

Author Acknowledgments

RAPS and lead editor, J. Michael Sprafka, MPH, PhD, thank the following subject matter experts for sharing their experience and knowledge and volunteering their time to contribute to this third edition of *Risk Management Principles for Devices and Pharmaceuticals*.

Nayan Achayara, MBBS,
MRCP, MFPM
Chapter 1

Jessica D. Albano, PhD, MPH
VP, Epidemiology & Analytics
Syneos Health
Chapter 14

Krishna Bahadursingh, MD,
FRCS, MBA, LLB, FFPM
Head of WorldWide Patient
Safety-Japan
Bristol Myers Squibb

Judy Bingham, MHA, GAICD
Executive Director
Easington Pty Ltd
Chapter 4

Mariette Boerstoele-Streefland,
MD, MSc, MBA
Chief Safety Officer, SVP
Patient Safety
AstraZeneca
Chapter 16

Brian Buysse, PhD
Senior Director, Epidemiology
Syneos Health
Chapter 14

Jemma Contreras, PhD
Advisory Group Lead, R&D
Consulting
Syneos Health
Chapter 23

Lindsay Crampton, BSc
Advisory Group Lead, Risk
& Program Management,
Consulting
Syneos Health
Chapter 23

George Cusatis MS, RAC
Sr. Regulatory Affairs Manager
Medtronic
Chapter 3

Karin de Haart, MSc
Product Strategy Lead
IQVIA
Chapter 13

Bruce R. DeMark, PhD
Retired Research Fellow
Procter & Gamble
Pharmaceuticals
Chapter 20

Debashish Dey, MD, PhD,
MPH
Vice President & Head, Drug
Safety & Pharmacovigilance
Intellia Therapeutics

Bernadette Dwan, BSc,
Mpharm, MPSI
Product Strategy Lead
IQVIA
Chapter 13

Michael Engwall, DVM, PhD,
DSP
Chapter 6

Sara Ephross, PhD
Senior Director, Epidemiology
Syneos Health
Chapter 14

Matthew Francis, MS, PhD
Epidemiologist
Procter and Gamble
Chapter 10

Angie Graves, MBA,
MLS(ASCP)
Senior Director, Business
Operations, Real World &
Late Phase
Syneos Health
Chapter 14

Mark Heinemann, BSc
Associate Director, Regulatory
Advice & Delivery
Syneos Health France SARL
Chapter 12

Lisette Hoogendoorn, PhD
Epidemiology Director
IQVIA
Chapter 13

Leo Hovestadt, MSc
Director Governmental Affairs
EU

Elekta
Chapters 7, 11 and 15

Yong Huang, MD, PhD
Associate Director
Bristol Myers Squibb Japan
Chapter 2

Tara Isherwood, MSc, BSc
(Hons)
Senior Director, Regulatory
Advice and Delivery
Syneos Health
Chapter 12 and 14

David Konadu, MSc, MASc
Senior Analyst, Quality
Systems
Edwards Lifesciences
Chapter 5

Richard Loomis, MD
Chief Informatics Officer,
Clinical Solutions
Elsevier
Chapter 19

Nadja Merkusheva, MD
Sr. Principal, Strategic RW
Solutions
IQVIA
Chapter 13

Andrej Miotk, PhD
Senior Product Vigilance
Manager
P&G
Chapter 10

Elaine H. Morrato, DrPH,
MPH, CPH
Founding Dean and Professor
Parkinson School of Health
Sciences and Public Health
Loyola University Chicago
Chapter 21

Hiroshi Nakane
Senior Manager
Gilead Sciences
Chapter 2

Darin Oppenheimer DRSc,
FRAPS, RAC
AVP Regulatory Affairs
Agilent Technologies
Chapter 3

Debra Porter, MS
Associate Director, Project
Management
Eli Lilly and Company
Chapter 1

Russ Roberson, PhD, MBA,
MScME, BScAgE
Chapter 9

Peter Schiemann, PhD, MBA
Managing Partner and
Co-Founder
Widler & Schiemann Ltd.
Chapter 8

Paul Sheehan, MSJ, BSc
Vice President
Synoes Health
Chapter 23

Meredith Y. Smith, PhD, MPA,
FISPE
Senior Director,
Implementation Science
Evidera, Inc., PPD, a part of
Thermo Fisher Scientific
Chapter 22

Michael Steinbuch, PhD,
FISPE
Senior Director, Global Head
of Postmarket Product
Vigilance
Procter & Gamble
Chapter 10

Tjeerd-Pieter van Staa, MD,
MSc, MA, PhD
Professor of Health eResearch
University of Manchester
Chapter 17

Priscilla Velentgas, PhD
Senior Principal
IQVIA
Chapter 13

Angela Walker, MD
Senior Director of Quality
Clinical Solutions
Chapter 19

Beat Widler, PhD, dipl. pharm.
med.
Managing Partner and
Co-Founder
Widler & Schiemann Ltd.
Chapter 8

Fei Xue, MD, MSC, ScD
Global Safety Medical Director,
Safety Officer
Amgen Inc.
Chapter 18

Brande Yaist, MS
Associate Vice President,
Value, Evidence and
Outcomes-Immunology
Eli Lilly and Company
Chapter 1

SECTION

I

Risk Management Regulations

Section I: Risk Management Regulations
Chapter 1: Risk Management Regulations in the US

1

Risk Management Regulations in the US

Brande Yaist, MS; Debra Porter, MS; Debashish Dey, MD, PhD, MPH; and Nayan Achayara MBBS, MRCP, MFPM

Introduction

The role of risk management in the drug development and postmarket environment is to optimize user benefits while minimizing risk and maintaining appropriate access. Managing risk involves many diverse individuals, including scientists, regulators, policymakers, physicians, healthcare providers, and patients. In early development, nonclinical study data are used to initiate the development of a human testing safety profile. During Phase 1 development, risks are managed at the individual patient level through careful monitoring and observation. As the drug progresses further into Phase 2 and 3 clinical trials, safety data are aggregated to assess risk at a population level. Following approval, the population exposed to the drug becomes more diverse, expanding the breadth and complexity of data and information on the drug's benefits and risks.

The science and process of risk management have evolved over time. This evolution is reflected in the activities conducted as well as the governing regulations and guidelines. Risk management is becoming increasingly complex, with the globalization of requirements, increased availability of potential data sources through

advanced technology, digitization, and changes to the healthcare delivery system. The complexity and nature of clinical development and postmarket experience require a proactive, systematic, and scientific approach to measuring or assessing risk and developing strategies to manage or mitigate it.

Risk Management Concepts

Pharmacovigilance Overview

Pharmacovigilance (PV) refers to scientific activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem.¹ One PV objective is to maintain a current safety profile, which includes information regarding the drug's known and potential risks in the context of its efficacy information, forming the benefit-risk profile under which the product is used. When discussing risk, it is important to differentiate between harm (the damage resulting from taking the drug) and risk (the probability that harm could result from taking the drug).

Safety information is collected to monitor and maintain biopharmaceutical products' safety profile. In the US and many other countries,