

Preface

Mammalian cells have now become common cell hosts for the production of biologics, and more than 50 % of approved recombinant protein therapeutics currently on the market are being manufactured in mammalian cell lines. Since the approval of Orthoclone OKT3 (the first biologic drug to be produced in mammalian cells) in 1986, routine titers, cell-specific productivities, and cell densities have increased dramatically. These improvements have been the result of decades of developmental work in multiple areas, including cell line development, process operations, and equipment.

This volume was put together to highlight the progress in using mammalian cell cultures for the manufacture of therapeutic biologics. It consists of ten chapters which provide an overview of biologics development and manufacturing in mammalian cell cultures. The first chapter entitled “[Mammalian Cell Cultures for Biologics Manufacturing](#)” provides an overview of licensed therapeutic biologics currently on the market, including details on market size, as well as commonly used production cell lines and cell culture operation modes. The second chapter entitled “[Mammalian Cell Line Developments in Speed and Efficiency](#),” provides an overview of the cell line development process, including host cell line selection, available expression systems, and commonly used selection strategies. In the third chapter “[Cell Culture Process Operations for Recombinant Protein Production](#),” an overview of current operation models for mammalian cell culture is presented, including batch, fed-batch, and perfusion processes. Details regarding process monitoring and control, including data analysis, are also included. The fourth chapter, entitled “[Equipment for Large-Scale Mammalian Cell Culture](#),” provides an overview of the commonly used equipment in industrial mammalian cell culture, with an emphasis on bioreactors. This chapter also provides insight into the use of disposables during seed train and production.

The next chapter, entitled “[Development and Characterization of a Cell Culture Manufacturing Process Using Quality by Design \(QbD\) Principles](#)” provides a case study of the application of quality by design principles during late stage process development. In the sixth chapter, “[Product Quality Considerations for Mammalian Cell Culture Process Development and Manufacturing](#),” a review of common product quality consideration in mammalian cell culture is provided. This chapter also includes a summary of the impact of cell culture conditions on product quality, and current strategies to control product quality profiles.

An overview of testing of adventitious agents is provided in the next chapter, entitled “[Safety Assurance for Biologics Manufactured in Mammalian Cell Cultures: A Multitiered Strategy](#).” In this chapter, a general overview of the tiered safety strategy commonly employed by the biopharmaceutical industry to mitigate adventitious agent contamination is presented. The eighth chapter, entitled “[Mammalian Cell Culture Capacity for Biopharmaceutical Manufacturing](#),” provides an overview of the current global manufacturing capacity and an analysis of market trends that will impact the future manufacturing expansions and utilization. The ninth chapter, entitled “[Transcriptomics as a Tool for Assessing the Scalability of Mammalian Cell Perfusion Systems](#),” provides a case study of the use of transcriptome analysis in mammalian cell culture process development. The final chapter, “[Lifecycle Management for Recombinant Protein Production Using Mammalian Cell Culture Technology](#),” provides a case study for product lifecycle management.

In summary, this volume represents a comprehensive overview of biologics manufacturing in mammalian cell lines, and includes a number of relevant industrial case studies. While it is inevitable that certain topics or areas were omitted from this volume, the authors have sought to provide extensive references to additional sources of information. We hope this volume will provide readers with a concise summary of state-of-the-art practices in the industry and an overview of the current challenges faced by biologics manufacturers. The editors would like to thank all of the contributors to this volume, the series editor and the publisher, who have made this volume possible.

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