

Table of Contents

1	Introduction	9
1.1	Purpose.....	10
1.2	Rationale for the Second Edition	10
1.3	Structure of This Guide	11
1.4	Key Terms	11
2	Scope	13
2.1	Aspects and Challenges of GCP Systems.....	13
3	Regulatory and Industry Guidance Overview	17
3.1	Key Regulations.....	17
4	Process Overview	21
4.1	The Project Nature of Clinical Studies	21
4.2	Conducting a Clinical Trial	22
4.3	Layer Model Approach.....	23
4.4	Stakeholders in Clinical Trials.....	25
4.5	Dataflows and Management of Outsourcing.....	30
4.6	Oversight Activities Including Audits/Assessments.....	32
4.7	Change of Service Provider.....	36
4.8	Archiving	36
4.9	Quality by Design and Inspection Readiness	39
4.10	Quality Risk Management for Setup and Validation of Computerized Clinical Systems.....	41
5	Process Model.....	49
5.1	Process: Study Protocol and Submission for Approval.....	49
5.2	Process: Project and Clinical Study Management.....	51
5.3	Process: Electronic Data Capture System Life Cycle and Validation	55
5.4	Process: Electronic Patient-Reported Outcome System Life Cycle and Validation	62
5.5	Process: Site/Service Providers Qualification.....	63
5.6	Process: Data Collection by Clinical Trial Investigator Site Systems.....	69
5.7	Process: Investigational Medicinal Product Management	86
5.8	Process: Participant Recruitment, Inclusion, and Randomization	96
5.9	Process: Data Aggregation and Review	100
5.10	Process: Severe Adverse Event Reporting.....	110
5.11	Process: Mid-Study Changes and Change Management.....	115
5.12	Process: Statistical Analysis and Programming.....	116
5.13	Process: Study Report, Study Closure, And Submission.....	118
5.14	Process: QA and Quality Control	125
5.15	Process: Laboratory Analysis and Sample Logistics	128

6	Data Integrity	131
6.1	Data Integrity Definition.....	131
6.2	Data Integrity Risks.....	132
6.3	Data Governance and Ownership.....	141
6.4	Data Life Cycle and Dataflow.....	145
6.5	Data Integrity in Computerized Systems Used in Clinical Trials: Electronic Source Data (eSource Data).....	150
6.6	Data Integrity in Computerized Systems Used in Clinical Trials: Audit Trails and Audit Trail Reviews.....	152
6.7	Interfaces and Their Validation.....	155
6.8	Data Integrity for Electronic Records Used in Clinical Trials: Electronic Signatures and Digital Signatures.....	157
6.9	Data Integrity for Electronic Records Used in Clinical Trials: Certified Copy of Original Documents (Source Documents).....	159
7	Appendix 1 – Data Privacy in Clinical Trials	161
7.1	Introduction.....	161
7.2	Key Definitions.....	161
7.3	Applicable Regulations.....	163
7.4	Roles and Responsibilities.....	164
7.5	Supplier Management and International Data Transfers.....	166
7.6	Clinical Data and Personal Data.....	167
7.7	Privacy by Design.....	168
8	Appendix 2 – Decentralized Clinical Trials	171
8.1	Introduction.....	171
8.2	Prerequisites.....	172
8.3	Providers.....	174
8.4	Data.....	174
8.5	Digital Health Technologies and Devices.....	175
8.6	Establishing Fitness for Use.....	176
8.7	Training.....	176
8.8	IMP/Investigational Product (IP).....	177
9	Appendix 3 – Assessment of Clinical Site Systems	179
10	Appendix 4 – Good Clinical Laboratory Practice (GCLP)	183
10.1	Process Overview.....	183
10.2	Regulations/Guidance.....	183
10.3	Partners.....	184
10.4	Logistics and Analysis of Samples.....	185
10.5	Data and Risks Associated with the Process.....	186
10.6	Data Transfer from Laboratories.....	187
10.7	Patient Sample Analysis Versus Clinical Trial Sample Analysis.....	187
10.8	Retention and Archiving Records.....	188
10.9	Laboratory Responsibilities and Facilities.....	189
10.10	SOPs in a GCLP Environment.....	189

11 Appendix 5 – Use of Data Science and AI-Enabled Systems in Clinical Trials ...	191
11.1 Introduction and Overview	191
11.2 Overview of Concepts in Data Science, AI, and ML	192
11.3 Overview of Standards and Regulatory Guidance Relevant for the Application of Data Science and AI	193
11.4 Evolution from Clinical Data Management to Clinical Data Science	194
11.5 Guidance on AI-Enabled Systems	197
11.6 Guidance on Specific AI-Based Support for Clinical Trial Activities	204
12 Appendix 6 – Real-World Data/Real-World Evidence	209
12.1 Growing Importance of RWD/RWE and Challenges	209
12.2 Key Terms	210
12.3 What Makes This Different	210
12.4 Regulatory and ICH Frameworks	212
12.5 Potential Uses of RWD and RWE	215
12.6 RWD/RWE Process and Data Validation	216
12.7 Selection of Data Sources	219
12.8 Data Preparation and Curation	221
12.9 Data Privacy Aspects	224
12.10 Data Management	225
12.11 Data Retention	225
13 Appendix 7 – Open-Source Software in Clinical Trials	227
13.1 Introduction	227
13.2 Regulatory Positions	228
13.3 Validation, Security, and Risk Management	228
14 Appendix 8 – Historical Overview of GCP Regulations and Guidance	231
15 Appendix 9 – References	235
16 Appendix 10 – Glossary	247
16.1 Acronyms and Abbreviations	247
16.2 Definitions	251