### <sup>o</sup>Guide to Drug Development: a Comprehensive Review & Assessment

Bert Spilker

ISBN 9780781774246

#### **Contents**

About the Author xi Preface xiii Acknowledgments xv Abbreviations xvii

SECTION 1 - Introduction and Overview of a Company and the Industry

- 1 Introduction to Drug Development --- 3
- 2 Pharmaceutical Industry: Definitions --- 8
- 3 The Big Picture --- 15
- 4 Standards: Types, Uses, and Issues --- 34
- 5 Pharma-think, Academic-think, and

Government-think --- 45

6 Pharma Sense versus Common Sense --- 55

SECTION 2 - Basic Principles, Strategies, and Approaches

- 7 Overview of Factors Affecting Drug Discovery --- 61
- 8 The Drug Discovery Process --- 68
- 9 Golden Rules of Drug Discovery --- 97
- 10 The Drug Development Process --- 104
- 11 Golden Rules of Drug Development --- 114
- 12 Biotechnology --- 119
- 13 Extrapolating Animal Safety and Efficacy Data to Humans --- 132
- 14 Evaluating and Interpreting Data --- 143
- 15 Stimulating Innovation and Increasing Efficiency with the Right Questions, People,

Milieu, and Approaches --- 151

- 16 A New Paradigm of Drug Development --- 167
- 17 Future Environments for Drug Discovery and Development --- 172

SECTION 3 - Corporate Organization and Management Issues

- 18 Models of International Operations --- 183
- 19 Organization at the Corporate Level --- 191
- 20 Corporate Management --- 202
- 21 Reducing Pharmaceutical Risk --- 225
- 22 Enhancing Communication --- 231

23 Personnel and Staffing Issues 246
24 Competitive Intelligence 261
25 Conflicts of Interest and Bias 266
26 Crisis Management 280
27 Mergers, Joint Ventures, and Alliances 287
28 Pharmacopolitics 298
29 Institutional Memory 308
30 Differences among Pharmaceutical Companies 315
SECTION 4 - External Corporate Relationships and Interactions
31 Interactions and Relationships between Academicians and Industry 331
32 Investigator-sponsored Research Proposals Submitted to Industry 341
33 Technology Transfer from Academia to Industry 345
34 Interactions between Pharmaceutical Companies 349
35 Interactions with Trade Associations 354
36 Interactions with Legislators and Government Agencies 359
37 Interactions and Relationships with Healthcare Professionals 370
38 Interactions with Patients and the Public 374
39 Patient Package Inserts 384
40 Interactions and Relationships with the Media 391
SECTION 5 - Research and Development Organization, Management, and Assessments
41 Organizing Research and Development 401
42 Managing Research and Development and Avoiding Tangents 410
43 Personnel Issues in Drug Discovery and Development 429
44 Myths about the Pharmaceutical Industry and Drug Development 436
45 Fads and Fashions in Drug Development 441
46 The Many Facets of Reality: Approaches to Issues and Problems 446
47 International Organization and Management 451
48 Project Management: Balancing Line Function and Matrix Approaches 460
49 Choosing the Number and Types of Drugs to Develop 475
50 Choosing Standards for Developing Drugs 480
51 Creating and Using Benchmarks 489
52 Evaluating a Portfolio of Investigational Drug Projects 496
53 Compassionate Use Programs 529

54 Virtual Drug Development --- 533 55 Developing and Marketing Orphan Drugs for Rare Diseases --- 544 56 Productivity and Project Success --- 553 57 Overview of Safety and Risk Management --- 569 58 Developing Standard Operating Procedures --- 578 SECTION 6 - Clinical Activities and Issues 59 Introduction to Clinical Trials --- 589 60 Creating a Clinical Strategy and Development Plan for a New Drug or Indication ---603 61 Designing and Implementing a Clinical Trial --- 615 62 Questions to Ask about a Clinical Trial Protocol --- 640 63 Dose-response Relationships in Clinical Trials --- 644 64 Collecting and Interpreting Life Events Data in Clinical Trials --- 655 65 Quality of Life and Pharmacoeconomics in Clinical Trials --- 662 66 Overview of Phase 4 and Postapproval Clinical Activities --- 677 67 Phase 4 Trials and Postapproval Pharmacovigilance Methodologies --- 685 68 Feasibility of Multinational Trials --- 693 69 Groups that Influence Protocol Design --- 707 70 Monitoring and Auditing a Clinical Trial --- 712 71 Electronic Data Collection and E-clinical Trials --- 721 72 Principles of Patient Recruitment and Retention --- 733 73 Surrogate Endpoints and Biomarkers --- 737 74 Contract Research Organizations and Outsourcing Strategies --- 746 75 Conducting Clinical Trials Efficiently and Rapidly --- 756 76 Clinical Significance --- 765 77 Incorporating Benefit-to-risk Determinations in Drug Development --- 771 78 Interactions between Clinicians and Statisticians for Analysis and Interpretation of Clinical Data --- 780 79 The Concept of Normalcy --- 787 80 Recruiting and Training Clinical Investigators --- 797 81 Human Subject Protection and Ethical Issues in Clinical Trials --- 807 82 Improving the Standards of Clinical Trial Publications .819 83 Registries and Directories of Clinical Trials, plus Disclosure of Their Results and

Archiving Their Data --- 823

84 Clinical Trials Come of Age --- 832

# SECTION 7 - Regulatory Affairs Activities and Issues

- 85 Introduction to Regulatory Affairs --- 841
- 86 Negotiating and Interacting with Regulatory Agencies --- 859
- 87 Learning Which Regulatory Guidances and Standards May Be Modified --- 867
- 88 Preparing for and Holding Meetings with Regulatory Agencies --- 873
- 89 Food and Drug Administration Advisory Committee Meetings --- 884
- 90 Regulatory Applications for Marketing Approval and Global Interactions with Regulators --- 891
- 91 Regulatory Strategies in Real-life Product Development --- 902

#### SECTION 8 - Marketing Activities, Issues, and Interactions with Medical Affairs

- 92 Overview of Marketing Activities and Issues --- 911
- 93 Corporate Issues Regarding the Medical Marketing Interface --- 946
- 94 Organizational and Staffing Issues Regarding the Medical Marketing Interface --- 954
- 95 Marketing Needs, Wants, and Issues in Developing Drugs --- 963
- 96 Joint Medical and Marketing Activities --- 972
- 97 Switching Prescription Drugs to Over-the-counter Status --- 986
- 98 Costs and Pricing --- 993
- 99 Providing Product Information to Healthcare Professionals --- 1007

#### SECTION 9 - Functional Activities and Issues

- 100 Information Management --- 1021
- 101 Selected Statistical Issues --- 1038
- 102 Data Management --- 1049
- 103 Toxicology Activities and Issues --- 1058
- 104 Animal Testing and Animal Welfare --- 1065
- 105 Pharmacokinetics --- 1072
- 106 Licensing Activities and Issues --- 1077
- 107 Technical Development Activities and Issues --- 1102
- 108 Production Activities and Issues --- 1119
- 109 Patent Activities and Issues --- 1144
- 110 Legal Activities and Issues --- 1159
- 111 Financial Activities and Issues --- 1172

## SECTION 10 - Overview of Current and Future Development

112 Poor Development and Corporate Practices: Threats to a Pharmaceutical Organization --- 1191

- 113 Keys for Pharmaceutical and Development Success --- 1201
- 114 Computer Simulations and Modeling --- 1214
- 115 The Future of Drug Discovery and Development --- 1221

SECTION 11 - Case Studies in Clinical Development, Regulatory Affairs, and the Management of Drug Development

- 116 Clinical Case Studies --- 1231
- 117 Regulatory Affairs Case Studies --- 1237
- 118 Management of Drug Development Case Studies -- 1244

Index 1251