Contents

Preface ix
Acknowledgments xi

Chapter 1 Pharmaceutical Industry Overview 1
  1.1 Introduction 2
  1.2 Regulations 2
    1.2.1 Health Insurance Portability and Accountability Act 2
    1.2.2 The Code of Federal Regulations 3
    1.2.3 Guidance for Industry 4
    1.2.4 International Conference on Harmonisation of Technical Requirements 5
    1.2.5 Clinical Data Interchange Standards Consortium 6
  1.3 Documentation 7
  1.4 Standard Operating Procedures 7
    1.4.1 Companywide Standard Operating Procedures 7
    1.4.2 Department Standard Operating Procedures 8
    1.4.3 Task Standard Operating Procedures 8
  1.5 SAS Programming Guidelines 9
  1.6 Quality Control versus Quality Assurance 9
  1.7 Patient versus Subject 10
  1.8 Conclusion 10

Chapter 2 Validation Overview 11
  2.1 Introduction 12
  2.2 Validation versus Verification 12
  2.3 Why Is Validation Needed? 13
    2.3.1 Presenting Correct Information 13
    2.3.2 Validating Early Saves Time 13
    2.3.3 Developing a Positive Relationship 14
2.4 How Do You Approach Validation? 14
  2.4.1 Start with All the Information 14
  2.4.2 Have a Plan 15
  2.4.3 Make the Code Do the Work 16
  2.4.4 Ask Questions 16
  2.4.5 Be Proactive 16
  2.4.6 Validation Must Come First 17
2.5 Validation Methods 17
  2.5.1 Independent Programming 18
  2.5.2 Peer Review 19
2.6 Validation Checklists 20
2.7 Software Development Life Cycle 21
2.8 Conclusion 22

Chapter 3 Documentation and Maintenance 23
3.1 Introduction 24
3.2 Starting the Process 25
  3.2.1 Study Protocol 25
  3.2.2 Annotated Case Report Form 26
  3.2.3 Statistical Analysis Plan 29
  3.2.4 Meeting Minutes 31
3.3 Internal Program Documentation 32
  3.3.1 Program Header 32
  3.3.2 Body Comments 34
  3.3.3 Output Titles 35
3.4 External Documentation 35
  3.4.1 Data Definition Tables 35
  3.4.2 Program Directory 36
  3.4.3 Validation Files 37
3.5 Make Programs Maintainable 38
  3.5.1 Create and Follow Naming Conventions 38
  3.5.2 Make It Easy to Read 38
3.5.3 One Program, One Purpose  42
3.5.4 Comments, Comments, Comments  43
3.5.5 Use Macros Judiciously  44
3.6 Make Data Maintainable  44
  3.6.1 Order Your Data  44
  3.6.2 Label Everything  49
  3.6.3 Attach Formats Sparingly  50
  3.6.4 Consistency Is Key  51
  3.6.5 Good Housekeeping  51
  3.6.6 Look—but Don’t Touch  53
3.7 Conclusion  56

Chapter 4 General Techniques to Facilitate Validation  57
  4.1 Introduction  58
  4.2 Validation Tools  58
    4.2.1 Procedures  58
    4.2.2 SAS Options and Language Elements  67
    4.2.3 Using Macros Effectively  72
  4.3 Techniques That Facilitate Validation  80
    4.3.1 Start with a Clean Log  80
    4.3.2 Print Only What You Need—When You Need It  81
    4.3.3 Tracking Problems  82
    4.3.4 Using PROC TRANSPOSE or an Alternative Solution  85
    4.3.5 Tracking Dropped Data  89
  4.4 Conclusion  93

Chapter 5 Data Import and Export  95
  5.1 Introduction  96
  5.2 Validating the Import Process  96
  5.3 Validating the Export Process  98
  5.4 General Items to Watch For When Transferring Data  99
5.5 Working with SAS Files 100
  5.5.1 SAS Data Sets 100
  5.5.2 SAS Transport Files 101
5.6 Working with Other File Types 102
  5.6.1 Microsoft Excel Files 102
  5.6.2 Flat Files 103
5.7 Common Procedures Used for Validating Data Transfers 104
  5.7.1 PROC CONTENTS 104
  5.7.2 PROC COMPARE 108
5.8 Conclusion 112

Chapter 6 Common Data Types 113
  6.1 Introduction 114
  6.2 Study Populations 114
    6.2.1 Safety 115
    6.2.2 Intent-to-Treat 115
    6.2.3 Efficacy 116
  6.3 Common Data Domains 116
    6.3.1 Subject Demographics 116
    6.3.2 Inclusion/Exclusion Criteria 117
    6.3.3 Subject Disposition 118
    6.3.4 Medical History 118
    6.3.5 Physical Examination 120
    6.3.6 Vital Signs 120
    6.3.7 Treatment Exposure 122
    6.3.8 Concomitant Medications 123
    6.3.9 Adverse Events 124
    6.3.10 Clinical Laboratory Data 126
  6.4 Conclusion 137