

VOLUME THREE

Second Edition

Handbook of
**Pharmaceutical
Manufacturing
Formulations**

Liquid Products



SARFARAZ K. NIAZI

informa
healthcare

Contents

Preface to the Series—Second Edition v
Preface to the Series—First Edition viii
Preface to the Volume—First Edition ix
About the Author xi

PART I REGULATORY AND MANUFACTURING GUIDANCE

1. Manufacturing Practice Considerations in

Liquid Formulations 2

- I. Introduction 2
- II. Facilities 2
- III. Equipment 2
- IV. Raw Materials 3
- V. Compounding 3
- VI. Microbiological Quality 3
- VII. Oral Suspensions 3
- VIII. Product Specifications 3
- IX. Process Validation 4
- X. Stability 4
- XI. Packaging 4

2. Oral Solutions and Suspensions 5

- I. Introduction 5
- II. Facilities 5
- III. Equipment 5
- IV. Raw Materials 5
- V. Compounding 5
- VI. Microbiological Quality 6
- VII. Oral Suspension Uniformity 6
- VIII. Product Specifications 6
- IX. Process Validation 6
- X. Stability 6
- XI. Packaging 7

3. The FDA Drug Product Surveillance Program 8

- I. Background 8
- II. Implementation 8
 - A. Objectives 8
 - B. Strategy 8
 - 1. Biennial Inspection of Manufacturing Sites 8
 - 2. Inspection of Systems 8
 - 3. A Scheme of Systems for the Manufacture of Drugs and Drug Products 9
- III. Program Management Instructions 9
 - A. Definitions 9
 - 1. Surveillance Inspections 9
 - 2. Compliance Inspections 10
 - 3. State of Control 10

- 4. Drug Process 10
- 5. Drug Manufacturing Inspection 10
 - B. Inspection Planning 10
 - C. Profiles 11
- IV. Inspectional Observations 11
 - A. Investigational Operations 11
 - 1. General 11
 - 2. Inspection Approaches 11
 - 3. System Inspection Coverage 12
 - 4. Sampling 14
 - 5. Inspection Teams 14
 - 6. Reporting 14
 - V. Analytical Observations 15
 - A. Analyzing Laboratories 15
 - B. Analysis 15
 - VI. Regulatory/Administrative Strategy 15
- Glossary 16
- 4. Changes to Approved NDAs and ANDAs 20
 - I. Introduction 20
 - II. Reporting Categories 20
 - III. General Requirements 20
 - IV. Assessing the Effect of Manufacturing Changes 21
 - A. Assessment of the Effects of the Change 21
 - 1. Conformance to Specifications 21
 - 2. Additional Testing 21
 - B. Equivalence 21
 - C. Adverse Effect 21
 - V. Components and Composition 22
 - VI. Manufacturing Sites 22
 - A. General Considerations 22
 - B. Major Changes (Prior Approval Supplement) 22
 - C. Moderate Changes (Supplement—Changes Being Effected) 22
 - D. Minor Changes (Annual Report) 23
 - VII. Manufacturing Process 23
 - A. General Considerations 23
 - B. Major Changes (Prior Approval Supplement) 23
 - C. Moderate Changes (Supplement—Changes Being Effected) 24
 - D. Minor Changes (Annual Report) 24
 - VIII. Specifications 24
 - A. General Considerations 24
 - B. Major Changes (Prior Approval Supplement) 25

C. Moderate Changes (Supplement—Changes Being Effected) 25	25
D. Minor Changes (Annual Report)	25
IX. Package	26
A. General Considerations	26
B. Major Changes (Prior Approval Supplement)	26
C. Moderate Changes (Supplement—Changes Being Effected)	26
D. Minor Changes (Annual Report)	26
X. Labeling	27
A. General Considerations	27
B. Major Changes (Prior Approval Supplement)	27
C. Moderate Changes (Supplement—Changes Being Effected)	27
D. Minor Changes (Annual Report)	27
XI. Miscellaneous Changes	27
A. Major Changes (Prior Approval Supplement)	27
B. Moderate Changes (Supplement—Changes Being Effected)	28
C. Minor Changes (Annual Report)	28
XII. Multiple Related Changes	28
Glossary	29

5. Formulation Considerations of Liquid Products 30

I. Solubility	30
II. Chemical Modification	30
III. Preservation	30
IV. Sweetening Agents	31
V. Flavors	31
VI. Viscosity	31
VII. Appearance	31
VIII. Chemical Stability	31
IX. Physical Stability	31
X. Raw Material	31
XI. Manufacturing Equipment	32
XII. Manufacturing Directions	32
XIII. Packaging	32
XIV. Particle Size and Shape	32
XV. Suspensions	32
XVI. Emulsions	32
XVII. Powder for Reconstitution	33
XVIII. Nasal Spray Products	33
A. Inhalation Solutions and Suspensions	33
B. Inhalation Sprays	34
C. Pump Delivery of Nasal Products	34
D. Spray Content Uniformity for Nasal Products	34
E. Spray Pattern and Plume Geometry of Nasal Products	35
F. Droplet-Size Distribution in Nasal Products	35
G. Particle-Size Distribution for Nasal Suspensions	35

XIX. Emulsification and Solubilization	35
XX. Complexing	35
XXI. Hydrophilization	35
XXII. Stabilizing Suspensions	35

6. Container Closure Systems 37

I. Introduction	37
A. Definitions	37
B. Current Good Manufacturing Practice, the Consumer Product Safety Commission, and Requirements on Containers and Closures	37
C. Additional Considerations	37
II. Qualification and Quality Control of Packaging Components	37
A. Description	40
B. Information about Suitability	40
C. Stability Data (Packaging Concerns)	41
D. Inhalation Drug Products	41
E. Injection and Ophthalmic Drug Products	41
F. Liquid-Based Oral and Topical Drug Products and Topical Delivery Systems	42
G. Solid Oral Dosage Forms and Powders for Reconstitution	43
1. Polyethylene Containers (USP <661>)	44
2. Single-Unit Containers and Unit-Dose Containers for Capsules and Tablets (USP <671>)	44
3. Multiple-Unit Containers for Capsules and Tablets (USP <671>)	44
H. Other Dosage Forms	44
III. Postapproval Packaging Changes	44
IV. Type III Drug Master Files	44
V. Bulk Containers	45
References	45

7. Material for Containers 47

I. Glass Containers	47
II. Nonplasticized Poly(Vinyl Chloride) for Containers for Noninjectable Aqueous Solutions	47
III. Polyethylene Terephthalate for Containers for Preparations Not for Parenteral Use	48
IV. Nonplasticized Poly(Vinyl Chloride) for Containers for Dry Dosage Forms for Oral Administration	48
V. Plasticized Poly(Vinyl Chloride) for Containers for Aqueous Solutions for Intravenous Infusion	48
VI. Polyethylene Terephthalate for Containers for Preparations Not for Parenteral Use	48
VII. Polyolefines	48
VIII. Polyethylene with Additives for Containers for Parenteral Preparations and for Ophthalmic Preparations	49

- IX. Polypropylene for Containers and Closures for Parenteral Preparations and Ophthalmic Preparations 49
- X. Poly(Ethylene/Vinyl Acetate) for Containers and Tubing for Total Parenteral Nutrition Preparations 50
- XI. Plastic Containers for Aqueous Solutions for Infusion 50
- XII. Sterile Single-Use Plastic Syringes 51
- XIII. Rubber Closures for Containers for Aqueous Parenteral Preparations, for Powders, and for Freeze-Dried Powders 51
- XIV. Silicone Oil Used as a Lubricant 51
- XV. Silicone Elastomer for Closures and Tubing 51

8. Stability Testing of New Drug Substances and Products 52

- I. Introduction 52
 - A. Objectives of the Guideline 52
 - B. Scope of the Guideline 52
 - C. General Principles 52
- II. Guidelines 52
 - A. Drug Substance 52
 - 1. General 52
 - 2. Stress Testing 52
 - 3. Selection of Batches 52
 - 4. Container Closure System 52
 - 5. Specification 52
 - 6. Testing Frequency 53
 - 7. Storage Conditions 53
 - 8. Stability Commitment 53
 - 9. Evaluation 54
 - 10. Statements/Labeling 54
 - B. Drug Product 54
 - 1. General 54
 - 2. Photostability Testing 54
 - 3. Selection of Batches 54
 - 4. Container Closure System 54
 - 5. Specification 55
 - 6. Testing Frequency 55
 - 7. Storage Conditions 55
 - 8. Stability Commitment 57
 - 9. Evaluation 57
 - 10. Statements/Labeling 57

Glossary 58
References 59

9. Stability Testing: Photostability Testing of New Drug Substances and Products 60

- I. General 60
 - A. Preamble 60
 - B. Light Sources 60
 - C. Procedure 60
- II. Drug Substance 61
 - A. Presentation of Samples 61
 - B. Analysis of Samples 61
 - C. Judgement of Results 61
- III. Drug Product 61
 - A. Presentation of Samples 61
 - B. Analysis of Samples 62
 - C. Judgement of Results 62

- IV. Annex 62
 - A. Quinine Chemical Actinometry 62

10. Stability Testing for New Dosage Forms 63

- I. General 63
 - II. New Dosage Forms 63
- Glossary 63
Bibliography 63

11. Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products 64

- I. Introduction 64
 - A. Objectives of the Guideline 64
 - B. Background 64
 - C. Scope of the Guideline 64
- II. Guidelines 64
 - A. General 64
 - B. Applicability of Reduced Designs 64
 - C. Bracketing 64
 - 1. Design Factors 64
 - 2. Design Considerations and Potential Risks 65
 - 3. Design Example 65
 - D. Matrixing 65
 - 1. Design Factors 65
 - 2. Design Considerations 65
 - 3. Design Examples 65
 - 4. Applicability and Degree of Reduction 66
 - 5. Potential Risk 67
 - E. Data Evaluation 67

12. Evaluation of Stability Data 68

- I. Introduction 68
 - A. Objectives of the Guideline 68
 - B. Background 68
 - C. Scope of the Guideline 68
- II. Guidelines 68
 - A. General Principles 68
 - B. Data Presentation 69
 - C. Extrapolation 69
 - D. Data Evaluation for Retest Period or Shelf-Life Estimation for Drug Substances or Products Intended for Room Temperature Storage 69
 - 1. No Significant Change at Accelerated Condition 69
 - 2. Significant Change at Accelerated Condition 70
 - E. Data Evaluation for Retest Period or Shelf-Life Estimation for Drug Substances or Products Intended for Storage Below Room Temperature 70
 - 1. Drug Substances or Products Intended for Storage in a Refrigerator 70
 - 2. Drug Substances or Products Intended for Storage in a Freezer 71

3. Drug Substances or Products Intended for Storage Below -20°C 71	Product Quality Review 81
F. General Statistical Approaches 71	Quality Risk Management 81
III. Appendices 71	Chapter 2: Personnel 81
Appendix A: Decision Tree for Data Evaluation for Retest Period or Shelf-Life Estimation for Drug Substances or Products (Excluding Frozen Products) 71	Principle 81
Appendix B: Examples of Statistical Approaches to Stability Data Analysis 71	General 82
B.1. Data Analysis for a Single Batch 71	Key Personnel 82
B.2. Data Analysis for One-Factor, Full-Design Studies 71	Training 82
B.2.1. Evaluating whether all batches support the proposed retest period or shelf life 73	Personnel Hygiene 83
B.2.2. Testing for poolability of batches 74	Chapter 3: Premises and Equipment 83
B.2.2.1. Analysis of covariance 74	Principle 83
B.2.2.2. Other methods 74	Premises 83
B.3. Data Analysis for Multifactor, Full-Design Studies 74	Production Area 83
B.3.1. Evaluating whether all factor combinations support the proposed shelf life 74	Storage Areas 84
B.3.2. Testing for poolability 74	Quality Control Areas 84
B.3.2.1. Testing for poolability of batch factor only 74	Ancillary Areas 84
B.3.2.2. Testing for poolability of all factors and factor combinations 75	Equipment 84
B.3.2.2.1. Analysis of covariance 75	Chapter 4: Documentation 84
B.3.2.2.2. Other methods 75	Principle 84
B.4. Data Analysis for Bracketing Design Studies 75	General 85
B.5. Data Analysis for Matrixing Design Studies 75	Specifications for Starting and Packaging Materials 85
References 76	Specifications for Intermediate and Bulk Products 85
13. Stability Data Package for Registration	Specifications for Finished Products 85
Applications in Climatic Zones III and IV 77	Manufacturing Formula and Processing Instructions 85
I. Introduction 77	Packaging Instructions 85
A. Objectives of the Guideline 77	Batch Processing Records 86
B. Background 77	Batch Packaging Records 86
C. Scope of the Guideline 77	Procedures and Records 86
II. Guidelines 77	Sampling 86
A. Continuity with the Parent Guideline 77	Testing 86
B. Storage Conditions 77	Other 87
1. General Case 77	Chapter 5: Production 87
2. Aqueous-Based Drug Products Packaged in Semipermeable Containers 77	Principle 87
3. Tests at Elevated Temperature and/or Extremes of Humidity 78	General 87
C. Additional Considerations 78	Prevention of Cross-Contamination in Production 87
References 78	Validation 88
14. EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use 79	Starting Materials 88
I. Introduction 79	Packaging Materials 88
Part I: Chapter 1: Quality Management 80	Packaging Operations 88
Principle 80	Finished Products 89
Quality Assurance 80	Rejected, Recovered, and Returned Materials 89
Good Manufacturing Practice for Medicinal Products (GMP) 80	Chapter 6: Quality Control 89
Quality Control 81	Principle 89
	General 89
	Good Quality Control Laboratory Practice 90
	Documentation 90
	Sampling 90
	Testing 90
	Ongoing Stability Program 90
	Chapter 7: Contract Manufacture and Analysis 91
	Principle 91
	General 91
	The Contract Giver 91
	The Contract Acceptor 91
	The Contract 92
	Chapter 8: Complaints and Product Recall 92
	Principle 92
	Complaints 92
	Recalls 92

15. EDQM Certification 93

- I. 2.3.S Drug Substance 93
 - A.2.3.S.1 General Information 93
 - 1.2.3.S.1.1 Nomenclature 93
 - 2.3.S.1.2 General Properties 94
 - 2.3.S.2 Manufacture 94
 - 2.3.S.2.1 Manufacturer(s) (Name, Manufacturer) and Sites Involved in the Entire Process 94
 - 2.3.S.2.2 Description of Manufacturing Process and Process Controls 94
 - 2.3.S.2.3 Control of Materials 94
 - 2.3.S.2.4 Controls of Critical Steps and Intermediates 94
 - 2.3.S.2.5 Process Validation and/or Evaluation 94
 - 2.3.S.3 Characterization 94
 - 2.3.S.3.1 Impurities 94
 - 2.3.S.3.4 Control of the Drug Substance 94
 - 2.3.S.4.1 Specification 94
 - 2.3.S.4.2 Analytical Procedures 94
 - 2.3.S.4.3 Validation of Analytical Procedures 94
 - 2.3.S.4.4 Batch Analyses 94
 - 2.3.S.4.5 Justification of Specification 94
 - 2.3.S.5 Reference Standards or Materials 94
 - 2.3.S.6 Container Closure System 95
 - 2.3.S.7 Stability 95
 - 2.3.S.7.1 Stability Summary and Conclusions 95
 - 2.3.S.7.2 Postapproval Stability Protocol and Stability Commitment 95

16. Impurities: Guideline for Residual Solvents 96

- I. Introduction 96
- II. Scope of the Guideline 96
- III. General Principles 96
 - A. Classification of Residual Solvents by Risk Assessment 96
 - B. Methods for Establishing Exposure Limits 97
 - C. Options for Describing Limits of Class 2 Solvents 97
 - D. Analytical Procedures 98
 - E. Reporting Levels of Residual Solvents 98
- IV. Limits of Residual Solvents 98
 - A. Solvents to Be Avoided 98
 - B. Solvents to Be Limited 98
 - C. Solvents with Low Toxic Potential 98
 - D. Solvents for Which No Adequate Toxicological Data Was Found 98

Glossary 98

Appendix 1. List of Solvents Included in the Guideline 99

Appendix 2. Additional Background 101

A2.1 Environmental Regulation of Organic Volatile Solvents 101

A2.2 Residual Solvents in Pharmaceuticals 101

Appendix 3. Methods for Establishing Exposure Limits 101

17. Electronic Records and Signatures (CFR 21 Part 11 Compliance) 103

- I. Definitions 103
- II. Electronic Records—Controls for Closed Systems 103

- III. Controls for Open Systems 104
 - A. Signature Manifestations 104
 - B. Signature/Record Linking 104
 - C. Electronic Signatures 104
 - IV. Electronic Signature Components and Controls 104
 - V. Controls for Identification Codes/Passwords 105
 - VI. Explicatory Notes About 21 CFR Part 11 Compliance 105
 - A. Overall Approach to Part 11 Requirements 105
 - B. Details of Approach—Scope of Part 11 105
 - C. Definition of Part 11 Records 106
 - D. Approach to Specific Part 11 Requirements 106
 - E. Copies of Records 107
 - F. Record Retention 107
 - VII. Establishing a Compliance Plan 107
 - VIII. Software and Systems Support 109
- Bibliography 111

18. GMP Audit Template, EU Guidelines 112
Glossary 131**19. Bioequivalence Testing Protocols 134****20. Dissolution Testing of Liquid Dosage Forms 137****21. Approved Excipients in Liquid Forms 139****PART II MANUFACTURING FORMULATIONS**

- Manufacturing Formulations 167**
- Abacavir Sulfate Oral Solution 167
 - Abacavir Sulfate Oral Solution 167
- Acetaminophen, Chlorpheniramine, and Pseudoephedrine Syrup 168
- Acetaminophen Drops 169
- Acetaminophen Oral Suspension 170
- Acetaminophen Rectal Solution 170
- Acetaminophen Suspension 171
- Acetaminophen Syrup 171
 - Acetaminophen Syrup 172
 - Acetaminophen Syrup for Children 172
 - Acetaminophen Syrup 173
 - Acetaminophen Syrup 173
- Acne Scrub 174
- Acyclovir Oral Suspension (2% = 200 mg/10 mL) 174
 - Acyclovir Oral Suspension 174
 - Acyclovir Oral Suspension 175
- Adapalene Solution 175
- Albendazole Oral Suspension 176
- Albendazole Suspension 177
- Albuterol Inhalation Solution 177
 - Albuterol Inhalation Solution 177
- Alginate Acid + Aluminium Hydroxide + Magnesium Silicate Tablets (500 mg + 100 mg + 25 mg) 178
- Alpha-Bisabolol Aqueous Mouthwash Solution 178
- Alpha-Bisabolol Buccal or Topical Solution 178

- Alpha-Bisabolol Ethanolic Mouthwash Solution 179
 Alpha-Bisabolol Mouthwash Solution 179
 Aluminium Hydroxide + Magnesium Silicate
 Chewable Tablets (120 mg + 250 mg) 179
 Aluminum Chloride Solution 180
 Aluminum Hydroxide and Magnesium Carbonate
 Dry Syrup 180
 Aluminum Hydroxide and Magnesium Carbonate
 Dry Syrup 180
 Aluminum Hydroxide and Magnesium Hydroxide
 Antacid Suspension 181
 Aluminum Hydroxide and Magnesium Hydroxide
 Antacid Suspension 181
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 182
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 183
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 183
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 184
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 184
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 185
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 186
 Aluminum Hydroxide and Magnesium Hydroxide
 Suspension 186
 Aluminum Hydroxide, Magnesium Hydroxide, and
 Simethicone Suspension 187
 Aluminum Hydroxide, Magnesium Hydroxide, and
 Simethicone Suspension 187
 Aluminum Hydroxide, Magnesium Hydroxide, and
 Simethicone Suspension 188
 Aluminum Hydroxide, Magnesium Hydroxide, and
 Simethicone Suspension 188
 Aluminum Hydroxide, Magnesium Hydroxide, and
 Simethicone Tablets 189
 Aminacrine Hydrochloride Topical Solution 190
 Aminolevulinic Acid HCl for Topical Solution
 (20%) 190
 Amoxicillin Powder for Suspension 190
 Amoxicillin–Clavulanate Syrup 191
 Amoxicillin–Clavulanate Syrup 191
 Ampicillin Powder for Suspension 192
 Ampicillin Powder for Suspension 192
 Ampicillin and Cloxacillin Oily Suspension 193
 Amprenavir Capsules 193
 Amprenavir Capsules 193
 Amprenavir Oral Solution 194
 Anise Oil Solution 194
 Antipyrine and Benzocaine Elixir 194
 Antiseptic Wet Wipes 194
 Apraclonidine Hydrochloride Ophthalmic
 Solution 195
 Ascorbic Acid Solution 195
 Atovaquone Suspension 195
 Atovaquone Suspension 195
 Azelastine Hydrochloride Nasal Spray 196
 Azelastine Hydrochloride Nasal Spray 196
 Azithromycin Suspension 197
 Azithromycin Suspension 197
 Azulene Solution 198
 Azulene Solution (1%) 198
 Barium Sulfate Oral Suspension 198
 Beclomethasone Dipropionate Inhalation
 Aerosol 198
 Beclomethasone Dipropionate Inhalation
 Aerosol 199
 Beclomethasone Dipropionate and Salbutamol Sulfate
 Nasal Spray 199
 Benzethonium Chloride Solution 199
 Benzethonium Chloride and Benzocaine Topical
 Anesthetic 199
 Benzocaine and Tetracaine Topical Solution 199
 Benzyl Benzoate Solution 199
 Beta-Estradiol Vaginal Solution 200
 Betamethasone Syrup 200
 Bismuth Carbonate Suspension 200
 Bismuth Subsalicylate Suspension 201
 Bromazepam Drops 201
 Bromhexine Hydrochloride Syrup 202
 Bromhexine Hydrochloride Syrup—Alcohol
 Free 203
 Bromhexine Hydrochloride Syrup 204
 Budesonide Inhaler 204
 Butamirate Citrate Syrup 205
 Caffeine Citrate Oral Solution 205
 Calcipotriene Solution 205
 Calcitonin Nasal Spray 205
 Calcitonin Nasal Spray 205
 Calcium Carbonate and Guar Gum Suspension 206
 Calcium Iodide and Ascorbic Acid Syrup 207
 Carbamazepine Oral Suspension 2% 207
 Carbetapentane Tannate and Chlorpheniramine
 Suspension 208
 Carnitine and Coenzyme Q Solution 208
 Cefaclor Suspension 209
 Cefadroxil Monohydrate Oral Suspension 209
 Cefpodoxime Proxetil Oral Suspension 209
 Cefpodoxime Proxetil Oral Suspension 209
 Cefpodoxime Proxetil for Oral Suspension 210
 Cefuroxime Axetil Suspension 210
 Cetirizine Hydrochloride Syrup 210
 Chlophedianol, Ipecac, Ephedrine, Ammonium
 Chloride, Carbinoxamine, and Balsam Tolu
 Syrup 211
 Chlophedianol, Ipecac, Ephedrine, Ammonium
 Chloride, Carbinoxamine, and Balsam Tolu
 Syrup 212
 Chloramphenicol Palmitate Oral or Topical Emulsion
 (2.5% = 250 mg/10 mL) 213
 Chloramphenicol Palmitate Oral or Topical Emulsion
 (5% = 500 mg/10 mL) 213
 Chloramphenicol Ophthalmic Solution 213
 Chloramphenicol Palmitate Oral or Topical
 Emulsion 213
 Chlorhexidine Gel 214
 Chlorpheniramine Maleate Syrup 214
 Chloroxylenol Surgical Scrub 215
 Ciclopirox Topical Solution 215
 Cimetidine Syrup 215
 Ciprofloxacin Hydrochloride and Hydrocortisone Otic
 Suspension 216
 Cisapride Suspension 217

- Citalopram Hydrobromide Oral Solution 218
 Clarithromycin Suspension 218
 Clindamycin Phosphate Topical Solution 219
 Clotrimazole Topical Solution 219
 Clotrimazole Topical Solution (3%) 219
 Codeine Phosphate and Acetaminophen Elixir 219
 Colistin Sulfate, Neomycin, Thonzonium Bromide, and Hydrocortisone Otic Suspension 219
 Cotrimoxazole Oral Suspension 220
 Cromolyn Sodium Nasal Spray 221
 Cromolyn Sodium Oral Concentrate 221
 Crospovidone Oral Suspension (2000 mg/10 mL) 221
 Cyclosporin Oral Solution 221
 Cyclosporine Soft Gelatin Capsules 221
 Desmopressin Acetate Nasal Spray 221
 Dexamethasone Elixir 221
 Dextromethorphan and Chlorpheniramine Maleate Solution 222
 Dextromethorphan, Pseudoephedrine, and Chlorpheniramine Maleate Syrup 222
 Dextromethorphan Liquid 223
 Dextromethorphan Liquid 223
 Dextromethorphan, Pseudoephedrine, and Chlorpheniramine Maleate Syrup 224
 Dextromethorphan Solution 224
 Dextrose, Levulose, and Phosphoric Acid Solution 225
 Diazepam Rectal Solution 225
 Diclofenac Oral Solution 225
 Didanosine for Oral Solution 226
 Digoxin Capsules 226
 Digoxin Elixir Pediatric 226
 Dihydroergotamine Mesylate Drops 226
 Diphenhydramine and Ammonium Chloride Syrup 227
 Diphenhydramine Hydrochloride Liquid 227
 Dornase-Alpha Inhalation Solution 228
 Doxercalciferol Capsules 228
 Dyphylline, Guaifenesin Elixir 228
 Electrolyte Lavage Solution 228
 Eplerenone Solution 228
 Erythromycin Drops 229
 Erythromycin Topical Solution 229
 Estradiol Nasal Spray 230
 Ethchlorvynol Gelatin Capsule (200 mg) 230
 Eucalyptus and Mint Emulsion 230
 Eucalyptol Solution 231
 Eucalyptol Solution (8%) 231
 Fentanyl Citrate Nasal Spray 231
 Ferrous Sulfate Oral Solution 231
 Ferrous Sulfate Oral Syrup 232
 Fluconazole Oral Suspension 232
 Flunisolide Spray 232
 Fluocinonide Topical Solution 232
 Fluorouracil Solution 232
 Fluorouracil Topical Solution 232
 Fluticasone Suspension Spray 232
 Furosemide Syrup 233
 Ferrous Sulfate Oral Solution 233
 Ferrous Sulfate Oral Syrup 234
 Fir Needle Oil Solution 234
 Foot Bath 235
 Gabapentin Oral Solution 235
 Galantamine Hydrobromide Oral Solution 235
 Glucose, Fructose, and Phosphoric Acid Antiemetic Solution 235
 Glycol Foam, Nonaqueous 235
 Gramicidin Ophthalmic Solution 236
 Guaifenesin, Pseudoephedrine, Carbinoxamine, and Chlophedianol Drops 236
 Guaifenesin Pseudoephedrine, Carbinoxamine, and Chlophedianol Drops 237
 Haloperidol Oral Liquid 238
 Heparin Nasal Spray 238
 Hydrocodone Bitartrate Elixir 238
 Hydrocodone Polistirex Extended-Release Suspension 238
 Hydromorphone Hydrochloride Oral Liquid 238
 Hydroxyzine Pamoate Oral Suspension 238
 Hyoscine Butylbromide Syrup 239
 Hyoscyamine Sulfate Elixir 239
 Ibuprofen Topical Solution 239
 Ibuprofen Pediatric Suspension 240
 Iron Infant Drops 241
 Iron Polystyrene and Vitamin C Syrup 242
 Ibuprofen Pediatric Suspension 243
 Ibuprofen Solution 243
 Ibuprofen Suspension 244
 Ibuprofen Suspension, Sugar Free 244
 Ibuprofen and Domperidone Maleate Suspension 244
 Insulin Inhalation Spray 245
 Ipratropium Bromide Inhalation Solution 245
 Ipratropium Bromide Nasal Spray 245
 Iron Polystyrene and Vitamin C Syrup 246
 Isoproterenol Sulfate and Calcium Iodide Syrup 247
 Isotretinoin Capsules 247
 Itraconazole Oral Solution 247
 Kaolin, Pectin, and Aluminum Hydroxide Suspension 248
 Kaolin-Pectin Suspension 249
 Kaolin-Pectin Suspension 250
 Ketoprofen Topical Solution 250
 Ketotifen Syrup 251
 Lamivudine Oral Solution 251
 Levalbuterol Hydrochloride Inhalation Solution 251
 Levocarnitine Oral Solution 251
 Linezolid for Oral Suspension 251
 Lithium Carbonate Solution 251
 Lithium Citrate Syrup 251
 Lomustine Nasal Spray 251
 Loracarbef for Oral Suspension 251
 Loratadine Syrup 252
 Mafenide Acetate Topical Solution 252
 Magaldrate Instant Powder for Dry Syrup 252
 Magaldrate Suspension 253
 Magaldrate with Simethicone Suspension 253
 Magaldrate with Simethicone Suspension 254
 Mebendazole Oral Suspension 255
 Mebendazole Suspension 255
 Megestrol Acetate Oral Suspension 256
 Menthol and Benzocaine Solution 256
 Menthol Mouthwash 257
 Mesalamine Rectal Suspension Enema 257

- Mesalamine Rectal Suspension 257
 Metformin Liquid 257
 Metoclopramide Oral Solution 258
 Metoclopramide Syrup 259
 Metronidazole Suspension 260
 Mineral and Multivitamin Syrup 261
 Minoxidil Solution 262
 Mint–Menthol Mouthwash 262
 Mint–Menthol Mouthwash 263
 Mint Oil Solution 263
 Mint Oil Solution 264
 Mometasone Furoate Nasal Spray 264
 Monosulfiram Solution 264
 Multivitamin and Calcium Syrup 265
 Multivitamin and Mineral Syrup 266
 Multivitamin Drops 267
 Multivitamin Infant Drops 268
 Multivitamin Infant Drops 269
 Multivitamin Mineral Syrup 270
 Multivitamin Syrup 271
 Multivitamin Syrup 272
 Multivitamin with Fluoride Infant Drops 273
 Multivitamin Drops 274
 Multivitamin Syrup 274
 Multivitamin Syrup 275
 Multivitamin with Fluoride-Infant Drops 276
 Nafarelin Acetate Nasal Solution 277
 Naproxen Suspension 277
 Nevirapine Suspension 277
 Nicotine Spray 277
 Nimesulide Suspension 277
 Nimodipine Capsules 278
 Nitroglycerin Lingual Spray 278
 Norephedrine Syrup 278
 Norephedrine Syrup 278
 Nystatin Oral Suspension 279
 Nystatin Suspension 280
 Ofloxacin Otic Solution 280
 Ofloxacin Otic Solution 280
 Omeprazole Solution 280
 Ondansetron Hydrochloride Dihydrate Oral
 Solution 281
 Orciprenaline Sulfate and Clobutinol Hydrochloride
 Syrup 281
 Oxtripium and Formoterol Nasal Spray 281
 Oxycodone Hydrochloride Oral Concentrate
 Solution 281
 Oxymetazoline Hydrochloride Congestion Nasal
 Spray 281
 Oxymetazoline Hydrochloride Nasal
 Solution 282
 Oxymetazoline Moisturizing Nasal Spray 282
 Oxymetazoline Nasal Solution 282
 Oxymetazoline Nasal Spray 282
 Oxymetazoline Sinus Nasal Spray 282
 Peptide Topical Liquid 283
 Pheniramine Maleate Syrup 283
 Phenobarbital, Hyoscyamine Sulfate, Atropine
 Sulfate, and Scopolamine Hydrobromide
 Elixir 283
 Phenylephrine Tannate and Chlorpheniramine
 Tannate Pediatric Suspension 283
 Phenylephrine Tannate and Pyrilamine
 Tannate Suspension 283
 Phenylpropanolamine, Chlorpheniramine,
 Dextromethorphan, Vitamin C Syrup 284
 Phenylpropanolamine, Chlorpheniramine,
 Dextromethorphan, Vitamin C Syrup 285
 Phenylpropanolamine Controlled-Release
 Capsules 286
 Phenytoin Suspension 286
 Phenytoin Suspension 286
 Pipenzolate Methyl Bromide and Phenobarbital
 Drops 287
 Podofilox Solution 288
 Polidocanol Wound Spray 288
 Polidocanol Wound Spray 288
 Polyvinyl Pyrrolidone–Iodine Gargle Solution 289
 Polyvinyl Pyrrolidone–Iodine Gargle Solution
 Concentrate 289
 Polyvinyl Pyrrolidone–Iodine Liquid Spray 289
 Polyvinyl Pyrrolidone–Iodine Mouthwash 290
 Polyvinyl Pyrrolidone–Iodine Mouthwash and Gargle
 Solution Concentrate 290
 Polyvinyl Pyrrolidone–Iodine Scrub 291
 Polyvinyl Pyrrolidone–Iodine Solution 291
 Polyvinyl Pyrrolidone–Iodine Solution 292
 Polyvinyl Pyrrolidone–Iodine Solution 292
 Polyvinyl Pyrrolidone–Iodine Solution 292
 Polyvinyl Pyrrolidone–Iodine Solution 293
 Polyvinyl Pyrrolidone–Iodine Surgical Scrub 293
 Polyvinyl Pyrrolidone–Iodine Surgical Scrub 293
 Polyvinyl Pyrrolidone–Iodine Vaginal Douche
 Concentrate 294
 Polyvinyl Pyrrolidone–Iodine Viscous Solution 294
 Polyvinylpyrrolidone–Iodine Mouthwash 294
 Povidone–Iodine Concentrates for Broilers and
 Cattle 295
 Povidone–Iodine Foam Spray 295
 Povidone–Iodine Gargle 295
 Povidone–Iodine Gargle Solution Concentrate 296
 Povidone–Iodine Liquid Spray 296
 Povidone–Iodine Mouthwash and Gargle Solution
 Concentrate 296
 Povidone–Iodine Powder Spray 297
 Povidone–Iodine Pump Spray 297
 Povidone–Iodine Shampoo 297
 Povidone–Iodine Solution 298
 Povidone–Iodine Solution 298
 Povidone–Iodine Solution 299
 Povidone–Iodine Solution 299
 Povidone–Iodine Solution 299
 Povidone–Iodine Scrub 300
 Povidone–Iodine Surgical Scrub 300
 Povidone–Iodine Surgical Scrub 301
 Povidone–Iodine Vaginal Douche Concentrate 301
 Povidone–Iodine Viscous Solution 301
 Prednisone Oral Solution 302
 Prednisolone Sodium Phosphate Oral Solution 302
 Prednisolone Syrup 302
 Progesterone Capsules 302
 Promethazine and Codeine Syrup 302
 Promethazine and Dextromethorphan Syrup 302
 Promethazine Hydrochloride Syrup 302
 Promethazine Hydrochloride Syrup 303
 Promethazine Rectal Solution 303
 Promethazine Rectal Solution 304
 Pseudoephedrine Hydrochloride Syrup 304

- Pseudoephedrine Hydrochloride, Carbinoxamine Maleate Oral Drops 305
Pseudoephedrine Hydrochloride, Carbinoxamine Maleate Oral Drops 306
Pseudoephedrine and Carbinoxamine Drops 307
Pseudoephedrine Hydrochloride Syrup 308
Ribavirin Inhalation Solution 308
Risperidone Oral Solution 308
Ritonavir Capsules 308
Ritonavir Oral Solution 308
Ritonavir and Lopinavir Oral Solution 308
Rivastigmine Tartarate Oral Solution 309
Salbutamol Aerosol 309
Salbutamol Syrup Sugar Free 310
Salbutamol Syrup 310
Salicylic Acid Collodion 311
Salmeterol Xinafoate Inhalation Aerosol 311
Salmeterol Xinafoate Inhalation Aerosol 311
Scopolamine Nasal Spray 312
Selenium Sulfide Shampoo with Conditioner 312
Sertraline Hydrochloride Oral Concentrate 313
Sertraline Hydrochloride Solution 313
Simethicone Drops 313
Sirolimus Solution 314
Sodium Chloride Nasal Drops 314
Stavudine for Oral Suspension 314
Sucralfate Suspension 314
Sulfacetamide Sodium and Sulfur Cleanser and Suspension 315
Sulfadiazine and Trimethoprim Veterinary Oral Suspension 315
Sulfamethoxazole and Trimethoprim Suspension 316
Sulfamethoxazole and Trimethoprim Suspension 316
Sulfamethoxazole and Trimethoprim Suspension 317
Sulfathiazole Veterinary Oral Solution 317
Sulfidoxine Solution 317
Sulfidoxine and Pyrimethamine Suspension 318
Sumatriptan Nasal Spray 318
Sumatriptan Nasal Spray 318
Terfenadine Oral Suspension 319
Terfenadine Suspension 319
Theophylline Sodium Glycinate Elixir 320
Thiabendazole Suspension 320
Thiothixene Oral Concentrate 320
Timolol Maleate Ophthalmic Drops 320
Tolnaftate Foot Care Microemulsion 321
Tolu Balsam Cough Syrup 321
Tolu Balsam Cough Syrup 322
Tretinoin Solution (50 mg/100 g) 323
Tretinoin Solution 323
Triamcinolone Acetonide Nasal Spray 323
Triclosan Oral Solution 324
Triprolidine and Pseudoephedrine Hydrochloride Syrup 324
Tulobuterol Syrup 325
Tolnaftate Foot Care Microemulsion 325
Triprolidine and Pseudoephedrine Hydrochloride Syrup 326
Undecylenic Acid and Chloroxylonol Solution 327
Urea Peroxide Ear Drops 327
Valproic Acid Capsules 327
Valproic Acid Syrup 327
Vancomycin Hydrochloride Oral Solution 327
Vitamin A and Vitamin D Infant Drops 328
Vitamins A and D Infant Drops 329
Vitamin A and Vitamin D₃ Drops 329
Vitamin A and Vitamin D₃ Drops 330
Vitamin A and Vitamin D₃ Oral Solution 330
Vitamin A and Vitamin D₃ Oral Solution 330
Vitamin A and Vitamin D₃ Syrup 331
Vitamin A and Vitamin D₃ Syrup 331
Vitamin A and Vitamin E Drops 331
Vitamin A and Vitamin E Drops 332
Vitamin A and Vitamin E Drops 332
Vitamin A and Vitamin E Drops 332
Vitamin A Concentrate, Water-Miscible 333
Vitamin A Concentrate, Water-Miscible 333
Vitamin A Drops 333
Vitamin A Drops 334
Vitamin B Complex Syrup 334
Vitamin B Complex Syrup 335
Vitamin B Complex Syrup 336
Vitamin B Complex and Vitamin C Syrup 336
Vitamin B Complex (without B₁₂) Syrup 337
Vitamin B Complex, A, C, D, and Calcium Drops 338
Vitamin B Complex and Iron Syrup 339
Vitamin B Complex and Iron Syrup 340
Vitamin B Complex and Vitamin C Syrup 341
Vitamin B Complex and Vitamin C Syrup 342
Vitamin B Complex and Vitamin C Syrup 342
Vitamin B Complex, A, C, and D Syrup 343
Vitamin B Complex Syrup 344
Vitamin B Complex Syrup 345
Vitamin B Complex Syrup (without B₁₂) 346
Vitamin B Complex, Vitamin A, Vitamin C, and Vitamin D Syrup 347
Vitamin B Complex, Vitamin A, Vitamin C, Vitamin D, and Calcium Drops 348
Vitamin B Complex, Vitamin A, Vitamin C, Vitamin D, and Vitamin E Pediatric Drops 349
Vitamin B Complex, Vitamin C, and Iron Syrup 350
Vitamin B Complex, Vitamin C, and Iron Syrup 351
Vitamin C Drops 352
Vitamin E and Benzocaine Solution 352
Vitamin E Concentrate, Water-Miscible 352
Vitamin E Drops 353
Vitamin E Soft Gel Capsules 353
Vitamin E Solution with Ethanol 353
Vitamin E and Benzocaine Solution 354
Vitamin E and Benzocaine Solution 354
Vitamin E Capsules 354
Vitamin E Drops 355
Vitamin E Drops 355
Vitamin E Solution with Ethanol 355
Vitamin E Solution with Ethanol 355
Xylometazoline Hydrochloride Nasal Solution 356
Xylometazoline Hydrochloride Nasal Solution 356
Xylometazoline Hydrochloride Children's Nasal Solution 356
Zinc Pyrithione Shampoo 357
Commercial Pharmaceutical Products 357