## **Contents**

	face — V
List	of Contributing Authors —— IX
1	introduction —— 1
1.1	Industrial Use and Perspectives of Animal Cell Culture —— 1
2	Cell Lines —— 11
2.1	Generation of Cell Lines and Biotechnological Applications —— 11
2.2	CHO History, CHO Evolution and CHO Genomics –
	an Unsolvable Enigma? —— 38
2.3	Cell Lines for Vaccine Production —— <b>60</b>
2.4	Cell Line Monitoring: Molecular Cytogenetic Characterization —— 87
2.5	Quality Control Essentials in Human Cell Culture:
	Cell Line Cross-contamination and Microbiological Infections —— 10
3	Genetic Engineering of Cells —— 115
3.1	Cell Line Evolution and Engineering —— 115
3.2	Chromosome Rearrangements and Gene Amplification —— 127
3.3	Synthetic Biology Principles for Engineering Mammalian
	Designer Cells —— 144
3.4	Rational Approaches for Transgene Expression:
	Targeted Integration and Episomal Maintenance —— 173
3.5	Manipulation of Cell Growth, Metabolism
	and Product Quality Attributes —— <b>216</b>
4	Engineering of the Product —— 247
4.1	Control of Biotheraputics Glycosylation —— 247
4.2	Manufacturing of Complex Biotherapeutic Protein Products:
	Medical Need and Rational for Monoclonal Antibody Mixtures,
	Multispecific Formats, and Fc-fusion Proteins —— 280
5	Basic Aspects of Animal Cell Cultivation —— 301
<b>5.1</b>	Physiology and Metabolism of Animal Cells for Production —— 301
5.2	Functional -Omics for Cell Lines and Processes:
	The -Omics Technologies on the Example of CHO Cells —— 326
5.3	Nutrient Media for Cell Culture Technology —— 368
6	Upstream and Downstream Process Technology —— 389
6.1	Bioreactors for Animal Cell Culture —— 389
6.2	High Cell Density Cultivation Process —— 427



1/11	•	_				_
VII	_		on	te	nt	S

6.3	Industrial Cell Culture Process Scale-up Strategies
	and Considerations —— 455

6.4 Extraction and Purification of Biologics from
Cell Culture: Monoclonal Antibody Downstream Processing — 489

## 7 Monitoring and Control of Processes and Products — 523

- 7.1 Concepts and Technologies for Advanced Process Monitoring and Control 523
- 7.2 Analytical Techniques and Quality Control of Protein Therapeutics 571
- 7.3 Process Characterization for Upstream and Downstream Process Development —— 598
- 8 Pharmaceutical Aspects of Biologics from Animal Cell Culture Processes 649
- 8.1 Spatiotemporally Controlled Delivery of Biopharmaceuticals 649

Index --- 693