Experimental and Computational Fluid Dynamics Studies of Adherent Cells on Microcarriers in an ambr® 250 Bioreactor

Marco C. Rotondi1,2, Alvin W. Nienow1,3, John P. J. Betts1, A. Neil Bargh1, Ned Grace1, Barney Zoro1, Mariana P. Hanga2, Christopher J. Hewitt2, Qasim A. Rafiq1,4

1 Aston Medical Research Institute, School of Life and Health Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, UK. 2 Sartorius-Stedim, York Way, Royston, Hertfordshire SG8 5WY, UK. 3 University of Birmingham, Birmingham B15 2TT, UK. 4 Department of Biochemical Engineer, University College London, Gower Street, London, WC1E 6BT. For further information please contact: Royston-Info@sartorius.com. June 2018

Introduction

Interest in microcarriers-based processes for large-scale culture of adherent cells has grown due to increasing attention towards vaccine and cell therapy applications. This opportunity allows the need for effective, high-throughput, single-use, process development tools that can be transferred successfully into industrial-scale operations. The Sartorius ambr® 250 platform is one such technology, operating at a volume between 150 – 250 mL, is both high throughput and single-use. The ambr® 250 high throughput platform has been shown to be suitable for microcarrier-based processes for the culture of adherent cells.

The fluid dynamic characteristics of the stirred ambr® 250 bioreactor must be understood sufficiently to enable efficient scale-up to larger bioreactors, particularly because of the special issues arising from the presence of the solid phase.

In this work some R&D prototype vessels are investigated for adherent microcarrier cell culture. The prototypes are characterized by different impellers and the vessel can be baffled or unbaffled.

Process

• ambr® 250 high throughput
• Elephant ear impeller at 115 rpm

Biological Characterization

• Viable cell density: x10^-5 cells/mL

Methodology

• Biological characterization: cell culture with Vero cells on microcarriers.

Computational Characterization

• Eulerian-Eulerian CFD simulation, steady state, single liquid phase, solid microcarriers, unbaffled and baffled vessel

Conclusions

• Physical characterization of different ambr® 250 high throughput BM4 prototypes vessels with microcarriers, to determine power number, energy per unit volume. Reynolds number, minimum suspension speed, Reynolds number scale.

• Biological characterization: cell culture with Vero cells on Culture Duration (days)

References

• Axial flow: 250 h, 2000 rpm, Baseline

• Viable cell density 2.5x10^5 cells/mL, Cytodex 1: 2.0 g/L

• Viable cell density 2.0x10^5 cells/mL, Cytodex 1: 1.0 g/L

• Viable cell density 1.5x10^5 cells/mL, Cytodex 1: 0.5 g/L

Acknowledgments

Many thanks to Innovate UK for the financial contribution to this project.