Contents

Contributors xi
Preface xv
Acknowledgments xix

1. Introduction to vaccine development 1
Katherine E. Odneal
Vaccines: the greatest advancement of modern medicine 1
A brief historical review 2
The foundation of vaccine development 3
A summary of current strategies in vaccine development 4
Adjuvants 6
Summary 7
References 7

2. Overview of vaccine adjuvants 9
Rushit N. Lodaya, Sonia Gregory, Mansoor M. Amiji and Derek T. O'Hagan
Introduction 9
General classification of vaccine adjuvants 11
Specific types of adjuvants 13
Future considerations in the development of adjuvants 18
Conclusions 19
Trademark statement 20
References 20

3. Formulation design considerations and good practice for live attenuated vaccine development 27

Lee C. Smith and Paul Nelson

Introduction 27

Development of products with the end in mind 29

Development by design 34

Summary 76

References 76

4. Subunit-based vaccines: challenges in developing protein-based vaccines 79

Salvador F. Ausar, Nicholas R. Larson, Yangjie Wei, Akshay Jain and C. Russell Middaugh

Introduction 79

Similarities of vaccine proteins to therapeutic proteins 80

Pneumococcal protein-based vaccine development 82

Pneumococcal virulence factors 83

Licensed pneumococcal vaccines 84

Recombinant pneumococcal proteins as vaccine candidates 85

Alternative approaches for pneumococcal vaccines 91

Protective immunity against *Chlamydia trachomatis* 92

Chlamydia trachomatis vaccine candidates 93

Ricin vaccine candidates 101

NoV vaccine candidates 108

Clostridium difficile vaccine candidates 116

Acknowledgments 124

References 124

5. QbD approach to formulation development for protein-based vaccines 137
Malte Meppen and Daniela Stranges
Scope and challenges of protein bases formulation development 137
Quality by design as a guiding principle in vaccine formulation development 138
Preformulation studies 143
Formulation development and optimization studies 145
Conclusion 155
Acknowledgments 155
References 155

6. pDNA and mRNA vaccines 157
Kanwal Gill, Leanne Minall and Aslin Rodriguez Nassif
Introduction 157
Basic biology of pDNA and mRNA vaccines 162
Nucleic acid vaccine development 168
Process development; scalability and manufacturability 177
The future of nucleic acid vaccines 182
References 187

7. Antigen–adjuvant formulations—key considerations 207
Deep Bhattacharya, Chris Wiley, Aaron Latal and Vamsi Krishna
Introduction 207
Considerations for antigen–adjuvant compatibility 209
Drug product design and considerations for dose preparation and administration 215

Container closure 217
Lyophilization of antigen–adjuvant formulation considerations 219
Summary 222
References 223

8. Suspension properties and characterization of aluminum-adjuvanted vaccines 225
Alex Langford, Michael Bruchsaler and Manish Gupta
Introduction 225
Aluminum-containing adjuvant structure 231
Principles of suspension behavior 232
Properties and characterization 237
Considerations in vaccine development 254
Conclusion 260
References 260

9. Effect of shipping stresses on suspension vaccines 267
Jianxin Guo and Parag Kolhe
Introduction 267
Interplay between particle size, charge, and settling rate 268
Effect of shipping stress on thermodynamic suspension stability 271
Impact of individual shipping stresses on redispersion time 272
Mitigation strategy to reduce high redispersion time 276
Summary and recommendations 276
References 277

10. Control strategy development guide for vaccine drug product 279
Deep Bhattacharya and Parag Kolhe
Introduction to control strategy approach 279
Control strategy considerations 280
Application of control strategy concept 285
Raw material control strategy 293
Summary and considerations for control strategy 295
References 295

11. Lyophilized vaccine development 297
Nicole M. Payton, Rushit N. Lodaya and Adora M. Padilla
Introduction 297
Overview of lyophilization formulation and process 299
Vaccine-specific considerations 309
Considerations for lyophilization cycle scale-up 319
Summary 322
References 322

12. Conventional and nontraditional delivery methods and routes of vaccine administration 329
Roberta Antonia Diotti, Valeria Caputo and Giuseppe Andrea Sautto
The choice: the importance of the correct delivery system for an effective vaccination 329
Conventional delivery methods: subcutaneous and intramuscular route 330

Epidermis and dermis as new sites of vaccine delivery 334
Other areas of the body as targets for vaccine delivery 341
Conclusion 347
References 348

Index 357