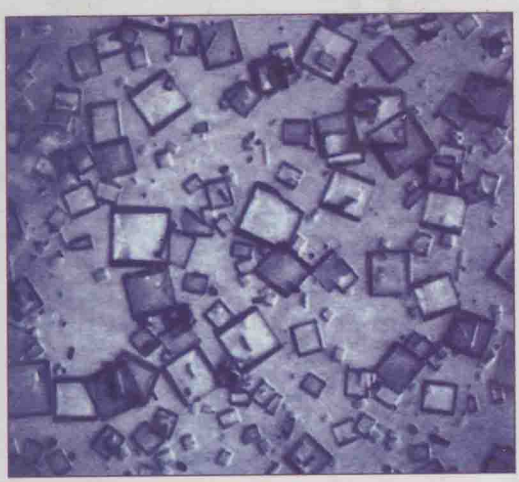
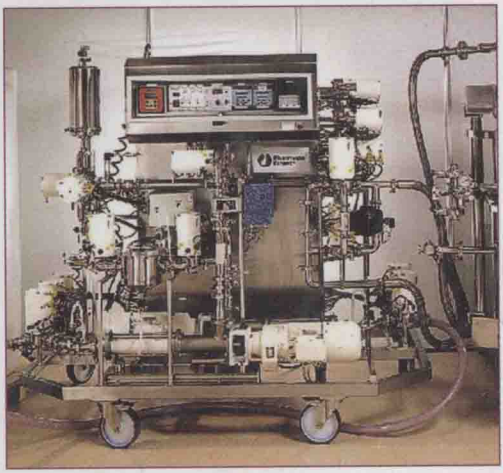
Advanced Technologies in Biopharmaceutical Processing

Roshni L. Dutton
and
Jeno M. Scharer





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ADVANCED TECHNOLOGIES IN BIOPHARMACEUTICAL PROCESSING

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PREFACE

In 2004 a United States Food and Drug Administration (FDA) white paper regarding the analysis of the biopharmaceutical pipeline[1] noted an unexpected decline in the number of new biopharmaceuticals reaching patients (US FDA, 2004) despite the exponential growth in drug discovery. This slowdown of drug submissions to regulatory agencies seems to be worldwide. The paper concluded that the "medical product development process is no longer able to keep pace with basic scientific innovation. Only a concerted effort to apply the new biomedical science to medical product development will succeed in modernizing the critical path." The gap between bench-scale drug discovery and manufacture is spreading. This is due, in part, to the shortage of scientists and engineers specializing in process development and manufacturing. Therefore, besides basic science, "scientific creativity and effort must also focus on improving the medical product development process itself".[1]

This book provides a complete overview of advanced and emerging biopharmaceutical manufacturing technologies—from the bioproduction system to the final dosage presentation—that will appeal to both novice technical staff with little or no previous background in manufacturing and biopharmaceutical professionals with expertise in only one or two production areas. The various chapters, written by practicing scientists and engineers in the field, encompass product and process development, production and production-step integration, and regulatory issues. The chapters reflect the authors' experience—the successes as well as the pitfalls to be avoided. They provide real-life, first-hand examples through case studies.

Only a handful of books are available today that address issues related to biopharmaceutical manufacturing, and most of them are focused on a single aspect of the subject, such as purification or regulatory compliance. The most notable exception is a detailed, four-volume treatise of biopharmaceutical development and manufacturing by Knablein[2] that was published in 2005.

[1]US Department of Health and Human Services, US Food and Drug Administration (2004). Challenge and Opportunity on the Critical Path to New Medical Products.

[2]Knablein, J. (editor, 2005). Modern Biopharmaceuticals: Design, Development and Optimization. John Wiley and Sons.

Advanced Technologies in Biopharmaceutical Processing thus provides a unique, up-to-date and comprehensive synopsis of biopharmaceutical manufacturing. It provides a starting point for the identification of technologies and potential problems, and offers simple, tried-and-proven solutions. The book is organized into nine chapters. Each chapter addresses a unique aspect of biopharmaceutical manufacturing and presents the best current information—ranging from current practice to emerging platforms and technologies. This book complements more detailed treatments of the subjects covered here—from genomics to cell therapy—and the reader is guided to those other publications through extensive bibliographies.

Roshni L. Dutton
Jeno M. Scharer
Editors

FOREWORD

I would first like to thank the editors, Drs. Roshni Dutton and Jeno Scharer, for the incredible effort they have put into planning, organizing and editing this extremely valuable reference book. In addition, I'd like to acknowledge the authors of the various chapters for pouring their hard-earned knowledge into what will surely be a well-referenced text for many years to come.

This book provides an anthology of information in essentially all area of bioprocessing, from genomics to final fill and finish, while it weaves the crucial elements of regulatory compliance throughout each step in the process. Though other texts have excelled in their coverage of more narrowly focused aspects of bioprocessing, this text provides a comprehensive approach to biopharmaceutical manufacturing that has been sorely needed.

The biopharmaceutical industry is starting to mature in its ability to produce certain product types, such as antibodies and recombinant proteins, but the nature of biologics makes development and production an art form with a continuing need for innovation and improvement. More novel products, such as those used for cell and gene therapy, will remain quite challenging for many years to come. They are harder to make and deliver with the desired functionality, plus they are much harder to characterize. This book provides essential information on proven techniques that can make the evolutionary art form of biologic manufacturing more manageable.

As analytical techniques become more powerful and produce more meaningful data, we learn more and more about the products and the raw materials used to make them. And the more we know, the more we need to learn about what makes them work and how we can produce them consistently. Heterogeneity is expected and may have a significant role in making the product work. Therefore, it may not be advisable to improve the purity of a product beyond a certain point. What matters are robust processes that can be validated and repeated, and products that are known to be consistently safe and effective. I feel the authors have provided a detailed roadmap for approaching these matters.

Product discovery techniques are also becoming increasing powerful, and the process development effort is being swamped with an ever-increasing number of product candidates. The key will be development strategies that give satisfactory results, but quickly produce enough product to keep the

pre-clinical and early clinical work moving. Then, the hope will be that the vast majority of the products fail early, so that time will be available to develop an even better process for product candidates that will move foreword. Process changes will become commonplace with later-stage clinical and licensed products, but the characterization data must sufficiently correlate with clinical outcome and show that the product has not changed in any meaningful way. Bridging several chapters, this text does an excellent job of covering these concepts.

Manufacturing and development capacity will always be a problem, and most firms will either have far too much or not enough. The key will be building flexibility into the facility and processing techniques, developing strategic relationships with the right partners, and learning how to effectively use outside services. Multiple products will have to be produced in the same facility, and the industry will continue to move toward the use of single-use, product-contact components as the cost of cleaning, and the risk of cross-contamination, will be too high.

I know you will enjoy this book and find its information to be highly valuable for your work. Whether you are a beginner in this field or a seasoned veteran, this text will give you the reference material you need to successfully develop and produce biologics, while satisfying regulatory requirements.

Keith L. Carson

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