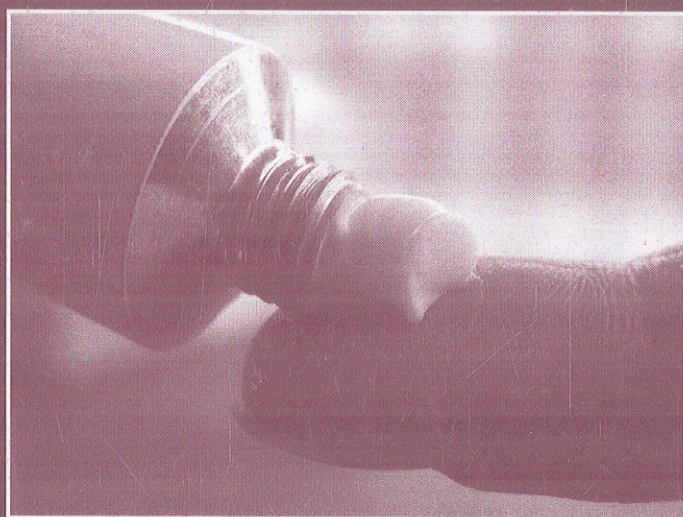


VOLUME FOUR

Second Edition

Handbook of
**Pharmaceutical
Manufacturing
Formulations**

Semisolid 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. Waiver of In Vivo Bioequivalence Study 2

- I. Introduction 2
- II. The Biopharmaceutics Classification System 2
 - A. Solubility 5
 - B. Permeability 5
 - C. Dissolution 5
- III. Methodology for Classifying a Drug Substance and for Determining the Dissolution Characteristics of a Drug Product 5
 - A. Determining Drug Substance Solubility Class 5
 - B. Determining Drug Substance Permeability Class 6
 1. Pharmacokinetic Studies in Humans 6
 2. Intestinal Permeability Methods 6
 3. Instability in the Gastrointestinal Tract 9
 - C. Determining Drug Product Dissolution Characteristics and Dissolution Profile Similarity 10
- IV. Additional Considerations for Requesting a Biowaiver 10
 - A. Excipients 10
 - B. Prodrugs 10
 - C. Exceptions 10
 1. Narrow Therapeutic Range Drugs 10
 2. Products Designed to Be Absorbed in the Oral Cavity 10
- V. Regulatory Applications of the BCS 10
 - A. INDs/NDAs 10
 - B. ANDAs 11
 - C. Postapproval Changes 11
- VI. Data to Support a Request for Biowaivers 11
 - A. Data Supporting High Solubility 11
 - B. Data Supporting High Permeability 11
 - C. Data Supporting Rapid and Similar Dissolution 11
 - D. Additional Information 12
 1. Excipients 12
 2. Prodrugs 12
 3. Exceptions 12

Animal Products 13
Species Selection 13
Subject Characteristics 13
Human Food Safety Considerations 13
Bibliography 14

2. Quality Risk Management 15

- I. Introduction 15
 - II. Scope 15
 - III. Principles of Quality Risk Management 15
 - IV. General Quality Risk Management Process 15
 - A. Responsibilities 16
 - B. Initiating a Quality Risk Management Process 16
 - C. Risk Assessment 16
 - D. Risk Control 17
 - E. Risk Communication 17
 - F. Risk Review 17
 - V. Risk Management Methodology 17
 - VI. Integration of Quality Risk Management into Industry and Regulatory Operations 18
- Glossary 18
Bibliography 19
- Annex I: Risk Management Methods and Tools 19
- I.1 Basic Risk Management Facilitation Methods 19
 - I.2 Failure Mode Effects Analysis Potential Areas of Use(s) 19
 - I.3 Failure Mode, Effects, and Criticality Analysis Potential Areas of Use(s) 19
 - I.4 Fault Tree Analysis Potential Areas of Use(s) 19
 - I.5 Hazard Analysis and Critical Control Points Potential Areas of Use(s) 20
 - I.6 Hazard Operability Analysis Potential Areas of Use(s) 20
 - I.7 Preliminary Hazard Analysis Potential Areas of Use(s) 20
 - I.8 Risk Ranking and Filtering Potential Areas of Use(s) 20
 - I.9 Supporting Statistical Tools 20
- Annex II: Potential Applications for Quality Risk Management 21
- II.1 Quality Risk Management as Part of Integrated Quality Management Documentation 21
Training and education 21
Quality defects 21

Auditing/Inspection	21	G. Design and Content Considerations	25
Periodic review	21	H. Quality Manual	25
Change management/change control	21	II. Management Responsibility	25
Continual improvement	21	A. Management Commitment	25
II.2 Quality Risk Management as Part of Regulatory Operations	21	B. Quality Policy	26
Inspection and assessment activities	21	C. Quality Planning	26
II.3 Quality Risk Management as Part of development	21	D. Resource Management	26
II.4 Quality Risk Management for Facilities, Equipment, and Utilities	22	E. Internal Communication	26
Design of facility/equipment	22	F. Management Review	26
Hygiene aspects in facilities	22	G. Management of Outsourced Activities and Purchased Materials	26
Qualification of facility/equipment/utilities	22	H. Management of Change in Product Ownership	26
Cleaning of equipment and environmental control	22	III. Continual Improvement of Process Performance and Product Quality	26
Calibration/preventive maintenance	22	A. Lifecycle Stage Goals	26
Computer systems and computer controlled equipment	22	1. Pharmaceutical Development	26
II.5 Quality Risk Management as Part of Materials Management	22	2. Technology Transfer	27
Assessment and evaluation of suppliers and contract manufacturers	22	3. Commercial Manufacturing	27
Starting material	22	4. Product Discontinuation	27
Use of materials	22	B. Pharmaceutical Quality System Elements	27
Storage, logistics, and distribution conditions	22	1. Process Performance and Product Quality Monitoring System	27
II.6 Quality Risk Management as Part of Production	22	2. Corrective Action and Preventive Action System	27
Validation	22	3. Change Management System	28
In-process sampling and testing	22	4. Management Review of Process Performance and Product Quality	28
Production planning	22	IV. Continual Improvement of the Pharmaceutical Quality System	28
II.7 Quality Risk Management as Part of Laboratory Control and Stability Studies	22	A. Management Review of the Pharmaceutical Quality System	29
Out of specification results	22	B. Monitoring of Internal and External Factors Impacting the Pharmaceutical Quality System	29
Retest period/expiration date	23	C. Outcomes of Management Review and Monitoring	29
II.8 Quality Risk Management as Part of Packaging and Labeling	23	Glossary	29
Design of packages	23	Annex 1	30
Selection of container closure system	23	Annex 2	31
Label controls	23	4. Pharmaceutical Development	32
3. Pharmaceutical Quality System	24	I. Introduction	32
I. Pharmaceutical Quality System	24	A. Approaches to Pharmaceutical Development	32
A. Introduction	24	II. Elements of Pharmaceutical Development	32
B. Scope	24	A. Target Product Profile	32
C. Relationship of ICH Q10 to Regional GMP Requirements, ISO Standards, and ICH Q7	24	B. Critical Quality Attributes	32
D. Relationship of ICH Q10 to Regulatory Approaches	24	C. Linking Material Attributes and Process Parameters to CQAs—Risk Assessment	33
E. ICH Q10 Objectives	24	D. Design Space	33
1. Achieve Product Realization	24	1. Selection of Variables	33
2. Establish and Maintain a State of Control	25	2. Defining and Describing a Design Space in a Submission	33
3. Facilitate Continual Improvement	25	3. Unit Operation Design Space(s)	33
F. Enablers: Knowledge Management and Quality Risk Management	25	4. Relationship of Design Space to Scale and Equipment	33
1. Knowledge Management	25		
2. Quality Risk Management	25		

5. Design Space vs. Proven Acceptable Ranges	33
6. Design Space and Edge of Failure	33
E. Control Strategy	34
F. Product Lifecycle Management and Continual Improvement	34
III. Submission of Pharmaceutical Development and Related Information in CTD Format	34
A. Quality Risk Management and Product and Process Development	34
B. Design Space	34
C. Control Strategy	35
D. Drug Substance Related Information	35
Glossary	35
Appendix 1: Differing Approaches to Pharmaceutical Development	35
Appendix 2: Illustrative Examples	36
Example of Use of a Risk Assessment Tool	36
Example of Depiction of Interactions	36
Illustrative Examples of Presentation of Design Space	36
5. Pharmaceutical Development in CTD	39
I. Introduction	39
A. Objective of the Guideline	39
B. Scope	39
II. Pharmaceutical Development	39
A. Components of the Drug Product	40
1. Drug Substance	40
2. Excipients	40
B. Drug Product	40
1. Formulation Development	40
2. Overages	40
3. Physicochemical and Biological Properties	40
C. Manufacturing Process Development	41
D. Container Closure System	41
E. Microbiological Attributes	41
F. Compatibility	41
Glossary	42
6. Scale-Up and Postapproval Changes for Nonsterile Semisolid Dosage Forms: Manufacturing Equipment	43
I. Preservative	43
II. Manufacturing Changes	43
III. Process	44
A. Batch Size (Scale-Up or Scale-Down)	44
IV. Manufacturing Site	44
I. Introduction	44
II. Particle Size Reduction and Separation	45
A. Definitions	45
1. Unit Operations	45
2. Operating Principles	45
B. Equipment Classifications	45
1. Fluid Energy Mills	45
2. Impact Mills	45
3. Cutting Mills	45
4. Compression Mills	45
5. Screening Mills	45
6. Tumbling Mills	45
7. Separators	45
III. Mixing	45
A. Definitions	45
1. Unit Operation	45
2. Operating Principles	46
B. Equipment Classification	46
1. Convection Mixers, Low Shear	46
2. Convection Mixers, High Shear	46
3. Roller Mixers (Mills)	46
4. Static Mixers	46
5. Low-Shear Emulsifiers	46
IV. Transfer	46
A. Definitions	46
1. Unit Operation	46
2. Operating Principles	46
B. Equipment Classification	46
1. Low Shear	46
2. High Shear	46
V. Packaging	46
A. Definitions	46
1. Unit Operation	46
2. Operating Principles	47
B. Equipment Classification	47
1. Holders	47
2. Fillers	47
3. Sealers	47
7. GOOD Manufacturing Practice Guide for Active Pharmaceutical Ingredients	48
1. Introduction	48
1.1 Objective	48
1.2 Regulatory Applicability	48
1.3 Scope	48
2. Quality Management	48
2.1 Principles	48
2.2 Responsibilities of the Quality Unit(s)	49
2.3 Responsibility for Production Activities	49
2.4 Internal Audits (Self-Inspection)	50
2.5 Product Quality Review	50
3. Personnel	50
3.1 Personnel Qualifications	50
3.2 Personnel Hygiene	50
3.3 Consultants	50
4. Buildings and Facilities	50
4.1 Design and Construction	50
4.2 Utilities	51
4.3 Water	51
4.4 Containment	51
4.5 Lighting	51
4.6 Sewage and Refuse	51
4.7 Sanitation and Maintenance	51
5. Process Equipment	52
5.1 Design and Construction	52
5.2 Equipment Maintenance and Cleaning	52
5.3 Calibration	52
5.4 Computerized Systems	52
6. Documentation and Records	53
6.1 Documentation System and Specifications	53
6.2 Equipment Cleaning and Use Record	53

- 6.3 Records of Raw Materials, Intermediates, API Labeling and Packaging Materials 53
 - 6.4 Master Production Instructions (Master Production and Control Records) 53
 - 6.5 Batch Production Records (Batch Production and Control Records) 54
 - 6.6 Laboratory Control Records 54
 - 6.7 Batch Production Record Review 54
 - 7. Materials Management 54
 - 7.1 General Controls 54
 - 7.2 Receipt and Quarantine 54
 - 7.3 Sampling and Testing of Incoming Production Materials 55
 - 7.4 Storage 55
 - 7.5 Reevaluation 55
 - 8. Production and In-Process Controls 55
 - 8.1 Production Operations 55
 - 8.2 Time Limits 56
 - 8.3 In-process Sampling and Controls 56
 - 8.4 Blending Batches of Intermediates or APIs 56
 - 8.5 Contamination Control 56
 - 9. Packaging and Identification Labeling of APIs and Intermediates 56
 - 9.1 General 56
 - 9.2 Packaging Materials 56
 - 9.3 Label Issuance and Control 57
 - 9.4 Packaging and Labeling Operations 57
 - 10. Storage and Distribution 57
 - 10.1 Warehousing Procedures 57
 - 10.2 Distribution Procedures 57
 - 11. Laboratory Controls 57
 - 11.1 General Controls 57
 - 11.2 Testing of Intermediates and APIs 58
 - 11.3 Validation of Analytical Procedures (see Subsection 12) 58
 - 11.4 Certificates of Analysis 58
 - 11.5 Stability Monitoring of APIs 58
 - 11.6 Expiry and Retest Dating 59
 - 11.7 Reserve/Retention Samples 59
 - 12. Validation 59
 - 12.1 Validation Policy 59
 - 12.2 Validation Documentation 59
 - 12.3 Qualification 59
 - 12.4 Approaches to Process Validation 59
 - 12.5 Process Validation Program 60
 - 12.6 Periodic Review of Validated Systems 60
 - 12.7 Cleaning Validation 60
 - 12.8 Validation of Analytical Methods 60
 - 13. Change Control 61
 - 14. Rejection and Reuse of Materials 61
 - 14.1 Rejection 61
 - 14.2 Reprocessing 61
 - 14.3 Reworking 61
 - 14.4 Recovery of Materials and Solvents 61
 - 14.5 Returns 61
 - 15. Complaints and Recalls 62
 - 16. Contract Manufacturers (Including Laboratories) 62
 - 17. Agents, Brokers, Traders, Distributors, Repackers, and Relabelers 62
 - 17.1 Applicability 62
 - 17.2 Traceability of Distributed APIs and Intermediates 62
 - 17.3 Quality Management 62
 - 17.4 Repackaging, Relabeling and Holding of APIs and Intermediates 62
 - 17.5 Stability 62
 - 17.6 Transfer of Information 62
 - 17.7 Handling of Complaints and Recalls 63
 - 17.8 Handling of Returns 63
 - 18. Specific Guidance for APIs Manufactured by Cell Culture/Fermentation 63
 - 18.1 General 63
 - 18.2 Cell Bank Maintenance and Record Keeping 63
 - 18.3 Cell Culture/Fermentation 64
 - 18.4 Harvesting, Isolation, and Purification 64
 - 18.5 Viral Removal/Inactivation Steps 64
 - 19. APIs for Use in Clinical Trials 64
 - 19.1 General 64
 - 19.2 Quality 64
 - 19.3 Equipment and Facilities 65
 - 19.4 Control of Raw Materials 65
 - 19.5 Production 65
 - 19.6 Validation 65
 - 19.7 Changes 65
 - 19.8 Laboratory Controls 65
 - 19.9 Documentation 65
- Glossary 65
- 8. Validation of Analytical Procedures 68**
- I. Introduction 68
 - II. Types of Analytical Procedures to be Validated 68
- Glossary 69
- 9. Validation of Analytical Procedures: Methodology 70**
- I. Introduction 70
 - II. Specificity 70
 - A. Identification 70
 - B. Assay and Impurity Test(s) 70
 - 1. Impurities Are Available 70
 - 2. Impurities Are Not Available 70
 - III. Linearity 71
 - IV. Range 71
 - V. Accuracy 71
 - A. Assay 71
 - 1. Drug Substance 71
 - 2. Drug Product 71
 - B. Impurities (Quantitation) 71
 - C. Recommended Data 71
 - VI. Precision 72
 - A. Repeatability 72
 - B. Intermediate Precision 72
 - C. Reproducibility 72
 - D. Recommended Data 72

- VII. Detection Limit 72
 - A. Based on Visual Evaluation 72
 - B. Based on Signal-to-Noise 72
 - C. Based on the Standard Deviation of the Response and the Slope 72
 - 1. Based on the Standard Deviation of the Blank 72
 - 2. Based on the Calibration Curve 72
 - D. Recommended Data 72
 - VIII. Quantitation Limit 72
 - A. Based on Visual Evaluation 72
 - B. Based on Signal-to-Noise Approach 72
 - C. Based on the Standard Deviation of the Response and the Slope 73
 - 1. Based on Standard Deviation of the Blank 73
 - 2. Based on the Calibration Curve 73
 - D. Recommended Data 73
 - IX. Robustness 73
 - X. System Suitability Testing 73
- 10. Bioequivalence Testing of Topical Drugs 74**
- I. Inactive Ingredients 74
 - II. Waiver of Bioequivalence 74
 - III. Bioequivalence Approaches 74
 - A. Dermatopharmacokinetic Approaches 74
 - 1. Performance and Validation of the Skin Stripping Technique 75
 - IV. Sample Pilot Study 75
 - A. DPK Bioequivalence Study Protocol 76
 - 1. Protocol and Subject Selection 76
 - 2. Application and Removal of Test and Reference Products 76
 - 3. Sites and Duration of Application 76
 - 4. Collection of Sample 76
 - 5. Procedure for Skin Stripping 76
 - B. Metrics and Statistical Analyses 77
 - V. Pharmacodynamic Approaches 77
 - A. In Vitro Release Approaches (Lower Strength) 77
 - B. In Vitro Release: Extension of the Methodology 78
 - C. Systemic Exposure Studies 78
- 11. Good Manufacturing Requirements for Active Pharmaceutical Ingredients 79**
- I. Introduction 79
 - II. FDA's Risk-Based, Systems Approach to API Inspections 79
 - The Quality System 80
- 12. FDA Active Pharmaceutical Ingredient Manufacturing Facility Inspection 81**
- Part I—Background 81
 - General 81
 - Scope of APIs Covered by This Program 81
 - Part II—Implementation 82
 - Objective 82
 - Program Management Instructions 82
 - Inspection Planning 83
 - Profile Classes 83
 - Types of Inspections 83
- Part III—Inspectional 83
 - Inspection Approaches 84
 - Full Inspection Option 84
 - A Full Inspection Is Appropriate 84
 - Abbreviated Inspection Option 84
 - Compliance Inspections 84
 - Selecting Systems for Coverage 84
 - Preparing the Inspection Strategy 84
 - Special Inspection Reporting Instructions 85
 - Special Instructions for Foreign Drug Inspections 85
 - Part IV—Analytical 85
 - Part V—Regulatory/Administrative Strategy 86
 - Part VI—References, Attachments, and Program Contacts 87
 - Bibliography 87
 - Part VII—Center Responsibilities 87
 - Appendix A: Description of Each System and Areas of Coverage 87
 - Quality System 87
 - Facilities and Equipment System 88
 - Materials System 88
 - Production System 89
 - Packaging and Labeling System 89
 - Laboratory Control System 89
 - Glossary 90
- 13. Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances 94**
- I. Introduction 94
 - A. Objective of the Guideline 94
 - B. Background 94
 - C. Scope of the Guideline 94
 - II. General Concepts 94
 - A. Periodic or Skip Testing 94
 - B. Release vs. Shelf life Acceptance Criteria 95
 - C. In-process Tests 95
 - D. Design and Development Considerations 95
 - E. Limited Data Available at Filing 95
 - F. Parametric Release 95
 - G. Alternative Procedures 95
 - H. Pharmacopoeial Tests and Acceptance Criteria 96
 - I. Evolving Technologies 96
 - J. Impact of Drug Substance on Drug Product Specifications 96
 - K. Reference Standard 96
 - III. Guidelines 96
 - A. Specifications: Definition and Justification 96
 - 1. Definition of Specifications 96
 - 2. Justification of Specifications 96
 - B. Universal Tests/Criteria 97
 - 1. New Drug Substances 97
 - 2. New Drug Products 97
 - C. Specific Tests/Criteria 98
 - 1. New Drug Substances 98
 - 2. New Drug Products 99
- Glossary 102
 - References 103
 - IV. Attachments 104

14. Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products 115

- I. Study Designs 115
 - A. Recommendations for a Cumulative Skin Irritation Study 115
 - 1. Sample Size 115
 - 2. Exclusion Criteria 115
 - 3. Duration of Study 115
 - 4. Study Design 115
 - 5. Patch Application 115
 - 6. Evaluations 115
 - 7. Data Presentation and Analysis 115
 - B. Recommendations for a Skin Sensitization Study (Modified Draize Test) 115
 - 1. Sample Size 115
 - 2. Exclusion Criteria 115
 - 3. Duration of Study 115
 - 4. Study Design 115
 - 5. Patch Application 115
 - 6. Data Presentation and Analysis 116
 - C. Combined Studies 116

Appendix A: Skin Irritation Scoring Systems 116

Appendix B: Adhesion Score 116

Appendix C: Statistics 116

Bibliography 117

15. Impurities in New Drug Substances 118

- I. Preamble 118
- II. Classification of Impurities 118
- III. Rationale for the Reporting and Control of Impurities 118
 - A. Organic Impurities 118
 - B. Inorganic Impurities 119
 - C. Solvents 119
- IV. Analytical Procedures 119
- V. Reporting Impurity Content of Batches 119
- VI. Listing of Impurities in Specifications 119
- VII. Qualification of Impurities 120

Glossary 120

16. Impurities in New Drug Products 123

- I. Introduction 123
 - A. Objective of the Guideline 123
 - B. Background 123
 - C. Scope of the Guideline 123
- II. Rationale for the Reporting and Control of Degradation Products 123
- III. Analytical Procedures 123
- IV. Reporting Degradation Products Content of Batches 124
 - V. Listing of Degradation Products in Specifications 124
- VI. Qualification of Degradation Products 125

Glossary 125

17. Formulation Factors in Semisolid Dosage Forms 130

- I. Potency Uniformity 130
- II. Equipment and Production Control 130
 - A. Mixers 130
 - B. Filling and Packaging 130
 - C. Process Temperature Control 130

- III. Cleaning Validation 131
 - A. Detailed Cleaning Procedures 131
 - B. Sampling Plan for Contaminants 131
 - C. Equipment Residue Limits 131
- IV. Microbiological 131
 - A. Controls (Nonsterile Topicals) 131
 - 1. Deionized Water Systems for Purified Water 131
 - 2. Microbiological Specifications and Test Methods 132
 - B. Preservative Activity 132
- V. Change Control 132
- VI. Transdermal Topical Products 132
 - A. General Considerations 132
 - B. The Role of In Vitro Release Testing 133
 - C. In Vivo Bioequivalence Studies 133

References 134

Glossary 134

18. GMP Audit Template, EU Guidelines 136

Glossary 155

19. Dissolution Testing of Semisolid Dosage Forms 158**20. Approved Excipients in Semisolid Dosage Forms 159****PART II. MANUFACTURING FORMULATIONS****Regulatory and Manufacturing Guidance 182**

Acetoclofenac Gel Cream 182

Acetaminophen Suppositories 182

Acetaminophen Suppositories 183

Acetaminophen Suppositories 183

Acetaminophen Suppositories 183

Acetaminophen Suppositories 184

Acetaminophen Suppositories 184

Acetylsalicylic Acid Suppositories 184

Acne Cover Cream 185

Acne Treatment Cream 185

Acyclovir Cream 186

Acyclovir Ointment 186

Adapalene Cream 187

Alclometasone Dipropionate Cream and Ointment 187

Aloe Vera Gel 187

Alum Cream 187

6-Aminonicotinamide Ointment 188

6-Aminonicotinic Acid Methyl Ester Ointment 188

6-Aminonicotinic Acid Ointment 188

Aminacrine Hydrochloride Cream 188

Amoxicillin Lotion 188

Ampicillin Lotion 189

Analgesic Clear Gel 189

Analgesic Cream 189

Analgesic Lotion 190

Anthralin Cream 190

Antiacne Gel 190

Antifungal Foot Powder 190

Antifungal Topical Cream 191

- Antiseptic Cream 191
- Antiseptic Lotion 191
 - Antiseptic Lotion 192
- Arginine and Oleoresin Capsicum Cream 192
- Arginine Cream 192
- Arginine–Aspartate Cream 193
- Atropine Ophthalmic Ointment 193
- Azelaic Acid Cream and Gel 194
- Baby Cream, Benzalkonium Chloride, and Zinc Oxide 194
- Baby Lotion 195
 - Baby Lotion 195
- Baby Shampoo 196
- Bacitracin Zinc and Polymyxin B Sulfate Ophthalmic Ointment 196
- Base Cream 197
- Base Ointment 197
 - Base Ointment 197
 - Base Ointment 198
 - Base Ointment 198
- Becaplermin Gel (0.01%) 199
- Benzalkonium Chloride and Zinc Oxide Cream 199
- Benzalkonium Chloride Contraceptive Gel 200
- Benzocaine Cream 200
- Benzoyl Peroxide and Alpha-Bisabolol Gel 200
- Benzoyl Peroxide Antiacne Microemulsion 201
- Benzoyl Peroxide Cream 201
- Benzoyl Peroxide Gel 202
- Benzoyl Peroxide Lotion 202
 - Benzoyl Peroxide Lotion 202
- Betamethasone and Cinchocaine Suppositories 203
- Betamethasone and Neomycin Gel Cream 203
- Betamethasone and Salicylic Acid Lotion 203
- Betamethasone Cream 204
 - Betamethasone Cream 204
- Betamethasone Dipropionate Cream, Lotion, and Ointment 204
- Betamethasone Dipropionate Ointment 205
- Betamethasone Gel 205
- Betamethasone Ophthalmic Ointment 205
- Betamethasone Valerate and Cinchocaine Ointment 206
- Betamethasone Valerate Cream 206
- Betamethasone Valerate Foam 207
- Betamethasone Valerate Ointment 207
 - Betamethasone Valerate Ointment 207
- Bifonazole Cream (1%) 208
- Bisacodyl Suppositories 208
 - Bisacodyl Suppositories 208
- Biscarboxychromonyloxy Propanol Ointment 209
- Bleaching and Antimicrobial Dentifrice 209
- Breast Care Cream 209
- Budesonide Cream 210
- Budesonide Ointment 210
- Buprenorphine Hydrochloride Suppository 211
- Burn Cream 211
 - Burn Cream 211
- Butenafine Hydrochloride Cream 212
- Butesin Picrate and Metaphen Ointment 212
- Butesin Picrate Ointment 213
- Butoconazole Nitrate Vaginal Cream 214
- Calamine and Diphenhydramine Hydrochloride Lotion 214
- Calamine and Pramoxine Hydrochloride Lotion 215
- Calamine Cream 215
 - Calamine Cream 215
- Calamine Lotion 216
- Calcipotriene Cream 216
 - Calcipotriene Cream 216
- Calcium Carbonate Ointment 216
- Camphor, Eucalyptus Oil, and Menthol Ointment 217
- Carbamazepine Cream 217
- Carbamazepine Gel 217
- Carbamazepine Ointment 217
- Carbamide Peroxide Chewing Gum 217
- 2-Carbamoylpyrazinamide Ointment 218
- Castor Oil Ointment 218
- Cefaclor and Benzoyl Peroxide Gel 218
- Cefaclor and Benzoyl Peroxide Lotion 218
- Cetrimide Antiseptic Cream 219
- Cetrimonium Bromide Cream 219
- Chloramphenicol Ophthalmic Ointment 219
- Chlorhexidine and Cetrimonium Bromide Cream 219
- Chlorhexidine Gel 220
- Chlorpromazine Suppositories 220
- Ciclopirox Cream, Lotion, and Gel 220
- Ciclopirox Nail Varnish 220
 - Ciclopirox Nail Varnish 220
- Ciprofloxacin Hydrochloride Ophthalmic Ointment 221
- Clindamycin Gel 221
- Clindamycin Lotion and Gel 221
- Clindamycin Phosphate Suppository 221
- Clindamycin Phosphate Topical Gel 221
- Clindamycin Phosphate Vaginal Cream 221
- Clindamycin Phosphate Vaginal Suppository 221
- Clobetasol Propionate Cream 222
- Clobetasol Propionate Cream, Ointment, and Gel 223
- Clobetasol Propionate Ointment Gel 223
- Clotrimazole and Betamethasone Cream and Lotion 223
- Clotrimazole Cream 223
- Clotrimazole Lotion 224
 - Clotrimazole Lotion 224
- Clotrimazole Vaginal Cream 225
 - Clotrimazole Vaginal Cream 225
- Clotrimazole Vaginal Cream Inserts 225
- Clotrimazole and Clindamycin Cream 225
- Clotrimazole and Clindamycin Suppositories 226
 - Clotrimazole and Clindamycin Suppositories 226
- Coal Tar and Allantoin Cream 226
 - Coal Tar and Allantoin Cream 227
- Coal Tar Cream 227
- Collagenase Ointment 227
- Conjugated Estrogens Vaginal Cream 227
- Cyanocobalamin Gel 227
- DBcAMP Ointment 227
- Desonide Cream, Ointment, and Lotion 228
- Desoximetasone Emollient Cream, Gel, and Ointment 228
- Dexamethasone Sodium Phosphate Ointment 228
- Dexpanthenol Cream 228
- Dexpanthenol Gel Cream 229
- Diclofenac Diethylamine Gel 229

- Diclofenac Diethylammonium Gel 230
 Diclofenac Sodium Suppositories 230
 Diclofenac Sodium Suppositories 230
 Diclofenac Sodium Suppositories 231
 Diclofenac Sodium Suppositories 231
 Dichlorobenzyl Alcohol Tooth Gel 231
 Dienestrol Vaginal Cream 232
 Diethylamine Salicylate Cream 232
 Diflorasone Diacetate Cream and Ointment 232
 Dimethicone and Zinc Oxide Ointment 232
 Dinoprostone Cervical Gel 232
 Dinoprostone Vaginal Insert and Suppositories 233
 Diphenhydramine Hydrochloride and Zinc Acetate
 Ointment 233
 Docosanol Lotion 233
 Econazole Nitrate and Benzoyl Peroxide Cream 233
 Econazole Nitrate and Benzoyl Peroxide Lotion 234
 Eflornithine Hydrochloride Cream 234
 Enzyme Extract Ointment 234
 Erythromycin and Neomycin Ointment 235
 Erythromycin Gel 235
 Erythromycin Ointment 235
 Erythromycin Ointment 236
 Estradiol and Norethindrone Acetate Transdermal
 System 236
 Estradiol Transdermal System 236
 Estradiol Vaginal Cream 236
 Estradiol Vaginal Cream 237
 Ethylenediamine Tetracetate Ointment 238
 Eucalyptus and Mint Ointment 238
 Foot Freshener Cream 239
 Foot Mousse 239
 Fluocinonide Cream 240
 Fluocinonide Cream, Ointment, and Gel 240
 Fluorometholone Ophthalmic Ointment 240
 Fluorouracil Cream 240
 Flurandrenolide Lotion 241
 Flurandrenolide Topical Film 241
 Fluticasone Ointment 241
 Fluticasone Propionate Ointment 241
 Fluticasone Propionate Cream 242
 Fluticasone Propionate Cream 242
 Folic Acid Suppository 242
 6-Formylaminonicotinamide Ointment and
 Lotion 242
 Foscarnet Cream 243
 Gamma Benzene Hexachloride Lotion 243
 Gentamicin Sulfate Cream 244
 Gentamicin Sulfate Ointment 244
 Gentamicin Sulfate Ointment 245
 Glycerin Suppositories 245
 Glycerin Suppositories 245
 Glycolic Acid Cream 246
 Gramicidin, Neomycin, Nystatin, and Triamcinolone
 Ointment 246
 Halobetasol Propionate Cream and Ointment 247
 Hemorrhoid Cream 247
 Heparin Gel Cream 247
 Hexachlorophene Cream 248
 Hydrocortisone Acetate and Pramoxine
 Hydrochloride Cream and Lotion 249
 Hydrocortisone Acetate Suppositories 249
 Hydrocortisone and Nitrofurazone Cream 249
 Hydrocortisone Butyrate Cream and Ointment 250
 Hydrocortisone Cream 250
 Hydrocortisone Cream 251
 Hydrocortisone Cream 251
 Hydrocortisone Cream and Ointment 252
 Hydrocortisone Gel 252
 Hydrocortisone Gel 252
 Hydrocortisone Gel 253
 Hydrocortisone Ointment 253
 Hydrogen Peroxide and Carbamide Peroxide
 Bleaching Oral Dentifrice 253
 Hydrogen Peroxide Bleaching Dentifrice Paste 254
 Hydrogen Peroxide Ointment 254
 Hydrophilic Ointment USP 255
 Hydroquinone Cream 255
 Hydroquinone Cream and Gel 256
 Hydroquinone Gel 256
 Ibuprofen and Domperidone Maleate
 Suppository 257
 Ibuprofen Cream 257
 Ibuprofen Gel 257
 Ibuprofen Gel 258
 Ibuprofen Gel 258
 Ibuprofen Gel Cream 258
 Ibuprofen Gel Cream 259
 Ibuprofen Gel Cream 259
 Imiquimod Cream 259
 Indomethacin Gel 259
 Indomethacin Gel 260
 Indomethacin Gel 260
 Indomethacin Suppositories 261
 Indomethacin Suppositories 261
 Indomethacin Suppositories 261
 Insect Bite Cream 262
 Keratolytic Cream 262
 Ketoconazole Cream 263
 Ketoconazole Cream 263
 Kojic Dipalmitate Cream 263
 Lactic Acid Cream 264
 Lanolin Cream 264
 Lidocaine Adhesive System Gel 264
 Lidocaine and Prilocaine Topical Adhesive System
 Cream 264
 Lidocaine and Tribenoside Cream 265
 Lidocaine and Tribenoside Ointment 265
 Lidocaine and Tribenoside Suppositories 266
 Lidocaine Anorectal Cream 266
 Lidocaine, Eugenol, and Menthol Dental
 Ointment 266
 Lidocaine Gel 267
 Lidocaine Gel 267
 Lidocaine Ointment 267
 Lindane Lotion 268
 Mafenide Acetate Cream 268
 Malathion Lotion 268
 Mandelic Acid Cream 268
 Medicated Foot Cream 269
 Menthol, Methyl Salicylate, and Menthol Cream and
 Ointment 269
 Mercuric Oxide Ointment 269
 Mesalamine Suppository 269
 Methotrexate Cataplasms 270
 Methotrexate Cream 270

- Methotrexate Gel 270
 Methotrexate Lotion 271
 Methoxsalen Lotion 271
 Methyl Salicylate and Menthol Cream 271
 Methyl Salicylate and Menthol Gel 272
 Methyl Salicylate and Menthol Lotion 272
 Methyl Salicylate and Menthol Ointment 272
 Methyl Salicylate Clear Gel 273
 Methyl Salicylate Cream 273
 Methyl Salicylate Cream 274
 Methyl Salicylate Heat Rub Lotion 274
 Methyl Salicylate Lotion 275
 Methyl Salicylate, Thyme, Pine, and Menthol Foot
 Cream 275
 Metoclopramide Suppositories 276
 Metoclopramide Suppositories 276
 Metoclopramide Suppositories 277
 Metoclopramide Suppositories 277
 Metronidazole Cream 277
 Metronidazole Gel Solution 278
 Metronidazole Lotion 278
 Metronidazole Vaginal Gel 278
 Miconazole Cream 278
 Miconazole Mouth Gel 279
 Miconazole Nitrate Cream 279
 Miconazole Nitrate Vaginal Suppositories 280
 Miconazole Nitrate Vaginal Suppositories
 (400 mg) 280
 Minoxidil Gel 281
 Minoxidil Gel 281
 Minoxidil Gel 281
 Minoxidil Gel 282
 Mometasone Furoate Cream 282
 Mometasone Furoate Lotion 282
 Monobenzene Cream 283
 Multivitamin Oral Gel Veterinary 283
 Multivitamin Oral Gel with Linoleic and Linolenic
 Acid 284
 Mupirocin Calcium Cream 284
 Mupirocin Ointment 284
 Mupirocin Ointment 285
 Naftifine Hydrochloride Cream 285
 Naftifine Hydrochloride Cream 285
 Nanoxynol Suppository with Bacterial Culture 286
 Neomycin and Bacitracin Ointment 287
 Neomycin Gel 287
 Neomycin, Polymyxin B Sulfate, and Bacitracin Zinc
 Ophthalmic Ointment 288
 Nicotine Polymer Gel 288
 Nitrofurazone Cream 288
 Nondetergent Neutral Dry Skin Cream 289
 Nystatin Cream 289
 Nystatin Ointment 290
 Nystatin, Neomycin Sulfate, Gramicidin, and
 Triamcinolone Acetonide Cream 291
 Nystatin, Neomycin Sulfate, Gramicidin, and
 Triamcinolone Acetonide Ointment 292
 Octyl Methoxycinnamate, Octyl Salicylate, and
 Oxybenzone Gel 292
 Olibanum Gum Cream 292
 Oxiconazole Cream and Lotion 293
 Oxymorphone Hydrochloride Suppositories 293
 Oxytetracycline Ointment 293
 Panthenol and Chlorhexidine Lotion 293
 Panthenol Ointment 294
 Panthenol Lotion 294
 Pantoprazole–Cholesterol Complex Suppository 295
 Papain Chewing Gum 295
 Papain Ointment 295
 Penciclovir Cream 295
 Peppermint Cream 295
 Permethrin Cream and Lotion 296
 Petrolatum and Lanolin Ointment 296
 Phenylephrine Ointment, Cream, Suppositories,
 and Gel 296
 Piroxicam Ointment 296
 Piroxicam and Dexpanthenol Gel 296
 Polymyxin, Bacitracin, Hydrocortisone, and Zinc
 Ointment 297
 Povidone–Iodine and Lidocaine Gel 297
 Povidone–Iodine Bar Soap 297
 Povidone–Iodine Bar Soap 298
 Povidone–Iodine Bar Soap 298
 Povidone–Iodine Cream 298
 Povidone–Iodine Cream 299
 Povidone–Iodine Cream 299
 Povidone–Iodine Gel 299
 Povidone–Iodine Gel 300
 Povidone–Iodine Gel 300
 Povidone–Iodine Gel Cream 300
 Povidone–Iodine Gels 301
 Povidone–Iodine Glucose Ointment 301
 Povidone–Iodine Glucose Ointment 301
 Povidone–Iodine Mastitis Cream for Cattle 302
 Povidone–Iodine Soft Gel 302
 Povidone–Iodine Transparent Ointment 302
 Povidone–Iodine Vaginal Ovule 303
 Povidone–Iodine Vaginal Ovule 303
 Povidone–Iodine Vaginal Ovules 303
 Povidone–Iodine Vaginal Ovules 303
 Pramoxine Cream 304
 Pramoxine Hydrochloride and Zinc Acetate Lotion
 and Ointment 305
 Pramoxine Suppositories 305
 Pramoxine Suppositories 305
 Pranoprofen Ointment 306
 Prednicarbate Emollient Cream 306
 Prochlorperazine Suppositories 306
 Progesterone Gel 306
 Promethazine Hydrochloride Suppositories 306
 Promethazine Suppository 306
 Psoriasis Cream 306
 Psoriasis Cream 307
 Resorcinol Acne Cream 307
 Rubefacient Analgesic Ointment 307
 Salicylic Acid Cream 308
 Salicylic Acid Cream 308
 Salicylic Acid Gel 309
 Scopolamine Transdermal Therapeutic System 309
 Selenium Sulfide Detergent Lotion 310
 Selenium Sulfide Lotion 311
 Silicone Cream 311
 Silver Sulfadiazine Cream 311
 Silver Sulfadiazine Cream 311
 Sodium Chloride Ointment 312
 Sodium Sulfacetamide Lotion 312

Spermatocidal Effervescent Suppository	313
Squalene Cream	313
Starch Ointment	313
Sucralafate and Hyaluronic Acid Ointment	313
Sucralafate Ointment	314
Sucralafate Ophthalmic Ointment	314
Sulfacetamide Ointment	314
Sulfacetamide Sodium and Prednisolone Acetate Ophthalmic Ointment	314
Sulfanilamide Suppositories	314
Sulfathiazole Cream	315
Sulfur Ointment	315
Tacrolimus Ointment	315
Terconazole Vaginal Cream	315
Terconazole Vaginal Suppositories	315
Testosterone Gel	315
Testosterone Transdermal System	316
Tetracaine Gel and Cream	316
Tetracycline Hydrochloride Ointment	316
TGF Alpha-Ointment	316
Therapeutic Skin Lotion	317
Tolnaftate and Undecylenate Cream	317
Tretinoin and Alpha-Bisabolol Gel	318
Tretinoin and Dexpanthenol Gel	318
Tretinoin Cream	319
Tretinoin Cream	319
Tretinoin Gel	319
Tretinoin Gel Microsphere	320
Triacotanol Ointment	320
Triclosan Foot Care Cream	320
Triclosan Foot Cream	321
<i>Tridax procumbens</i> Ointment	321
Trolamine Salicylate Cream	322
Ulinastatin Suppository	322
Ultrasonic Adhesive Gel	322
Vitamin A Ointment	323
Vitamin A Suppositories	323
Vitamin C Vaginal Ointment	323
Vitamin E Gel Cream	324
Wound Debriding Ointment	324
Zinc Oxide and Vitamin E Cream	324
Zinc Oxide Lotion	325
Zinc Oxide Ointment	325
Zinc Oxide Ointment	325
Zinc Oxide Ointment with Vitamin E and Aloe	326
Zinc Pyrithione Detergent Lotion	326
Zinc Undecylenate Cream	326
Zirconium Oxide Lotion	327
Commercial Pharmaceutical Formulations	327
<i>Index</i>	335