INDEX

Absorption:
  enteric coatings, 214
  gastric retention devices, 186
  nonuniform abilities, 4
  peptide/protein drug absorption, 4
Abuse deterrence, 306–308
Accelerated stability testing, 149
Acceptance criteria, 13–14
Achievable release profiles, 28
Active pharmaceutical ingredient (API), 41
  bilayer osmotic tablet processing, 143–144
  coating systems and, 108–109
  excipient impurities and API compatibility, 149
  fast-dissolving (fast disintegrating) tablets, 163
  preformulation protocols, 59–66
  dissolution rate, 65
  equilibrium solubility, 59–61
  food effect, 64–65
  intrinsic dissolution, 65
  kinetic solubility, 61
  pH profile, 62
  pKₐ values, 62–63
  salt/buffer/chloride ion effects, 63–64
  simulated biological fluid, 63
  thermodynamically stable polymorph, 65–66
Alginate, 75–76
Alza Corporation, 198
5-Aminosalicylic acid:
  colon-specific drug delivery, 229–231
  polymeric prodrugs, 234–235
Angle of repose, 50
Animal studies:
  gastric retention devices, 195–196
  permeability assessment, 36
  preclinical studies, 309
Antiadherents, 106
Aphthous ulceration, 172
Apparatus design and selection, 246–247
Applicability mapping, 135–136
Aqueous-based polymer coatings, 120–122
Aqueous solubility, 4–5
  biopharmaceutical evaluation, 33–35
Aspect ratio parameter, 48–49
Assisted floating systems, devices, 193
Asymmetric membrane, 131–132
Atomization air pressure, 125
Azo-polymers, 232–233
Bacterial, 219
Barrier membrane coatings, 93–94
Batch report, 295
Bilayer osmotic tablet technology:
  advantages, 133–134
  applications, 135–137
  controlled release feasibility, 135–136
  core properties, 137–138
  delivery orifice, 141–142
  disadvantages, 134–135
  drug solubilization, 150–151
  in vitro performance testing, 146–149
  membrane coating, 139–141
  physiologic factors, 136–137
  processing operations, 142–146
  delivery port manufacture, 146
  film coating, 145–146
  material properties, 142–143
  tablet compression, 144–145
INDEX

Bilayer osmotic tablet technology: (Continued)
push-pull design, 137
stability testing, 149–150
swelling core, 132–133
swelling layer properties, 138–139
Bioadhesive controlled release systems:
buccal drug delivery, 174–178
design innovations, 261
polymer-based modified oral release systems, 81–83
carbomers, 81–82
polyethylene oxide, 82–83
Bioavailability, 344–345
Biodegradable controlled release systems:
buccal drug delivery, 174–178
design innovations, 261
polymer-based modified oral release systems, 81–83
carbomers, 81–82
polyethylene oxide, 82–83
Biodegradable coated tablets:
targeting of oral cavity, 173–174
toxicity and irritancy, 179–180
Bioavailability, 344–345
Bioequivalence:
generic compounds, 330–331
RLD characterization, 324–326
life cycle management, 309–310
regulatory guidelines, 344–345
Biopharmaceutical Classification System (BCS):
Class II drugs, aqueous solubility, 4–5
permeability, 35–36
quality by design, 285–286
Biopharmaceuticals:
generic compounds, 330–331
oral controlled release formulation, 4–5
colonic stability, 36–37
design approaches, 263–266
dissolution, 38–39
drug candidate evaluation, 33–41
future research issues, 28
gastrointestinal metabolism and elimination, 37
in vivo study and pharmacokinetics simulation, 39–41
permeability, 35–36
solubility, 33–35
Biorelevant media, dissolution testing, 250
Biowaivers, 345
Bottom spray systems, 122–124
Bristol-Meyers Squibb Co., 198
Buccal drug delivery systems:
buccal/gingival mucosa permeability, 172–173
diseases of oral cavity, 172
formulations, 174–180
bioadhesives, 174–175
films and patches, 175–176
liquid dosage forms, 178–179
particulates, 175–176
semisolids, 176–177
solid dosage forms, 174–178
tablet adhesives, 175
microbial ecology in oral cavity, 171–172
oral cavity anatomy and physiology, 169–172
permeation enhancers, 173
targeting of oral cavity, 173–174
toxicity and irritancy, 179–180
Buccastem®️, 176–177
Buffer solutions, dissolution testing, 250
Bulk powder properties, 49–52
Butylated hydroxytoluene (BHT), 149
Carbomers, 81–82
Cardiazem®️ CD, 313
Cardiazem®️ LA, 313–314
Carr’s index, 50
Carvedilol phosphate extended release capsules, 315–316
Cellulose acetate phthalate (CAP) coating:
barrier membrane coatings, 93–94
enteric coatings, 206
evolution, 23
polymer-based membrane controlled oral release systems, 79–80
Cellulose derivatives, 90
Cellulose ethers, 79
Chemical structure
partition coefficient estimation, 67
Chemical vapor deposition (CVD), 219
Chemometrics, 297
Chitosan:
buccal drug delivery systems, 177–179
hydrophilic matrix systems, 73–75
structure and properties, 72–73
Chloride ion transfers, 63–64
Clearance mechanisms, 4
Clinical manufacturing, 148
Clinical study design, 148–149
Clinical trials:
FDA review, 338–339
life cycle management, 310
regulatory guidelines, 346
Coacervation, 218–219
Coating systems:
bilayer osmotic tablets:
film coating solution preparation, 145–146
membrane coatings, 139–141
cellulose acetate phthalate (CAP) coating, 23
defects, 109–110
drug and substrate considerations, 108–109
dry coating techniques, 109
enteric coatings:
historical background, 21–23
polymethacrylates, 81
semisynthetic/synthetic polymers, 24
excipients, 104–106
antiadherents, 106
pigments, 106
plasticizers, 104–105
solvents, 104
surfactants, 106
extended release hydrophilic matrices:
barrier membrane coating, 93–94
press coating modulation, 95
film coatings, 101–102
polymer adhesion, film-tablet interface, 109
fluid bed coating and granulation:
aqueous-based polymer coatings, 120–122
bottom spray systems, 123–124
controlled release development process, 122–126
formulation considerations, 117–122
functional coating, 120–122
Design space development (Continued)
first principles methods, 296
process analytical technology, 298–299
Dexamethasone, 312
Dextran prodrugs, 235–236
Didanosine, 213–214
Diffusion:
Fick’s first law, 2–3
matrix systems, 27
Diffusion-controlled reservoir systems:
fluidized bed coating systems, 117
oral controlled release drugs, 6
Dilacor® XR, 314–315
Diltiazem, 313–315
Direct power coating systems, 122
Disease effect, 212–213
Disintegrants, 158–159
Disintegration-controlled matrix tablet, 259
Disintegration profile, 164–165
Dissolution-controlled release:
biayer osmotic tablets:
formulation development and testing, 147–148
in vitro measurement, 147
solubilization process, 150–151
fast-dissolving (fast disintegrating) tablets, 164–165
fluidized bed coating systems, 117
quality by design principles, 284–287
Dissolution profiles, 10–11
biopharmaceutical evaluation, 38–39
Dissolution rate, 65
Dissolution testing:
apparatuses, 246–247
extrinsic factors, 246–251
formulation development, 251–252
hydrodynamics, 247–248
intrinsic factors, 246
in vivo-in vitro correlation, 252–253
media properties, 248–250
parameters, 245–251
particle size, 246
postapproval manufacturing and scale-up, 253–254
solubility parameters, 246
solution detection, 250–251
Dosage form:
active pharmaceutical ingredient, 41
enteric coatings, 209–212
generic compounds:
design principles, 324–330
pharmacokinetics, 326–330
Dose dumping risk, 288–289
Dose volume, 136
Draining mechanisms, 228
Drug-excipient compatibility and stability, 327
Drug interactions:
enteric coatings, drug-polymer interactions, 217
gastric retention devices, 187–188
Drug-polymer interactions, 149–150
Drug release rate, 147
Dry coating techniques, 109
Dry granulation, 143–144
DuraSolv technology, 162
Effervescence, 161
Egalet®, 259–260
Electrostatic dry-coating, 271–273
Emulsion diffusion, 218–219
Emulsion solvent evaporation, 218–219
Enantiomers, 306–308
Engineering Process Control (EPC), 299
EnSoTrol system, 7
Enteral coating mycophenolate sodium (EC-MPS), 213–214
Enteric coatings:
absorption enhancement, 214
colon-specific drug delivery, 230–231
disease effects, 212–213
dosage forms, 209–212
drug absorption and toxicity, 214
food effects, 212
gastrointestinal physiology, 212–213
GI toxicity reduction, 213–214
historical background, 205–209
matrix systems, 210–212
oral controlled release formulation:
biopharmaceuticals, 263–266
historical background, 21–23
semisynthetic/synthetic polymers, 24
polymer properties, 217
poly(meth)acrylates, 81
processing issues, 217–219
substrate properties, 217
targeted drug design and formulation, 214–217
pH-dependent solubility, 214–216
pore formation, 216–217
Enterion™ capsule, 36
Entraining agents, 138
Enzyme degradation, 231
Equilibrium solubility, 59–61
Erodible molded multilayer tablet, 259–260
Ester polymers, 206–209
Ethyl cellulose:
barrier membrane coatings, 93–94
colon-specific drug delivery systems, 230–231
polymer-based membrane controlled oral release systems, 80
Eudragit®:
colon-specific drug delivery, 230–231
fluid bed coating systems, 120
historical background, 210–212
plasticizer, 105
polymer-based membrane controlled oral release systems, 81
European Pharmacopoeia, 51–52
Excipients:
bilayer osmotic tablets:
disadvantages, 135
impurities and API compatibility, 149
in coating systems, 104–106
antiadherents, 106
pigments, 106
plasticizers, 104–105
solvents, 104
surfactants, 106
dissolution/release assessment, 287–289
FDA guidelines, 341–342
generic compounds, 327
preformulation protocols:
compatibility, 56–58
solid excipient degradation, 58–59
properties, 273–274
Exclusivity principles, 322–324
Expandable materials, 195
Extended release dexamethylphenidate, 312
Extended release hydrophilic matrices:
applications, 93–97
barrier membrane coating, 93–94
classification, 89–90
minimatrix alternative, 96–97
multilayer modulation, 94–95
pH microenvironmental control, 96
polymer blends, 95–96
predicted release, 92–93
press coating modulation, 95
release mechanisms, 90–92
Failure modes and effect analysis (FMEA), 289–290
Fast-dissolving (fast disintegrating) tablets (FDTs):
active ingredient selection, 163
current products, 156–157
formulation methods, 156–161
compression method, 157–161
crystalline transition, 159–160
disintegrant addition, 158–159
effervescence, 161
phase transition, 160
spray drying, 161
sublimation, 160–161
lyophilization (freeze drying), 156
molding method, 156–157
patented technologies, 161–163
DuraSolv, 162
Flashdose, 162
FlashTab technology, 163
Frosta, 162–163
Lyoc and QuickSolv, 161
OraSolv, 161–162
Pharmaburst technology, 163
WOW Tab, 162
Zydis, 161
performance evaluation, 164–165
taste masking, 163–164
Fiber-optic detection, 251
Fick’s first law of diffusion:
fluidized bed coating systems, 116–117
intrinsic dissolution, 65–66
oral controlled release formulation, 2–3
Film coatings:
aqueous polymer dispersion, 101–102
basic properties, 101–102
bilayer osmotic tablets:
solution preparation, 145–146
thickness properties, 141
buccal drug delivery, 177–178
colon-specific drug delivery, 230–231
defect analysis, 109–110
enteric coatings, 206–209
polymer adhesion, 109
First principles knowledge:
design space analysis, 296–297
process understanding, 293
Fish oil capsules, 210
Flashdose technology, 162
FlashTab technology, 163
Floatable gastric retention devices, 189–193
Flow measurement, 142–143
Flowmeter analysis, 51
Fluidized bed coating systems:
aqueous-based polymer coatings, 120–122
direct powder coating systems, 122
bottom spray systems, 123–124
controlled release development process, 122–126
formulation considerations, 117–122
functional coating, 120–122
multiparticulate release mechanisms, 116–117
oral controlled release drug coatings, 106–108
process variables, 125
rotary spray systems, 124
scale-up protocols, 125–126
subcoats, 119–120
substrate preparation, 117–119
granules, 119
minitablets, 119
pellets, 118–119
top spray systems, 124
Food and Drug Administration (FDA), 338–339
excipient guidelines, 341–342
Food effect:
active pharmaceutical ingredient solubility, 64–65
enteric coatings, 212
Formulation development:
dissolution testing, 251–252
generic compounds, 327–330
life cycle management, 308–309
freeze-drying, 156
Friability testing, 164–165
Frosta technology, 162–163
Functional coatings:
bilayer osmotic tablets, 137–138
fluid bed coating systems, 120–122
Gamma scintigraphy, 11
Gas-driven floatable systems, 189–191
Gastric emptying:
gastric retention devices, 187
oral controlled release limitations, 3
Granulation:
aids and binders, 138
enteric coatings, 209–212
fluid bed coating systems:
aqueous-based polymer coatings, 120–122
direct powder coating systems, 122
binder melting points, 119
top spray systems, 123–124
controlled release development process, 122–126
formulation considerations, 117–122
functional coating, 120–122
multiparticulate release mechanisms, 116–117
process variables, 125
rotary spray systems, 124
scale-up protocols, 125–126
subcoats, 119–120
substrate preparation, 117–119
granules, 119
mimitables, 119
pellets, 118–119
top spray systems, 124

Helicobacter pylori, 186
High-performance liquid chromatography (HPLC), 251
Higuchi equation, 91–92
Hollow core carriers, 191–192
Hot melt extrusion (HME):
enteric coatings, 211–212
oral controlled release design, 266–268
system properties, 122
Hybrid systems, 26–28
Hydrodynamically balanced systems (HBS), 189–193
Hydrodynamics:
bilayer osmotic tablet release rate independence, 133
dissolution testing, 247–248
Hydrogels:
complexation, 264–266
swellable platforms, 194–195
Hydrophilic matrix systems:
chitosans, 73–75
extended release formulation and design:
aplications, 93–97
barrier membrane coating, 93–94
classification, 89–90
minimatrix alternative, 96–97
multilayer modulation, 94–95
pH microenvironmental control, 96
polymer blends, 95–96
predicted release, 92–93
press coating modulation, 95
release mechanisms, 90–92
gel-forming polymers, 24–25
N-(2-Hydroxypropyl)methacrylamide (HPMA) copolymer,
colon-specific drug delivery systems, 235
Hydroxypropyl methylcellulose (HPMC):
coating excipients, 106
colon-specific drug delivery systems, 231
floatable gastric retention devices, 189–193
Life cycle management: (Continued)
quetiapine fumarate extended release tablets, 317
product development, 308–310
Liquid crystal (LC) substances, 80
Liquid dosage formulations, 179
Low density core carriers, 191–192
LTS Lohmann Therapie-System AG, 198
Lyoc technology, 161
Lyophilization, 156

Magnetic resonance imaging (MRI), 11
Magnetic systems, 195
Malvern® Matersizer, 49–50
Manufacturing protocols:
generic compounds, 330
postapproval changes, 252–253
quality by design, 288
Materials properties:
bilayer osmotic tablet processing, 142–143
oral controlled-release drugs, 273–274
Mathematical modeling, 91–92
Matrix systems:
eric coatings, 210–212
extended release technology:
hydrophilic matrices:
applications, 93–97
barrier membrane coating, 93–94
classification, 89–90
minimatrix alternative, 96–97
multilayer modulation, 94–95
pH microenvironmental control, 96
polymer blends, 95–96
predicted release, 92–93
press coating modulation, 95
release mechanisms, 90–92
generic compounds, 327–330
oral controlled release drugs, 8
classification, 26–27
disintegration-controlled tablet, 259
dissolution profiles, 38–39
polymer-based modified oral release systems, 72–79
alginate, 75–76
cellulose ethers, 79
chitosan, 72–75
hydroxypropyl methylcellulose, 77–79
pectins, 76–77
membrane-controlled systems, 79–81
cellulose acetate, 79–80
ethylcellulose, 80
polymethacrylates, 81
Merck & Co, 198
Metabolism, 227
Methylphenidate:
life cycle management, 312–313
OROS® methylphenidate, 311–312
Metronidazole (MZ), 192–193
Microbial ecology, 171–172
Microflora, 227
Micronization, 48–50
Microscopic imaging, 48–49
Minimatrixses, 96–97
Minitablets:
extended release hydrophilic matrices, 96–97
fluid bed coating systems, 119
Modified oral release systems:
bioadhesive controlled release systems, 81–83
carbomer, 81–82
polyethylene oxide, 82–83
classification, 71–72
matrix systems, 72–79
alginate, 75–76
chitosan, 72–75
hydroxypropyl methylcellulose, 77–79
pectins, 76–77
Moisture sorption model, 159–160
Moisture uptake, 164–165
Molding process, 156–157
Monitoring procedures, 196
Monolithic diffusion-controlled systems, 117
Monolithic swelling tablets, 132
Motility mechanisms:
colon-specific drug delivery, 226
gastric retention devices, 187
Mucadhesion systems, 193–194
Mucosal barriers, 226
Mucus lining, 227
Multilayer matrix technology:
erodible molded multilayer tablet, 259–260
extended release hydrophilic matrices, 94–95
Multiparticulates:
oral controlled release drugs, 8
dissolution profiles, 38–39
release mechanisms, 116–117
Multivariate Statistical Process Control (MSPC), 300
Mycophenolic acid (MPA), 213–214
Nalmefene, 229
Naloxone, 229
Nanosuspensions, 218–219
Natural food ingredients, 274
Natural polysaccharides, 233
New Chemical Entity (NCE) definition, 322–323
New Clinical Investigation (NCI), 323
Nifedipine, 315
Noncellulose derivatives, 90
Nonfringement principles, 322
Nonoral controlled-release dosage forms, 347
Nonporous reservoir system, 117
Nonuniform absorption, 4
Noyes-Whitney equation, 34–35
Nucleotides, 263–266
OCAS™, 13
One-step dry coating (OSDrC), 272–273
Optical evaluation, 324–326
Oral cavity:
anatomy and physiology, 169–172
microbial ecology, 171–172
Oral controlled release formulation. See also specific
delivery systems, e.g., Buccal drug delivery systems
biodhesive delivery, 261
biopharmaceuticals, 28, 263–266
computer modeling, 261–263
current developments, 22–23
design fundamentals, 1–4
advantages/disadvantages, 1–2
computer-aided design, 8–9
limitations, 3–4
mechanisms and formulation approaches, 5–8
nonconventional systems, 11–13
overview, 1
pharmacokinetics/pharmacodynamics, 10–11
polymers, 9–10
preformulation/biopharmaceutical considerations, 4–5
process approaches, 8
regulatory and legal aspects, 13–14
release theories, 2–3
development history, 308–309
disintegration-controlled matrix tablet, 259
erodible molded multilayer tablet, 259–260
evolution, 21
future research issues, 274
generic vs. innovator products, 14
historical background, 21–26
hydrophilic gel-forming polymers, 24–25
osmotic delivery systems, 25–26
semisynthetic/synthetic polymer enteric coatings, 24
Spansule® technology, 24
hybrid systems, 26–28
achievable release profiles, 28
material innovations, 273–274
matrix systems, 26–27
membrane systems, 26–27
nucleotides, 265–266
platform technologies, 266–273
dry coatings, 270–273
hot melt extrusion, 266–268
injection molding, 268–269
printing techniques, 269–270
terminology and potential benefits, 23
vaccines, 265
water-insoluble drugs, 257–259
OraSolv technology, 161–162
OROS® methylphenidate, 311–312
OROS® nifedipine, 315
OROS® osmotic device, 7
OROS® oxybutynin hydrochloride, 317
Orphan Drug Exclusivity, 323
Osmogens, 138–139
Osmotic drug delivery (osmotic pump systems):
bilayer tablets:
advantages, 133–134
applications, 135–137
controlled release feasibility, 135–136
core properties, 137–138
delivery orifice, 141–142
disadvantages, 134–135
membrane coating, 139–141
physiologic factors, 136–137
push-pull design, 137
stability testing, 149–150
swelling core, 132–133
swelling layer properties, 138–139
coating materials, 103–104
controlled release tablet comparisons, 135
drug solubilization, 150–151
generic compounds, 327–330
in vitro performance testing, 146–149
oral controlled release formulation:
dissolution profiles, 38–39
invention and commercialization history, 25–26
membrane systems, 27
tablet formation, 8
pH release independence, 133
porous coating tablets, 131–132
bilayer tablets, 132–133
monolithic swelling core, 132
processing:
delivery port manufacturing, 146
film coating preparation, 145–146
material properties, 142–143
tablet compression, 144–145
pump devices:
elementary pump and liquid OROS, 130–131
history, 129–130
tablet components, 130
tablet technology classification, 130–133
Oxidative degradation:
excipient impurities and API compatibility, 149
solution-state forced degradation analysis, 54
Paliperidone ER (INVEGA®), 310–311
Particle size analysis:
disintegrate properties, 158–159
dissolution testing, 246
generic compounds, 327
quality by design:
critical quality attributes, 284–285
dissolution/release assessment, 286–287
Particulate properties:
- buccal drug delivery, 177–178
- preformulation, 47–53
  - bulk powder properties, 49–52
  - compression properties, 52–53
  - particle size analysis, 48–50
- Partition coefficient, 66–68
- Passive transport, 35–36
- Patches, 177–178

Patented technologies:
- fast-dissolving (fast disintegrating) tablets, 161–163
  - DuraSolv, 162
  - Flashdose, 162
  - FlashTab technology, 163
  - Frosta, 162–163
  - Lyoc and QuickSolv, 161
  - OraSolv, 161–162
  - Pharmaburst technology, 163
  - WOW Tab, 162
  - Zydis, 161
- gastric retention devices, 196–198
- generic compounds, 322–324
- life cycle management, 310

Patient protection, 14

Pectins, 76–77

Pediatric Exclusivity, 323

Pellets:
- enteric coatings, 209–212
- fluidized bed coating systems, 118–119

Peptides, 4

Performance analysis:
- bilayer osmotic tablets, 146–149
- fast-dissolving (fast disintegrating) tablets, 164–165

Periodontal disease, 172

Perio Products Ltd, 198

Permeability:
- buccal drug delivery:
  - enhancement of, 173
  - oral cavity mucosa and, 172–173
  - generic compounds, 326
  - oral controlled release formulation, 5
  - biopharmaceutical evaluation, 35–36
  - biopharmaceuticals, 263–266

Pfizer, Inc., 198

Pharmaceutical equivalence, 345

Pharmacokinetics:
- generic compounds, 326
- life cycle management, 309–310
- oral controlled release drugs, 10–11
  - in vivo study, 39–41

Pharmacodynamics, 10–11

Phase transition, 160

pH profile:
- basic principles, 3
- bilayer osmotic tablet release rate independence, 133
- luminal pH, 227–228
- medium pH, 248–249
- microenvironmental control, 96
  - pH-solubility profile, 62–63
  - solubility evaluation, 34–35
    - coating materials, 104
    - sustained-release formulas, 214–215

Physicochemical stability:
- generic compounds, 326–327
- oral controlled release formulation, 5

Pigments, 106

pKₐ values:
  - pH-solubility profile, 62–63

Plasticizers:
- coating excipients, 104–105
  - dry coating systems, 270–273
- fluid bed polymer coatings, 120–122

Platform technologies, 266–273
- dry coatings, 270–273
- hot melt extrusion, 266–268
- injection molding, 268–269
- printing techniques, 269–270

Polyethylene glycol (PEG):
- excipient impurities and API compatibility, 149
  - membrane composition and thickness, 140–141

Polyethylene oxide (PEO):
- bilayer osmotic tablet processing:
  - basic properties, 142–143
  - compression formulation, 143–144
  - excipient impurities and API compatibility, 149
  - tablet compression, 144–145
  - polymer-based modified oral release systems, 82–83

Polymers:
- aqueous-base polymer coating systems, 120–121
- bioadhesive compounds, 174–176
- coating systems:
  - adhesion and film-tablet interface, 109
  - aqueous polymer dispersion, 101–102
  - release mechanisms, 116–117
- colon-specific drug delivery systems:
  - azo-polymers, 232–233
  - enzyme-driven degradation, 231
  - natural polysaccharides, 233
  - prodrugs, 234–235
  - synthetic saccharides, 233–234
  - enteric coatings, 217

extended release hydrophilic matrices:
- blended polymers, 95–96
- classification, 89–90

modified oral release systems:
- bioadhesive controlled release systems, 81–83
- carbomers, 81–82
- polyethylene oxide, 82–83
- classification, 71–72

matrix systems, 72–79
  - alginate, 75–76
  - chitosan, 72–75
  - hydroxypropyl methylcellulose, 77–79
  - pectins, 76–77
- membrane-controlled systems, 79–81
  - cellulose acetate, 79–80
ethylcellulose, 80
polyacrylates, 81
oral controlled release formulation:
evolution, 9–10, 23
hydrophilic gel-forming polymers, 24–25
semisynthetic/synthetic coatings, 24
organic solvent-based coating systems, 120
Polymethacrylates:
bioadhesive compounds, 176
polymer-based membrane controlled oral release systems, 81
Polymorphism, 326–327
Polysaccharides:
natural polysaccharides, 233
synthetic saccharides, 233–234
Porous coating:
formation mechanisms, 216–217
osmotic tablet technology, 131–132
Porous reservoir systems, 117
Powder blend processing, 143–144
Powder coating systems, 270–273
Powder density, 50
Preclinical in vivo testing, 148
Prediction models, 92–93
Preformulation protocols:
active pharmaceutical ingredient solubility, 59–66
dissolution rate, 65
equilibrium solubility, 59–61
food effect, 64–65
intrinsic dissolution, 65
kinetic solubility, 61
pH profile, 62
pKₐ values, 62–63
salt/buffer/chloride ion effects, 63–64
simulated biological fluid, 63
thermodynamically stable polymorph, 65–66
basic principles, 4–5, 47
particulate and mechanical properties, 47–53
bulk powder properties, 49–52
compression properties, 52–53
particle size analysis, 48–50
partition coefficient, 66–68
stability and compatibility, 53–59
degradant identification, 55–56
excipient compatibility, 56–58
microenvironmental modulation, 55
solid excipient degradation, 58–59
solid-state forced degradation, 53–55
solution-state forced degradation, 53–54
Press coating systems, 95
Presystemic clearance, 4
Printing techniques, 269–270
Process analytical technology (PAT), 298–299
Processing systems:
enteric coatings, 217–219
quality by design principles, 292–294
Prodrugs:
dextran prodrugs, 235–236
steroid-based glycosidic/glucuronic acids, 234
Product and exhaust temperature, 125
Protein drugs:
absorption limitations, 4
biopharmaceuticals, 263–266
Purdue Research Foundation, 199
Push-pull design, 137
Quality attributes, 342
Quality by design (QbD):
continual improvement principles, 301
control strategy, 299–300
criticality process, 291–292
critical process parameters, 292
critical quality attributes, 284–289
design space development, 294–299
chemometrics, 297
design of experiments, 295–296
first principles methods, 296
process analytical technology, 298–299
representation, 295
dissolution/release factors, 284–287
dose dumping risks, 288–289
excipient properties, 287–288
knowledge management, 282
manufacturability issues, 288
process analysis, 292–294
quality target product profile, 283–284
research background, 279–281
risk assessment, 289–291
risk management, 281–282
Quality risk management (QRM), 281–282
Quality target product profile (QTPP):
product/process design and development, 293–294
quality by design principles, 282–285
Quantitative structure-property relationship (QPSR), 93
Quetiapine fumarate extended release tablets, 317
QuickSolv technology, 161
Ranbaxy Laboratories Ltd, 198
Real-time release testing (RTRT), 299
Regulatory issues:
controlled-release dosage forms:
bioavailability and bioequivalence, 344–345
biowaiver, 345
clinical applications, 346
combined products, 347
definitions, 339–341
excipient issues and guidelines, 341–342
FDA review, 338–339
inspection, 347
IVIVC, 342–344
labeling, 347
nonoral standards, 347
pharmaceutical equivalence, 345
quality attributes, 342
scale-up issues, 345–346
stability issues, 346–347
Regulatory issues: (Continued)
- generic compounds, 332
- life cycle management, 310
- Relative colonic bioavailability, 35–36
- Reservoir controlled systems, 327–330
- Reservoir diffusional system, 102–103
- Reverse polymers, 219
- Ring shear tester, 52
- Risk assessment, 289–291
- Risk management, 281–282
- Risk priority number (RPN), 290
- RLD characterization, 324–326
- RNAi, 265–266
- Rotary spray systems, 124
Saliva composition and physiology, 170–172
Salt/buffer systems:
- active pharmaceutical ingredient solubility, 63–64
- generic compounds, 326–327
Scale-up:
- fluid bed coating configuration, 125–126
- oral controlled release drugs, 9
- postapproval changes, 252–253
- regulatory guidelines, 345–346
SCOT®, 7
Semipermeable membrane:
- coating properties, 139–141
- film coatings solution preparation, 145–146
Semisolid compounds, 178–179
Semisynthetic/synthetic polymers:
- enteric coatings, 24
- hydrophilic gel-forming polymers, 24–25
Sennoside, 228–229
Shear cell tester, 51–52
Shellac enteric coating, 206
Sieve analysis, 49, 51
SimCYP ADME simulator, 262–263
Simulated biological fluids, 63
Single photon emission computed tomography (SPECT), 11
Size-dependent technologies, 194–195
Slow-release systems, 230–231
Sodium sulisatin, 228–229
Solid excipient degradation, 58–59
Solid-state forced degradation analysis, 54–55
Solubility:
- active pharmaceutical ingredient solubility, 59–66
dissolution rate, 65
equilibrium solubility, 59–61
food effect, 64–65
kinetic solubility, 61
pH-solubility profile, 62–63
pKa values, 62–63
salt/buffer and chloride ion effects on stomach, 63–64
simulated biological fluids, 63
thermodynamically stable polymorphs, 65–66
aqueous solubility, 4–5
bilinear osmotic tablets, 137–138
biopharmaceutical evaluation, 33–35
dissolution testing:
- basic parameters, 246
detection, 250–251
generic compounds, 326
Solubilization process, 150–151
Solution-diffusion mechanism:
dissolution testing, 250–251
membrane systems, 27
Solution layering, 118–119
Solution-state forced degradation analysis, 53–54
Solvents:
- coating excipients, 104
- coating solution composition, 141
- organic polymer-based coating systems, 120
Spray Flow Tester FT-300, 51
Spansule® technology, 24
Spray drying:
- enteric coating processing, 219
- fast-dissolving (fast disintegrating) tablet compression, 161
Spray rate, 125
Stability properties:
- bilayer tablets, 149–150
- preformulation protocols, oral controlled release drugs, 53–59
degradant identification, 55–56
excipient compatibility, 56–58
microenvironmental modulation, 55
solid excipient degradation, 58–59
solid-state forced degradation, 54–55
solution-state forced degradation, 53–54
regulatory guidelines, 346
Starches, 273–274
Statistical Process Control (SPC), 299
Steroid-based glycosidic/glucuronic acids, 234
Stomach physiology, 186–187
Subcoating, 119–120
Sublimation, 160–161
Substrates:
- coating systems, 108–109
- film-tablet interface, 109
- fluidized bed coating systems, 117–119
- enteric coatings, 217
Sulfasalazine, 229
Superdisintegrants, 158–159
Surface area, 327
Surfactants:
- coating excipients, 106
dissolution testing, 249–250
Suscard Buccal®, 176–177
Suspending agent, 138
Suspension layering, 118–119
Sustained release (SR) drug formulas:
- enteric coatings, 214–217
- fluidized bed coating systems:
  - aqueous-based polymer coatings, 120–122
direct powder coating systems, 122
- bottom spray systems, 123–124
controlled release development process, 122–126
- formulation considerations, 117–122
INDEX  363

functional coating, 120–122
multiparticulate release mechanisms, 116–117
oral controlled release drug coatings, 106–108
process variables, 125
rotary spray systems, 124
scale-up protocols, 125–126
subcoats, 119–120
substrate preparation, 117–119
granules, 119
minitablets, 119
pellets, 118–119
top spray systems, 124
quality by design, 280–281
Sustained-release drug formulations, 102–104
Swellable matrix tablets, 24–25
Swellable platforms, 194–195
Swelling core:
  bilayer tablets, 132–133
  monolithic tablets, 132
Swelling/erosion mechanisms, 27
Swelling layer properties, 138–139
Swelling pressure, 158–159
Synthetic saccharides, 233–234

Tablet compression, 144–145
Tablet wetting time, 164–165
Target dissolution profiles, 10–11
Targeted drug systems, 214–217
Taste masking, 163–164
Temperature effects, 60–61
Tensile strength values:
  fast-dissolving (fast disintegrating) tablets, 164–165
  materials properties, 142–143
  Teva Pharmaceutical Industries Ltd, 198
  Thermodynamically stable polymorphs, 65–66
  Three-dimensional printing, 269–270
  TIMERx™, 2–3
  Top spray systems, 122, 124
  Toxicity:
    buccal drug delivery systems, 179–180
    gastrointestinal toxicity reduction, 213–214
  Transport pathways, 35–36
  Unigene delivery system, 264–266
  United States Pharmacopoieia (USP), 60
  Vaccines, 265
  van’t Hoff plot, 65–66
  Water-insoluble drugs, 257–259
  West Pharmaceutical, 198
  Wet granulation, 143–144
  “Window for absorption,” 4
  Wireless M2A Capsule Camera, 11
  WOW Tab technology, 162
  Xerostomia, 172
  Zegrid®, 209–212
  Zein enteric coatings, 206
  Zero-order release technology, 94–95
  Zydis technology, 161