
Contents

Preface..... xv
Introduction.....xvii

SECTION I Study Startup

Chapter 1 The Data Management Plan 3

 History of Data Management Plans 3

 What Goes into a DMP? 4

 Signing Off on the DMP 5

 Revising the DMP 5

 DMPs and the Study Files 6

 Using DMPs with CROs 6

 Quality Assurance and DMPs 7

 SOPs for DMPs and Study Files 7

 Using Data Management Plans 8

Chapter 2 CRF Design Considerations 9

 Primary Goals of CRF Design 9

 Collecting Required Data: Visits, Procedures, Fields 10

 Protocol Compliance 12

 Collecting Analyzable Data 13

 Secondary Goal: Reducing Queries 14

 Avoiding Duplicate Data 14

 Eliminating Missing or Ambiguous Responses 15

 CRFs with Data Processing Impact 16

 Log Forms 17

 Questionnaires 18

 Diagrams and Analog Scales 19

 Early Termination Visits 20

 Revisions to the CRF 20

 Quality Assurance for CRFs 21

 SOPs on CRF Design 22

 Reuse and Refine CRF Modules 22

Chapter 3 Database Design Considerations 23

 Making Design Decisions 23

 Basic Clinical Database Concepts 24

 Field Data Types 24

	Numeric Fields	25
	Dates	26
	Texts	28
	Coded Data	28
	Identifier Fields	30
	Calculated or Derived Values	31
	Tall-Skinny versus Short-Fat Tables	32
	Using Standards	34
	After Deciding on a Design	35
	Quality Assurance for Database Design	35
	SOPs for Database Design	35
	Responsibilities in Database Design	36
Chapter 4	Edit Checks	37
	Choosing Edit Checks	37
	Missing Values	38
	Simple Range Checks	38
	Logical Inconsistencies	38
	Cross-Form or Cross-Page Checks	39
	Protocol Violations	39
	Specifying Edit Checks	40
	Quality Assurance of Edit Checks	40
	SOPs for Edit Checks	40
	The Connection to Queries	42
Chapter 5	Preparing to Receive Data	43
	Overview of Creating Study Databases	43
	Validating Study Databases	44
	A Study Validation Plan	45
	Database Specifications	45
	Paper Studies	45
	EDC Studies	46
	How Building Impacts Specifications	46
	Testing Study Databases	46
	Testing Environment	47
	Testing Paper Studies	47
	Testing EDC Studies	48
	Final Steps in Testing	48
	Moving to Production	48
	Study Database Change Control	49
	Quality Assurance for Building Studies	51
	SOPs for Preparing for Data	51
	Study Creation Is Programming	52

SECTION II Study Conduct

Chapter 6	Receiving Data on Paper	55
	Transcribing Data	55
	Double Entry	55
	OCR Plus Review	56
	Single Entry	56
	How Close a Match to the CRF?	57
	Dealing with Problem Data	58
	Illegible Fields	58
	Notations in Margins	58
	Using Preentry Review	59
	Changing Data after Entry	59
	Quality Assurance and Quality Control for Entry	60
	Audit Plan	60
	Audit Process	61
	Audit Report	62
	SOPs for Data Entry	62
	Entry Quality	62
Chapter 7	Overseeing Data Collection	65
	Monitoring EDC Data Collection	65
	Monitoring Paper Data Collection	65
	Paper CRF Workflow	66
	Tracking Challenges	67
	Repeating Pages	67
	Pages with No Data	68
	Duplicate Pages	68
	Studies without Page Numbers	68
	Missing Pages Reports	69
	What Pages Do You Expect?	69
	CROs and Tracking Pages	70
	Principal Investigator Signatures	71
	Using Tracking for Quality Assurance and Quality Control	71
	SOPs for Overseeing Data Collection	72
	Tracking throughout the Process	72
Chapter 8	Cleaning Data	73
	Identifying Discrepancies	73
	Automatic Checks	74
	Manual Queries	74
	Clinical and Listing Review	74

Problems during Entry from Paper.....	75
Discrepancies Identified by External Programs	75
The EDC Query Process	75
Creating Manual Queries	76
Resolving an EDC Query	76
Getting PI Signatures	76
The Paper Query Process	77
Resolving Discrepancies Internally	77
Turning a Discrepancy into a Query	79
Sending Queries to the Sites.....	80
Resolving Paper Queries	80
Getting PI Signatures.....	81
Applying the Resolution	81
Tracking Queries	82
Links to Quality Assurance and Quality Control	83
SOPs for Discrepancy Management.....	84
Using Queries to Improve Efficiency	84
 Chapter 9 Managing Lab Data.....	 87
Storing Lab Data	87
Advantages of the Tall-Skinny Format	88
Disadvantages of the Tall-Skinny Format.....	89
Identifying Lab Tests.....	90
Storing Units	91
Ranges and Normal Ranges	91
Laboratory IDs	92
Normal Range Storage	92
Using the Normal Ranges.....	93
Lab Result Trends.....	93
Using Central Labs.....	93
Using Specialty Labs.....	94
Auditing the Lab.....	94
Monitoring the Data	95
Quality Assurance around Lab Data.....	95
SOPs for Processing Lab Data	96
Why Lab Data Needs Special Attention	96
 Chapter 10 Non-CRF Data	 97
Receiving Electronic Files from a Vendor	97
Transferring Files	97
Formatting the Data.....	98
Loading Data	98
Identifying File Contents.....	99
Cleaning Non-CRF Data.....	100

Quality Assurance for External Data.....	101
SOPs for Non-CRF Data.....	101
When Non-CRF Data Is outside Data Management.....	102
Chapter 11 Collecting Adverse Event Data	103
Collecting Adverse Events	103
Adverse Event Forms.....	104
Special Considerations for Paper AE Forms.....	106
Storing and Cleaning AE Data.....	107
Coding Adverse Event Terms.....	108
Reconciling Serious Adverse Events.....	109
Methods for Reconciliation	110
Easing the Reconciliation Process	110
Quality Assurance and Quality Control.....	110
SOPs for AE Data.....	111
Impact of AEs on Data Management.....	111
Chapter 12 Creating Reports and Transferring Data	113
Specifying the Contents	113
From Where?	113
Exactly What?	114
When?	114
Standard and Ad Hoc Reports.....	115
Data Transfers	116
Transfer Checklists.....	116
Transfer Metrics	117
Quality Control Review of Printed Reports and Presentations.....	118
SOPs for Reports and Transfers	118
Putting in the Appropriate Effort.....	118

SECTION III *Study Closeout*

Chapter 13 Study Database Lock.....	123
Final Data.....	123
Final Queries	124
Final Quality Control	124
Database Audits.....	124
Summary Review	125
Reconciling.....	126
Final Steps for EDC	127
Using a Checklist to Lock a Study	127
Setting Database Lock	129

Time to Study Database Lock	129
Quality Assurance around Lock	130
SOPs for Study Closeout	130
Reducing Time to Study Lock	131
Chapter 14 After Database Lock	133
Complete Study Files	133
Assess Study Conduct	133
Site eCRF Copies	134
Unlocking	134
Avoiding Unlocks	134
Approval for Unlocking.....	135
Unlocking for Paper Studies.....	135
Unlocking for EDC Studies.....	135
Quality Assurance.....	136
SOPs for Study Database Unlock.....	136
Avoid Unlocks	136

SECTION IV Necessary Infrastructure

Chapter 15 Standard Operating Procedures (SOPs)	139
What Is an SOP?	139
SOPs for Data Management	140
Creating Standard Procedures.....	141
Starting from Scratch	141
Procedures for New CDM Systems.....	143
Complying with Standard Procedures	143
Training on SOPs	144
Designing for Compliance.....	144
Proving Compliance	145
How Data Management SOPs Are Different from	
Clinical SOPs	146
SOPs on SOPs	146
SOP Work Never Ends	147
Chapter 16 Training	149
Who Gets Trained on What?.....	149
Study-Specific Training.....	150
How to Train.....	152
Training Records	153
SOPs on Training	154
Allotting Time for Training	154

Chapter 17	Controlling Access and Security	155
	Account Management	155
	Usernames	156
	Passwords	156
	Account Timeouts	157
	Access Control	157
	How to Grant Access	158
	Who Had Access?	158
	SOPs and Guidelines for Accounts	159
	Taking Security Seriously	159
Chapter 18	Working with CROs	161
	The CRO Myth	161
	Auditing CROs	162
	Defining Responsibilities	163
	Oversight and Interaction	163
	Study Startup	163
	Study Conduct	164
	Closing the Study	166
	EDC Vendors as CROs	166
	CROs as Functional Service Providers	167
	SOPs for Working with CROs	167
	Benefiting from CROs	167

SECTION V CDM Systems

Chapter 19	Clinical Data Management Systems	171
	CDM System Characteristics	171
	Where CDM Systems Come From	172
	Choosing a CDM System	172
	Using CDM Systems Successfully	173
	SOPs for CDM Systems	173
	CDM Systems Are for More than Data Entry	174
Chapter 20	EDC Systems	175
	What Makes EDC Systems Different?	175
	Multiple Data Streams	176
	Coding	176
	Where the Servers Are—Hosting	176
	Study Setup	177
	The Need for Data Repositories	177

Working with EDC Systems	178
Main Advantages of EDC	179
Some Problems with EDC.....	179
Will Data Management Groups Disappear?	180
SOPs for EDC.....	181
Making EDC Successful	181
 Chapter 21 Choosing Vendor Products.....	183
Defining Business Needs.....	183
Initial Data Gathering	184
Requests for Information.....	184
Evaluating Responses.....	185
Extended Demos and Pilots	185
Hands-On Demos	186
Pilots	186
Additional Considerations	187
What Is Missing?.....	189
Preparing for Implementation	189
 Chapter 22 Implementing New Systems.....	191
Overview and Related Plans	191
Essential Preparation.....	192
Integration and Extensions	193
Migration of Legacy Data	194
Benefiting from Pilots	194
Validation	196
Preparation for Production	196
Successful Implementation	196
 Chapter 23 System Validation.....	199
What Is Validation?	199
Validation Plans or Protocols	200
Introduction and Scope.....	200
Assumptions and Risks	201
Business Requirements and Functional Specification.....	201
Installation	201
Testing Overview	202
Vendor Audit	202
Security Plan	203
SOPs and Guidelines	203
Completion Criteria	203
Maintaining Validation Plans.....	203
Change Control and Revalidation	204

What Systems to Validate	204
SOPs for Validation	205
Requirements and Benefits	206
Chapter 24 Test Procedures	207
Traceability Matrix	207
Test Script Contents	208
Purchasing Test Scripts	209
Training for Testers	210
Reviewing Results	210
Test Outcome	211
Retaining the Test Materials	212
Chapter 25 Change Control	213
What Changes Should Be Controlled?	213
Changes to Software Systems	213
Changes to Study Databases	214
Documenting the Change	214
Describe or Propose the Change	215
Assess the Impact	215
Plan Testing	216
Document the Outcome	216
Releasing Changes	217
Problem Logs	217
Considering Version Control	218
The Value of Change Control	218
Chapter 26 Coding Dictionaries and Systems	219
Common Coding Dictionaries	219
MedDRA	220
WHO Drug	220
Using Autocoders	220
Collecting the Term	221
Storing the Results	222
Failure to Code	222
Special Considerations for AE Terms	224
Dictionary Maintenance	225
Quality Assurance and Quality Control for Coding	226
SOPs for Coding and Dictionaries	226
Effective Coding	227
Chapter 27 Migrating and Archiving Data	229
Simple Migrations within Systems	229

Why Migrate between Systems?	230
Complex Migrations	231
Migration by Hand	232
Migrating Audit Trails	232
Archiving Data	232
Level of Archive Access	233
What to Archive	233
Migration and Archive Plans	234
Future Directions	234
 Appendix A: Data Management Plan Outline	235
Appendix B: Clinical Data Management SOPs	239
Appendix C: CRO-Sponsor Responsibility Matrix	243
Appendix D: Implementation Plan Outline	247
Appendix E: Validation Plan Outline	249
Appendix F: CDISC and HIPAA	251
Bibliography	253
Index	255