Nucleo™ Bioreactor
The Next-Generation Single-Use Bioreactor

ATMI LifeSciences
The Source of Bioprocess Efficiency™
Overview

The Nucleo™ single-use bioreactor was developed to provide a complete turn-key solution to cell culturists as a next generation alternative to stainless steel classical bioreactors and existing single-use bioreactors, without need for extended validations. The Nucleo bioreactor platform is the result of the combined expertise of Pierre Guerin - Biolafitte (bioreactors and control systems), ATMI LifeSciences (ultra-pure bioprocess films and disposable mixing technology) and Artelis (cell culture and cell culture process optimizations).

Nucleo, the next generation of single-use bioreactors, represents the state of the art response to the evolution of biotech processes. It is perfectly suited to laboratory environments, process development centers, clinical material supply and flexible GMP manufacturing. The Nucleo bioreactor vessel, which offers comparable functionality to classical stirred tank bioreactors, is a single use bag (ATMI) integrating an internal paddle mixing and sparger system (ATMI). The bag, paddle and fittings are single-use and all contact surfaces are discarded after use. The paddle is enclosed in a medical grade ULDPE sleeve, with the same contact material as the bag itself, and is coupled on top of the vessel with the mechanical mixing head.

Highlights & Benefits

• Superior mixing capabilities with drastically reduced shear stress
• Innovative sparging device for superior oxygenation and kLa
• Adapted for cultivation of suspended or adherent cells at very high densities
• Compatible with batch, fed-batch and perfusion processes
• Scalable customizable system
• Ergonomic: modular or fully integrated configuration
• Control of all process parameters ensuring optimal cultivation conditions
• No need for CIP/SIP (disposable bag technology)
• Avoid all cross contamination risks
• User-friendly control interface fully compliant to GAMP V5 and 21 CFR PART 11
• Very low working volume
• All product contact surface of same material (ATMI medical grade ULDPE)
Bag and Container

- Available vessel sizes: 25, 50, 250, 600 liters, cubical geometry (available in the near future: 1200 liters)
- Film material: multi-layer film with contact layer in ULDPE, gamma sterilizable, USP - Class VI compliant, fully ADCF (Animal Derived Component Free)
- Temperature control via jacketed container (thermostatic bath as option)

Mixing System

- Mixing system equipped with patented ATMI paddle
- Adjustable speed: 20-110 RPM

Qualification and Validation

- FAT/SAT Protocols
- Comprehensive test and documentation package designed to ease and support validation

Nucleo Selection Guide

<table>
<thead>
<tr>
<th>Code</th>
<th>Total/Working Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>N50–25</td>
<td>25/20L</td>
</tr>
<tr>
<td>N50–50</td>
<td>50/40L</td>
</tr>
<tr>
<td>N1000–250</td>
<td>250/200L</td>
</tr>
<tr>
<td>N1000–600</td>
<td>Contact your local sales professional for results</td>
</tr>
<tr>
<td>N1000–1200</td>
<td>Contact your local sales professional for results</td>
</tr>
</tbody>
</table>

**Line** | **Description**                                                                                                                                 |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1...4</td>
<td>Multi port fitment - can be used for: nutrient addition, gas exhaust/foam trap, acid addition, media filling, inoculation...</td>
</tr>
<tr>
<td>5...8</td>
<td>Multi port fitment - can be used for: nutrient addition, gas exhaust/foam trap, acid addition, media filling, inoculation...</td>
</tr>
<tr>
<td>9</td>
<td>Disposable bioreactor bag (ATMI LifeSciences TK8 ADCF film)</td>
</tr>
<tr>
<td>10</td>
<td>Sampling port</td>
</tr>
<tr>
<td>11</td>
<td>Perfusion connection/extra sampling connection</td>
</tr>
<tr>
<td>12</td>
<td>Connection for pH, T or DO probe with aseptic Kleenpak connector</td>
</tr>
<tr>
<td>13</td>
<td>Sensing probe assembly to be connected to (12) by Kleenpak counterpart</td>
</tr>
<tr>
<td>14</td>
<td>Easy drain connector</td>
</tr>
<tr>
<td>15</td>
<td>Micro (20μm) or macro (2mm holes) rigid and in motion sparger device</td>
</tr>
<tr>
<td>16</td>
<td>ATMI paddle mixing stick surrounded by sleeve</td>
</tr>
<tr>
<td>17</td>
<td>Gas inlet through sparger device</td>
</tr>
</tbody>
</table>
Aeration

- Dual gas inlet including oxygen supply via micro-sparger or optional macro-sparger and air/CO2 supplies to the head space, both with rotameter and solenoid valve or optional mass flow meters
- 0.2μm absolute filters on gas inlet and outlet
- Gas outlet line fitted with foam trap set
- Optional N2 supply to the sparger with rotameter and solenoid valve or mass flow meter, additional air supply to the sparger with rotameter and solenoid valve or mass flow meter, CO2 supply to the sparger instead of the head place

Accessories and Product Lines

- Up to four fixed speed peristaltic pumps (two included in the basic configuration) and two external variable speed peristaltic pumps for fed-batch and perfusion applications
- Three to six ports for probes and sensors
- 14 multi-purpose ports for inoculation, nutrients, reagent additions, sampling, etc.
- Easy drain: flush bottom harvest valve
- Additive and sampling bags with holders as option

Instrumentation and Control System

- Digital Control System with embedded touch screen operator panel (OP), SIEMENS controller and NEPTUNE OP-WinCC software
- Up to 16 highly flexible control loops for all process parameters: temperature, speed, pH, pO2, optional gas flow rates, weight and optical density
- Control types include PID, digital on/off and others, cascade mode
- Optional PC working station with the NEPTUNE SCDA-iFix or Intouch software for remote control and supervision of up to eight Nucleo bioreactors

Neptune™ SCADA Software

“Standard” Version: OP-WinCC software

- Process control via synoptic views
- Alarm management
- Controller profiles for dynamic set points
- Management of user’s access complying with 21 CFR PART 11
- Monitoring of controller set points and alarms
- Data logging and trends with file export/import

“Advanced and Expert” Versions (Optional SCADA software)

- Calculation module allowing user to define additional calculations and apply control based on these calculations
- Strategy module for process strategy optimization

System Dimensions

<table>
<thead>
<tr>
<th>Dimension</th>
<th>N50</th>
<th>N1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Width</td>
<td>1330mm</td>
<td>1800mm</td>
</tr>
<tr>
<td>Minimum depth with bag holder</td>
<td>1020mm</td>
<td>1245mm</td>
</tr>
<tr>
<td>Maximum depth with bag holder and scale</td>
<td>1210mm</td>
<td>1875mm</td>
</tr>
<tr>
<td>Minimum height for installation</td>
<td>1880mm</td>
<td>1880mm</td>
</tr>
<tr>
<td>Maximum height in use</td>
<td>1880mm</td>
<td>2330mm</td>
</tr>
<tr>
<td>Weight without bag holder</td>
<td>400kg</td>
<td>650kg</td>
</tr>
</tbody>
</table>

Touch Screen Control

Neptune SCADA Software

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For more information, please contact us at: roman_rodriguez@atmi.com, d.felezue@pierreguerin.fr, bacanna@dci-bio.com

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