
Table of Contents

Section I: General Information

Chapter 1	FDA and Related Regulatory Agencies.....1 <i>Updated by Mitchell Berger, MPH and Barry Berger, JD, MBA</i>
Chapter 2	History of Food, Drug and Cosmetic Laws17 <i>Updated by Mujadala Abdul-Majid, MS, JD, RAC</i>
Chapter 3	Overview of Drug, Biologic and Device Regulatory Pathways.....25 <i>Updated by Meredith Brown-Tuttle, RAC</i>
Chapter 4	FDA Communications and Meetings.....53 <i>Updated by Helen M. Ribbans, MBA, FRAPS</i>
Chapter 5	Preparing for Key FDA Meetings and Advisory Committee Meetings61 <i>Updated by William K. Sietsema, PhD</i>
Chapter 6	Crisis Management71 <i>Updated by Meredith May, MS, RAC</i>
Chapter 7	Health Technology Assessment.....77 <i>Updated by Richard A. Vincins, CBA, CQA, RAC (US and EU)</i>
Chapter 8	Good Laboratory Practice Regulations87 <i>Updated by Christopher V. Braudis, Jr., MSc, RQAP-GLP and Anne E. Maczulak, PhD, RQAP-GLP</i>
Chapter 9	Clinical Trials: GCPs, Regulations and Compliance101 <i>Updated by Nancy J. Perrella, JD, RAC</i>
Chapter 10	Current Good Manufacturing Practices and Quality System Design121 <i>Updated by Jocelyn Jennings, MS, RAC and Carrie Kuehn, MA, MPH, RAC</i>
Chapter 11	FDA User Fees133 <i>By Allison C. Komiyama, PhD, RAC</i>
Chapter 12	Regulatory Strategy139 <i>By Maje Babatola, MS, RAC and Naseem Kabir, MS, RAC (US & EU)</i>

Section II: Drugs

Chapter 13	Prescription Drug Product Submissions147 <i>Updated by Wm. Trey Putnam, PhD, RAC</i>
Chapter 14	Postapproval Prescription Drug Submissions and Compliance169 <i>Updated by Nathalie Innocent, MS, RAC</i>

Chapter 15	Generic Drug Submissions.....	183
	<i>Updated by Samrat Sisodia, MS, MBA, MRSC, RAC</i>	
Chapter 16	Patents and Exclusivity.....	197
	<i>Updated by Clark G. Sullivan, JD</i>	
Chapter 17	Over-the-Counter (Nonprescription) Drug Products	209
	<i>Updated by Shekhar Natarajan, MSc, MRSC</i>	
Chapter 18	Prescription Drug Labeling, Advertising and Promotion	217
	<i>Updated by Mitchell E. Parrish, JD, CIP, RAC</i>	
Chapter 19	Pharmacovigilance and Risk Management.....	231
	<i>Updated By Treena Jackson, MS, CQA, CSSGB, RAC (US)</i>	
 Section III: Medical Devices		
Chapter 20	Medical Device Submissions	241
	<i>Updated by Sharad Mi. Shukla, RAC (US and EU) and Rajaram Balasubramanian, RAC (US and EU)</i>	
Chapter 21	Medical Device Compliance and Postmarketing Activities	265
	<i>Updated by Andrew P. Zeltwanger, MS and Anthony P. Schiavone</i>	
Chapter 22	Advertising, Promotion and Labeling for Medical Devices and In Vitro Diagnostics.....	277
	<i>Updated by Rajaram Balasubramanian, RAC (US and EU) and Sharad Mi. Shukla, RAC (US and EU)</i>	
Chapter 23	In Vitro Diagnostics Submissions and Compliance	287
	<i>Updated by Jocelyn Jennings, MS, RAC</i>	
 Section IV: Biologics		
Chapter 24	Biologics Submissions	295
	<i>Updated by Irina Kulinets, PhD, CQE, RAC</i>	
Chapter 25	Biologics Compliance.....	317
	<i>Updated by Nisha Pandya, MS, RAC</i>	
Chapter 26	Biologics Labeling, Advertising and Promotion	329
	<i>Updated by Jennifer Wilhelm, MSc, MBA, RAC</i>	
 Section V: Other Product Classifications		
Chapter 27	Combination Products.....	341
	<i>Updated by Michael D'Amico</i>	
Chapter 28	Products for Small Patient Populations.....	349
	<i>Updated by Brian E. Harvey, MD, PhD</i>	
Chapter 29	Blood and Blood Products	357
	<i>Updated by Jennifer Wilhelm, MSc, MBA, RAC</i>	
Chapter 30	Human Cell and Tissue Products	365
	<i>Updated by Martha Wells, MPH, RAC</i>	
Chapter 31	Regulating Regenerative Medicine: Cell Therapy, Gene Therapy and Tissue Engineering.....	373
	<i>By James Smith, DPhil Candidate, Brock Reeve, MBA, MPhil, Andy Carr, MA, ChM, Dsc, FRCS, FMedSci, and David A. Brindley, DPhil, MEng</i>	

Chapter 32	Laws and Regulations Pertaining to Pediatrics	387
	<i>Updated by Mitchell E. Parrish, JD, CIP, RAC</i>	
Chapter 33	Dietary Supplements and Homeopathic Products	395
	<i>Updated by Abhishek K. Gurnani, JD and Ashish R. Talati, JD, MS, RAC</i>	
Chapter 34	Cosmetics	419
	<i>Updated by Vic Mencarelli</i>	
Chapter 35	Veterinary Products	435
	<i>Updated by Adria Tyndall, RAC</i>	
Chapter 36	Food Products	451
	<i>Updated by Edward A. Steele, Charles Breen, Elizabeth Campbell, Robert Martin, PhD</i>	
Chapter 37	Companion Diagnostics	467
	<i>Updated by Maham Ansari, MS, RAC</i>	
Chapter 38	Medical Foods	475
	<i>Updated by Maruthi Prasad Palthur, PhD, PMP, RAC (US)</i>	

Section VI: Inspection and Enforcement

Chapter 39	FDA Inspection and Enforcement	483
	<i>Updated by Anthony P. Schiavone and Andrew P. Zeltwanger, MS</i>	
Chapter 40	Healthcare Fraud and Abuse Compliance	491
	<i>Updated by H. Carol Saul</i>	

Section VII: Resources

Chapter 41	Regulatory Information Resources in Review	503
	<i>By Auresa Thomas, PhD, RAC (US, Global)</i>	

Appendices

Comparative Matrix of Regulations Across Product Lines	525
Glossary	557
Index	581

Figures

Figure 1-1.	FDA Organizational Chart (as of April 2015)	6
Figure 3-1.	Decision Tree for Drug and Device Development and Approval for Situations that Require FDA Premarket Review	31
Figure 3-2.	CTD Organization	37
Figure 4-1.	Timeline for Meetings During Drug and Biologics Development	55
Figure 5-1.	Major Milestone Timeline	64
Figure 5-2.	Sample Project Management Chart	66
Figure 7-1.	An HTA Model	79
Figure 7-2.	Importance of the Relevant Technology for the Patient's Everyday Life (Børlum 2007)	81
Figure 7-3.	The Overall Synthesis Process as Shown in the HTA Danish Handbook	82
Figure 8.1.	Study Reconstruction and Evaluation	95
Figure 8-2.	FDA Inspection Classifications	99
Figure 10-1.	Quality System Elements	123
Figure 10-2.	Design Control Process Required by FDA for Medical Device Design and Development (21 CFR § 820)	124
Figure 12-1.	Tools for Regulatory Landscape	141
Figure 12-2.	Risk Tool	142

Figure 12-3.	Decision Tree	143
Figure 12-4.	Quality Target Product Profile.....	144
Figure 12-5.	Regulatory Strategist—Skills	145
Figure 13-1.	FDA IND Review Process.....	153
Figure 13-2.	Diagrammatic Representation of the ICH Common Technical Document (CTD)	158
Figure 13-3.	Timeline and Product Review Clock	161
Figure 13-4.	Timeline and PDUFA Review Clock for Products Under “The Program” Described in <i>PDUFA V</i>	162
Figure 14-1.	Summary of Reporting Categories for Postapproval Changes	172
Figure 14-2.	Example of CMC Index	177
Figure 15-1.	Pending ANDAs	186
Figure 15-2.	Median ANDA Approval Times.....	187
Figure 15-3.	FDA’s ANDA Approval Process.....	188
Figure 17-1.	Example of an OTC Drug Facts Label	214
Figure 31-1.	Framework for Assessing Risk of Gene Therapy-Related Delayed Adverse Events	382
Figure 33-1.	Sample Supplement Facts Boxes.....	401
Figure 37-1.	Drug-Diagnostic Co-Development Process	470
Figure 40-1.	Fraud Detection Technology	500

Tables

Table 2-1.	Other Laws, Regulations and Guidelines.....	22
Table 3-1.	21 CFR Parts Most Relevant to Drug and Device Development	29
Table 3-2.	Key Questions to be Addressed in a Drug Development Program	33
Table 3-3.	IND Safety Reporting Timeframes.....	38
Table 3-4.	Summary of Device Classification System	39
Table 4-1.	Description of FDA Product Application Meetings and Associated Timelines.....	57
Table 7-1.	Comparison of HT Regulation and HTA Regulation.....	78
Table 7-2.	Types of HTA Products and Search Approaches	80
Table 11-1.	Cost of Principal User Fee Programs for Fiscal 2014 and Fiscal 2015*.....	135
Table 15-1.	Median ANDA Approval Times.....	191
Table 16-1.	180-Day Exclusivity Forfeiture Snapshot.....	204
Table 16-2.	Differences Among Applications Submitted and Approved Under FD&C Act Section 505	205
Table 17-1.	NDA vs. OTC Drug Monograph.....	211
Table 17-2.	OTC monograph therapeutic category subtopics evaluated* as part of the OTC review process. (Therapeutic category subtopics in BOLD are codified in the final monographs)	212
Table 18-1.	PLR Format, Associated Regulations and Guidance Documents	222
Table 21-1.	Domestic Establishments	267
Table 21-2.	Foreign Establishments	268
Table 21-3.	Annual Registration Process	271
Table 21-4.	UDI Implementation Compliance Dates	274
Table 24-1.	Key Milestones in the Regulatory Oversight of Biologics.....	300
Table 24-2.	Key CMC Guidance for Biological Product Development	306
Table 24-3.	BLA Review Timetable.....	309
Table 24-4.	Biosimilarity Guidance Documents.....	312
Table 27-1.	Unique Proposed Postmarket Safety Reporting Provisions for Combination Products	347
Table 30-1.	21 CFR 1271	366
Table 30-2.	Overview of the Core CGTP Requirements (21 CFR 1271, Subpart D).....	369
Table 30-3.	FDA Regulation of Minimally Manipulated Cord Blood Products.....	370
Table 31-1.	Summary of Select Revenue-Generating Regenerative Medicine Products Currently on the Market	374
Table 31-2.	Definition of Minimal Manipulation	375
Table 31-3.	361 and 351 Product Classification and Regulation	376
Table 31-4.	Examples of Potential Regenerative Medicine Combination Products	378

Table 31-5.	Summary of Important IND Information for Generation of Cell Populations for Therapeutic Use	379
Table 31-6.	Integration Properties of Current Commonly Used Gene Therapy Vectors in Clinical Trials	383
Table 31-7.	Guidance Available for Regenerative Medicine Products (In Reverse Chronological Order)	384
Table 32-1.	Definition of Pediatric Subpopulations	393
Table 34-1.	Examples of Claims That Misbrand or Adulterate Cosmetic Products	423
Table 35-1.	Summary of Veterinary Product Types	438
Table 37-1.	Principal FDA Policy and Guidance Documents	469
Table 39-1.	FDA Enforcement Actions	487
Table 40-1.	State Laws on Manufacturer Interaction With Healthcare Providers.....	499
Table 41-1.	Agencies, Organizations, Institutes, Centers and Offices Associated With Healthcare Product Regulation	506
Table 41-2.	Publisher Resources.....	508
Table 41-3.	Databases for Healthcare Product Regulatory-Related Intelligence	510
Table 41-3.	Databases for Healthcare Product Regulatory-Related Intelligence (con't.)	512
Table 41-4.	Societies, Trade Associations, Advocacy Groups and Associations Providing Learning Resources	520