This edition is dedicated to the victims of the fungal meningitis outbreak of 2012, who serve as an enduring reminder of the consequences of poor compounding practice.

E. Clyde Buchanan
Philip J. Schneider
Ryan A. Forrey
# Table of Contents

Acknowledgments ............................................................................................................................ ix  
Preface ............................................................................................................................................... xi  
Contributors .................................................................................................................................... xiii  
Reviewers ......................................................................................................................................... xv  

## Part I Sterile Preparation

1 Imperative for Change: Adverse Sterile Compounding Events ............................................. 1  
   Philip J. Schneider, MS, FASHP, FFIP, FASPEN  

2 Standards for Compounded Sterile Preparations ................................................................. 7  
   E. Clyde Buchanan, RPh, MS, FASHP  

3 Immediate-Use Compounding ............................................................................................... 35  
   Jeannell M. Mansur, PharmD, RPh, FASHP  

4 Sterile Preparation Formulation ........................................................................................... 51  
   Mark G. Klang, RPh, MS, BCNSP, PhD  

5 Parenteral Nutrition Compounding ....................................................................................... 67  
   Todd W. Canada, PharmD, BCNSP, BCCCP, FASHP, FTSHP  

6 Special Considerations in Pediatric Compounding ............................................................... 81  
   Kathleen M. Gura, PharmD, BCNSP, FASHP, FPPAG, FASPEN  

7 Special Considerations in Compounding Biologicals ........................................................... 113  
   Susan Spivey, PharmD; Kelley Reece, PharmD; and Ryan K. Roux, PharmD, MS, RPh, FASHP  

8 Ancillary Equipment and Supplies ......................................................................................... 121  
   Ryan A. Forrey, PharmD, MS, FASHP  

9 Primary Engineering Controls ................................................................................................. 133  
   Richard C. Capps, PharmD  

10 Personnel Cleansing and Garbing ......................................................................................... 153  
   Richard B. Osteen, DPh  

11 Aseptic Technique .................................................................................................................. 161  
   Linda F. McElhiney, PharmD, MSP, RPh, FIACP, FASHP, FACA  

12 Handling and Compounding Hazardous Drugs ................................................................. 171  
   Luci A. Power, RPh, MS and Joseph W. Coyne, BS Pharm, RPh  

13 Radiopharmaceuticals As Compounded Sterile Preparations ........................................... 203  
   George H. Hinkle, RPh, MS, BCNP
14 Storage and Beyond-Use Dating ................................................................. 213
  Caryn Dellamorte Bing, RPh, MS, FASHP

15 Labeling Sterile Preparations ...................................................................... 227
  Patricia Kuban, RPh, MBA

16 Documentation of Compounded Sterile Preparations ............................... 243
  Ryan A. Forrey, PharmD, MS, FASHP

17 Sterility Assurance of Compounded Sterile Preparations ............................. 249
  Angela W. Yaniv, PharmD

18 Finished Preparation Release Checks and Tests ........................................... 257
  Angela W. Yaniv, PharmD

19 Microbiological Issues in Compounding Sterile Preparations ....................... 267
  Keith H. St. John, MT(ASCP), MS, CIC, FAPIC and Radhakrishna S. Tirumalai, PhD

20 Handling Sterile Commercial Products and Compounded Sterile Preparations within the Pharmacy ........................................................... 283
  Ryan A. Forrey, PharmD, MS, FASHP

21 Maintaining Sterility, Purity, and Stability of Dispensed and Distributed CSPs .......................................................... 295
  Caryn Dellamorte Bing, RPh, MS, FASHP

22 Batch Compounding ..................................................................................... 303
  Richard B. Osteen, DPh

Part II QUALITY MANAGEMENT

23 Pharmacist Education ................................................................................. 315
  Philip J. Schneider, MS, FASHP, FFIP, FASPEN

24 Pharmacy Technician Education, Certification, Training, Evaluation, and Regulation.... 323
  Mary Ann Stuhan, PharmD, RPh

25 Secondary Engineering Controls ................................................................... 333
  E. Clyde Buchanan, RPh, MS, FASHP

26 Sterile Compounding Technology .................................................................. 363
  Bruce A. Erickson, RPh, MS and Craig Boyce, RPh

27 Cleaning and Disinfecting .......................................................................... 409
  Ryan A. Forrey, PharmD, MS, FASHP

28 Environmental Quality and Control .............................................................. 425
  Patricia C. Kienle, RPh, MPA, FASHP

29 Dealing with Latex Allergies ........................................................................ 437
  Stephen K. Hetey, RPh, MS, FASHP

30 Personnel Training and Competency Evaluation of Garbing and Aseptic Work Practices .......................................................... 445
  Linda F. McElhiney, PharmD, MSP, RPh, FIACP, FASHP, FACAC

31 Policies, Procedures, and Quality Assurance Programs ............................... 453
  Patricia C. Kienle, RPh, MPA, FASHP

32 Outsourcing the Compounding of Sterile Preparations ............................... 473
  E. Clyde Buchanan, RPh, MS, FASHP
APPENDIXES
Appendix A: ASHP Guidelines on Compounding Sterile Preparations .......................... 489
Appendix B: ASHP Guidelines on Handling Hazardous Drugs ....................................... 517
Appendix C: Selected ASHP Guidelines Pertaining to Sterile Compounding ..................... 545
Appendix D: Selected Websites Pertaining to Compounding Sterile Preparations ............... 547

Glossary ......................................................................................................................... 551
Index ............................................................................................................................... 567
Every day many pharmacists and pharmacy technicians participate in compounding sterile preparations. In the vast majority of cases, their preparations are accurate, stable, pure, and sterile. We salute these health professionals who maintain essential high standards. Such work requires great attention to detail and genuine care for patients.

We are grateful to Ruth Bloom, Beth Campbell, Kristin Eckles, and the many other ASHP staff members who reviewed and edited each chapter of this text. We express special gratitude to Jack Bruggeman, former ASHP Director of Special Publishing, who began working with us on this book in 2014. Without his encouragement and support, our work would not have been possible.

Finally, to our family members and friends who gave us the space and emotional support to finish, we express our heartfelt appreciation.

E. Clyde Buchanan
Philip J. Schneider
Ryan A. Forrey
This professional reference for pharmacists and pharmacy technicians who compound sterile preparations also will serve well as a textbook for student pharmacists and pharmacy technicians. To assist with classroom use, ASHP plans to publish learning objectives and review questions and answers for each chapter. There is a robust list of references at the end of each chapter for those scholars who wish to dig deeper into this rich material.

Since the current version of USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations became official in June 2008, much has happened in the world of sterile compounding. Perhaps the most significant event, as well as the most tragic, was the multistate outbreak of fungal meningitis and other infections that occurred in 2012 (www.cdc.gov). The Centers for Disease Control and Prevention (CDC) counted 753 infected patients in 20 states, and 64 of those infected patients died. Contaminated steroid injections compounded at the New England Compounding Center in Framingham, Massachusetts, caused these infections. As a direct consequence, in 2013 the U.S. Congress passed the Drug Quality and Security Act (DQSA) to be enforced by the Food and Drug Administration. The meningitis outbreak also sparked concerns about compounding pharmacies and prompted an investigation by the Office of the Inspector General (OIG) regarding the use of compounding pharmacies by hospitals and oversight of hospital compounding by the Centers for Medicare & Medicaid Services (CMS) and its accreditating organizations (OIG report OEI-01-13-00400). The OIG recommended that accreditation surveyors be trained on standards for safe compounding practices and that CMS amend its interpretive guidelines to address hospitals’ contracts with standalone compounding pharmacies. In October 2015, CMS did so. In May 2016, one of the CMS accreditation agencies, the Healthcare Facilities Accreditation Program, published updates to its pharmaceutical standards. These standards identify extensive and specific requirements for compounded sterile preparations. The other agencies that accredit pharmacies and healthcare organizations will update their pharmacy standards too.

In February 2016, the United States Pharmacopeia finalized USP Chapter <800> Hazardous Drugs—Handling in Healthcare Settings. This enforceable chapter applies to all healthcare personnel and entities that handle hazardous drugs. Compounding Sterile Preparations, Fourth Edition, updates all chapters for DQSA and USP Chapter <800> but refers to the 2008 version of USP Chapter <797>, which is current as of this publication. The fourth edition does not cover USP Chapter <797> proposed in late 2015 which is still under review and revision. When a new, final USP Chapter <797> becomes available, ASHP will publish a revised edition.

All previous chapters have been updated, and several new chapters and chapter authors have been added. New chapters include the following:

- Imperative for Change: Adverse Sterile Compounding Events
- Immediate-Use Compounding
- Special Considerations in Pediatric Compounding
• Special Considerations in Compounding Biologicals
• Microbiological Issues in Compounded Sterile Preparations
• Sterile Compounding Technology

New authors include Craig A. Boyce, Todd W. Canada, Richard C. Capps, Bruce A. Erickson, Ryan A. Forrey, Kathleen M. Gura, Patricia C. Kienle, Mark G. Klang, Jeannell M. Mansur, Linda F. McElhiney, Richard B. Osteen, Kelley Reece, Ryan K. Roux, Keith H. St. John, Susan Spivey, Mary Ann Stuhan, Radhakrishna S. Tirumalai, and Angela W. Yaniv. All chapter authors are listed with their credentials in the front matter and anyone who compounds sterile preparations will recognize the experts assembled for this work.

With all the new material, we needed another coeditor, so we are fortunate to welcome Ryan A. Forrey and his expertise. Having served as the Associate Director of Pharmacy and Infusion Services at the Ohio State University Wexner Medical Center and as the Director of Pharmacy at Emory University Hospital Midtown, he is now Senior Manager for Market Development of Hazardous Drug Safety at Becton, Dickinson and Company. Dr. Forrey is also on the Compounding Expert Committee for the United States Pharmacopeia.

Many challenges face the pharmacy staff members who compound sterile preparations. Let us meet those challenges by providing our patients with the safest compounded sterile preparations possible and protecting the healthcare employees who handle hazardous drugs. Our professional reputation depends on it.

E. Clyde Buchanan
Philip J. Schneider
Ryan A. Forrey
September 2017
Contributors

Caryn Dellamorte Bing, RPh, MS, FASHP
Co-Editor, Extended Stability for Parenteral Drugs
CB Healthcare Consulting
Las Vegas, Nevada

Craig A. Boyce, RPh
Pharmacy Systems Consultant
ARxIUM Inc.
Buffalo Grove, Illinois

E. Clyde Buchanan, RPh, MS, FASHP
Senior Director of Pharmacy (Ret.)
Emory Healthcare
Atlanta, Georgia

Todd W. Canada, PharmD, BCNSP, BCCCP, FASHP, FTSHP
Clinical Pharmacy Services Manager & Nutrition Support Team Coordinator
Division of Pharmacy
University of Texas MD Anderson Cancer Center
Houston, Texas

Richard C. Capps, PharmD
Manager of Pharmacy Operations
GHS Oconee Memorial Hospital
Seneca, South Carolina

Joseph W. Coyne, BS Pharm, RPh
Director of Field Operations
Clinical IQ, LLC
Mundelein, Illinois

Bruce A. Erickson, RPh, MS
Pharmacy Automation Consultant (Ret.)
Director of Pharmacy (Ret.)
VA Medical Center, Minneapolis
Placida, Florida

Ryan A. Forrey, PharmD, MS, FASHP
Senior Manager, Market Development for Hazardous Drug Safety
Becton, Dickinson and Company
Franklin Lakes, New Jersey

Kathleen M. Gura, PharmD, BCNSP, FASHP, FPPAG, FASPEN
Pharmacy Clinical Research Program Manager
Clinical Pharmacist, Gastroenterology/Nutrition
Boston Children’s Hospital
Assistant Professor of Pediatrics
Harvard Medical School
Boston, Massachusetts

Stephen K. Hetey, RPh, MS, FASHP
Associate Chief Pharmacy Officer (Ret.)
Department of Pharmacy
Duke Children’s Hospital and Health Center
Duke University Medical Center and Health System
Durham, North Carolina

George H. Hinkle, RPh, MS, BCNP
University Radiation Safety Officer
Radiation Safety Section—Environmental Health & Safety
Faculty Emeritus
Pharmacy Practice and Science
The Ohio State University
Columbus, Ohio

Patricia C. Kienle, RPh, MPA, FASHP
Director, Accreditation and Medication Safety
Cardinal Health Innovative Delivery Solutions
Lafayette, Pennsylvania
Lisa D. Ashworth, BS Pharm, RPh, FACA
Compounding Specialist and Clinical Pharmacist (All Campuses)
Children’s Health
Dallas, Texas