Contents

1 Clinical Trial Simulation and Quantitative Pharmacology .......... 1
Carl C. Peck and Holly H. C. Kimko

Part I Application of M&S in Regulatory Decisions

2 Contribution of Modeling and Simulation Studies in the Regulatory Review: A European Regulatory Perspective ...... 15
Siv Jönsson, Anja Henningssson, Monica Edholm, and Tomas Salmonson

3 Contribution of Modeling and Simulation in the Regulatory Review and Decision-Making: U.S. FDA Perspective ................. 37
Christine E. Garnett, Joo-Yeon Lee, and Jogarao V.S. Gobburu

Part II Strategic Applications of M&S in Drug Development

4 Decision-Making in Drug Development: Application of a Model Based Framework for Assessing Trial Performance .......................................................... 61
Mike K. Smith, Jonathan L. French, Kenneth G. Kowalski Matthew M. Hutmacher, and Wayne Ewy

5 Decision-Making in Drug Development: Application of a Clinical Utility IndexSM ......................................................... 85
Timothy J. Carrothers, F. Lee Hodge, Robert J. Korsan, William B. Poland, and Kevin H. Dykstra

6 Adaptive Trial Designs ...................................................... 109
José C. Pinheiro, Frank Bretz, and Chyi-Hung Hsu
7 Keys of Collaboration to Enhance Efficiency and Impact of Modeling and Simulation ............................................. 131
Anthe S. Zandvliet, Rik de Greef, Anton F.J. de Haan, Pieta C. IJzerman-Boon, Maya Z. Marintcheva-Petrova, Bernadette M.J.L. Mannaerts, and Thomas Kerbusch

8 Leveraging Pharmacometrics in Early Phase Anti-inflammatory Drug Development ........................................ 149
Ene I. Ette and Christopher J. Godfrey

Part III Application of M&S in Selected Therapeutic Areas

9 The Application of Drug-Disease Models in the Development of Anti-Hyperglycemic Agents ..................... 175
Jenny Y. Chien and Vikram P. Sinha

10 Modeling and Simulation in the Development of Cardiovascular Agents .................................................. 199
Diane R. Mould, Bill Frame, and Timothy Taylor

11 Viral Dynamic Modeling and Simulations in HIV and Hepatitis C .......................................................... 227
Philippe Jacqmin and Eric Snoeck

12 A Model-Based PK/PD Antimicrobial Chemotherapy Drug Development Platform to Simultaneously Combat Infectious Diseases and Drug Resistance ......................... 251
N. L’ntshotsholé “Shasha” Jumbe and George L. Drusano

13 PKPD and Disease Modeling: Concepts and Applications to Oncology .................................................... 281
Oscar E. Della Pasqua

14 Application of Pharmacokinetic–Pharmacodynamic Modeling and Simulation for Erythropoietic Stimulating Agents .............. 311
Juan José Pérez-Ruixo, Sameer Doshi, and Andrew Chow

15 Model Based Development of an Agent for the Treatment of Generalized Anxiety Disorder .................... 329
Peter A. Lockwood and Jaap W. Mandema

16 Balancing Efficacy and Safety in the Clinical Development of an Atypical Antipsychotic, Paliperidone Extended-Release ...... 345
Filip De Ridder and An Vermeulen
Part IV  Expanded Applications of M&S

17  Application of Modeling and Simulation in the Development of Protein Drugs ................................................................. 365
    Lorin K. Roskos, Song Ren, and Gabriel Robbie

18  Modeling and Simulation in Pediatric Research and Development ................................................................. 401
    Jeffrey S. Barrett

Part V  Evolving Methodologies in M&S

19  Disease Progression Analysis: Towards Mechanism-Based Models ................................................................. 437
    Stephan Schmidt, Teun M. Post, Massoud A. Boroujerdi,
    Charlotte van Kesteren, Bart A. Ploeger
    Oscar E. Della Pasqua, and Meindert Danhof

20  Using a Systems Biology Approach to Explore Hypotheses Underlying Clinical Diversity of the Renin Angiotensin System and the Response to Antihypertensive Therapies .......... 461
    Arthur Lo, Jennifer Beh, Hector De Leon, Melissa K. Hallow,
    Ramprasad Ramakrishna, Manoj Rodrigo, Anamika Sarkar,
    Ramesh Sarangapani, and Anna Georgieva

21  Recent Developments in Physiologically Based Pharmacokinetic Modeling ................................................................. 487
    Vikash Sinha and Holly H.C. Kimko

22  Covariate Distribution Models in Simulation ................................................................. 505
    Peter L. Bonate

Index ............................................................................ 527
Clinical Trial Simulations
Applications and Trends
Kimko, H.H.C.; Peck, C.C. (Eds.)
2011, XVI, 540 p., Hardcover