreactor consists of a single-use SCINUS culture bag within a controller cabinet. The system supports the growth of both adherent cell types (using microcarriers) or suspension cells, through the use of two different single-use SCINUS culture bags (Figure 1).

### SINGLE-USE SCINUS CULTURE BAG

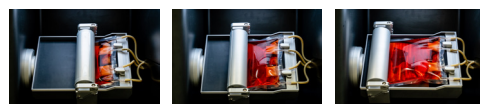
The single-use SCINUS culture bag (Figure 1) is the heart of the SCINUS cabinet. The bag is part of a closed perfusion loop that maintains pH and DO. It also includes connections for containers for fresh medium, waste containers for spent medium and connections for sampling of medium and cells. Sterile welding maintains a closed environment for every operation during culture (addition of cells, medium, removal of excess waste, sampling, etc.). In addition, sterile welding is also used to integrate the SCINUS bioreactor in the complete production cycle, including upstream and downstream processes (USP/DSP). The SCINUS culture bag has integrated sensor technology that monitors the culture environment at the point of cell growth. The roller defines the volume available for cell culture. The volume can be limited clamping the culture bag (Figure 2, left), and can then gradually be increased to accommodate a growing cell population. The volume can be increased more than ten-fold to over 1,4L (range 100 mL – 1400 mL, Figure 2, right). A schematic presentation of the perfusion loop is shown in Figure 3.



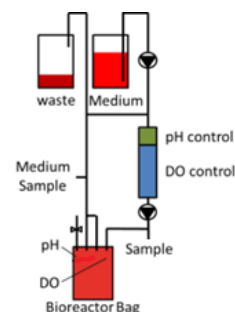
**FIGURE 1** The single-use SCINUS adherent culture bag (left) and the suspension culture bag (right), with incorporated sensors to the right

The single-use SCINUS culture bag and tubing include:

- USP Class VI plastic throughout
- Integrated sensors for pH and oxygen
- Filters to prevent the cells from entering the perfusion loop
- One inflow port for addition of medium
- Outflow for medium removal and harvest
- One outflow for removal of gas
- Pressure sensor
- Tygon weldable tubing for connections to
  - Fresh medium addition
  - Waste removal
  - Sampling
  - Third party USP/DSP systems



**FIGURE 2** Volume expansion of the bag. Minimal volume (left), half the volume (middle) and maximum volume (right).



**FIGURE 3** Schematic presentation of the perfusion loop of the SCINUS culture bag.

## SCINUS CABINET

Cell culture inside the SCINUS culture bag is done in a hardware enclosure (Figure 4). This hardware enclosure houses a unique expansion platform, integrated controller software, an oxygenation system, and all other required hardware such as pumps and heaters.

- Full touchscreen interface for parameter setting with different login levels (operator, engineer, service, etc.)
- A unique agitation (rocker) and volume-expandable (roller) platform that also houses the integrated transmitters for sensors
- Control loops for pH, oxygen and temperature
- A patented oxygenation system for accurate gas control
- Supports on-device data logging, storage, and audit trails.
- Modest footprint: 87 x 52 x 84 cm



**FIGURE 4** The SCINUS bioreactor

### EXPANSION PLATFORM

A homogenous cell culture environment is maintained by a unique platform (Figure 5). The SCINUS culture bag is positioned on a platform that can rock, thereby mixing the content of the bag and maintaining a homogeneously distributed cell suspension. The settings of agitation can be optimized for every individual cell culture application, depending for example on cell type, growth speed or sensitivity to shear stress. The expansion platform houses the clamp that is used to define the available culture volume inside the SCINUS culture bag. The clamp can be repositioned to increase or decrease the available volume.



**FIGURE 5** The expansion platform of the SCINUS cabinet.

### EXPANSION PLATFORM PARAMETERS

PARAMETER	RANGE
Volume range	0.05 – 1.4 L
Rocking angle	+/- 100 °
Rocking velocity	0 – 500 ° /s
Rocking time	0 to 100 hours
Horizontal hold	0 to 100 hours

### ENVIRONMENTAL CONTROL

The SCINUS cabinet maintains an optimal culture environment with strict control of temperature, oxygen and pH levels. Oxygen and pH levels are measured by the sensors that are integrated in the SCINUS culture bag. Transmitters are built into the rocking expansion platform and generated data is transmitted to the controller software of the SCINUS cabinet. The controller software subsequently maintains the pre-defined culture environment by controlling the addition of gases. A patented oxygenation system ensures that setpoints are maintained within minimal bandwidths. The system's unique rocking approach ensures minimal levels of shear.

- Accurate control of pH, oxygen and temperature
- Homogenized culture through rocking with minimized levels of shear
- Temperature control
- Mass-flow controllers for gas flow control

PARAMETER	REQUIREMENTS
DO control	N <sub>2</sub> and compressed air or O <sub>2</sub>
pH control	CO <sub>2</sub>
DO range	0 – 500 % air saturation
pH range	5.5 – 8.5
Temperature range	Ambient to +45 °C

### RECIPE MANAGEMENT AND DATA ACQUISITION

The SCINUS bioreactor comes with on-device data logging, storage, and audit trail features. These features enable the equipment to store data locally, which can be accessed at a later time. This data is also secured through an audit trail, which tracks any changes or modifications made to the data. This feature ensures that all data is accurate and trustworthy, providing users with confidence in their data. It is also 21CFR Part 11 compliant and OPC compatible, enhancing its interoperability with other systems, allowing users to integrate the equipment into their existing processes and systems.