Index

A

acceptance criteria for software usability 152
Agile development process
for software 103
gated development 113
increments of 115
risk management in 111–114
AIMDICP 175
AI/ML-based devices
assessment for bias in 172–181
change according to device legislation 166–181
change boundaries and ACP for 165
change dynamics in 162–181
compliance with existing legislation 176
controllability and human oversight of 167–181
ethical algorithms in 171–181
federated learning in 161–181
global model for training versus local change 160–181
lack of regulatory framework for 71
overtrust in 168–181
postmarket significant change 164–181
pre-determined change 161–181
standards for 175–181
technical documentation for IVD SaMD 36
transparency and explicability of 169–181
algorithm change protocol (ACP) 164, 165–181
Application Programming Interface (API) 6
Artificial General Intelligence (AGI) 159
artificial intelligence (AI) 159. See also AI/ML-based devices
clinical evaluation of 67
considerations for 67–73
definition 159–181
techniques and uses of 159–181
Artificial Intelligence Medical Device Innovation and Cooperation Platform (AIMDICP) 175
Australian, health app use survey 183
automation bias 168

B

Belgium
mHealth validation pyramid 201
process for mobile health apps 201
Blue Guide
common rules in EU 187–196
intent to place a product on EU market 187–196
placing on the market clarification 189

C

Canada
classification of IVD SaMD in 32–41
device definitions in 25
qualification of IVD software in 24
SaMD in 8
card sorting method in usability testing 150
CE marking/certification
compliance with EU regulations 224
for OEM/OBL 126
market access and reimbursement 204, 207
of apps 193
centralized machine learning techniques 161
change boundaries 164
change control plan 164
China
AI legislation in 174–181
SaMD classification in 43
Classification Rule 11
impact of 55–62
MDSW classification 50
Rule 11b 55–62
Rule 11c 55
Classification Rule 12 55–62
Classification Rule 15 55–62
Classification Rule 22 55–62
clinical commissioning groups (CCGs) 198
clinical development plan (CDP) 63
clinical evaluation of software 63
AI/ML-based SaMD 67–73
applicable regulations for 68–73
evidence components for 66
general principles of 63–73
guidelines and standards for 70
IVD SaMD support of validity 37
process 64
specific guidelines for 64
clinical evaluation plan (CEP) 64
clinical evaluation report (CER) 64
coding guidelines 88
commercial software. See open-source and third-party software components
Common Attack Pattern Enumeration and Classification (CAPEC) 96
Common Weakness Enumeration (CWE) 96
connected medical devices (CMDs)
benefits and challenges of 1
reimbursement 205
requirements for 205
security risk management with 93
continuous integration (CI) 89
core functionality in software design 146–158

D
data privacy, federated learning for 161
dependent MDSW 48
design validation 118
Diagnosis Related Groups (DRGs), in reimbursement 200
digital distribution models 187
distributor role in 189–196
fulfilment service provider (FSP) role in 190–196
identification of distributors for 193
intent to offer product 189
ordering/shipping system inclusion 189–196
Digital Healthcare Act 209
Digitale-Versorgungs-Gesetz (DVG) 209
digital health applications (DiGAs) 209
digital health technologies (DHTs)
benefits of 197–202
function and evidence requirements for 203
market access for and reimbursement 197
Digital Spain 214
distributors. See economic operators
DREAD threat modeling framework 96
drive or influence the use relation to hardware 46–62
types of 47–62
Dutch Healthcare Authority (NZa) 211

E
economic operators
requirements for 187
responsibilities of 194
roles under EU MDR and EU IVDR 188
eHealth Platform 202
embedded software 5, 6
emergence/emergent software development strategy 105
ergonomics in usability 136, 156
Essential Principles (EP) 82
ethics frameworks for AI 171
European Committee for Electrotechnical Standardisation (CENELEC) 183
EU In Vitro Diagnostic Medical Devices Regulation (EU IVDR)
AI/ML-based SaMD 67
clinical association requirements 36–41
economic operators 188, 189–196
fulfilment service provider 190
information society service provider 191–196
legal requirement compliance 224
market access requirements 187
negligence or fault liability 224
performance evaluation and clinical evidence 35
risked-based classification of 34
safety and performance requirements 82
software classification 9, 29, 45, 44–62
software qualification 22, 22–24
software usability 155
EU Medical Device Regulation (EU MDR)
classification of software 9
economic operator role in software market 189–196
implementing rules in 45–62
IVD medical device software 22
market access requirements 187
requirements for security 104
software classification 44
software usability and safety 155
wearable and software as a system 17
European Union (EU)
AI legislation in 173–181
classification of IVD MDSW in 34–41
expectations for OSS 124
liability law updates 226
MDSW use in 9–19
Medical Device Software (MDSW) usage in 5
qualification of IVD software in 22–41
terminology used for SaMD 5
evolutionary strategy in software development 105

F

failure assertion programming 88
Federal Agency for Medicine and Health Products 202
federated learning 161–181
fever detection app (example) 6
firmware
  hardware medical devices and 6
  qualification as MDSW 22
formative evaluation 142
fourth hurdle 198, 199
France
  DHT assessment process 206
  DHT market access in 205
telemedicine disciplines 208
telemedicine reimbursement in 208
frontloading 87
fulfilment service provider (FSP) 190
functionality 10, 133

G

General Data Protection Regulation 101, 207
General Safety and Performance Requirements (GSPR)
  compliance with 155
  for wearables 17
  security requirements of 104
  single fault safety of SaMD 82
Germany
digital health application reimbursement in 209–212
Digital Healthcare Act (Digitale-Versorgungs-Gesetz, DVG) 209
Global Harmonization Task force (GHTF).
  See International Medical Device Regulators Forum (IMDRF)
global model for machine training 160

H

hardware in SaMD and SiMD definitions 6
harm, definition of 78
HartWacht app 213
Haute Autorité de Santé (HAS) 205
hazard/hazardous situation 78
health and wellness apps
  assessment system for 185
  barriers to adoption 183–185
  health professionals recommendation for 183
  quality and reliability of 183
  quality criteria for 184–185
  safety and reliability concerns with 183–186
  specific use-case and national requirements 185
health app assessment frameworks 184
Health Insurance Portability and Accountability Act 101
health technology assessment (HTA) body
  market access approval by 197
  reimbursement decisions and 199
Helsinki procedure 56–62
heuristics analysis 144
High-Level Expert Group on AI (HLEG) 173

I

IEC 61508-3 87
IEC 62304
  configuration management process 110
IEC 61508-3 comparison 87
lifecycle model for software 2
lifecycle processes 103
requirements for software quality 87
risk management in development process 75
software development processes 114, 115, 116
software lifecycle process 75
IEC 62306 106
IEC 62366-1
  in clinical evaluation 66
  incremental execution development processes 116
role in software development 2
software safety compliance 155
usability engineering 105, 109
IEEE 80001
  operational security 101
  postmarket activities 119
  product lifecycle activities 105
IEEE Personal Health Devices Cybersecurity Standards Roadmap 96
incremental strategy in software development 105
independent MDSW 45, 49
information architecture 136
information society service provider
download portals and app-stores as 192
role in software distribution 191–196
intended use/intended purpose 78
definition for IVD 27
definition for IVD SaMD 25–41
elements of 28
in MDSW definition 44
security risk management and 100
intent to place on market 189
interaction design 136
International Electrotechnical Commission (IEC) 183
International Medical Device Regulators Forum (IMDRF) 43
draft definition of machine learning device 159
Essential Principles (EP) 82
guidance for clinical evaluation of SaMD 65
guidance for SaMD 5
guidance on clinical evaluation 63
issues of interpretation of risk framework 54
medical purposes of 21–41
SaMD risk framework interpretation 51–62
software vulnerabilities and design flaws 96
terminology creation for SaMD 1
International Standards Organization (ISO) 183
in vitro diagnostic medical device software (IVD SaMD) 21
analytical performance analysis for 37–41
clinical association of output and condition 36–41
clinical performance demonstration 38–41
hazards of 81
performance evaluation and clinical evidence for 35–41
qualification as IVD device 21
qualification as IVD SaMD 21–41
qualification in Canada 24–41
regulation by IVD regulations 21
regulatory classification of 29–41
sequence of events for 81
ISO 9241 156
ISO 13485
design control and development validation 104
gated development 113–114
postmarket activities 120
traceability requirements 109, 110
user needs 108
validation requirements 117
ISO 14971
application of risk management 75
estimating probability of software errors 84
guidance on software application of 131
probability estimates for software 80
product safety and 93
Risk Control Measures in SaMD 86
risk management in software 77–91
safety definition 78
safety definition for devices 95
verification requirements 105
ISO DTS 82304-2
health app assessment framework 184
health app quality and reliability standard 183
in assessment system 185
iterative development strategy 105
IVD SaMD. See in vitro diagnostic medical device software (IVD SaMD)

L

labeling
CEN-ISO/TS 82304 clauses and 193 claims made in 29
device classification and 35 for intended use 25
Health App Quality Label standards 192
intended use requirements and 38
liability. See software liability
lifecycle control
for digital health technologies 198–199
OTS and 97
with third-party software 124
Liste des Produits et Prestations Remboursables (LPPR) 205
local change 162
Luchtbrug app 213
Lusciii app 212

M

machine learning (ML) devices
current device legislation and 159
device characteristics 160–181
market access
catalogue or website for offer 189
defor digital health technologies 197
HTA body assessment as fourth hurdle 199
market authorization comparison 198–202
reimbursement relation to 200
wearable and software as a system 17
market access and reimbursement 197
clinical and process-related outcomes in 214–219
Digital Healthcare Act (Digitale-Versorgungs-Gesetz, DVG) 209
economic analysis of 204
EU examples of 201–202
evidence for patient benefits from 204
importance of market access in 217–219
link to funding 200–202
MAST framework for 216–219
outcomes and frameworks for 214–219
pathways for 205
PICOS framework in 215–219
market authorization/approval 198
MATLAB scripting language 88
Medical Device and Health Technology Evaluation Committee (CNEDiMTS) 205
Medical Device Coordination Group (MDCG)
clinical evaluation guidance 117
MDSW terminology introduction 44–62
security guidance from 104
medical device software classification 43
code-based 43–62
comparison and use of types of 61
rule-based classification 43–62
medical device software (MDSW)
device qualification in EU 23
intent to place on market 188
international definitions of 39
IVD qualification in US 24–41
jurisdictional differences in consideration of 18
methods of classification for 43
qualification as IVD SaMD in EU 22–41
Medicines and Healthcare products Regulatory Agency (MHRA) usability guidance 156
Model Assessment of Telemedicine (MAST) framework 216–219
modules, grouping 10–19

N

National eHealth Living Lab (NeLL) 212
National Institute for Food and Drug control (NIFDC) 174
National Institute for Health and Care Excellence (NICE) 202
National Institute for Health and Disability Insurance (NIHDI) 201
National Medical Products Administration (NMPA) 117, 174
Network Information Security Directive (NIS) 101
NHS Apps Library 204
Nictiz 211
no-fault liability 224
non-compliance with legal requirements 224

O

OCTAVE threat modeling framework 96
Off-The-Shelf Software (OTS) guidance for use 97, 124
open-source and third-party software
components 123, 124

case study 126–130

quality management case study 126

regulatory requirements for 124–130

safety concerns 123–130, 124–130

open-source software (OSS) 123

Open Web Application Security Project (OWASP) 96

Organization Center for Medical Device Evaluation (CMDE) 174

original equipment manufacturer (OEM) 125, 126

overtrust 168

Own-Brand Labeller (OBL)

CE certificate loss by OEM 126

definition of 123

full documentation for software 125

P

Patient, Intervention, Comparator, Outcomes, and Settings (PICOS) framework

HTA body assessment 199

reimbursement framework 215

Picture Archiving and Communication System (PACS) 10

placing on the market. See intent to place on market

Platform as a Service (PaaS), business model 187

postmarket clinical follow-up (PMCF) 64

global change in AI/ML-based devices 161

in usability engineering of software 156

postmarket performance follow-up (PMPF), software usability 156

postmarket surveillance (PMS)

comments in app-store and download portals 192

in usability engineering of software 156

requirements for healthcare software 131–158

Precertification (Pre-Cert) Program 175

pre-determined change 161

pre-specifications 164

probability 79

qualitative and semi-quantitative 79

strategies for estimation of software errors 84

probability of occurrence of harm (PO) 78

Product Liability Directive 221, 225

Programmable Electrical Medical Systems (PEMS) 94

programming language selection 88

putting into service 187

R

reimbursement 197. See also market access and reimbursement

residual risk 78

Risk Control Measures 78, 83, 86

risk framework and management

assessment of 82

challenges with software 80–91

class implications in US and EU 58–62

clinical evaluation and 64

definition of 78

interpretation of IMDRF SaMD 51

in usability engineering 154–158

matrix example 80

security of SaMD 93

soft factors in 89

strategies for successful 84–91

rule-based software classification 43–62

S

safety, definition 78

safety risk management of software 75

security risk management 93

aspects covered by 95–102

for SaMD 94–102

overlapping legislative requirements 101–102

shared responsibility for 100–102

standards addressing 100

system interconnection and 93–102

threat modeling in 96–102

total lifecycle requirements 98–102

vulnerability management and security monitoring 97–102

severity 78, 79, 84

Single Ease Question (SEQ) 149–158

single fault conditions, management strategy for 85

SkinVision app 212
Software as a Medical Device (SaMD); See also in vitro diagnostic medical device software (IVD SaMD) as a product 221
classification in EU 5
defectiveness of 222
estimating probability of errors 84
for monitoring of physiological processes 55–62
independent 49
liability 221
MDSW and SaMD comparison 9, 10–19
open-source and third-party components for 123
risk assessment challenges 80–91
risk assessment strategies for 84
risk management for 75
safety risk management history 76–91
systematic failures 80
types of applications 34–41
usability engineering of 131
Software as a Medical Device (SaMD) 5
acronyms and terminology for 106
advantages of open source and third-party software use in 123–130
creation of terminology for 1
for population health 6–19
in Canada 8
international differences in meanings 5
in the US 7–19
managing single fault condition 85
MDSW comparison 10
open source and off-the-shelf third-party 2
overview of 1
product liability for software 221–227
relation to MDSW 9
risk assessment for third-party or OSS software 129
safety concerns with OSS 124–130
strategies for Risk Control Measures in 86
terminology for 123
software as an IVD Medical Device (IVD SaMD) 21
Software as a Service (SaaS)
business model 187
qualification as IVD software 22
software development 103
defining requirements in 120
definitions used in 105–114
postmarket activities 119–122
processes for 106–114
standards and guidance for 103–105
validation requirements and guidance 117
software download portals (app-stores) 187
Software in a Medical Device (SiMD)
FDA use of 6
regulatory definition and use of 6
relation to SaMD 5
software items 112
software liability 221
in US 223
liability in contract 226–227
negligence or fault liability 224–227
update in EU liability laws 226–227
Software of Unknown Provenance (SOUP)
definition 106
in security risk management 97
software system 106, 112
software unit, definition 106
Spain, health app reimbursement 213
stage-gated development 113
STRIDE threat modeling framework 96
subject matter experts (SMEs), third-party and OSS evaluation 127
Systematic Failure 78
System Usability Score (SUS) 150–158

T
technical specification (TS) for health/wellness apps 183
teleassistance (TLA) 209
TELECARE (or Télésoin in French) 209
teleconsultation (TLC) 208
tele-expertise (TLX) 209
tele-surveillance (remote monitoring (TLS) 208
test-driven development (TDD) 89
The Netherlands
examples of reimbursed health apps in 212
reimbursement model in 211–212
threat modeling for security assessment 96–102
TRIKE threat modeling framework 96
U

Unified Modeling Language (UML) 88
United Kingdom (UK)
  DHT reimbursement in 202–208
  virtual manufacturer of software 123
United States (US)
  AI legislation in 175
  IVD classification in 28
  qualification of IVD software in 24, 29–41
  SaMD in 7–19
  software liability in 223
unreasonable conduct 224
usability engineering of software 131
  acceptance criteria 152–158
  avoiding frustration by 132–158
  core functionality focus 146–158
  determining intended users of product 134–158
  documentation of goals 140–158
  evaluation of usability 140–158
  formative evaluation 142–158
  functionality vs. usability in 133
  heuristics analysis 144–158
  identifying goals for 139–158
  information architecture principles in 148–158
  intended user needs and expectations of 133–158
  interface requirements and design specifications 141–158
  mobile first 148–158
  number of testers for 149
  product safety risk management 154–158
  regulatory standards and requirements 154–158
  roles and responsibilities in 135–158
  self-evident and self-learnable 147–158
  severity scale of flaws 146
  Single Ease Question (SEQ) 149
  System Usability Score (SUS) for assessment 150–158
  tester training 149
  testing in development 105
  understandability before simplicity 147–158
  usability and user interfaces 133–158
  usability sensitive user needs 136–158
  user expectations and safety 131–158
  user needs, requirements and specifications for 134–158
  user observation for 142–158
  use scenarios 138–158
  verification and validation 149
  walkthrough evaluation 143–158
  user experience design (UXD) specialist 136–158
  user interface (UI)
    accessibility needs in 133, 136
    definition of 133
    design in software development 104
    user experience design (UXD) specialist 135
US Food and Drug Administration (FDA)
  clinical evaluation of SaMD guidance 65
  commercial software guidance 124
  declaration of conformity for safety 155
  design control guidance 103
  device risk classifications 30
  expectations for OSS 124
  gated development guidance 113–114
  generic device regulation 30
  OTS software use 97
  product classification database 32
  regulatory pathway for AI 175
  SaMD guidance 6
  software device levels of concern 33
  software validation guidance 87, 117
  usability requirements guidance 156

V

validation
  intended use fulfillment by device 105
  in usability engineering of software 149–158
  of user needs in software development 104
  requirements for software 117–122
VAST threat modeling framework 96
verification
  definition of 105
  in usability engineering of software 149–158
virtual manufacturer 123

W

walkthrough evaluation 143
waterfall model
  for software development  103, 107
  once-through strategy in  105
wearables  12–19
word association cards in user testing  150
World Health Organization (WHO)
  market access monitoring by  198

Z

Zorginstituut Nederland (ZIN)  213