Preface

It is now more than 15 years ago when the first edition of the book 'Mammalian Cell Biotechnology in Protein Production' was published. At that time, realization of the book was driven by the requirements of academia and industry working on cell-based research and production processes to intensify their biological and technological understanding for bringing their inter-disciplinary knowledge to an applicable know-how and for using their technological capacities to an all-embracing capability.

During the last 20 years the biopharmaceutical market showed a substantial growth and can be described as the age of blockbusters. While at the beginning drugs dominated targeting genetic defects (Antithrombin III or Factor VIII), more and more therapeutics for treatment of cancer, cardiovascular, immunological and neurological diseases have been produced. However, treatment of diseases with a broad diversity and physiological dependency on the genetic background of the host is less predictable. As a consequence, not all patients benefit from blockbusters. Current clinical research increasingly reveals information about the molecular basis of these diseases, especially through reliable omics data. Patient stratification methods lead to a facilitated prediction if a certain drug will be effective or if it is better not used. This generates the "virtual patient" and asks for individualized medicines, leading to reduced use of blockbusters and request for a diversification of medications, even if they are only of interest for smaller patient groups. Thus, the next decade will be characterized by more sophisticated direct-to-consumer distribution channels which will diminish the role of wholesalers. The blockbuster sales model will be more and more replaced by products or combinations of drugs that are primarily focused on specialized medication and treatment procedures.

Meanwhile, industry was able to develop new products of the second and third generation and launched the so-called biosimilars that allow companies to rely, at least in part, on the safety and efficacy data of the reference brand product. Increases in knowledge and the more rational approach to drug discovery have contributed to the discovery of many important new classes of biopharmaceuticals but the costs for licensing a product constantly increased and amounts up to more than 1 billion USD.

The regulatory authorities have continuously strengthened their rules and guidelines. This concern not only the quality of the production process and the product, it also influences the average number of patients enrolled in clinical trials. While in 1970 approximately 2,000 individuals were needed for approval of a certain drug, more than 5,000 have been requested in 1990.

Today, the research and development process typically spans more than a decade and still remains subject to considerable risk and uncertainty. This is reflected by the low probability of success. In 2010, Ernst and Young presented an estimation of 5,000 products in phase I/II development and another 20,000 products in preclinical development. This reflects the failure rate in this step. The high number indicates the potential revenues but as well the requirement for new drugs as stated above. Also,

the high number requests cheaper, faster and more efficient procedures to obtai clinical trial materials. The capacity to develop manufacturing processes in a com petitive time period is often not available at the critical phase and the flexibility o the facility is missing. New cheaper and flexible production facilities are necessar to satisfy the increasing demand. At the same time, the considerable increase in th number of new drug candidates, their use in individualized medicine leads to a reduc tion of the manufacturing volume forcing companies to leave their established route and set up flexible facilities.

While the above considerations concern recombinant proteins, mainly antibo dies, gene and cell therapies represent a new class of drugs that have the potentia for cure. As of 2012, over 2,030 clinical gene therapy trials for human and anima health have to be completed or have been ongoing. Around 200 companies are invol ved in developing gene therapeutics and their number increased 4-fold during th last decade.

The new book encompasses the major aspects for the development and manu facturing of biopharmaceuticals and cell-based processes ranging from the genetic molecular and cellular issues up to the final product. It is mainly directed to th expression and production of proteins and builds bridges to other biologics lik those based on viral genomes. All these therapeutics have particular requirement on purity, potency and safety with tight specification ranges guaranteed by robus processes of highest efficiency run under cGMP conditions. The book also addresse researchers in industry and academia that need higher amounts of recombinant pro teins from animal cells for functional tests and structural investigation.

The chapters have been written by outstanding experts in the respective biotech nological areas. The content is aimed at students interested in the blooming field o protein and virus-based biotechnology for the development and manufacturing o biotherapeutics and at researchers working in this scientific field in academics an industry as well as at all scientists interested in specific aspects of the applied anima cell culture-based biotechnology.

Berlin, in March 2014 *Hansjörg Hauser and Roland Wagner*