



# Ambr<sup>®</sup> 15 Cell Culture

Selected Bibliography

Simplifying Progress

**SARTORIUS**

# Ambr<sup>®</sup> 15 Cell Culture

This bibliography covers many key applications and topics for the Ambr<sup>®</sup> 15 Cell Culture system. Cell and product types and application areas are shown as icons on the next page.

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- 5 Screening
- 8 Media Development
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- 16 Working With Scale Down Models
- 21 Advanced Therapies
















# Key

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## Culture Type











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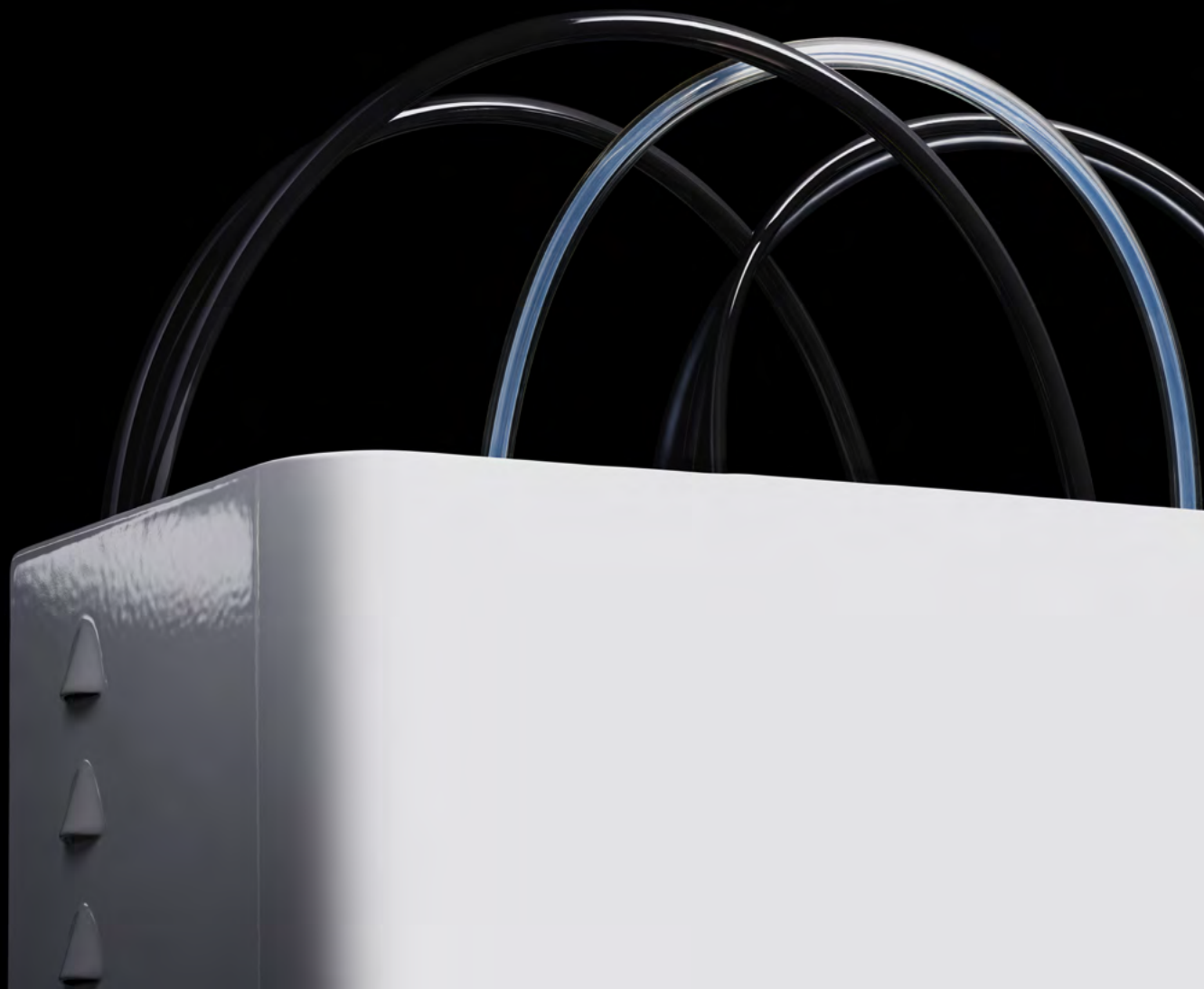
-  Cell Therapy
-  Chemical
-  CHO
-  HEK
-  Insect Cells
-  mAb
-  Microbial
-  Microcarriers
-  Protein
-  Stem Cell
-  T-Cells
-  Vaccine
-  Viral Based Therapy

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## Technology

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-  Bioreactor Process Control
-  Bioreactor Vessel Characterization
-  Consistency | Reproducibility
-  Design of Experiment (DOE)
-  Multivariate Data Analysis (MVDA)
-  Perfusion Mimic
-  Product Quality
-  Scalability
-  Spectroscopy
-  Transient Transfection





### Integrating Metabolome Dynamics and Process Data to Guide Cell Line Selection in Biopharmaceutical Process Development

Gianmarco Barberi, Antonio Benedetti, Paloma Diaz-Fernandez, Daniel C.Sévin, Johanna Vappiani, Gary Finka, Fabrizio Bezzo, Massimiliano Barolo, Pierantonio Facco

University of Padova, via Marzolo, 9, 35131, Padova, PD, Italy.  
GlaxoSmithKline R&D, Stevenage, UK,  
Cellzome GmbH, GlaxoSmithKline R&D, Heidelberg, Germany

2022

<https://doi.org/10.1016/j.ymben.2022.03.015>



### Simplifying Adeno-Associated Virus Vector Production

Véronique Blouin-Tavel, Magalie Penaud-Budloo, Christophe Chevé, Maïlys Pennors, Marie Enga, Cécile Robin, Amélie Boulais, Franziska Bollmann, Robert Zuban, Timo Schmidberger, Chloe Lang, David Retour, Oumeya Adjali, Piergiuseppe Nestola

University of Nantes, France  
INSERM UMR 1089  
Sartorius

2021

Request from your Sartorius representative. Celum ID 116764



### Rapid Development of Viral Vector Production Processes: Iterative Parameter Optimization

Jakub Krakowiak, Qian Liu, Lara Nascimento-Brooks

OXGENE, UK.  
Sartorius

2021

<https://bioprocessintl.com/sponsored-content/modde-software-for-rapid-development-of-viral-vector-production-processes-iterative-parameter-optimization/>

**“Our studies explored multiple innovative ideas in a single platform, significantly reducing the time required to enhance and validate a viral vector platform by up to 50%.”**



### Evaluation of a Microbioreactor System as a Screening Tool for Optimizing Lentiviral Vector Process Development in Suspension Culture

Nolan Sutherland, Lesley Chan, Kelly Kral, Franziska Bollmann

bluebird bio, Inc  
Sartorius

2021

<https://doi.org/10.18609/cgti.2021.136>

**“...this study demonstrates the suitability of the Ambr® 15 system as a process screening tool which has the potential to reduce costs and timelines of the development of scalable LVV production systems in suspension culture.”**

**“Using an Ambr® 15 system we now have the capability to screen multiple different factors at the same time and the screening doesn’t cost as much as we’re using smaller volumes of media and expensive reagents. We can also test at the extreme ranges of a factor, which is something we have not been able to do in the past. This has led us to developing final processes that are up to ten-times more efficient in terms of titer increases.”**



### Novel Automated Micro-Scale Bioreactor Technology: A Qualitative and Quantitative Mimic for Early Process Development

Gareth Lewis, Richard Lugg, Ken Lee, and Richard Wales

MedImmune, Cambridge, United Kingdom  
Sartorius

2021

<https://doi.org/10.12665/J91.Wales>

**“The study indicates that Ambr® can help predict the clone performance in bench-scale bioreactors and may help in ranking clones and selecting the optimum clone to take forward into further process development work.”**



### An Integrated Cell Line Development Platform For Generation of High Yielding CHO Stable Cell Lines Expressing a Stabilized Trimeric Pre-Fusion RSV F Recombinant Viral Glycoprotein

Amritha Menon, Mingzhong Chen, Giulia Fabozzi, Althaf Hussai

Vaccine Research Center, NIAID, NIH

2016

[https://dc.engconfintl.org/cellculture\\_xv/79/](https://dc.engconfintl.org/cellculture_xv/79/)



### Webinar - Ambr® 15 Generation 2: Enhancing Cell Line Selection and Early Process Development

Alison Rees-Manley

Sartorius

2020

Request from your Sartorius representative. Celum ID 72502



### High-Throughput Screening and Selection of Mammalian Cells for Enhanced Protein Production

Joseph J. Priola, Nathan Calzadilla, Martina Baumann, Nicole Borth, Christopher G. Tate, Michael J. Betenbaugh

John Hopkins University, Baltimore, MD, USA

Austrian Centre of Industrial Biotechnology, Graz, Austria  
MRC Laboratory of Molecular Biology, Cambridge, UK

2018

<https://doi.org/10.1002/biot.201500579>



### High-Throughput Screening of Multiple Protein Complexes

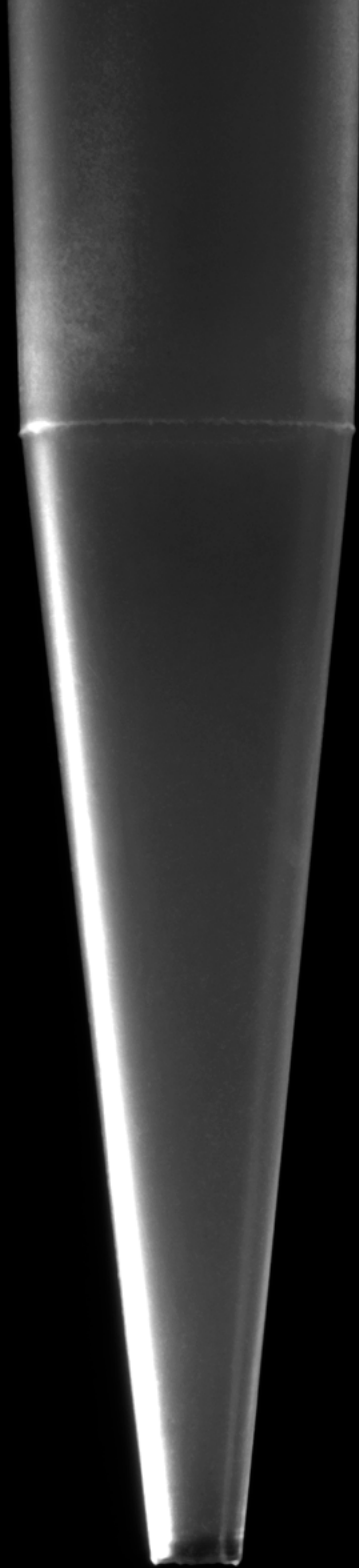
Imre Berger, Maxime Chaillet, Frederic Garzoni, Sinyee Yau-Rose, Barney Zoro

European Molecular Biology Laboratory (EMBL), Grenoble Cedex 9, France  
Sartorius

2013

<https://www.americanlaboratory.com/914-Application-Notes/140723-High-Throughput-Screening-of-Multiple-Protein-Complexes/>

**“The observed results confirm that sf21 insect cells can be successfully grown, maintained, and infected in the Ambr® bioreactors to express multiprotein complexes.”**





## Developing a Medium Combination to Attain Similar Glycosylation Profile to Originator by DOE and Cluster Analysis Method

Jian Xu, Zhihui Shao, Zhanqing Wang, Yingfeng Huang, Xun Zou, Yaling Shen

East China University of Science and Technology, Shanghai, 200237, China  
Chinese Academy of Sciences, Shanghai, China  
Dragon Sail Pharmaceutical, Shanghai, China  
Dragonboat Biopharmaceutical, Shanghai, China  
Shanghai Sanjin Bioscience and Technology, Shanghai, China

2021

<https://doi.org/10.1038/s41598-021-86447-0>



## Webinar - Ambr® 15 for Cell Culture Process Optimization

Marta Ruiz Guillén, Javier Lobo

3P Biopharmaceuticals  
Sartorius

2018

<https://3pbio.com/ambr15-for-cell-culture-process-optimization-webinar-3p-biopharmaceuticals-and-sartorius-stedim-biotech>

**“The system can be implemented within the Upstream process workflow to generate early process development data at the small scale with very low demands on operator time, set-up and turn around due to automation and single-use components.”**



## Use of High-Throughput Automated Microbioreactor System for Production of Model IgG1 in CHO Cells

Sai Rashmika Velugula-Yellela, Casey Kohnhorst, David N. Powers, Nicholas Trunfio, Anneliese Faustino, Phillip Angart, Erica Berilla, Talia Faison, Cyrus Agarabi

Division of Biotechnology Review and Research II, U.S. Food and Drug Administration.

2018

<https://doi.org/10.3791/58231>

**“There are numerous advantages provided by the microbioreactor system, as it enables multiple controlled cultures to be run in parallel at a small scale with greater control than shake flasks. Therefore, the system facilitates the execution of screening studies, DOEs, high throughput clone studies and transfection studies.”**



## A Rapid Approach for Basal and Feed Media Optimization in Ambr® 15 Bioreactors

Michael Gillmeister, Greg Bremer, Christophe Grimm, Marc Mitchell, Rida Sheikh, Alexis Bossie

Lonza Walkersville Inc  
Sartorius

2016

[https://dc.engconfintl.org/cellculture\\_xv/131](https://dc.engconfintl.org/cellculture_xv/131)





# Process Development



## Automated Single-Cell Cloning in Chemically Defined Medium for New Suspension Mdck Cell Lines and Scale-Down of Influenza a Virus Production Into Ambr®15 Microbioreactors

Tilia Zinnecker, Ilona Behrendt, Maverick Lau, Angelika Hinkelmann, Kristin Thiele, Najd Badri, Diogo Araujo, Yvonne Genzel, Udo Reichl

Max Planck Institute for Dynamics of Complex Technical Systems, Germany  
Otto-von-Guericke University Germany  
Sartorius

2022

[https://dc.engconfintl.org/vaccine\\_viii/55](https://dc.engconfintl.org/vaccine_viii/55)



## Application of a Simple Unstructured Kinetic and Cost of Goods Models to Support T-Cell Therapy Manufacture

Maryam Shariatzadeh, Adriana G. Lopes, Katie E. Glen, Andrew Sinclair, Rob J. Thomas

Loughborough University, Epinal Way, Loughborough University, Loughborough, UK  
Biopharm Services, Chesham, UK

2021

<https://doi.org/10.1002/btpr.3205>

**“Ambr® 15 microbioreactor vessel mimics the characteristics of lab scale bioreactors to enable optimal cell growth, productivity and product quality.”**



## How to Intensify Upstream Process Development With Ambr® 15 & 250

James Edwards, Don Traul

Sartorius

2021

<https://www.sartorius.com/en/pr/webinar-how-to-intensify-upstream-process-development-with-ambr15250>

**“This study demonstrated the ease, simplicity and speed of performing multiple conditions in one experiment using Ambr® 15 Cell Culture by assessing five different media compositions on two different clones.”**



## Scalable Upstream Process Development for the Suspension-Based Production of Lentivirus Vectors for CART Cell Therapies With Multiparallel & Benchtop Bioreactor Systems & DOE Methodology

Diana Riethmüller, Alengo Nyamay'antu, Franziska Bollmann

Polyplus-transfection, Illkirch, France  
Sartorius

2021

<https://insights.bio/cell-and-gene-therapy-insights/journal/article/2128/Scalable-upstream-process-development-for-the-suspension-based-production-of-lentiviral-vectors-for-CAR-T-cell-therapies-with-multiparallel-benchtop>



## Stress-Induced Increase of Monoclonal Antibody Production in CHO Cells

Jana Schellenberg, Tamanna Nagraik, Ole Jacob Wohlenberg, Sebastian Ruhl, Janina Bahnemann, Thomas Scheper, Dörte Solle

Leibniz Universität Hannover, Callinstr. 5, 30167 Hannover, Germany.  
Sartorius

2021

<https://doi.org/10.1002/elsc.202100062>

# Process Development



## Cell Line Development: Accelerating Process Optimization by Combining Ambr® 15 Cell Culture with Octet® Titer Measurements

Jonathan Kirby, Alison Rees-Manley, David Apiyo, Lukas Klein, Eva Diem, Tim Dale

Sartorius

2021

Request from your Sartorius representative. Celum ID 115331



## Spectroscopy Integration to Miniature Bioreactors and Large Scale Production Bioreactors - Increasing Current Capabilities and Model Transfer

Ruth C. Rowland-Jones, Alexander Graf, Angus Woodhams, Paloma Diaz-Fernandez, Steve Warr, Robert Soeldner, Gary Finka, Marek Hoehse

GlaxoSmithKline R&D, Stevenage, UK. Sartorius

2021

<https://doi.org/10.1002/btpr.3074>

**“It was demonstrated that a predictive model for glucose concentration using spectral data acquired of cell culture at small scale could be used to accurately measure glucose concentration at 50 L scale.”**



## Establishment and Optimization of a High-Throughput Mimic Perfusion Model in Ambr® 15

Lu Jin, Zhen-Shou Wang, Yun Cao, Rui-Qiang Sun, Hang Zhou, Rong-Yue Cao

China Pharmaceutical University, #639 Longmian Dadao, Jiangning District, Nanjing 211198, Jiangsu, China  
WuXiBiologics, #288 Fute Middle Road, Waigaoqiao FreeTrade Zone, Shanghai 200131, China

2020

<https://doi.org/10.1007/s10529-020-03026-5>

**“A small-scale high-throughput perfusion model in Ambr® 15 was developed, optimized to improve cell viability, and as a result, utilized for media screening in two cell lines.”**

# Process Development



## Development of a Novel, High-Throughput Screening Tool for Efficient Perfusion-Based Cell Culture Process Development

Thomas M. Gagliardi, Rahul Chelikani, Yang Yang, Gioia Tuozzolo, Hang Yuan

Shire, 300 Shire Way, Lexington, MA 02421

2019

<https://doi.org/10.1002/btpr.2811>

**“This process matches the cellular microenvironment of true perfusion systems, and gives excellent cell culture.”**



## A Novel Scale-Down Mimic of Perfusion Cell Culture Using Sedimentation in an Automated Microbioreactor (SAM)

Steffen Kreye, Rainer Stahn, Karina Nawrath, Vicky Goralczyk, Barney Zoro, Steffen Goletz

2019

Glycotope  
Sartorius

<https://doi.org/10.1002/btpr.2832>



## Optimization of the HEK293T Suspension Cultivation With a DOE-Approach in Ambr® 15 Cell Culture

Franziska Bollmann, Diana Riethmüller, Erik Johansson, Alexander Tappe Sartorius

2019

Request from your Sartorius representative. Celum ID 112375



## Up and Down Scale Considerations for the Continuous Production of Glycooptimized Biopharmaceuticals

Steffen Kreye, Rainer Stahn

Glycotope GmbH, Robert-Roessle-Str. 10, 13125 Berlin, Germany

2017

[https://dc.engconfintl.org/biomanufact\\_iii/38](https://dc.engconfintl.org/biomanufact_iii/38)



## Integrating a Programmable Robotic Bioreactor System With a Biochemical Analyser for Real-Time Analysis

Jareatha Abdul-Raheem, Jean-Francois P. Hamel

Massachusetts Institute of Technology, Department of Chemical Engineering, Cambridge, MA 02139

2017

Request from your Sartorius representative. Celum ID 166182

**“Integrated platform can automate real time secondary data analysis (glucose consumption rate) and implement it in an automated control strategy.”**



## Comparison of Spectroscopy Technologies for Improved Monitoring of Cell Culture Processes in Miniature Bioreactors

Ruth C. Rowland-Jones, Alexander Graf, Angus Woodhams, Paloma Diaz-Fernandez, Steve Warr, Robert Soeldner, Gary Finka, Marek Hoehse

BBTC, Newcastle University, Newcastle Upon Tyne NE1 7RU, UK  
Lonza Biologics plc, 228 Bath Road, Slough SL1 4DX, UK  
University of Copenhagen, Rolighedsvej 30, Frederiksberg DK- 1958, Denmark  
University of Leeds, Leeds LS2 9JT, UK

2017

<https://doi.org/10.1002/btpr.2459>

# Process Development



## **Impact of Media and Antifoam Selection on Monoclonal Antibody Production and Quality Using a High Throughput Micro-Bioreactor System**

Sai Rashmika Velugula-Yellela, Abasha Williams, Nicholas Trunfio, Chih-Jung Hsu, Brittany Chavez, Seongkyu Yoon, Cyrus Agarabi

U.S. Food and Drug Administration, Center for Drug Evaluation and Research, Office of Product Quality, Office of Biotechnology Products, Division of Biotechnology Review and Research II, Silver Spring, MD  
Dept. of Chemical Engineering, University of Massachusetts, Lowell, MA

2017

<http://doi.org/10.1002/btpr.2575>



## **Application of Multivariate Data Analysis in the Monitoring and Control of Mammalian Cell Processes**

Stephen Goldrick, Richard Turner  
MedImmune Marcel  
Kuiper MedImmune Kenneth Lee,  
Rahul Pradhan

University College London,  
Medimmune

2016

[https://dc.engconfintl.org/cellculture\\_xv/40/](https://dc.engconfintl.org/cellculture_xv/40/)



## **Optimizing Performance of Semi-Continuous Cell Culture in an Ambr® 15 Microbioreactor Using Dynamic Flux Balance Modeling**

William Kelly, S orelle Veigne, Xianhua Li, Shyam Sundar Subramanian, Zuyi Huang, Eugene Schaefer

Villanova University, Chemical Engineering, Villanova, PA, 19085  
Janssen R&D, cAPI Large Molecule Pharmaceutical, Development and Manufacturing Sciences, Malvern, PA  
Teva Pharmaceuticals, Biologics CMC, North Wales, PA

2017

<https://doi.org/10.1002/btpr.2585>



## **HEK293 Cell Adaptation To New Media And DOE For AAV Production In Suspension Using Sartorius Automated Small Scale Stirred Tank Bioreactor Platform: Ambr® 15**

Cecile Robin, Marie Enga, Lucie Menard, Mailys Pennors, Veronique Blouin, Oumeya Adjali, Virginie Houyoux, Chloe Lang, Robert Zuban, Quen Fn Vicard, Eduard Ayuso

INSERMUMR1089, University of Nantes, Centre Hospitalier Universitaire, Nantes, France  
Sartorius

2016

Request from your Sartorius representative. Celum ID 138439



## **Targeted Supplementation Design for Improved Production and Quality of Enveloped Viral Particles in Insect Cell-Baculovirus Expression System**

Francisca Monteiroa, Vicente Bernalc, Maxime Chailletd, Imre Bergerd, Paula M. Alvesa

iBET, Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal  
Universidade Nova de Lisboa, Oeiras, Portugal

Facultad de Química, Campus Internacional de Excelencia "Mare Nostrum", Universidad de Murcia, Murcia, Spain

The European Molecular Biology Laboratory, Grenoble, France

Unit of Virus Host Cell Interaction UVHCI, Université Grenoble Alpes, – EMBL – CNRS Unité Mixte de Recherche Grenoble, France  
University of Bristol, Bristol BS8 1TD, UK

2016

<http://dx.doi.org/10.1016/j.jbiotec.2016.06.029>

# Process Development



## Agitation Conditions for the Culture and Detachment of hMSCs From Microcarriers in Multiple Bioreactor Platforms

Alvin W. Nienow, Christopher J. Hewitta, Thomas R.J. Heathman, Veronica A.M. Glyn, Gonçalo N. Fonte, Mariana P. Hanga, Karen Coopman, Qasim A. Rafiq

Loughborough University,  
Leicestershire LE11 3TU, UK  
University of Birmingham, Birmingham  
B15 2TT, UK  
Aston University, Aston Triangle,  
Birmingham B4 7ET, UK Instituto  
Superior Técnico (IST),  
Universidade de Lisboa, Portugal

2015

<https://doi.org/10.1016/j.bej.2015.08.003>



## High-Throughput Miniaturized Bioreactors for Cell Culture Process Development: Reproducibility, Scalability and Control

Shahid Rameez, Sigma S. Mostafa, Christopher Miller, Abhinav A. Shukla

KBI Biopharma Inc., 2 Triangle Dr,  
Research Triangle Park, NC

2014

<https://doi.org/10.1002/btpr.1874>

**“This system offers the realistic possibility of decreasing the process development time for investigational biopharmaceutical to reach clinic by reducing the timeframe for process development experiments.”**



## Critical Process Parameter Identification Using The Ambr® 15 For Process Characterization

Matthew Zustiak, Stephanie Chakravarty, Matt Caple

Patheon Biologics

2016

[https://dc.engconfintl.org/cellculture\\_xv/103/](https://dc.engconfintl.org/cellculture_xv/103/)

**“Here we demonstrate the feasibility to use the Ambr® 15 as a tool for key and even critical process parameter identification to reduce timelines for process characterization.”**



## Transient Production of VLPs in HEK 293 Cells and the Evaluation of Parameters Influencing Transfection and Expression

Daniel Blackstock

NIH

2016

[https://dc.engconfintl.org/cellculture\\_xv/206](https://dc.engconfintl.org/cellculture_xv/206)



## MultiBac Expression System: Comparison of Growth and Multiprotein Production in Shake Flask and Automated Miniature Bioreactor (Ambr®) Cultures

Maxime Chaillet, Frederic Garzoni, Sinyee Yau-Rose, Barney Zoro, Imre Berger

European Molecular Biology  
Laboratory (EMBL)Grenoble, 6 Rue  
Jules Horowitz,38042 Grenoble  
Cedex 9, France.  
Sartorius

2016

Request from your Sartorius representative. Celum ID 1507



## Evaluation of the Advanced Microscale Bioreactor (Ambr®) System for Use in Production Cell Line Development

Frédéric Delouvroy, Guillaume Le Reverend, Boris Fessler, Gregory Mathy, Mareike Harmsen, Nadine Kochanowski, Laetitia Malphettes

UCB Pharma S.A., Chemin du Foriest,  
Braine l'Alleud, Belgium

2013

<https://doi.org/10.1186/1753-6561-7-S6-P73>



SARTORIUS

BoPAT / Process Insights

Match tip speed kLa

Scenarios > Scale stir based on kLa and tip speed compromise

Scale stir based on kLa and tip speed compromise

Comparison

Scale task

Anchor/Document

Anchor/Document

Tip scale

Anchor/Document

Simple Confidence Metric

Simple Metric

Relative Confidence Metric

Relative Confidence Metric

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Anchor/Document

Anchor/Document

Anchor/Document

Anchor/Document

Anchor/Document

Anchor/Document

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+ Scenario

Results > Optimum

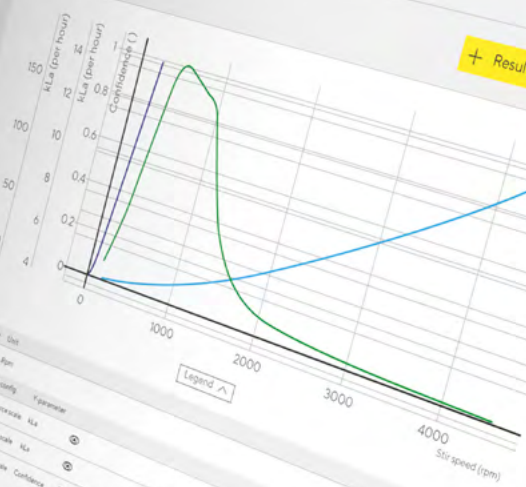
Duplicate

Export

+ Result set

+ Result

Optimum



2 Summary table

	Stir speed (rpm)	Tip speed (rpm)	kLa (per hour)
Source scale	500	(1) 0.581	(1) 6.12
Target scale	644	(1) 0.632	(1) 6.3



# Working With Scale Down Models



## MRI Hydrodynamic Characterization of an Ambr® 15 Bioreactor

Cloé Legrand, Matthew Cheeks, Christopher Sellick, Michael Mantle

University of Cambridge, Philippa Fawcett Drive, Cambridge CB3 0AS, UK  
BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK  
Kymab, The Bennet Building (B930), Babraham Research Campus, Cambridge, CB22 3AT, UK

2022

<https://doi.org/10.1016/j.bej.2021.108304>

**“The asymmetric Ambr® 15 vessel geometry and positioning of the impeller and gas sparge tube reduce vortex formation and create flow profiles more typical of larger scale baffled cylindrical bioreactors.”**



## Modeling Mass Transfer in Stirred Microbioreactors

Hooman Yadollahi Farsania, Johannes Wutz, Brian DeVincentis, John A.Thomas, Seyed Pouri Motevaliana

Pfizer Inc., Andover, MA 01810, USA  
M-Star Center Europe GmbH, Hauptstraße 3, 38822 Sargstedt, Germany  
M-Star CFD, 11100 Baltimore National Pike, Ellicott City, MD 21042, USA

2022

<https://doi.org/10.1016/j.ces.2021.117146>



## Shedding Light On the Dark Art Of Bioprocess Scaling

Kevin McHugh, Sinyee Yau-Rose, Katy McLaughlin

Sartorius

2022

<https://www.biopharminternational.com/view/shedding-light-on-the-dark-art-of-bioprocess-scaling>



## Webinar - Double Your Development Speed: A New Approach to Viral Vector Design

Lara Nascimento-Brooks, Jakub Krakowiak

Oxgene | Wuxi Biologics  
Sartorius

2022

<https://www.sartorius.com/en/applications/cell-and-gene-therapy/double-your-development-speed-a-new-approach-to-viral-vector-design-webinar/double-your-development-speed-a-new-approach-to-viral-vector-design-webinar-success>



# Working With Scale Down Models



## Next Level Scale-Up: How DOE and MVDA Improved Scale-Up Performance at a CDMO

Matthias Müller, Chloe Lang, Timo Schmidberger, Henrik Widmark, Lara Nascimento-Brooks, Annette Kahlig

Polyplus Transfection  
Sartorius

2021

Request from your Sartorius representative. Celum ID 109507



## Webinar - The Concept of Upstream Scaling: From Theory to Practice

Vincent Lam, Sherwin Ting, Sinyee Yau-Rose

Sartorius

2020

<https://www.sartorius.com/en/pr/webinar-the-concept-of-upstream-scaling-from-theory-to-practice>



## A Novel, Risk-Based Approach for Predicting the Optimum Set of Process and Cell Culture Parameters for Scaling Upstream Bioprocessing

Adrian Stacey, Jochen Scholz, and Sinyee Yau-Rose

Sartorius

2020

Request from your Sartorius representative. Celum ID 114923



## A Rapid, Low Risk Approach for Process Transfer of Biologics From Development to Manufacturing Scale

Sebastian Ruhl, Naomi de Almeida, Melisa Carpio, Jens Rupprecht, Gerhard Greller, Jens-Christoph Matuszczyk

Sartorius

2020

<https://bioprocessintl.com/upstream-processing/upstream-single-use-technologies/biostat-str-bioreactors-a-rapid-low-risk-approach-process-transfer-of-biologics-from-development-to-manufacturing-scale/>

**“Using the new scale-conversion tool, miniature and multiparallel bioreactors for process development, and a three-step pilot-to-manufacturing scale-up approach potentially enables faster and cost-effective manufacturing of biologics in fed-batch cell cultures.”**



## Multivariate Data Analysis Methodology to Solve Data Challenges Related to Scale-Up Model Validation and Missing Data on a Micro-Bioreactor System

Stephen Goldrick, Viktor Sandner, Matthew Cheeks, Richard Turner, Suzanne S. Farid, Graham McCreath, Jarka Glassey

University College London, Gower Street, London, WC1E 6BT UK  
FUJIFILM Diosynth Biotechnologies, Process Design and Data Science, Belasis Ave, Stockton-on-Tees, Billingham, TS23 1LH, UK  
MedImmune, Cambridge, CB1 6GH, UK  
Newcastle University, Newcastle upon Tyne, NE1 7RU, UK

2019

<https://doi.org/10.1002/biot.201800684>

# Working With Scale Down Models



## **A Protocol to Transfer a Fed-Batch Platform Process into Semi-Perfusion Mode: The Benefit of Automated Small-Scale Bioreactors Compared to Shake Flasks as Scale-Down Model**

Sabrina Janoschek, Markus Schulze, Gerben Zijlstra, Gerhard Greller, Jens Matuszczyk

Sartorius

2018

<https://doi.org/10.1002/btpr.2757>

**“The benefit of the automated small-scale bioreactor as scale-down model was clearly shown compared to the shake flasks.”**



## **Scale-Down Model Development in Ambr systems: An Industrial Perspective**

Viktor Sandner, Leon P. Pybus, Graham McCreath, Jarka Glassey

FUJIFILM Diosynth Biotechnologies, Belasis Avenue, Billingham, TS23 1LH, United Kingdom

University of Newcastle, Newcastle Upon Tyne, NE1 7RU, United Kingdom

2018

<https://doi.org/10.1002/biot.201700766>

**“...qualified Ambr® could be utilized to start process characterization studies much earlier (during cell line selection and process optimization) and speed up the development life-cycle of today’s drug manufacturing process.”**



## **Development of an N-1 Perfusion Process and Optimized Scale-Down Models for Implementation in a Platform CHO Cell Culture Manufacturing Process**

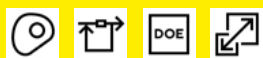
Frank V. Ritacco, Yongqi Wu, Luzmary Sabino, Mina Chaudhry, Tim Erlandson, Joon Chong Yee, Anurag Khetan, Zhengjian Li

Bristol-Myers Squibb, Devens, MA, and Hopewell, NJ, USA

2017

[https://dc.engconfintl.org/biomanufact\\_iii/21/](https://dc.engconfintl.org/biomanufact_iii/21/)

# Working With Scale Down Models



## Application of High-Throughput Mini-Bioreactor System for Systematic Scale-Down Modeling, Process Characterization, and Control Strategy Development

Vijay Janakiraman, Chris Kwiatkowski, Rashmi Kshirsagar, Thomas Ryll, Yao-Ming Huang

Biogen, Inc., Research Triangle Park, NC, 27709 Biogen, Inc., Cambridge, MA, 02142

2015

<http://doi.org/10.1002/btpr.2162>

**“The resulting control strategy generated from the Ambr® system was comparable to the bench scale bioreactors, and confirmed the utility of the Ambr® 15 system for process characterization studies and control strategy development.”**



## The Physical Characterization of a Microscale Parallel Bioreactor Platform With an Industrial CHO Cell Line Expressing an IgG4

Alvin W. Nienow, Christopher D. Reilly, Kathryn Brosnan, Neil Bargh, Kenneth Lee, Karen Coopman, Christopher J. Hewitt

Loughborough University, Leicestershire LE11 3TU, UK, University of Birmingham, B15 2TT, UK Sartorius

2013

<https://doi.org/10.1016/j.bej.2013.04.011>



## Steady State and Dynamic Control Performance of the ambr Automated Micro Bioreactor System in a CHO Cell Batch Culture

Sin Yee Yau Rose, Kenneth Lee, Barney Zoro

Sartorius

2011

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## Changes to Culture pH and Dissolved Oxygen Can Enhance CAR T-Cell Generation and Differentiation

Rodrigo Lamas, Robert Ulrey, Sanjeev Ahuja, Alex Sargent

MedImmune LLC, One MedImmune Way, Gaithersburg, MD

2022

<https://doi.org/10.1002/btpr.3275>

**“We used the automated mini-bioreactor (Ambr®) 15 platform to assess how differences in pH and DO affect CAR T-cell transduction, proliferation, and differentiation.”**



## Scalable MSC Suspension-Based Process Adaptation and Optimization in Ambr® 15 Cell Culture Microbioreactors Using DOE

Namitha Haridas, Alison Rees-Manley, Erik Johansson, Alexander Tappe, Ashok Mundrig, Julia Hupfeld

Sartorius

2021

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**“The Ambr® 15 Cell Culture bioreactor system in combination with MODDE® DOE software allows rapid screening of different MC and media combinations.”**



## Webinar: Single-use Technologies for Viral Vector Production

Lara Nascimento-Brooks, Franziska Bollmann

Sartorius

2021

<https://www.icheme.org/membership/communities/special-interest-groups/biochemical-engineering/events/03-02-21-single-use-technologies-for-viral-vector-production/>



## Optimized Suspension-Based Production of Lentiviral Vectors with a DOE Approach

Franziska Bollmann

Sartorius

2020

<https://doi.org/10.1089/gen.40.12.14>



## Demonstrating Scalable T-Cell Expansion in Stirred-Tank Bioreactors

Alex Klarer, David Smith, Ryan Cassidy, Thomas Heathman, Qasim Rafiq

Hitachi Chemical Advanced Therapeutics Solutions, Allendale, NJ  
Sartorius

2018

<https://bioprocessintl.com/manufacturing/cell-therapies/demonstrating-scalable-t-cell-expansion-in-stirred-tank-bioreactors/>

**“The results of this study demonstrate that a stirred-tank bioreactor system could be used for more efficacious T-cell expansion and reduced cost of goods with shortened culture periods.”**



**Process Development of Human Multipotent Stromal Cell Microcarrier Culture Using an Automated High-Throughput Microbioreactor**

Qasim A. Rafiq, Mariana P. Hanga, Thomas R. J. Heathman, Karen Coopman, Alvin W. Nienow, David J. Williams, Christopher J. Hewitt

University College London, Gower Street, London, WC1E 6BT, United Kingdom, Aston University, Aston Triangle, Birmingham B4 7ET, United Kingdom, Loughborough University, Leicestershire LE11 3TU, United Kingdom, PCT, A Hitachi Group Company, Allendale, New Jersey School of Chemical Engineering, University of Birmingham, Edgbaston, Birmingham, United Kingdom

2017

<https://doi.org/10.1002/bit.26359>

**“The findings of this study demonstrate that the Ambr® 15 microbioreactor is an effective tool for bioprocess development of hMSC microcarrier cultures and that a combination of serum-free medium, control and automation improves both process yield and consistency.”**



**Embryoid Bodies and the Ambr® 15: Improving Expansion of Pluripotent Stem Cells in Stirred Tank Reactors**

Rhys Macown, Isabel Uwagboe, Shai Senderovich, Davide Grandolfo, Moira Francois, Evangelia Rologi, Nicole Nicholas, Mark Bell, Garikai Kushinga, Ilaria Schena, Beata Surmacz-Cordle, Damian Marshal, Marc-Oliver Baradez, Sarah Callens, Ricardo P. Baptista

Cell and Gene Therapy Catapult, 12th Floor, Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT

2016

<https://ct.catapult.org.uk/sites/default/files/publication/Improving%20Expansion%20of%20Pluripotent%20Stem%20Cells%20in%20Stirred%20Tank%20Reactors%20-%20Rhys%20Macown.pdf>



**Production of Erythrocytes From Directly Isolated or delta1 Notch Ligand Expanded CD34<sup>D</sup> Hematopoietic Progenitor Cells: Process Characterization, Monitoring and Implications for Manufacture**

Katie E. Glen, Victoria L. Workman, Forhad Ahmed, Elizabeth Ratcliffe, Adrian J. Stacey, Robert J. Thomas

Loughborough University, Loughborough, Leicestershire, UK, Sartorius

2013

<https://doi.org/10.1016/j.jcyt.2013.04.008>



## A Novel Automated Bioreactor for Scalable Process Optimization of Haematopoietic Stem Cell Culture

Ratcliffe E, Glen K.E., Workman V.L., Stacey A.J., Thomas R.J

Loughborough University,  
Loughborough, Leicestershire,  
LE11 3TU, UK

Sartorius

2013

[https://doi.org/10.1016/j.jbio-  
tec.2012.06.025](https://doi.org/10.1016/j.jbio-tec.2012.06.025)

**“This system will be valuable for the further HSC suspension culture cost reduction and optimization necessary before the application of conventional stirred tank technology to scaled manufacture of HSC derived products.”**



## Bioreactor Design and Bioprocess Controls for Industrialized Cell Processing

John E. Hambor

The Cell Therapy Group

2012

[https://bioprocessintl.com/  
upstream-processing/upstream-  
single-use-technologies/bioreactor-  
design-and-bioprocess-controls-for-  
industrialized-cell-processing-331147/](https://bioprocessintl.com/upstream-processing/upstream-single-use-technologies/bioreactor-design-and-bioprocess-controls-for-industrialized-cell-processing-331147/)

**“Until TAP Biosystems introduced its Ambr® system, the minimal volume required for experiments was quite large, demanding higher starting cell numbers and increasing the costs associated with optimization studies.”**



## Assessment of Ambr® as a Model for High-Throughput Cell Culture Process Development Strategy

Sarath Moses, Matthew Manahan,  
Alexandre Ambrogelly, Wai Lam W. Ling

Merck Research Laboratories, Union,  
USA

2012

<https://doi.org/10.4236/abb.2012.37113>

**“The results indicate that the Ambr® system can be used to streamline the process development effort and facilitate a rapid and robust cell culture process development effort for mAb programs in a HTP manner.”**



## Novel Platform Technologies for Scaled Down Process Development and Optimization for Regenerative Medicine

Alison Rees-Manley,, Barney Zoro

Sartorius

2013

Request from your Sartorius  
representative. Celum ID 64199



## Stem Cell Production: Overcoming the Technical and Commercial Challenges

Dave Thomas

Sartorius

2012


[http://www.iptonline.com/articles/  
public/TAPBiosystems.pdf](http://www.iptonline.com/articles/public/TAPBiosystems.pdf)

**Germany**

Sartorius Stedim Biotech GmbH  
August-Spindler-Strasse 11  
37079 Goettingen  
Phone +49 551 308 0

**USA**

Sartorius Stedim North America Inc.  
565 Johnson Avenue  
Bohemia, NY 11716  
Toll-Free +1 800 368 7178

 For further contacts, visit  
[www.sartorius.com](http://www.sartorius.com)