

Contents

| | |
|--|---------------|
| List of Figures | xx |
| List of Tables | xxix |
| List of Forms | xxxii |
| Series Preface | xxxiii |
| Preface | xxxiii |
| Acknowledgments | lxxvii |
| About the Author | lxxx |
| 1 Introduction, Scope, and General Requirements of the BPE | 1 |
| 1.1 Introduction | 1 |
| 1.2 Scope of the ASME BPE Standard | 2 |
| 1.3 Intent of the BPE Standard | 6 |
| 1.4 ASME B31.3 Chapter X | 7 |
| 1.5 Terms and Definitions | 8 |
| 1.6 Quality Assurance | 11 |
| 1.6.1 <i>Documentation</i> | 13 |
| 1.7 An Essential Understanding of Codes and Standards | 17 |
| 1.8 Source of BPE Content | 20 |
| 1.8.1 <i>Government Regulations</i> | 20 |
| 1.8.2 <i>Generally Accepted Principals and Practices of the Industry</i> | 21 |
| 1.8.3 <i>Research and Testing Done by the BPE Membership</i> | 21 |
| 1.9 ASME B31.3 Process Piping Code Chapter X | 22 |
| 1.9.1 <i>B31.3 Chapter X as Supplement to the Base Code</i> | 23 |
| 1.9.2 <i>Harmonization of the BPE Standard and B31.3 Chapter X</i> | 24 |

| | | |
|----------|---|-----------|
| 2 | Materials | 25 |
| 2.1 | Scope of this Chapter | 25 |
| 2.2 | Materials of Construction | 25 |
| 2.3 | Metallic Materials | 26 |
| 2.3.1 | <i>Understanding ASTM Material Designations</i> | 27 |
| 2.3.2 | <i>Stainless Steel</i> | 36 |
| 2.3.3 | <i>The World of Crystallography</i> | 37 |
| 2.3.4 | <i>Pitting Resistance Equivalent Number (PREn)</i> | 42 |
| 2.3.5 | <i>Alloying Constituents in Austenitic Stainless Steel</i> | 45 |
| 2.3.6 | <i>Dual Certified Stainless Steels</i> | 46 |
| 2.3.7 | <i>So Why 316L Stainless Steel?</i> | 47 |
| 2.4 | Nonmetallic Materials | 49 |
| 2.4.1 | <i>What Are Nonmetallic Materials?</i> | 49 |
| 2.4.2 | <i>Extractables and Leachables</i> | 52 |
| 2.4.3 | <i>Single-Use Systems and Components</i> | 54 |
| 2.5 | Surface Finish | 57 |
| 2.6 | Rouge | 63 |
| 2.6.1 | <i>Class I Rouge</i> | 64 |
| 2.6.2 | <i>Class II Rouge</i> | 65 |
| 2.6.3 | <i>Class III Rouge</i> | 66 |
| 2.6.4 | <i>Background on Rouge</i> | 68 |
| 2.6.5 | <i>Source of Rouge</i> | 69 |
| 2.7 | Electropolishing | 70 |
| 2.7.1 | <i>Irregularities or Flaws in Electropolishing</i> | 74 |
| 2.8 | Passivation | 76 |
| 3 | Process Components | 81 |
| 3.1 | Process Components | 81 |
| 3.2 | Pressure Ratings | 81 |
| 3.2.1 | <i>Pressure Ratings of Welded Components</i> | 81 |
| 3.2.2 | <i>Pressure Ratings and Other Fundamentals of Hygienic Clamp Joint Unions</i> | 86 |
| 3.3 | Hygienic Clamp and Automatic Tube Weld Fittings | 89 |
| 3.4 | Sanitary Valves | 101 |
| 3.5 | Seals | 102 |
| 3.6 | Instruments | 105 |
| 3.6.1 | <i>Coriolis Flow Meter</i> | 106 |
| 3.6.2 | <i>Radar Level Instruments</i> | 106 |
| 3.6.3 | <i>Pressure Instruments</i> | 106 |
| 3.6.4 | <i>Temperature Instruments</i> | 106 |
| 3.6.5 | <i>Analytical Instruments</i> | 106 |
| 3.6.6 | <i>Optical Devices</i> | 107 |

| | | |
|----------|--|------------|
| 4 | Fabrication, Assembly, and Installation | 108 |
| 4.1 | Scope and Introduction to this Chapter | 108 |
| 4.1.1 | <i>Scope</i> | 108 |
| 4.1.2 | <i>Introduction</i> | 108 |
| 4.2 | Fabrication | 111 |
| 4.2.1 | <i>Fabrication Drawings and Spool Pieces</i> | 111 |
| 4.3 | Fabrication of Metallic Tubing | 116 |
| 4.3.1 | <i>Welding Documentation and Retention</i> | 116 |
| 4.3.2 | <i>Welding for Piping Systems</i> | 119 |
| 4.4 | Fabrication of Nonmetallic Piping and Tubing | 126 |
| 4.4.1 | <i>Fabrication of Polymeric Components</i> | 126 |
| 4.5 | Assembly and Installation | 131 |
| 4.5.1 | <i>General</i> | 131 |
| 4.5.2 | <i>Characteristics of the Hygienic Clamp Joint</i> | 131 |
| 4.6 | The Piping Installation Process | 140 |
| 4.6.1 | <i>Field Assembly and Installation (Stick Built)</i> | 140 |
| 4.6.2 | <i>As-Built and Other Drawings</i> | 142 |
| 4.6.3 | <i>Skid or Module Fabrication</i> | 144 |
| 5 | Examination, Inspection, and Testing | 147 |
| 5.1 | Examination, Inspection, and Testing | 147 |
| 5.2 | Examination | 148 |
| 5.2.1 | <i>Weld Examination</i> | 150 |
| 5.3 | Inspection | 153 |
| 5.4 | Leak Testing of Piping | 155 |
| 6 | Equipment and Component Quality | 157 |
| 6.1 | Assured Quality | 157 |
| 6.2 | BPE Certification | 157 |
| 6.3 | A Quality Management System | 161 |
| 6.4 | Purpose | 164 |
| 7 | Design | 166 |
| 7.1 | BPE Scope of Design | 166 |
| 7.2 | Intent of Part SD | 167 |
| 7.3 | It's a Bug's Life | 168 |
| 7.3.1 | <i>Perspective on Bacteria</i> | 168 |
| 7.4 | A Preamble to Design | 177 |
| 7.4.1 | <i>Undeveloped Subject Matter</i> | 177 |
| 7.4.2 | <i>Containment</i> | 177 |
| 7.4.3 | <i>Working with BPE and B31.3</i> | 180 |
| 7.4.4 | <i>Fabrication</i> | 183 |

| | | |
|----------|---|------------|
| 7.4.5 | <i>Materials of Construction</i> | 185 |
| 7.4.6 | <i>Cleanability and Drainability</i> | 186 |
| 7.4.7 | <i>Bioprocessing System Boundaries</i> | 186 |
| 7.5 | Design | 186 |
| 7.5.1 | <i>The System</i> | 187 |
| 8 | BPE Appendices | 202 |
| 8.1 | Mandatory and Nonmandatory Appendices | 202 |
| 8.2 | Mandatory Appendices | 203 |
| 8.2.1 | <i>Mandatory Appendix I: Submittal of Technical Inquiries to the BPE Committee</i> | 203 |
| 8.2.2 | <i>Mandatory Appendix II: Standard Units</i> | 204 |
| 8.3 | Nonmandatory Appendices | 204 |
| 8.3.1 | <i>Nonmandatory Appendix A—Commentary: Slag</i> | 204 |
| 8.3.2 | <i>Nonmandatory Appendix B: Material and Weld Examination/Inspection Documentation</i> | 204 |
| 8.3.3 | <i>Nonmandatory Appendix C: Slope Measurement</i> | 204 |
| 8.3.4 | <i>Nonmandatory Appendix D: Rouge and Stainless Steel</i> | 204 |
| 8.3.5 | <i>Nonmandatory Appendix E: Passivation Procedure Qualification</i> | 205 |
| 8.3.6 | <i>Nonmandatory Appendix F: Corrosion Testing</i> | 205 |
| 8.3.7 | <i>Nonmandatory Appendix G: Ferrite</i> | 205 |
| 8.3.8 | <i>Nonmandatory Appendix H: Electropolishing Procedure Qualification</i> | 205 |
| 8.3.9 | <i>Nonmandatory Appendix I: Vendor Documentation Requirements for New Instruments</i> | 206 |
| 8.3.10 | <i>Nonmandatory Appendix J: Standard Process Test Conditions (SPTC) for Seal Performance Evaluation</i> | 206 |
| 8.3.11 | <i>Nonmandatory Appendix K: Standard Test Methods for Polymers</i> | 206 |
| 8.3.12 | <i>Nonmandatory Appendix L: Spray Device Coverage Testing</i> | 207 |
| 8.3.13 | <i>Nonmandatory Appendix M—Commentary: 316L Weld Heat-Affected Zone Discoloration Acceptance Criteria</i> | 207 |
| 8.3.14 | <i>Nonmandatory Appendix N: Guidance When Choosing Polymeric and Nonmetallic Materials</i> | 207 |
| 8.3.15 | <i>Nonmandatory Appendix O: General Background/Useful Information for Extractables and Leachables</i> | 207 |
| 8.3.16 | <i>Nonmandatory Appendix P: Temperature Sensors and Associated Components</i> | 208 |
| 8.3.17 | <i>Nonmandatory Appendix Q: Instrument Receiving, Handling, and Storage</i> | 208 |
| 8.3.18 | <i>Nonmandatory Appendix R: Application Data Sheet</i> | 208 |
| 8.3.19 | <i>Nonmandatory Appendix S—Polymer Applications: Chromatography Columns</i> | 208 |
| 8.3.20 | <i>Nonmandatory Appendix T: Guidance for the Use of US Customary and SI Units</i> | 208 |

| | | |
|------------------------|---|------------|
| Appendices | | |
| Appendix A | Cleaning and Leak Testing Procedure | 209 |
| Appendix B | Biotechnology Inspection Guide Reference Materials and Training Aids | 251 |
| Appendix C | Guide to Inspections of High Purity Water Systems | 286 |
| Appendix D | Guide to Inspections of Lyophilization of Parenterals | 304 |
| Appendix E | Guide to Inspections and Validation of Cleaning Processes | 322 |
| Appendix F | Guide to Inspections of Dosage Form Drug Manufacturer's—CGMPR's | 331 |
| Appendix G | Guide to Inspections Oral Solutions and Suspensions | 349 |
| Appendix H | Guide to Inspections of Sterile Drug Substance Manufacturers | 356 |
| Appendix J | Guide to Inspections of Topical Drug Products | 366 |
| Appendix K | BPE History—Letters and Notes | 375 |
| Appendix L | Component Dimensions | 420 |
| Further Reading | | 440 |
| Index | | 445 |