# Table of Contents

## SECTION I: Fundamentals of US Medical Device Regulations

### Chapter 1 History of Food, Drug and Cosmetic Laws
- Chapter 1: History of Food, Drug and Cosmetic Laws
- Updated by Meredith Brown-Tuttle, RAC, FRAPS

### Chapter 2 Overview of Drug, Biologic, Device, Combination Product or Food Regulatory Pathways
- Chapter 2: Overview of Drug, Biologic, Device, Combination Product or Food Regulatory Pathways
- Updated by Michael R. Hamrell, PhD, RQAP-GCP, CCRA, FACRP, RAC, FRAPS

### Chapter 3 Clinical Trials: GCPs, Regulations and Compliance for Drugs, Biologics and Medical Devices
- Chapter 3: Clinical Trials: GCPs, Regulations and Compliance for Drugs, Biologics and Medical Devices
- Updated by Monique Carter, MS, RAC and Samantha Zappia, MS, RAC

### Chapter 4 Current Good Manufacturing Practices and Quality System Design
- Chapter 4: Current Good Manufacturing Practices and Quality System Design
- Updated by Joscelyn Bowersock, MS-RA, and Richard Vincins, CQP, MCQL, CBA, CQA, RAC

### Chapter 5 Medical Device Submissions
- Chapter 5: Medical Device Submissions
- Updated by Maria Connolly, MPharm and Thomas McNamara, MSE, RAC

### Chapter 6 Medical Device Compliance and Postmarketing Activities
- Chapter 6: Medical Device Compliance and Postmarketing Activities
- Updated by Ryan Burke, RAC and Elizabeth Goldstein, RAC

### Chapter 7 In Vitro Diagnostics Submissions and Compliance
- Chapter 7: In Vitro Diagnostics Submissions and Compliance
- Updated by Jocelyn Jennings, MS, RAC

### Chapter 8 Advertising, Promotion and Labeling for Medical Devices and In Vitro Diagnostics (IVDs)
- Chapter 8: Advertising, Promotion and Labeling for Medical Devices and In Vitro Diagnostics (IVDs)
- Updated by Carol M. Cooper, MS, IM(ASCP), RM(AAM), RAC

## Appendices

- Glossary of Terms
- Index of Laws and Guidances
- Index by Subject

## Figures

- Figure 2-1: Decision Tree for Drug and Device Development and Approval When FDA Premarket Review is Required
- Figure 2-2: CTD Organization
- Figure 3-1: Types of Pharmaceutical and Biologic Clinical Trials and Typical Pathway
- Figure 3-2: Types of Medical Device Clinical Trials and Typical Pathway
- Figure 4-1: Quality System Documentation Elements
- Figure 4-2: Design Control “V” Model Process Flow

## Tables

- Table 1-1: Electronic Resources for US Laws and Regulations
- Table 1-2: Other Laws, Regulations and Guidelines
SECTION II: Fundamentals of EU Medical Device Regulations

Chapter 1  The New Medical Device Regulation and In Vitro Diagnostic Device Regulation
By Gert Bos, PhD, FRAPS and Erik Vollebregt, LLM

Chapter 2  The European Medical Devices Legal System
By Gert Bos, PhD, FRAPS and Erik Vollebregt, LLM

Chapter 3  Medical Devices: Legislation and Classification
Updated by Nicole Beard, MSc, PhD

Chapter 4  In Vitro Diagnostic Medical Devices
Updated by Erik Vollebregt, LLM

Chapter 5  General Safety and Performance Requirements and Technical Documentation (MDR, IVDR)
By Wan-Li Liao, MD, PhD

Chapter 6  Medical Device Preclinical Testing
By Sharad Mi, Shukla, RAC (US, EU) and Rajaram Balasubramanian, RAC

Chapter 7  Clinical Evaluation and Clinical Evaluations
By Loes Pelgrim, MSc and Gert Bos, PhD, FRAPS

Chapter 8  Medical Device Conformity Assessment Procedure
Updated by Gert Bos, PhD, FRAPS

Chapter 9  Medical Device Compliance: Postmarket Requirements
Updated by Peter Osterhoff, PhD and Gert Bos, PhD, FRAPS

Chapter 10 Medical Device National Particularities
Updated by Elizabeth Goldstein, RAC
Appendices

Comparative Matrix of Regulations Across Product Lines .......................................................... 111
Glossary ........................................................................................................................................ 153
Index ............................................................................................................................................ 173

Figures

Figure 1-1. Supply Chain Controls .................................................................................................. 3
Figure 1-2. Proposed EU IVDR Classification Rules ................................................................. 4
Figure 1-3. Governance Structure for the EU MDR and EU IVDR ........................................... 7
Figure 2-1. Simplified EU Legislative Process .............................................................................. 11
Figure 2-2. Flow Chart for the Conformity Assessment Procedures Provided for In Directive 93/42/EEC on Medical Devices .................................................................................. 13
Figure 2-3. Flow Chart for the Conformity Assessment Procedures Provided for In Directive 90/385/EEC on Active Implantable Medical Devices ..................................................................... 14
Figure 2-4. Flow Chart for the Conformity Assessment Procedures Provided for In Directive 98/79/EEC on In Vitro Diagnostic Medical Devices ........................................................................... 15
Figure 3-1. Classification Guidance Chart—Noninvasive Devices per MDD .............................. 42
Figure 3-2. Classification Guidance Chart—Rule 5 per MDD ................................................... 43
Figure 3-3. Classification Guidance Chart—Rule 5 per MDD ................................................... 43
Figure 3-4. Classification Guidance Chart—Rule 7 per MDD ................................................... 44
Figure 3-5. Classification Guidance Chart—Rule 8 per MDD ................................................... 45
Figure 3-6. Classification Guidance Chart—Active Devices per MDD ...................................... 46
Figure 3-7. Classification Guidance Chart—Special Rules per MDD ......................................... 46
Figure 3-8. IVD Classification Chart per MDD ...................................................................... 47
Figure 8-1. Class III Device Conformity Assessment Procedure Options ................................ 84
Figure 8-2. Class IIb Conformity Assessment Procedures ......................................................... 85
Figure 8-3. Class IIa Conformity Assessment Procedure ......................................................... 85
Figure 8-4. Class I Device, Self-Declaration or Self-Certification ............................................ 86
Figure 8-5. AIMDD Conformity Assessment Procedure .......................................................... 86
Figure 8-6. IVD Conformity Assessment Procedure ................................................................. 87
Figure 8-7. Self-Testing IVD Conformity Assessment Procedure ............................................ 87
Figure 8-8. IVDD Annex II List B Conformity Assessment Procedures .................................... 88
Figure 8-9. High-Risk IVD Conformity Assessment Procedure ................................................ 89

Tables

Table 2-1. New Approach Areas .................................................................................................. 12
Table 2-2. EU Member States and Affiliated Countries Competent Authorities ...................... 17
Table 2-3. European Commission Working Groups and Their Activities ................................. 22
Table 2-4. European Industrial Trade Associations ................................................................. 24
Table 2-5. MEDDEV Guidance Documents ............................................................................. 29
Table 2-6. European Commission Consensus Statements ......................................................... 30
Table 2-7. Informative Documents Issued by the European Commission ................................. 31
Table 2-8. NBOG Documents (NBOG Best Practice Guides) ................................................ 32
Table 4-1. Examples of General Laboratory Use Products and IVD Medical Devices ............... 51
Table 5-1. Example of a Partial GSPR Checklist ....................................................................... 60
Table 8-1. Conformity Assessment Procedures ....................................................................... 81
Table 8-2. AIMDD Conformity Assessment Documentation .................................................... 82
Table 8-3. MDD Conformity Assessment Documentation ........................................................ 83
Table 8-4. IVDD Conformity Assessment Documentation ........................................................ 84
Table 8-5. Internal Production Control ..................................................................................... 88
Table 8-6. EC Type-Examination ............................................................................................. 88
Table 8-7. Production Quality Assurance .................................................................................. 88
Table 8-8. Product Quality Assurance ...................................................................................... 89
SECTION III: Fundamentals of International Medical Device Regulations

Chapter 1 Medical Device Premarket Requirements ................................................................. 1
Updated by Amina Abdal, MS, MBA

Chapter 2 Technical and Regulatory Requirements ................................................................. 19
Updated by Robin Stephens and Echo (Yuanyuan) Yu, MS, RAC

Chapter 3 Device Quality Systems ......................................................................................... 27
Updated by Sharad Mi. Shukla, RAC, and Rajaram Balasubramanian, RAC

Chapter 4 In Vitro Diagnostic Medical Devices ...................................................................... 37
Updated by Gert Bos, PhD, FRAPS, and Jocelyn Jennings, MS, RAC

Chapter 5 Active Implantable Medical Devices ..................................................................... 57
By Gert Bos, PhD, FRAPS

Chapter 6 Software .................................................................................................................. 67
Updated by Echo (Yuanyuan) Yu, MS, RAC, and Raajdeep (Raaj) Venkatesan, MS (EE BME, MDDE), RAC

Chapter 7 Postmarket Requirements ......................................................................................... 79
Updated by Pei-Ting S. Chou, RAC

Appendices
Comparative Matrix of Regulations Across Product Lines ...................................................... 89
Glossary .................................................................................................................................... 115
Index ........................................................................................................................................ 131

Figures
Figure 1-1. Decision Tree for Noninvasive Device Classification .......................................... 12
Figure 1-2. Decision Trees for Invasive Device Classification ............................................... 13
Figure 1-3. Decision Tree 2 for Invasive Devices ................................................................... 14
Figure 1-4. Decision Tree 1 for Active Device Classification ................................................ 15
Figure 1-5. Decision Tree 2 for Active Device Classification ................................................ 16
Figure 1-6. Decision Tree for Device Classification With Additional Rules ............................ 17
Figure 2-1. Premarket Use of the STED ................................................................................. 21
Figure 2-2. Postmarket Use of the STED .............................................................................. 22
Figure 3-1. Influence of Design Controls on the Design Process .............................................. 30
Figure 3-2. Process Validation Decision Tree .......................................................................... 32
Figure 3-3. Key Activities for Supplier Control ......................................................................... 33
Chapter 1 Health Canada ................................................................................................................................. 1
  Updated by Don Boyer, RAC, FRAPS

Chapter 2 Investigational Testing and Special Access Programme ................................................................. 9
  By Annie Levesque, MSc, RAC (CAN) and Jennifer Cabralda, RAC (US, CAN)

Chapter 3 Medical Device Submission and Approval Process ........................................................................ 19
  By Dinar Suleman RAC (US, Can) and Karen Long RAC (US, EU, Can, GS)

Chapter 4 In Vitro Diagnostic Medical Devices .............................................................................................. 39
  By Ugbaad Elmi and Sabrina Sharif

Chapter 5 Medical Device Quality System Requirements .................................................................................. 47
  Updated by Karen Fan, MSc, RAC, Peng, Charles Tam, MBA, and Danuta Zylka

Chapter 6 Medical Device Classification ........................................................................................................... 61
  Updated by Melissa Lake, RAC (US, CAN) and Janice Wright

Chapter 7 Medical Device Labelling, Advertising, Promotion ........................................................................ 75
  By Karen Long, RAC (US, EU, Can, GS) and Dinar Suleman RAC (US, Can)

SECTION IV: Fundamentals of Canadian Medical Device Regulations
Chapter 8  Medical Device Postmarketing Activities ................................................................. 85
   Updated by Kathryn Ronalds, RAC and Ana Bascom, MSc

Chapter 9  Medical Device Establishment Licensing .......................................................... 107
   Updated by Danuta Zylka, RAC

Index ........................................................................................................................................... 111

Figures

Figure 1-1.  Health Canada ........................................................................................................ 2
Figure 1-2.  Branches with Responsibility for the Regulation of Healthcare Products .......... 3
Figure 5-1.  MDSAP Audit Sequence ...................................................................................... 54
Figure 5-2.  MDSAP Nonconformity Grading Overview ......................................................... 55
Figure 5-3.  MDSAP Nonconformity Grading Matrix ............................................................... 56
Figure 5-4.  MDSAP Post-Audit Activities and Timeline ......................................................... 57
Figure 7-1.  Sample Letter of Attestation .............................................................................. 82
Figure 7-2.  Flowchart H—Changes to Labelling ................................................................. 83
Figure 8-1.  Export Certificate ............................................................................................... 88
Figure 8-2.  Complaint Form ................................................................................................. 95

Tables

Table 2-1.  Stages of Product Development for Medical Devices .......................................... 10
Table 2-2.  Record Requirements per MDR Section 81 ......................................................... 11
Table 2-3.  Content of an ITA Application for Non-IVDDs and IVDDs ................................. 12
Table 2-4.  Examples of Additional Information that May be Requested from the Manufacturer .......................................................... 15
Table 3-1.  Types of Medical Device Licence Applications ................................................... 22
Table 3-2.  Required Information for Medical Device Licence (MDL) Application Form ........ 24
Table 3-3.  Accepted Formats for Device Submissions .......................................................... 27
Table 3-4.  Table of Contents (ToC) Submission Folder Structure and Naming Conventions .......................................................... 28
Table 3-5.  Specific Content Requirements for Devices in ToC Format ................................ 29
Table 3-6.  Class III Medical Device Health Canada Non-IVDD Submission Folder Structure and Naming Conventions .......................................................... 30
Table 3-7.  Health Canada IVDD Submission Folder Structure and Naming Conventions .......................................................... 31
Table 3-8.  Class IV Medical Device Health Canada Non-IVDD Submission Folder Structure and Naming Conventions .......................................................... 32
Table 3-9.  STED-Based IVDD Submission Folder Structure and Naming Conventions .......................................................... 33
Table 3-10.  STED-Based non-IVDD Submission Folder Structure and Naming Conventions .......................................................... 36
Table 4-1.  IVDD Classifications ............................................................................................ 40
Table 6-1.  Classification Examples ....................................................................................... 63
Table 6-2.  Classification Rules and Associated Device Classes—Non-IVDDs ................. 68
Table 6-3.  Classification Rules and Associated Device Classes—IVDDs ............................ 70
Table 7-1.  Directions for Use Sections ................................................................................. 77
Table 7-2.  Schedule 2 Implant Devices (Require Implant Registration Cards) ................... 77
Table 7-3.  Additional Requirements for Some Devices ......................................................... 78
Table 7-4.  IVDD Package Insert Information ....................................................................... 80
Table 8-1.  Type of TPD Authorization Required for the Importation of Devices for Various Uses .......................................................... 87
Table 8-2.  Regulatory Requirements Assessed During HPFB Inspection of Medical Device-Related Companies ..... 102