

Spring 5-11-2016

# A holistic approach to the scale-up of a microcarrier-based perfusion cell culture process for the production of a therapeutic enzyme

Jin Yin

Genzyme, jin.yin@genzyme.com

Follow this and additional works at: [http://dc.engconfintl.org/cellculture\\_xv](http://dc.engconfintl.org/cellculture_xv)



Part of the [Biomedical Engineering and Bioengineering Commons](#)

---

## Recommended Citation

Jin Yin, "A holistic approach to the scale-up of a microcarrier-based perfusion cell culture process for the production of a therapeutic enzyme" in "Cell Culture Engineering XV", Robert Kiss, Genentech Sarah Harcum, Clemson University Jeff Chalmers, Ohio State University Eds, ECI Symposium Series, (2016). [http://dc.engconfintl.org/cellculture\\_xv/146](http://dc.engconfintl.org/cellculture_xv/146)

This Abstract is brought to you for free and open access by the Proceedings at ECI Digital Archives. It has been accepted for inclusion in Cell Culture Engineering XV by an authorized administrator of ECI Digital Archives. For more information, please contact [franco@bepress.com](mailto:franco@bepress.com).

# **A HOLISTIC APPROACH TO THE SCALE-UP OF A MICROCARRIER-BASED PERFUSION CELL CULTURE PROCESS FOR THE PRODUCTION OF A THERAPEUTIC ENZYME**

Jin Yin

Late Stage Process Development, Genzyme, A Sanofi Company

Jin.Yin@genzyme.com

Ben Wright, Late Stage Process Development, Genzyme, A Sanofi Company

Tom Hayes, Late Stage Process Development, Genzyme, A Sanofi Company

Armin Opitz, Network Manufacturing Sciences and Technology, Genzyme, A Sanofi Company

Shikha Kaji, Network Manufacturing Sciences and Technology, Genzyme, A Sanofi Company

Yogesh Waghmare, Late Stage Process Development, Genzyme, A Sanofi Company

Zheng Huang, Network Manufacturing Sciences and Technology, Genzyme, A Sanofi Company

Claudia Buser, Late Stage Process Development, Genzyme, A Sanofi Company

Chris Hwang, Late Stage Process Development, Genzyme, A Sanofi Company

Key Words: scale-up, microcarrier, computation fluid dynamics (CFD) simulation

This case study describes our holistic approach of scaling up a microcarrier-based perfusion cell culture process for the production of a therapeutic enzyme directly from a 12L benchtop glass bioreactor to a commercial scale stainless steel bioreactor. Besides conventional scale-up challenges such as mixing, shear stress and mass transfer, the scale-up of this microcarrier-based cell culture process posed its own challenges, e.g. the original design of the commercial scale stainless steel bioreactor had difficulty suspending microcarriers. Additional challenges included achieving effective cell attachment after seeding, balancing microcarrier stratification and culture turbulence, and minimizing bubble shear stress and foaming. To mitigate risks and maximize the chance of success in scaling up this process within an aggressive project timeline, we carried out a series of studies to systematically tackle these challenges.

First, physical modifications necessary to adapt the existing commercial scale stainless steel bioreactor for this microcarrier-based cell culture process, e.g. impeller, baffle and sparger designs, were implemented based on computation fluid dynamics (CFD) simulation, high speed imaging, and at scale bioreactor characterization. Second, 12L small scale bioreactor studies were performed in concert with simulation and mathematical modeling to define operating ranges for scale-dependent parameters for the commercial scale bioreactor. Third, strategies to mitigate potential negative effects of scale-dependent parameters on the commercial scale process such as stratification, turbulence and foaming were established and tested at the 12L scale.

Through our systematic work using CFD simulation, mathematical modeling, bioreactor characterization, and small scale bioreactor experimentation, we were able to achieve comparable bioreactor performance including product quality in the first large scale run; this allowed us to meet an accelerated project timeline.