Ambr® 15
Cell Culture
Generation 2
Advanced Microbioreactor System
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Generation 2

An automated, high throughput microscale bioreactor system that replicates laboratory scale bioreactor performance

The system comprises single-use vessels, an automated workstation and powerful software. Installed in a biological safety cabinet for aseptic operation, Ambr® 15 monitors and controls 24 or 48 microbioreactor cultures in parallel.

As biotherapeutics become more complex, and processes more intensified, laboratories around the world are facing bigger challenges developing clones, media and processes.

With key performance enhancements, improved flexibility and significant novel functions, the Ambr® 15 Generation 2 system helps scientists accelerate their research.

- New functions enhance performance in applications such as:
  - Clone selection
  - Media and feed optimization
  - Process intensification
  - Development of advanced cell therapies
- New Flexible Deck increases walk-away time to maximize operator productivity
- New Ambr® Clone Selection software provides powerful options for enhanced decision making
- New Generation 2 liquid handling capability for rapid, accurate completion of multifactorial DoE investigations
- Ambr® 15 is the industry standard microbioreactor system, implemented in laboratories world wide
- Integrated metabolite analysis fast tracks implementation of Quality by Design (QbD) principles
- Ambr® 15 reduces the cost per experiment by saving substantial amounts on facility space, capital, labour, media and consumables
- Ambr® 15 helps teams to select better clones, screen more media and optimize processes, faster

For more information, please visit
New Workstation

New Liquid Handler
Automates the transfer of media, feed and reagents into microbioreactor vessels or labware on the deck. It also performs sampling from the microbioreactors into the sample cup for integrated at-line analysis or into plates for off-line analysis.

The Liquid Handler includes pipette mandrels for picking 1 mL and 5 mL sterile disposable tips, microbioreactor decapper and plate delidding. New Liquid Handler design provides greater dispense accuracy during high intensity pipetting operations.

New Culture Stations
Each culture station holds 12 microbioreactors, there are 4 culture stations on the system pictured, operating up to 48 cultures in parallel. Culture stations maintain and monitor temperature and stirrer speed set points. New culture station design improves temperature performance and stirrer speed control. Individual bioreactor pH and DO is achieved by independent gas mixture delivery and closed feedback control.

New Large Tip Bin
Increased capacity for discarding pipette tips used for liquid additions and sampling of Ambr® cultures. The large tip bin is easily disconnected from the system for emptying and cleaning. The large tip bin is also interchangeable with a small tip bin either at the start of a process or during processing.

The additional capacity of the new large tip bin complements the increased capacity for tips offered by the Flexible Deck and means that the system can run for longer without an operator present.

New Labware Lid Locations
Pipette and plate lids are automatically removed prior to liquid transfer and replaced afterwards to ensure sample, reagent and media integrity. New process steps allow multiple locations for plates, plate lids and tip box lids to facilitate and speed up operations such as media mixing and culture passaging.

01
02
03
04
New Flexible Deck
Flexible positions for pipette tip boxes, plates, tip box lids and plate lids allowing the operator to define their set up according to specific process needs and to change labware configurations during the process. There are 6 flexible labware positions on the 24 microbioreactor system and 9 flexible labware positions on the 48 microbioreactor system.

More information on the New Flexible Deck on page 6

New Rapid Vessel Drain
The Rapid Vessel Drain is optionally available to allow removal of large volumes of culture or spent media from a bioreactor in a single step via a dedicated pipette mandrel and vessel drain assembly. Applications include passaging of cultures, media exchanges and performing perfusion mimic processes in the Ambr® microbioreactors.

More information on the New Rapid Vessel Drain option on page 8

New Software Application
Powerful Ambr® software allows easy experiment construction, effective process monitoring and control and detailed recording & data analysis. New software steps are included for media mixing, passaging and Rapid Vessel Drain operations.

New clone selection software application powered by Umetrics® is included as a 1 year license to provide simplified, streamlined multivariate capability for efficient clone selection.

More information on the new Ambr® Clone Selection application on page 11
Offering a high level of flexibility, the labware configurations can be changed by the operator both at the start and during the process. For example to take into account additional pipette tips needed over a weekend or during media mixing steps where multiple plates and plate lid locations are required.

In combination with the large tip bin for additional disposal capacity, the new Flexible Deck functionality reduces the need to visit the system to replace labware. This increases operator walk-away time.

Flexible deck positions can accommodate:
- 1-well, 4-well, 24-well or 96-well plates
- Cell counter sample cups
- 1 mL pipette tip boxes
- 5 mL pipette tip boxes
- Tip box lids
- Plate lids

Rapid Vessel Drain

Available with Ambr® 15 Cell Culture Generation 2 to allow removal of large volumes of culture or spent media from a bioreactor in a single step.

Liquid is pumped through vessel drain line. This part of the line is internally routed.

Liquid is drawn up from vessel via 1 mL pipette tip Pump 2 L Waste bottle.

Rapid Vessel Drain option includes:
- Additional 1 mL pipette tip mandrel in the Liquid Handler dedicated to vessel drain operations
- Internally routed vessel drain line
- Vessel drain pump and pump tubing set
- 2 L waste bottle for vessel drain
- New software process steps

A dedicated 1 mL pipette tip mandrel collects a sterile tip and moves down to the height corresponding to the final volume required in the microbioreactor.

Culture or spent media is pumped through the vessel drain line to a 2 L waste bottle. A new sterile tip is used for each bioreactor. User defined software steps fully automate the vessel drain operations and refill of cultures with fresh media.

With a significant reduction in time, the Rapid Vessel Drain enables passaging of cultures in Ambr® 15 during cell expansion stages or for generation clone stability studies, spent media removal can be performed for media exchanges or for perfusion mimic processing.
Ambr® 15 workstation
Fully automated parallel processing, monitoring, control and data capture of all bioreactor experiments, with:
- Standard and cooled workstation configurations available
- Cooled workstation increases culture temperature range from 33 – 40°C to 20 - 40°C, and includes chilled plate positions
- Individual set point, monitoring and closed-loop control of pH and DO
- Independent control of $O_2$, $CO_2$ and $N_2$ for each microbioreactor
- User defined temperature and stirring set point for each culture station
- Extended low speed stirring range, from 150 - 2000 rpm
- Flexible Deck layout allows different labware positions to be defined
- Interchangeable tip bins in two sizes; large tip bin significantly expands tip disposal capacity

- Option: Integrated Ambr® Analysis Module for automated at-line pH calibration and in-process checks
- Option: Integrated Nova Flex2 metabolite analyzer
- Option: Integrated ViCell XR and Cedex HiRes cell counters

Ambr® 15 Liquid Handler
Automated liquid handling robotics (LHR) manage all liquid transfer steps during the culture process:
- Media, feed and reagents are dispensed using 1 mL and 5 mL sterile pipette tips
- Samples are taken from the microbioreactors using 1 mL sterile pipette tips
- Larger volumes of microbioreactor culture are removed in a single step using the Rapid Vessel Drain option
- Updated LHR design improves tip picking reliability
- Vessel cap and labware lid handling ensure culture integrity

Ambr® 15 microbioreactor vessel
Mimics the characteristics of lab scale bioreactors to enable optimal cell growth, productivity and product quality:
- 10 – 15 mL working volumes
- Single-use pH and DO sensors
- Integrated pitched blade impeller
- Port for liquid additions and for sampling
- Vessels available with sparge tube for gassing into impeller mixing zone, or without for headspace gassing
- Vessels available with temperature compensation for lower temperature applications

Micro bioreactor vessel
The core disposable micro bioreactor technology includes sensors, stirring impeller, gas sparging and sample port.

1. Gas sparge tube
2. Sample port with cap
3. pH and DO sensor spots
4. Impeller
Ambr® 15 is increasingly used to accelerate development of newer approaches, such as cell and gene based therapies, bispecifics, next generation vaccines and antibody drug conjugates.

Ambr® 15 Cell Culture is used as a microscale model to eliminate bottlenecks in a range of applications such as:
- Clone selection
- Media, feed and early stage process optimization
- Screening under perfusion mimic conditions

Applications

Ambr® 15 is the industry standard microbioreactor system, extensively used to develop therapies including monoclonal antibodies and recombinant proteins.
Clone Selection

Clone selection remains a critical step in the cell line development process, as the choice of clone has significant impacts on further development activities, and is a time consuming process, potentially involving hundreds of candidates.

Globally, clone selection is the application most frequently performed on the Ambr® 15, and using the system for this purpose has been shown by many biopharma companies to significantly reduce timelines and increase laboratory productivity. Ambr® 15 enables selection of robust clones with high productivity, and optimal product quality profiles.

New Ambr® Clone Selection Powered by Umetrics®
A one year licence is included for the Ambr® Clone Selection software with every Ambr® 15 Cell Culture Generation 2 system. This standalone application solves the problems associated with inconsistent data analysis methods, subjective decision making and the burden of manually creating and managing spreadsheet ranking methods.

Users can now choose between traditional univariate methods for analyzing the data that result from clone ranking experiments, and the simplified, streamlined multivariate capability provided by the Ambr® Clone Selection software.

For more information, please visit
Many biopharma companies are focusing on intensification of their work streams, to cut costs, increase productivity and ensure consistent product quality. Clones selected under fed batch conditions may behave differently when transferred to an intensified process. Existing bench scale methods are both time consuming and expensive to execute, resulting in a demand for a microscale solution.

New Ambr® 15 Cell Culture Generation 2 offers perfusion mimic capabilities to fast track identification of clones and media.

The Rapid Vessel Drain option provides capability to bleed large volumes of culture and quickly remove spent media from the Ambr® 15 microbioreactors. The latest Ambr® software includes novel process steps to automate perfusion mimic protocols.

Development teams are facing significant new challenges, driven by innovations such as CAR-T cell therapy. In addition, novel, complex processes must be rapidly understood in order to manufacture viral vectors and next generation vaccines on time, and to the required specification.

Ambr® 15 offers high throughput experimentation to address these major development bottlenecks, cutting timelines and deepening scientists’ knowledge of cultivations including HEK293, stem cells and immune derived cell lines.

Scientists are using Ambr® 15 to rapidly establish protocols for stable and transient cell lines, select suitable clones, and optimize media and processes to facilitate scale up for implementation in new manufacturing facilities.

Optimizing media and feeds can deliver important improvements in cell growth and productivity. Traditionally, executing these studies in shake flasks or bench top bioreactors required significant investment of time and effort.

The Ambr® 15 Cell Culture Generation 2 system includes novel functions to streamline and simplify media, supplement and feed investigations.

New mixing steps in the Ambr® software allow the creation of media blends in plates on the deck or directly in the microbioreactors. Media blends can be defined by volume or as percentages. Automated liquid handling saves time and reduces the chance of error.
Scalability

Single-Use from Cell Line and Process Development to Production Scale

- Advanced bioreactor capability and performance
- Single-use solutions at different scales
- Consistent mixing and gassing strategies
- Effective automation and optimization using online and at-line sensor technology
- New software tools for data analysis

Similar geometry and sensors - scaling up from 0.25 L to 2000 L