Index

A

Academy of Managed Care Pharmacy (AMCP)
evidence requirements 186
accelerated filings
ancillary activity considerations with 248–252
ANVISA initiatives for 250–252
communication with FDA 246–252
compassionate use/single patient IND 248–252
COVID-19 pandemic and 251
expanded access 246
FDA initiatives 245–252
HDE and 248
rolling reviews for 246–252
state-level “Right to Try” laws 249
surrogate endpoint use 249
Advisory Committee (AC) Meetings
NDA review and approval 60
review and approval process 62
Agencia Nacional de Vigilancia Sanitaria
(ANVISA) Initiatives 250
annual product review updates 180
artificial intelligence (AI) in regulatory writing 10
audience requirements
for CSR 99
for labeling 151–154
for value dossiers 185
integrated nonclinical discussions 121
labeling for globalization 152–154
labeling for nontechnical 151–154
regulatory versus publication writing 253

B

background packages
draft briefing package for EU 165–166
FDA meeting package content and format 162–164
FDA meeting request content and format 161–164
final briefing package for EU 165–166
for scientific advice and protocol assistance 164–169
medical device meetings 166
pre-submission meeting 165–166
Q-Submission package 167–169
submission and meeting feedback 167–169
submission process 165–166
submission process for FDA 163–164
US pharmaceutical and biologics 159
Belmont Report 79, 79–87, 95
Bioresearch Monitoring (BIMO) protocol violations 74
biosimilars
analytical similarity demonstration 206
animal studies for evaluation 207
clinical considerations for 207
comparability versus biosimilarity 209
development process for 205–213
efficacy and safety of 208
extrapolation of indications 208
geographic jurisdiction for 209
immunogenicity assessment for 208
interchangeability 209
labeling of 210
naming and pharmacovigilance for 210
pharmacokinetics and pharmacodynamics 208
regulation of generics 196
stakeholder education 211–213
versus generics 203–213
Biosimilars Action Plan (BAP) 211
biotechnology-derived products 193

C

Centralised Procedure 173
chemistry, manufacturing and controls (CMC) 111
documentation for 111
format and content of documentation 112–114
lifecycle management of documentation 114
preparing documentation for 113–114
regional information for 114
Clinical and Laboratory Standards Institute (CLSI) 31
clinical study report (CSR)
changes to 108–109
content of 99–109
finalization and notification 107–109
guidance for 99–109
ICH requirements for 103–109
narratives for 105
planning meeting for 102–109
preparation 106–109
publication writing and 256
public disclosure of 107
redaction for disclosure 107
requirements for appendices 103–109
results review 106–109
shell preparation 105–109
single study with multiple 108–109
source materials for 100–109
timelines and milestones for 103–109
types of 100–109
writing and reviewing of 105
writing conventions 105–109
clinical study results. See lay summaries of study results
Clinical Summary
content of 136
in integrated clinical documentation 130
ISE/ISS relationship to 140

clinical trial protocols
amendments to 75–77
development of 72–77
endpoint for study 74
ethical requirements for 71–77
for biosimilars 208
for publication and peer review 76
key elements of 73–77
population and methodology 74
protocol synopsis 72
registration of trial 76–77
regulatory agency requirements 72–77
safety and reporting requirements 74–77
sponsor and funding agency roles 72–77
statistical analysis plan 75–77
study design and methodology 73–77
study endpoint definitions 74
templates for 73–77
violations of 74
ClinicalTrials.gov 95
Code of Federal Regulations
integrated summary requirements for 138
writing guidance in 30
Code of Federal Regulations (CFR)
combination product requirements 216–223
Federal Register history and use 29–40
informed consent regulations 79
regulatory writing requirements for 29
safety update reporting 142
combination product design and development
categorization of constituent parts 218–219
CGMP requirements for 216–223
constituents with prior marketing approval 218–223
definition of product 215–223
general recommendations for 221–223
human factors application to 220–223
IND applications and 220–223
pivotal clinical study use of device 221–223
risk management for 219–223
special regulatory considerations 217–218

Common Technical Document (CTD)
clinical sections of 131–137
CMC information in 111
information assembly and 18
information presentation in 25
marketing application format 57
modular structure in 25–27
Company Core Data Sheet (CCDS) 181
complete response letter (CRL) 172
CONSORT 96, 254
contract research organization (CRO) 72
COVID-19 public health emergency
  accelerated approval pathways due to 251
  adjustments to CSRs 108–109
  conducting clinical studies in 126
  effects on SAPs 90
  FDA requests for information and 171
  ICF requirement with 85–87
  impact on clinical trials 75–77
  medical device submissions and 41–43
  new vaccine and biologic guidelines for 190
  orphan designations and 235
  pharmaceutical industry impact of 145–149
  statistical guidance with 89

D

data analysis plans
  clinical trial ethics and transparency in 95–98
  data collection and handling quality for 93–98
  data handling for trials 94–98
  data-handling methods in therapeutic area 96
  guidance document updates 89–98
  ICH E9 content for 90–98
  SAP development 96–98
  scope of SAPs 93
  study reporting requirements 94–98
  therapeutic area statistical analysis 95
  writing statistical analysis plan 90–98
Decentralised Procedure 173
Declaration of conformity, updating 181
Declaration of Geneva 79
Declaration of Helsinki 71, 76, 79, 94, 95
Development International Birth Date (DIBD) 148
Development Safety Update Report (DSUR) 181
discipline review 171
document inventory lists 18
dossier maintenance 179
  annual reports for 182–184
  clinical safety update 181
  consequences of maintenance failure 183–184
  documents requiring maintenance 180–184
  identification of requirements 179–184
Drug Master Files, updating 180

E

endpoints
  accelerated filings and 249–252
  biomarkers and 249
  in lay summaries 271
  surrogate 249
EQUATOR network 96, 254
ethical requirements
  in clinical trials 71–77
  transparency of trial results 95
EudraCT 95
EU Marketing Authorization Application (MAA ) 63–70
  Centralised Procedure timeline for 66
  overview of review process 65
EU medicinal products
  background packages for meetings 164
European Federation of Good Clinical Practice (EFGCP) 271
European Federation of Pharmaceutical Industries Association (EFPIA) 271
European Federation of Pharmaceutical Industries (EFPIA) 107
European Medicines Agency (EMA)
  accelerated approval pathways 249–252
  COVID-19 impact on clinical trials 90
  data monitor committee checklist 89
  guidance on EU requirements 30
  medical device regulatory framework 31–40
  PIP requirements 237
  PIP submissions 241
  protocol assistance 72
  rare disease definition 225
European Union (EU)
  comment or information requests from 172–173
  General Data Protection Regulation 85–87
  interventional trial information 76
  lay summaries regulatory requirements 266–275
  regulatory pathways in 173–174
  scientific advice and protocol assistance meetings 164
  expanded access (compassionate use), IND for 192
  expedited reporting, IB contents and 145

F

first-in-human study, nonclinical data for 74
Food and Drug Administration (FDA)
  adoption of ICH recommendations 29
  application review by 6
  Biosimilars Action Plan 211
Clinical Summary replacement for ISS/ISE 130
COVID-19 guidance from 126
COVID-19 impact on clinical trials 90, 146
CSR guidance 100
formal meetings 160–164
guidance for industry 31–40
IFC development 80
medical device regulatory framework 31–40
meeting types and purposes 160–169
New Drug Application (NDA) review 59–70
orphan drug designation request 225
rare disease definition 225
regulations pertaining to 29
Special Protocol Assessment 72
support for master protocols 75
trial registration 76
types of formal meetings with 160–169
Formal Communication Plan 59
formatting/format
importance of 25–27
nonclinical reports 118–124
Form FDA 483 observations for GDPs 20–22

G

General Data Protection Regulation (EU) 85
General Safety and Performance Requirements, updating 181
Good Clinical Practice (GCP)
Investigator’s Brochure requirement 145
statistical analyses in 95
Good Documentation Practices (GDPs)
21 CFR good practices resources 39
basic principles for 16–22
consistency, clarity, completeness in 17
creating a system for 20–22, 21–22
documenting procedures 17–22
for SAPs 94–98
goals of documentation 16–22
guidelines and resources for 18–22
overview of 15
principles and development of 15
transparency and disclosure in 18
guidance documents and resources
identifying guidelines 18–22
professional societies 40
sources for 38–40

H

health technology assessments (HTAs). See value dossiers
humanitarian device exemption (HDE)
HUD marketing 234
Humanitarian Device Exemption (HDE)
accelerated filings for 248
Humanitarian Use Device (HUD)
HDE application for 248
requests for 234

I

Independent Monitoring Committee (IDMC) 74
individual study reports 199
information request letter 172
informed consent form (ICF)
audience considerations for 82–87
development of 84–87
history and purpose of 79–87
information provided in 80–87
in protocol development 83–87
scope of clinical activity 83–87
sponsor requirements for 83–87
updates to 83

Integratesd Summary of Safety (ISS) 138
integrated clinical documentation
attention to regulations and guidelines in 127–143
benefit and risk conclusions 135
Clinical Overview 132
Clinical Summary 136
CTD clinical sections 131
CTD format in 131–132
goals for 126–143
guidance and updates with COVID-19 125–143
ICH guideline updates on clinical documentation 126–143
integrated data discussions 126–143
Integrated Summary of Efficacy in 138
Integrated Summary of Safety in 140
lifecycle management of documentation 129
maintaining consistency in 127–143
medical writers role in 131–132
Module 5 137
multiple clinical trial comparisons 125–143
post-approval summaries at marketing application 129–143
regulatory documents in 129–132
safety update reporting 142
systematic approach for consistency 128–143
tables included in studies 138
transparency in data from trials 128–143
US requirements for 138
integrated CMC documentation. See chemistry, manufacturing and controls (CMC)
integrated nonclinical documentation
authoring discussions in 121–124
CTD safety structure 120–124
discussions of 119–124
electronic publishing readiness 118–124
for biologics 197
overview format and content 120–124
qualities of 115–124
study reports 117–124
style guides for 119
written and tabulated summaries for 121–124
Integrated Summary of Efficacy (ISE) 138
Integrated Summary of Safety (ISS) 129, 140
interdisciplinary documents. See dossier maintenance
International Committee of Medical Journal Editors (ICMJE) criteria 254–258
International Council for Harmonisation for Technical Requirements for Pharmaceuticals for Human Use (ICH) 29
International Council for Harmonisation (ICH) harmonized submissions 7
International Council on Harmonisation (ICH) CSR requirements for appendices 103–109
drug substance documentation 112–114
estimand and sensitivity analysis 89
guidelines from 31–40
guidelines on CSR 99
harmonized submission evolution 12–13
IFC development guidance 80
Investigator’s Brochure requirement 145
nonclinical format and content 120–124
scope of biotechnology-derived products 193
species specificity of biologics 197
statistical plan guidance 75, 90
International Medical Device Regulators Forum (IMDRF) Table of Contents structure 25
International Organization for Standardization (ISO) 31
Interventional Study 74
Invented Name Review 63
Investigational Medicinal Product Dossier (IMPD) 145
Investigational New Drug (IND) submission
Investigator’s Brochure for 145
protocol review 72
Investigator’s Brochure (IB)
content contributors for 146
content development for 146–149
contents of 145
essential components of 146–149
purpose of 145–149
updates to 148–149
with multiple product indications 148

K
key opinion leaders (KOLs) 72

L
labeling
audience requirements for 151–154
consequence statement 156
draft review 61
general content principles 154
hazard description for 156
IB content and 145
of biosimilars 210
prevention measures in 156
regulatory sources for 156–157
risk control measures for 154
risk statement content and layout 154
risk statements in 154
standards for 157
symbols, colors and codes in 153–154
updating 180
writing for global audience 152–154
writing for nontechnical audience 151–154
lay summaries of study results 265
development of 273
endpoint inclusion in 271
EU CTR requirements for 266
European expert group recommendations 266–275
for children 272
good practices for 270
implementation guide for 270–275
MRCT guidance document 267–275
non-promotional language for 269–275
studies in healthy volunteers 272–275
lifecycle management
CMC documentation 114
integrated clinical documentation 129
integrated nonclinical documentation 122
Investigator’s Brochure 148–149
updating documents 179
literature reviews
information sources 261–263
narrative (non-systematic) and systematic 259–263
reporting and methodological guidelines 260–263
search strategies for 262–263
M
master protocol, for clinical trials 75–77
MedDRA 94
medical device submissions
background packages for 166–168
considerations for writing 41–43
refuse to accept notification 172
regional requirements for 42–43
regulatory framework for 31–35
Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines 260
Multi-Regional Clinical Trial (MRCT) working group 265
Mutual Recognition Procedure 173
N
National Cancer Institute (NCI), protocol templates 73
National Research Act 79
New Chemical Entity (NCE), development process 111
New Drug Application (NDA)
filming and review timeline 59–70
Formal Communication Plan 59–70
preapproval inspections 62–70
prescribing information draft 62–70
Proprietary Name Review 61–70
review and approval process 59–70
review process and milestones 60–70
New Molecular Entity’s (NME), development process for 111
Notification of Clinical Hold 172
Nuremberg Code 79–87
O
Observational Study 74
Office of Orphan Products Development (OOPD) 225
orphan designation/rare diseases
accelerated review for 248
business benefits from 226
clinical superiority demonstration 231
criteria for 225
criteria in EU 249
humanitarian use devices 234–236
In FDA versus EU 226
in US 226–236
orphan designation for 225
pediatric priority review for 231
preparing request for designation 229–236
regulatory definition of 225
resources for 231
Special Protocol Assessment for 72
supporting evidence for designation 229–236
P
Parent Consent for Child to Act as a Research Subject” form 83
Patient-Reported Outcomes (PROs) 271
Pediatric Investigational Plan (PIP)
compliance check for 242–243
contents of 239–243
development of 238–243
legal framework for 237–243
modifying agreed plan 241–243
notification of discontinuation 242–243
submission process for 241–243
Periodic Benefit-Risk Evaluation Report (PBRER) 181
Periodic Safety Update Report (PSUR) 181
Pharmaceutical Research and Manufacturers of America (PhRMA)
code of ethics 95
data sharing principles 107
guidance and ethical code 31
Plain Language Summary (PLS) 265
planning and strategy documents (PSDs)
definition of 46
development of 46
for regulatory submissions 46–55
Post Market Surveillance Report (PMSR) 181
preapproval Inspections 62
Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) 260
Prescribing Information (PI), development of 62 professional societies, guidelines from 40
Proprietary Name Review (PNR) 61–70
Protocol Review Committee. 72
publication
clinical trial data disclosure and transparency in 255
good publication practice (GPP) guidelines 253
investigator’s roles and responsibilities in 254
planning for 253
protocol submission for 76–77
regulatory versus publication writing 253
SAP for 90
statistical analyses for 96

Q
Quality Assessment tool of Diagnostic Accuracy Studies (QUADAS) 260
Quality Management Systems (QMS) 17
Quality of Reporting of Meta-analyses (QUOROM) Statement. 260
questions/requests for information
FDA communication with sponsors 171
from EU regulatory authorities 172–173
preparation and planning for 57–70
written responses to 174

R
rare pediatric disease designation 233–236
Recommendation for Interventional Trials (SPIRIT) 73
Reference Safety Information for Assessment of Expectedness of Serious Adverse Reactions 145
refuse to accept hold notifications 172
regulatory writing
audience needs in 24–27
audiences for writing 2
automated redaction, translation and big data summaries 278–280
barriers to effective communication in 23–27
before harmonization 3
changes in audience for 9
comprehension aids for 26–27
design for comprehension 25–27
documents produced by 2
document type and development stage 25–27
editing of 26
format in 25–27
harmonized submissions 7
key information presentation 25–27
plain language in 26–27
structured content management 278–280
submission procedure changes and 6
technology impact on 4
written content as data 277
reporting requirements 74–77
review and approval process
CTD for submission 57–70
EU Marketing Authorization Application 63–70
New Drug Application 59–70
preparation for information requests 57–70
risk management, updating 181
risk statements
content and layout 154–157
in labeling 154
labeling risk control measures 154
rolling reviews 246

S
Safety Update Reporting 142
signal word in labeling 154
solicited reports, updating 182
SPIRIT checklist 255
standard operating procedures (SOPs)
defined 46
development of 46, 46–55
importance of 45, 45–55
in integrated discussions 123
regional differences for 54–55
scope of 47–55
updating 40
updating of 181
statistical analysis plans (SAPs)
collaboration for 96–98
elements of 93–98
endpoint analysis 74
for publications 96
guidelines for 96
ICH E9 content overview 90–98
in clinical trial protocol 75–77
rationale for 90–98
reporting requirement in 94
style guides
   clinical study reports 105
   integrated nonclinical documentation 123
Summary of Data and Guidance for the Investigator 145
surrogate endpoints 249
Suspected Unexpected Serious Adverse Reactions (SUSARs)
   reporting timeline 74

T
TransCelerate
   guidance for submissions 31
   harmonization for CSR disclosure 107
   implementation guide 270
   layperson summary 265
   non-promotional language guidance 269
   non-promotional language guidance and recommendations 269
   non-promotional language recommendations 269
   template from 73
transparency and disclosure for GDPs 18

U
United States (US)
   biologics regulation 193–201
   NDA/BLA milestones 61
   returning study results to participants 266–275

v
vaccines and biologics
   biologics definitions 192
   expanded access for 246–252
   guidance updates and adjusted definitions for 189
   integrated documentation 199
   regulation of biologics 193
   regulatory documentation for 198–201
   special documentation for vaccines 198–201
   specialized content for documents 189
   therapeutic areas for 197–201
   therapeutic areas of 197
   vaccine subset 193
value dossiers
   audience for 185
   compilation of 188
   purpose of 185
   regional differences and format of 186–188
   resources for writing 188

W
WHO-DDE 94
World Health Organization (WHO) 31
written responses to questions/information requests
   best practices for preparing 174
   content and organization of 174
   timing 176