

## TABLE OF CONTENTS

Dedication .....	iii
Introduction .....	xi
<b>1 The Clinical Research Coordinator (CRC).....</b>	<b>1</b>
Role and Responsibilities of the CRC .....	1
Personality and Skills .....	3
Where Do CRCs Work? .....	3
CRC Responsibilities .....	5
Influence of Technology .....	8
Problems and Opportunities .....	9
<b>2 Quality Documentation and Data Characteristics .....</b>	<b>11</b>
Handwritten Documentation In Clinical Research.....	12
Certified Copies of Paper Documents .....	16
Electronic Documentation in Clinical Research .....	16
Certified Copies of Electronic Documents .....	17
Summary of CRC Duties and Responsibilities .....	18
<b>3 Regulations and Good Clinical Practices (GCPs) .....</b>	<b>19</b>
The Declaration of Helsinki (1964) .....	19
The Belmont Report (1979).....	20
Good Clinical Practice (GCP) .....	20
ICH Guideline for Good Clinical Practice .....	21
FDA Regulations for Clinical Trials .....	21
FDA Guidelines and Information Sheets .....	22

FDA BIMO and CPGMs .....	23
Office for Human Research Protections (OHRP).....	23
U.S. HIPAA Privacy Rule.....	24
HIPAA Authorization .....	24
Obtaining Informed Consent under HIPAA .....	27
Key Takeaways .....	28
<b>4 An Overview of Product Development .....</b>	<b>31</b>
Drug Development and CDER .....	31
Preclinical Research .....	32
Clinical Trials .....	34
Notes on Studies in Women and Children .....	39
Biologics and CBER.....	40
Medical Device and CDRH .....	41
Summary .....	44
Key Takeaways .....	44
<b>5 Standard Operating Procedures (SOPs) .....</b>	<b>47</b>
Writing SOPs .....	48
Approval, Training and Implementation .....	52
SOPs for Investigative Sites .....	53
Key Takeaways .....	57
<b>6 Institutional Review Boards (IRBs) .....</b>	<b>61</b>
IRB Membership .....	62
IRB Operations .....	63
IRB Responsibilities .....	63
Vulnerable Subjects .....	65
State and Local Regulations .....	66
IRB Review of Proposed Research .....	66
Materials Submitted to the IRB by an Investigator .....	66
IRB Deliberations .....	68

Investigator Reporting Responsibilities .....	68
Continuing Review of a Research Study.....	69
Expedited Review .....	70
IRB Registration.....	70
Data Safety Monitoring Boards (DSMBs).....	71
CRC Responsibilities.....	73
Key Takeaways .....	73
<b>7 Informed Consent .....</b>	<b>77</b>
Required Elements of the Informed Consent Document .....	78
Developing the Study-Specific Informed Consent.....	82
Obtaining Informed Consent .....	86
The Consent Process .....	87
Exceptions from Consent .....	90
Common Informed Consent Deficiencies & Conclusion .....	93
Key Takeaways .....	94
<b>8 Pre-study: Preparing for a Study.....</b>	<b>97</b>
Sponsor Site Qualification .....	98
How to Succeed in Getting Studies.....	100
Protocol Feasibility .....	101
Grants, Budgeting and Contracts .....	102
Investigation Site Trial Master File (TMF).....	104
Storage of Study Materials .....	108
Trial Master File (TMF) .....	109
Financial Disclosure .....	110
Investigator Meetings and Site Initiation Visits .....	112
Working with CRAs .....	114
Other Sponsor Interactions .....	115
Shipping of Biological Samples .....	115
Key Takeaways .....	116

<b>9</b>	<b>Protocols .....</b>	<b>119</b>
	Protocols .....	119
	Protocol Complexity .....	128
	Protocol Amendments.....	128
	During the Study.....	130
	Key Takeaways .....	130
<b>10</b>	<b>Case Report Forms (CRFs) and Electronic Data Capture (EDC) .....</b>	<b>133</b>
	CRFs.....	133
	Electronic Data Capture (EDC) .....	139
	Internal Quality Control vs. Quality Assurance .....	141
	Key Takeaways .....	141
<b>11</b>	<b>Investigational Product (IP) Accountability .....</b>	<b>145</b>
	Responsibilities .....	145
	During a Clinical Trial .....	148
	Key Takeaways .....	150
<b>12</b>	<b>Working with Study Subjects .....</b>	<b>153</b>
	Recruitment of Study Subjects .....	153
	New Strategies for Subject Recruitment .....	160
	Scheduling Subjects .....	165
	Retention of Study Subjects .....	167
	Subject Compliance .....	172
	Key Takeaways .....	177
<b>13</b>	<b>Study Closure or Termination .....</b>	<b>181</b>
	Orderly Study Closure .....	181
	Closure Procedures .....	182
	Record Retention .....	184
	Post-Study Lessons Learned .....	185
	Key Takeaways .....	186

<b>14</b>	<b>Adverse Events (AEs) and Safety Monitoring .....</b>	<b>189</b>
	Drug Regulations .....	189
	Adverse Events (AEs) in Clinical Trials .....	191
	Investigator Reporting Responsibilities .....	196
	Differences Between Clinical Studies and Clinical Practice .....	197
	Assessing the Relationship of an AE to the Study Drug .....	197
	Common Reporting Problems .....	199
	Key Takeaways .....	199
<b>15</b>	<b>Audits and Inspections.....</b>	<b>203</b>
	Sponsor Audits of Investigative Sites .....	203
	IRB Audits of Investigative Sites .....	204
	FDA Audits of Investigative Sites .....	204
	Consequences .....	212
	Key Takeaways .....	213
	Afterword.....	217
	<b>Appendix A Abbreviations &amp; Acronyms .....</b>	<b>219</b>
	<b>Appendix B Glossary .....</b>	<b>221</b>
	<b>Appendix C Resources .....</b>	<b>229</b>
	Books and Videotapes .....	229
	Agencies .....	230
	Other Information .....	231
	<b>Appendix D Sample Forms, Checklists and Logs.....</b>	<b>233</b>
	<b>Appendix E Title 21—Food and Drugs .....</b>	<b>273</b>
	Part 11—Electronic Records; Electronic Signatures.....	273
	Part 50—Protection Of Human Subjects.....	277
	Part 54—Financial Disclosure by Clinical Investigators.....	291
	Part 56—Institutional Review Boards.....	294
	Part 312—Investigational New Drug Application.....	305