Contents

Preface ..... vii
Acknowledgments ..... xi
Contributors ..... xv

Part 1: Introduction and Specific Requirements

1. The Common Technical Document—A Global Format for Registration Files  1
   Anthony C. Cartwright

2. The Electronic Common Technical Document  14
   Geoffrey Williams

3. CTD Module 1—Administrative Information  26
   Roger Croswell and Anthony C. Cartwright

4. Environmental Risk Assessment  47
   David J. Snodin

Part 2: Common Technical Document Summaries

5. Quality Overall Summary  78
   Anthony C. Cartwright

6. The Nonclinical Overview and Summary  89
   Richard Lee

7. The Clinical Overview and Summary  107
   Chantal Le Floch and Patricia Maillère

Part 3: Quality—Drug Substance and Drug Product

8. Drug Substance—General Information  119
   Anthony C. Cartwright

9. Drug Substance—Manufacture  124
   Anthony C. Cartwright

10. Drug Substance—Characterization  136
    Anthony C. Cartwright and David J. Snodin

11. Control of Drug Substance  154
    Anthony C. Cartwright

12. Drug Substance and Drug Product—Container/Closure  169
    Brian R. Matthews
Contents

13. Drug Product—Description and Composition 179
   Brian R. Matthews

14. Drug Product—Pharmaceutical Development 184
   J. Michael Morris

15. Drug Product—Manufacture and Process Validation 210
   Brian R. Matthews

16. Drug Product—Excipients 234
   Brian R. Matthews

17. Control Tests on the Finished Product 248
   Henk J. de Jong

18. Reference Standards or Materials 264
   Anthony C. Cartwright

19. Drug Substance and Drug Product Stability 269
   Anthony C. Cartwright

20. Transmissible Spongiform Encephalopathy Agent and Adventitious Agent
    Requirements for Non-Biological Pharmaceutical Products 290
    Brian R. Matthews

Part 4: Nonclinical Studies

21. Nonclinical Testing Strategy 300
    Klaus Olejniczak and Rolf Bass

22. Pharmacology 323
    James W. McBlane

23. Nonclinical Pharmacokinetics and Toxicokinetics 336
    Richard J. Weaver and Roeline Jochemsen

24. Single and Repeat Dose Toxicity 377
    Barry S. Levine

25. Genotoxicity 402
    Peter Kasper

26. Carcinogenicity 419
    Gerd Bode

27. Reproductive and Developmental Toxicity 429
    John Baldwin

    Paul Baldrick

29. Immunotoxicology 467
    Danuta Herzyk

30. Local Tolerance and Other Toxicity Studies 478
    Andrew Makin
Part 5: Clinical Studies

31. Bioavailability and Bioequivalence Studies 490
   lain J. McGilveray

32. Pharmacokinetics in Man 520
   Don J. Nichols and Don K. Walker

33. Pharmacodynamics 537
   Corinne Seng Yue, Pina D'Angelo, and Murray P. Ducharme

34. Statistical Concepts in the Design and Analysis of Clinical Trials 554
   Richard Kay

35. Efficacy and Safety Clinical Studies 574
   David Jefferys

36. Postmarketing Evaluation 589
   H. Guenter Hennings

37. Pharmacovigilance and Risk Management 603
   Brian Edwards, Mary Teeling, and Markku Toivonen

38. Pregnancy and Children 622
   H. Guenter Hennings

39. Ageing Populations and Development of Medicinal Products 633
   Jean-Marc Husson and Jean-Marie Vetel

40. Good Clinical Practice 658
   Laura Brown

41. Prevention and Detection of Fraud in Clinical Trials 685
   Jane Barrett

Part 6: Special Products and Modeling

42. Aspects of Biological and Biotechnological Medicinal Products 697
   Manfred G. Haase

43. Device-Drug Combination Products 717
   Brian R. Matthews

44. Recommendations for Toxicological Evaluation of Nanoparticle Medicinal Products 755
   Jean-Roger Claude and Members of Afsaps Working Party

45. Modeling and Medical Product R&D 762
   Jean-Pierre Boissel, Michel Cucherat, Patrice Nony, François Gueyffier, and
   François-Henri Boissel

Annex 1: List of Acronyms and Abbreviations .... 774
   Anthony C. Cartwright

Annex 2: List of Key Technical and Regulatory Information Sources .... 784
   Anthony C. Cartwright and Brian R. Matthews

Index .... 787