Contents

Foreword xiv
Book Audience xvi
Preface xvii
About the Author xviii
Acknowledgments xix
List of Abbreviations xx
Glossary xxiii

Chapter 1 The Case for Considering Biosecurity in Synthetic Biology 1

1.1 Overview of Synthetic Biology 2
1.2 The Emergence of Biosecurity Concerns 6
1.3 Notable Case Studies in Biomedical Synthetic Biology 10
1.4 Historical Biosecurity Incidents: Lessons and Consequences 11
1.5 Recent Accomplishments in Synthetic Biology and Biorisk Governance Updates 13
1.6 Scope and Objectives of This Book 18
1.7 Concluding Thoughts 19
1.8 Key Takeaways 20
1.9 Thought-Provoking Questions 20

Chapter 2 Synthetic Biology and Its Role in Biomedicine 22

2.1 Definitions and Key Concepts 23
2.2 Tools and Techniques in Synthetic Biology 24
2.3 Synthetic Tissues and Organs 30
2.4 Personalized Medicine 31
2.5 Other Advancements 32
2.6 Concluding Thoughts 33
2.7 Key Takeaways 34
2.8 Thought-Provoking Questions 34

Chapter 3 Biosecurity Risks in Synthetic Biology 35

3.1 Biosafety & Biosecurity: Differences and Commonalities 36
3.2 Potential Misuse and Dual-Use Concerns 39
3.2.1 Dual-Use Research of Concern (DURC) 40
3.2.2 The Potential Misuse of Synthetic Biology 40
3.2.3 Intellectual Property (IP) and Data Security 42
3.3 Threats Posed by Engineered Pathogens 44
3.4 The Risk of Organisms or Genetic Traits Escaping 45
3.4.1 Mitigation Strategies 46

3.5 Implications of Human Germline Editing 47
3.6 Unintended Consequences of Synthetic Biology in Biomedical Applications 49
3.7 Other Biosecurity Challenges in Synthetic Biology 50
3.7.1 Environmental Effects in the Context of "One Health" 50
3.7.2 Veterinary and Wildlife Effects of Synthetic Biology 51
3.8 Concluding Thoughts 52
3.9 Key Takeaways 52
3.10 Thought-Provoking Questions 53

Chapter 4 The Role of Artificial Intelligence (AI) in Synthetic Biology and Biosecurity Implications 54

4.1 AI Applications in Synthetic Biology 55
4.1.1 Application of AI Tools Used to Generate *de novo* Genes 56
4.1.2 Employing AI Tools for Modifying Gene Sequences 57
4.1.3 AI Applications in Gene Screening Prior to Manufacturing 58
4.1.4 AI-Assisted Vaccine Development 59
4.1.5 AI-Trained Library Screenings 61
4.1.6 Benefits of AI Modeling in Drug Screening 62
4.2 Using AI Tools to Manage and Mine Large Datasets 62
4.3 Using AI Tools for Public Health Surveillance 63
4.4 Incorporating AI in Comprehensive "One Health" Solutions 64
4.5 Vulnerabilities of Using AI Technology 65
4.5.1 Risks of Data and Intellectual Property Theft Using AI Technology 67
4.6 Unintended Consequences of AI Applications in Synthetic Biology 69
4.7 Biosecurity Gaps in AI Technology 70
4.8 Biosecurity Risk Assessment Guidelines for AI Use in Synthetic Biology 71
4.8.1 Step 1: AI Application and Its Contextual Risks 71
4.8.2 Step 2: Threats and Vulnerabilities 71
4.8.3 Step 3: Maturity and Automation Level 71
4.8.4 Step 4: Determine the Consequences 78
4.8.5 Steps 5–7: Mitigation, Monitor, and Review 78
4.9 Oversight Implications at a Global and National Scale 79
4.10 Legal and Ethical Considerations of AI Usage 83
4.11 Concluding Thoughts 86
4.12 Key Takeaways 86
4.13 Thought-Provoking Questions 87

Chapter 5 Global Regulatory Frameworks and Policies for Synthetic Biology.. 89

5.1 International Perspectives on Biosecurity 90
5.1.1 Biological and Toxin Weapons Convention (BTWC) 91
5.1.2 Cartagena Protocol on Biosafety 92
5.1.3 The Nagoya Protocol on Access and Benefit Sharing 92
5.1.4 World Health Organization (WHO) Laboratory Biosafety Manual 93
5.1.5 Consideration on the Status of International Efforts in Biosecurity 94
5.2 United States' Perspectives on Biosecurity 95
5.2.1 Legal Framework for Biosecurity: The United States' Prohibition of Biological Weapons 95
5.2.2 U.S. Department of Defense Biodefense Posture Review (BPR) 95
5.2.3 Biosafety in Microbiological and Biomedical Laboratories (BMBL) 96
5.2.4 The Ethics of Synthetic Biology and Emerging Technologies (2010) 97
5.2.5 NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules 98
5.2.6 Biodefense in the Age of Synthetic Biology Report 99
5.2.7 Consideration on Efforts in Biosecurity within the U.S. 100
5.3 Perspectives on Biosecurity Outside of the United States 101
5.3.1 The Canadian Biosafety Standard 101
5.3.2 The European Biosafety Network and the European Commission's Directorate-General for Health and Food Safety 102
5.3.3 African Union Biosafety and Biosecurity Initiative (AU-BBI) 103
5.3.4 Australia's Biosecurity Act 104
5.3.5 The Southeast Asia Strategic Biosecurity Dialogue 104
5.3.6 The Tianjin Biosecurity Guidelines for Codes of Conduct 105
5.3.7 Guidelines for Biosafety and Biosecurity in the Middle East and North Africa Region 106
5.3.8 The Brazilian Biosafety Network 107
5.3.9 Indian Council of Agricultural Research Guidelines & Agricultural Biosecurity Bill 108
5.3.10 Japan's Guidelines for Biosafety and Biosecurity in Laboratories 109
5.3.11 The Korean Virtual Biosecurity Center Guidelines 109

5.3.12 The Biosecurity Regime in Denmark 110
5.3.13 Argentina's Guidelines and Regulations for Biosafety and Biosecurity 111
5.3.14 Consideration on Efforts in Biosecurity Outside of the U.S. 111
5.4 Global Health Security 112
5.5 Concluding Thoughts 113
5.6 Key Takeaways 113
5.7 Thought-Provoking Questions 113

Chapter 6 Regulatory, Ethical, and Policy Considerations for Synthetic Biology 115

6.1 Current Regulatory Measures for Synthetic Biology 116
6.2 Ethical Guidelines and Institutional Oversight 116
6.3 Other Ethical Considerations 117
6.4 Equitable Access to Biosecurity Resources 118
6.5 Environmental Impact of Synthetic Biology 119
6.6 Intellectual Property Rights and Access to Technologies 120
6.6.1 Patents 120
6.6.2 Access and Benefit-Sharing 120
6.6.3 Open Science and Biohacking 121
6.6.4 Proprietary Technology and Access to Medicine 121
6.6.5 Ethics of Patenting Life 122
6.7 Recommendations for Policy, Research, and Education 122
6.7.1 Policy 122
6.7.2 Research 123
6.7.3 Education 124
6.8 Concluding Thoughts 124
6.9 Key Takeaways 124
6.10 Thought-Provoking Questions 125

Chapter 7 Biorisk Management in Synthetic Biology 126

7.1 WHO's "Biorisk Management – Laboratory Biosecurity Guidance" 127
7.2 CEN Workshop Agreement (CWA 15793) 127
7.3 ISO 35001:2019 Biorisk Management for Laboratories and Other Related Organizations 128
7.4 Artificial Intelligence-Aided Methods for Assessing Biosecurity Risks 129
7.5 Strategies for Containment and Prevention 130
7.6 Biosafety Protocols and Best Practices 132
7.7 Emergency Preparedness and Response 133
7.8 Biosecurity Incident Management 135
7.9 Institutional Biorisk Committees (IBCs) & Oversight 136
7.9.1 Institutional Biorisk Committees (IBCs) 136
7.9.2 Importance of Internal Review Process 137

7.10 Biosecurity Levels: Definition and Description 138
7.11 Best Practices for Laboratories & Research Institutions..... 149
7.12 Concluding Thoughts 157
7.13 Key Takeaways 157
7.14 Thought-Provoking Questions..... 158

Chapter 8 Developing a Synthetic Biology Laboratory Biosecurity Manual ... 159

8.1 The Laboratory Biosecurity Manual 160
8.2 The Role of International Organizations..... 162
8.3 Mandating a Risk Assessment in Federally Funded Research 163
8.4 Training in Biosecurity Principles..... 164
8.5 Collaborative Efforts to Increase Public Awareness..... 165
8.6 Technological Solutions to Manage Biorisks 166
8.7 Monitoring and Surveillance Technologies in Public Health 167
8.8 Concluding Thoughts 168
8.9 Key Takeaways 169
8.10 Thought-Provoking Questions..... 169

Chapter 9 Incorporating Human Factors in Biosecurity for Synthetic Biology.....171

9.1 Communication Breakdowns 172
9.2 Complacency 173
9.3 Unsafe Acts..... 173
9.4 Lack of Teamwork 174
9.5 Lack of Leadership..... 175
9.6 Inadequate Training 176
9.7 Lack of Resources 177
9.8 Lack of Standards..... 178
9.9 Stress..... 179
9.10 Fatigue 180
9.11 Human Error..... 181
9.12 Individual Differences..... 182
9.13 Mental/Emotional Health and Insider Threat to Biosecurity Best Practices 185
9.13.1 Promoting a Healthy Work Culture 185
9.13.2 Training and Awareness..... 187
9.13.3 Screening and Monitoring..... 188
9.13.4 Having Clear Policies and Procedures 189
9.13.5 Considering the "Glass Ceiling" Factor 190
9.14 Concluding Thoughts 192
9.15 Key Takeaways 192
9.16 Thought-Provoking Questions..... 193

Chapter 10 Implementation of Biosecurity Measures in Different Settings..... 194

10.1 Academic Setting 195
10.1.1 Large Research Universities..... 195
10.1.2 Small Colleges..... 195
10.2 Pharmaceutical Industry..... 196
10.2.1 Startups..... 196
10.2.2 Large-Scale Manufacturers..... 196
10.2.3 Vaccine Manufacturers 197
10.3 Military Labs..... 197
10.4 Government Labs 198
10.5 Clinical Studies Centers 199
10.6 Non-Profit Research Centers 200
10.7 Multinational Collaborative Centers 201
10.8 Garages, DIY Labs, iGEM Competitions, and High Schools..... 202
10.9 Concluding Thoughts 203
10.10 Key Takeaways 204
10.11 Thought-Provoking Questions..... 204

Chapter 11 Conducting a Biosecurity Risk Assessment..... 206

11.1 The Eight Biosecurity Priority Areas..... 207
11.2 Biosecurity Risk Assessment 213
11.3 The Five-Step Procedure for Conducting a Biosecurity Risk Assessment..... 213
11.4 Hypothetical Scenario – Conducting a Biosecurity Risk Assessment with *Shigella* sp..... 218
11.4.1 Risk Assessment Background Information: *Shigella* sp. 218
11.4.2 Biosecurity Risk Assessment for *Shigella* sp. 218
11.4.3 Biosecurity Concerns 224
11.4.4 Measures Taken to Address Biosecurity Concerns..... 225
11.5 Concluding Thoughts 225
11.6 Key Takeaways..... 226
11.7 Thought-Provoking Questions..... 226

Chapter 12 Promoting Responsible Conduct in Biomedical Synthetic Biology. 228

12.1 Education and Training for Scientists and Researchers 229
12.2 Weakness in Formal Education and Training Programs Regarding Biorisk Management..... 230
12.3 Collaboration and Information Sharing 231
12.4 Professional Codes of Conduct and Ethical Standards 232
12.5 Public Engagement and Stakeholder Involvement 233
12.6 Concluding Thoughts 234
12.7 Key Takeaways..... 234
12.8 Thought-Provoking Questions..... 235

Chapter 13 Ensuring a Safe Future in the Age of Synthetic Biology 236

13.1 Anticipating Future Research Directions and Challenges 237
13.2 Looking Ahead: Balancing Innovation and Security 238
13.3 Biosafety and Biosecurity in the Age of Space Exploration 239
13.4 Cyberbiosecurity in the Age of Synthetic Biology 241
13.5 Agricultural Biosecurity in the Age of Synthetic Biology 242
13.6 Global Call to Action: Ensuring Biosecurity in Synthetic Biology 243
13.7 Individual Call to Action: Ensuring Biosecurity in the Lab 244
13.7.1 Being Proactive in Biosecurity as a Synthetic Biologist 244
13.7.2 Ensuring the Biorisk Management in Your Labs, Research, and Data 244
13.7.3 Engaging in Continued Dialogue & Collaboration with Various Stakeholders 244
13.8 Concluding Thoughts 245
13.9 Key Takeaways 245
13.10 Thought-Provoking Questions 246

Afterword Notes 248

References 250

Index 261