Table of Contents

Section I: Quality Management Systems

Chapter 1 Setting up a Quality Management System 1
By Abhishek Harde, PMP, RAC

Chapter 2 Medical Device Quality Management Systems 35
By Gert Bos, MSc, PhD, FRAPS

Chapter 3 Canadian Medical Device Quality System Requirements 47
By Karen Fan, MSc, RAC, Peng, Charles Tam, MBA, and Danuta Zylka

Chapter 4 Quality Systems and Inspectorate Process for Pharmaceuticals 63
By Siegfried Schmitt, PhD

Chapter 5 Regulatory Requirements for Design and Process Validation 85
By Robert V. Packard and Leo Lagrotte

Chapter 6 Quality Risk Management—A Gateway to Quality by Design 93
By Peter Schiemann, PhD and Beat Widler, PhD

Chapter 7 Product Lifecycle Management Guidance 105
By Ajay Babu Pazhayattil, Naheed Sayeed-Desta, and Queenia Lee

Section II: Laboratory Testing

Chapter 8 Good Laboratory Practice for Nonclinical Laboratory Studies 113
By Navneet Sekhon

Chapter 9 Nonclinical Laboratory Testing 121
By Dorota Grabowska, PhD and Peter A. Takes, PhD, RAC, FRAPS

Chapter 10 Medical Device Preclinical Testing 135
By Jan-Paul van Loon, MSc, PhD and Gert Bos, MSc, PhD, FRAPS

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org

Chapter 11 Preclinical Testing and Good Laboratory Practice Regulations 145
By Anu Gaur, PhD, MBA, MSRA, RAC

Chapter 12 Good Laboratory Practice Regulations 155
By Kurt Stahl and Jennifer G. Brown, PhD, RAC

Section III: Production

Chapter 13 Manufacturing 169
By Andrea Armando, RAC

Chapter 14 Current Good Manufacturing Practices and Quality System Design 177
By Joscelyn Bowersock, MS-RA and Richard Vincins, CQP, MCQL, CBA, CQA, RAC

Chapter 15 Canadian Good Manufacturing Practices and Establishment Licensing 197
By Bocar Guisse, MSc and Fraidianie Sévigné

Chapter 16 Impact of Good Manufacturing Practices on Printed Packaging Components 215
By Debra Goetchius

Chapter 17 CMC Regulatory Strategy 237
By Stephen Antonelli and Michael Craig

Chapter 18 Fundamental Principles for Labeling and Promotion of Prescription Medical Products 247
By Joanne S. Hawana, MS, JD, Bethany J. Hills, MPH, JD, and Benjamin M. Zegarelli, MS, JD

Section IV: Clinical Studies

Chapter 19 Clinical Trials, Good Clinical Practice, Regulations, and Compliance 295
By Anu Gaur, PhD, MBA, MSRA, RAC, Bettina Merz-Nideroest, MPharm, and Andrea Zobel, PhD

Chapter 20 Canadian Clinical Trial Applications, Good Clinical Practices 313
By Mahdis Dorkalam, MSc, RHN, and Navneet Sekhon

Chapter 21 EU Clinical Evaluation and Clinical Investigations 325
By Loes Pelgrim, MSc and Gert Bos, MSc, PhD, FRAPS

Chapter 22 Clinical Trials: GCPs, Regulations and Compliance for Drugs, Biologics and Medical Devices 333
By Monique Carter, MS, RAC and Samantha Zappia, MS, RAC

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org

Section V: Inspection, Compliance, and Enforcement

Chapter 23 Compliance and Enforcement 377
By David W. Husman, PhD, ASQ CPGP, RAC and John Rossman, MBEE, RAC

Chapter 24 FDA Inspection and Enforcement 399
By Robert Rogers, MS, RAC

Chapter 25 Components of a REMS: Communication Plans and Implementation Systems 411
By Edward Tabor, MD

Chapter 26 Components of a REMS: Elements to Assure Safe Use 413
By Edward Tabor, MD

Chapter 27 Components of a REMS: REMS Assessment 419
By Edward Tabor, MD

Chapter 28 Risk Management in the Medical Device and Food Industries 423
By Salma Michor, PhD, MBA, CMgr, CQA, RAC

Tables

Table 1-1. Key Differences Between ISO 9001 and ISO 13485 1
Table 1-2. Similarities Between ISO 9001 and ISO 13485 2
Table 1-3. Comparison of ISO 13485:2003 and ISO 13485:2016 6
Table 1-4. Applicability of ISO 13485 in Various Global Jurisdictions 12
Table 1-5. Benefits and Barriers to Certification 20
Table 1-6. Certification Body QMS Assessment Objectives, Scope and Criteria 20
Table 1-7. Audit Duration for Medical Device ISO 13485 Audits Based on Staff Numbers 22
Table 1-8. Factors That May Increase or Reduce Audit Durations 22
Table 4-1. PIC/S Member States 78
Table 6-1. Traditional Quality Management vs. QRM Approach 101
Table 9-1. The Universal Elements of GLP 123
Table 9-2. Examples of GLP Violations From FDA Warning Letters 124
Table 9-3. Sources of Device Risk 125
Table 9-4. Biocompatibility Tests 125
Table 9-5. Medical Device Classification Based on the Nature of Body Contact and Contact Duration 126
Table 9-6. Basic Animal Study Protocol Elements 127
Table 9-7. Animal Models for In Vivo Medical Device Assessment 129
Table 9-8. International Animal Research Laws, Policies and Guidelines 129
Table 9-9. Useful Web Resources for Planning and Conducting Animal Studies in Accordance With the Three Rs' Principles 130
Table 9-10. Questions a Company Should Consider When Selecting a CRO 132
Table 16-1. Select Resources on Pictogram Use 222
Table 17-1. Centralised Procedure Requirements Based on Product Type 239
Table 17-2. Regulatory Authorities by Country 239

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org

Table 18-1. Selected FDA Regulations for the Labeling of Prescription Drugs 248
Table 18-2. Selected FDA Regulations for Device Labeling 249
Table 18-3. FDA's Categorization of Promotional Materials (21 CFR 202.1(l)) 250
Table 18-4. Summary of PI Sections Under the PLR, Including Relevant Regulations and Available Guidance 257
Table 18-5. Other Product Claim Types 266
Table 18-6. Risk-Related Sections of the PI Ranked From Most to Least Important 271
Table 19-1. Regional Regulatory Authorities 302
Table 19-2. Trial Master File Essential Documents 310
Table 20-1. Contents of a CTA Submission Package 317
Table 20-2. Quality Changes-Biologics and Radiopharmaceuticals 318
Table 20-3. Quality Changes—Pharmaceuticals 319
Table 20-4. Postapproval Requirements 322
Table 22-1. Significant Legislation Relevant to Clinical Trials in the US 335
Table 22-2. Comparison of 21 CFR and ISO-GCP Requirements for Protocol Deviations in Medical Device Clinical Trials .. 341
Table 22-3. Comparison of 21 CFR and ISO GCP Requirements for Investigator Responsibilities in Medical Device Clinical Trials .. 367
Table 22-4. Comparison of 21 CFR and ISO-GCP Requirements for Recordkeeping in Medical Device Clinical Trials 370
Table 22-5. Comparison of 21 CFR and ISO-GCP Requirements for Device Accountability in Medical Device Clinical Trials ...370
Table 23-1. Applicability of GxPs to Standardized Market Authorization Application Formats 388
Table 24-1. FDA Enforcement Actions 405
Table 26-1. ETASUs Approved Per Year 414
Table 28-1. Content Deviations Between ISO 14971:2007 and Directive 93/42/EEC on Medical Devices 424

Figures

Figure 1-1. Basic Process Model 3
Figure 1-2. PDCA Cycle in Resource Management 4
Figure 1-3. Mandatory Procedures and Documents for ISO 13485:2003 11
Figure 1-4. Implementing an ISO 13485:2016 QMS 13
Figure 1-5. Sample Schedule for QMS Implementation 15
Figure 1-6. QMS Documentation Defining Responsibilities 16
Figure 1-7. Typical QMS Document Hierarchy 17
Figure 1-8. Iterative PDCA Cycle 20
Figure 1-9. ISO 17021 QMS Certification Cycle 21
Figure 1-10. Design Process 27
Figure 2-1. Process Flow of Interrelated QMS Processes 36
Figure 2-2. PDCA Methodology 37
Figure 2-3. Requirements Clauses in ISO 13485:2016 38
Figure 2-4. Design and Development Control Steps 40
Figure 2-5. Influence of Design Controls on the Design Process 40
Figure 2-6. Process Validation Decision Tree 43
Figure 2-7. Key Activities for Supplier Control 45
Figure 3-1. MDSAP Audit Sequence 55
Figure 3-2. MDSAP Nonconformity Grading Overview 57
Figure 3-3. MDSAP Nonconformity Grading Matrix 58
Figure 3-4. MDSAP Post-Audit Activities and Timeline 59
Figure 4-1. Drug Lifecycle Regulations 63
Figure 4-2. Assessors and Inspectors 64

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org

Figure 4-3. EU Legal Instruments 67
Figure 4-4. Inspections as Part of the Drug Approval Process 68
Figure 6-1. Failure Mode and Effect Analysis Cycle 96
Figure 6-2. Three-step RPN-based Risk Evaluation 99
Figure 6-3. Example of QRM in Action 100
Figure 9-1. Strategy for Performing Animal Studies 128
Figure 16-1. NDC Number Example 218
Figure 16-2. Trade Bottle Label 225
Figure 16-3. Small Container Label (Small Label Exemption Rule) 225
Figure 16-4. Folding Carton for Pharmaceutical Drug Product 228
Figure 16-5. Biologic Label 231
Figure 16-6. Biologic Carton Label 231
Figure 19-1. Acceptance of Foreign Clinical Data 301
Figure 19-2. Quality Management System 306
Figure 22-1. Types of Pharmaceutical and Biologic Clinical Trials and Typical Pathway 342
Figure 22-2. Types of Medical Device Clinical Trials and Typical Pathway 361
Figure 23-1. TPLC Cycle for Devices 379
Figure 23-2. Medical Device Design Control and Review Process 380
Figure 28-1. The Risk Management Process 425
Figure 28-2. Principal Activities for Risk Management 427
Figure 28-3. The Risk Management Process 430

Sidebars

Sidebar 18-1. Enforcement Example Mirapex 9/2008 251
Sidebar 18-2. Enforcement Example Focalin XR 5/2011 265
Sidebar 18-3. Enforcement Example Idelvion, 2/2018 269
Sidebar 18-4. Enforcement Example Estring 6/2018 270
Sidebar 18-5. Enforcement Example Vantas 9/2012 273
Sidebar 18-6. Enforcement Example Contrave 5/2017 276
Sidebar 18-7. Enforcement Example Muse 5/2004 and 4/1998 277
Sidebar 18-8. Enforcement Examples MiraLax 3/2001 and Patanol 3/2001 279
Sidebar 18-9. Enforcement Example Tasigna 7/2010 284
Sidebar 18-10. Enforcement Example NCS Pearson 8/2015 289

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org

1 Setting up a Quality Management System

By Abhishek Harde, PMP, RAC

Introduction

Building a quality management system (QMS) from scratch can be challenging, especially when the appropriate regulatory standards or compliance guidelines are not followed. Management system standards make best practices available to organizations of all sizes, in all sectors. Any organization can implement a system to improve efficiency and effectiveness and manage its way of doing things by:

- ensuring nothing important is omitted
- clearly defining who is responsible
- describing what to do, why, when, how and where
- ensuring people are not just "doing their own thing"
- ensuring the organization goes about its business in an orderly way[1]

Quality management is the set of coordinated activities to direct and control an organization with regard to quality.[2] Quality management systems are central to the medical device regulatory process in many countries to ensure safe products entering the market perform as intended. Streamlining and automating design documentation and quality processes to align with major industry regulations and standards are key criteria for setting up a quality management system. In this chapter, the focus is on ISO 9001 and ISO 13485,[3,4] and subsequently, US FDA's *Quality System Regulation (QSR)*[5] contained in 21 CFR 820. ISO 13485:2016 *Medical Devices—Quality Management Systems—Requirements for Regulatory Purposes* is a QMS standard based on ISO 9001 *Quality Management Systems Requirements*. The ISO 9000 series, originally published in 1987, was based on the British Standards Institution's (BSI) BS 5750 series of standards.[6] ISO 9001 covers both product quality assurance (providing confidence that quality requirements will be fulfilled) and enhanced customer satisfaction. Key differences between ISO 9001 and ISO 13485 are shown in **Table 1-1**.[7] Similarities between ISO 9001 and ISO 13485 are shown in **Table 1-2.** The standard can be applied to all products and services. ISO 9001 is based on the eight quality management principles:

1. process approach
2. system approach to management
3. continual improvement
4. factual approach to decision making
5. mutually beneficial supplier relationship
6. customer focus
7. leadership
8. involvement of people[8]

Table 1-1. Key Differences Between ISO 9001 and ISO 13485

ISO 9001	ISO 13485
6 documents	27 documents
Aims for customer satisfaction through continuous improvement	Does not include customer satisfaction and continuous improvement as objectives
Covers all products	Different requirements for different types of products
Basis for voluntary certification	Basis for regulatory certification

Purchased from RAPS Library (library.raps.org) for the exclusive use of unknown.
© 2026 RAPS Library. Please report unauthorized use to raps@raps.org