

Table of Contents

1	Introduction	7
1.1	Background.....	7
1.2	Purpose and Scope	7
1.3	Key Concepts and Terms.....	9
1.4	Synopsis of Guide Chapters	12
2	Regulatory.....	15
2.1	Introduction	15
2.2	Regulatory Agencies, Directives, and Guidance.....	15
2.3	Process Definition, Critical Quality Attributes, and Critical Process Parameters	17
2.4	Risk Management and Risk Mitigation (Chapter 3)	18
2.5	Contamination Control (Chapter 4).....	20
2.6	Biosafety	20
2.7	Commissioning, Qualification, and Validation	24
3	Risk Management	25
3.1	Introduction	25
3.2	Benefits of Risk Management for Facility Design, Build, and Qualification.....	25
3.3	Risk Management Principles and Practices.....	26
3.4	Risk Management Tools and Techniques	31
4	Contamination Control Strategy.....	41
4.1	Introduction	41
4.2	Contamination.....	41
4.3	Contamination Control Strategy.....	46
5	Process Closure	53
5.1	Introduction	53
5.2	Process Zone.....	55
5.3	Impact of the Process Platform on Process Closure	57
5.4	Equipment and Components Used in Closed Systems	60
5.5	Points to Consider in Closed Process/System Validation	64
6	Operations.....	69
6.1	Introduction	69
6.2	Operations and GMPs	69
6.3	Appropriate Segregation of Bioprocess Operations.....	71
6.4	Operational Bioburden Control Measures.....	74
6.5	Mitigating the Risk of Contamination during Manufacture of a Biopharmaceutical Drug Substance	76
6.6	Impact of Open Processing on Operational Choices	77
6.7	Preparation and Assembly of Equipment for Closed Processing.....	78
6.8	Monitoring Operations.....	87
6.9	Supply Chain.....	90
7	GMP Layout Approaches.....	93
7.1	Introduction	93
7.2	Good Manufacturing Practices.....	94
7.3	Basics of Product CQAs and System CPPs	95
7.4	Environmental Grades	97
7.5	Primary Sources of Product Contamination.....	98
7.6	Segregation Application Concepts.....	99

7.7	Facility and GMP Flows	100
7.8	Production Corridor Concepts.....	101
7.9	Facility Conceptualization Tool.....	103
7.10	Airlock Concepts	105
7.11	Contract Production Considerations	113
7.12	Production Facility Configurations	113
7.13	Mix-Up Prevention	117
7.14	Facility Aspects of Equipment and Facility Cleaning.....	118
7.15	Clinical and Commercial Production	120
7.16	Vaccine and Biologic Hazard Facilities	121
7.17	Human Factors Considerations	122
8	Architectural Design	123
8.1	Introduction	123
8.2	Architectural Design Criteria	123
8.3	Early Phases: Alignment, Programming, and Concept Design.....	125
8.4	Site Design.....	131
8.5	Building Core and Shell	132
8.6	Codes, Permitting, and Insurance.....	133
8.7	Design and Delivery of Modular Facilities.....	134
9	Mechanical and Electrical Systems.....	137
9.1	Introduction	137
9.2	Mechanical Systems and Environmental Controls.....	138
9.3	HVAC Design as Part of a CCS	140
9.4	HVAC for Containment and Safety	141
9.5	General HVAC Design Practices for Biological Processes	144
9.6	Monitoring	156
9.7	Qualification of HVAC Systems.....	157
9.8	Cost Considerations for HVAC Systems.....	157
9.9	Cleaning and Maintenance of HVAC Systems.....	158
9.10	Fire Protection.....	159
9.11	Other Safety Concerns	159
9.12	Electrical	159
10	Sustainability	161
10.1	Introduction	161
10.2	Process/Facility Interface – Reducing Space and Energy Intensity.....	161
10.3	Process Sustainability.....	163
10.4	Raw Materials	164
10.5	Waste Management.....	165
10.6	Process Energy.....	166
10.7	Facility and Infrastructure.....	167
11	Appendix 1 – Conceptual Design Stage Gate Model	173
12	Appendix 2 – Sample Rooms List	175
13	Appendix 3 – References	177
14	Appendix 4 – Glossary	183
14.1	Acronyms and Abbreviations	183
14.2	Definitions	187