

# INDEX

- accelerated tests *see* ICH guidelines  
acceptable quality level (AQL) 106–107, 109–110, 119–121, 127–128, 132–134, 231–232  
ADD-Vantage (Abbotts) 67  
adhesives 169, 196, 389–393, 467, 475–78  
advertising 95  
adulteration 190–191  
aerosols 64, 66, 89, 100, 246, 341, 342, 404, 406, 408, 412, 415, 423–433, 455, 467, 550, 557, 577, 620  
    filling 433–434  
    propellants 100, 432–434, 552  
    testing 434, 488  
    valves 431–433  
air filtration 493  
allergies 614–615  
aluminium containers 401–404, 409–410  
    coatings 438–439  
    deadfold 467  
    diaphragms 440–441  
    foil 368, 374, 387–398, 405, 435–442  
    metallisation 441–442  
    pinholes 388, 439–440, 480, 538, 619  
    properties 410, 436, 437, 439, 440, 442  
    recycling 442  
    yield 436  
ASTM tests (American Society for Testing Materials) 283–291  
ampoules 220–221, 238, 243, 256, 278, 485–486, 494, 498, 506, 556–557  
    printing 243–244  
    testing 480  
anaphylactic shock 500  
annealing 215, 218, 219, 260, 303, 436  
antimicrobial preservatives 493–499  
arrhenius 335  
aseptic processes 24–25, 313–315 341, 492–93, 496, 509, 533, 620  
Association of British Pharmaceutical Industries (ABPI) 483, 526, 623, 625  
audit (of suppliers) 107–108, 124, 135–139  
autoclaving 16, 261, 289, 296, 304, 311, 312–313, 347, 358, 381, 383, 396–398, 401, 417, 514  
auto injectors 508–509  
Automatic Liquid packaging (ALP) 486, 554, 557–558, 617, 620  
  
bacteria 23, 314, 387, 455  
bar code(s) 142, 165, 179, 199–204, 526, 610, 624  
bar code reader 145, 173, 198–199, 240, 516, 560, 606  
batch samples 231–232,  
    *see also* sampling (statistical)  
binomial distribution 123–124, 129–133  
  
bioburden 436, 492–493, 497, 557, 623  
biological contamination 21–25  
blister packs (general) 367, 370, 396–397, 517–544, 540–544  
    cold forming 528–530, 535, 539, 554  
    de-blistering 539  
    design (and cost) 524, 529, 531–532, 539, 541–542, 554  
    equipment 519–524, 526–528, 531, 539, 541–542, 554  
    inspection 523  
    lidding 526–530  
    liquid fill 532–533  
    machinery 523–524, 539  
    perforation 522–524  
    protection 525  
    OPD 524, 526, 532  
    sealing 521–524, 542  
    tamper evidence 523–524, 526, 530–531, 536, 539–541  
board 160–164  
bottle finishes 491,  
    *see also* glass  
British Pharmacopoeia (BP) 314, 334, 347, 349–350, 493  
British Standards Institute (BSI) 70, 109, 121, 127, 150, 283, 285  
  
calendering 378  
calibration 137  
cartons 152, 174–178, 559–561  
cartridge tubes *see* syringes  
certificates 137–138, 145, 199  
certification of suppliers 144–145, 232, 344  
change 37, 57–59, 111, 145–146, 618–620  
child resistant closures 67, 102, 246, 358, 418, 468, 526, 531, 621, 623  
chlorobutyl rubber *see* rubber types  
chlorofluorocarbons (CFCs) 67, 100  
clean areas (controlled areas) 311, 514, 561, 620  
cling film 7, 367, 373, 379  
clinical trials 90, 335  
closure thread design 463–465  
    tamper evident 443–444, 449, 456, 458, 461–466, 481–484  
    tamper evident definition 482  
    torque 15, 237–238, 247, 250, 339, 447, 457, 460–465, 489  
    torque instruments 457  
    vacuum 464, 466  
    vacuum/pressure tests 452–455, 479–481  
    wads 456, 462  
    wadless 460  
    welds (soudronic) 469  
closures (general) 227, 237, 245–255, 268–69, 271, 276, 280, 296, 307, 310, 316, 329, 339, 416, 556  
    administration 484–485

- child resistant 443–444, 449, 466, 474, 483, 484  
 coatings 457  
 costs 443–444  
 drawings 454  
 evaluation test 449–452, 478, 481  
 ingress/egress 445, 446, 451–455  
 liners 247–249  
 membrane/diaphragms 465, 474–474  
 presentation 457  
 reclosable/non reclosable 467, 471  
 ROPP (rolled-on pilfer-proof) 461, 465  
 recycling 444, 477  
 sealing (adhesive) 475, 478  
 sealing (heat) 470, 474  
 standards 490–491  
 static 448, 451, 456, 566  
 stress cracking 488–489  
 Code of Federal Regulations (CFR) 124, 348, 340, 350  
 Code of Practice 135, 150, 198, 327, 346, 352  
 collapsible metal tubes 405, 410, 413, 417, 419–420, 440, 469–470, 588, 598, 599  
 collapsible metal tubes closures 421  
 collapsible metal tubes particulates 422–423  
 complaints 54, 142, 146, 149, 455  
 compliance 7–8  
 component specification 262  
 containment and convenience 7  
 contamination 17, 24  
 conformance testing 112, 114  
 continuous improvement 140, 142  
 control charts 141, 143  
 controlled monitored dosage systems 532, 625–626  
 corrugated board 181–186, 209, 569, 574  
 counterfeiting (security) 188–203, 577  
 crimping metal tubes 421–422, 468–469  
 Critical Path Network (CPN) 147  
 cullet 212, 216, 242, 627  
 current good manufacturing practice *see* GMP  
 cushioning 564–581  
 debossing 604, 624  
 defect classification 119–20  
   actions 121  
 degradation (products) 2  
 dermal patches 618  
 dessicant closures 418  
 device (medical) 57, 62–67, 75, 349, 354–357, 360, 364, 618, 622, 628  
 diaphragms 254, 468,  
   *see also* metal containers:  
     diaphragms  
 DIN (Deutsche Normenausschus) 239, 283, 286–290  
 directives—classification, packaging and labelling of hazardous materials 100, 101  
   general 95  
   labels and leaflets 96, 172  
   medical devices 628  
   packaging waste 53, 99  
   plastic materials in contact with food 93  
   polymers 102  
 distribution 39–40, 183–186, 337–340, 453–54, 570, 574–575, 577, 579–580  
 drug master files (DMF) 89, 316, 332  
 drug substances 46  
 economic order quantity (EOQ) 561, 562  
 efficacy 1, 77–78, 88  
 elderly patients 354–355, 444, 466, 484, 517, 532, 614, 616, 623  
 embossing 604, 624  
 engineering 107  
 environmental issues 28, 62, 92, 152, 186, 204, 345–346, 397 444, 448, 527, 539–540, 568, 616, 618–619, 626–627  
 environmental stress cracking (ESC) 58, 276, 283–284, 290–291, 297, 330, 380, 488–489  
 ethylene oxide 311, 313, 341–342, 397–398  
 European Medicines Evaluation Agency (EMEA) 79–81  
 European Pharmacopoeia (EP) 44, 91–92, 493, 512–13  
 expert reports 87–88, 335  
 extractives 380  
   tests 63, 291, 380  
 extrusion 319–320, 323–324, 387  
 failure mode and effect analysis (FMEA) 109  
 Fair Packaging and Labelling Act 229  
 fibreboard 181  
 filtration (sterilisation) 497  
 finished product controls 139, 142–143  
 first in first out (FIFO) 199  
 flaming (corona discharge) 329, 343, 359, 588, 607  
 flexible packaging *see* multilayer materials, *also* blister materials  
 FDA (Food and Drugs Administration) 63, 77, 87, 88, 91, 145, 197, 229, 246, 273, 291, 313–314, 318, 333, 351, 396, 422, 434, 483, 492, 500, 550  
 Food, Drug and Cosmetic Act (1938) 75, 77, 229  
 food packaging 396  
 form fill packaging 367  
 furnace 212, 215  
 gang printing 606;  
   *see also* rogue product  
 gas sterilisation *see* ethylene oxide 26, 397–398, 423, 497, 514  
 gauges 116–118, 234–235, 257  
 glass  
   additives 212  
   aerosols 246  
   autoclaving 261  
   blowing 216–218  
   bottle irradiation 26  
   bottles specification 262–263  
   cartoning (and outerisation 240–241  
   composition 211–213  
   cleanliness 236  
   closures 211, 226–227, 237–238, 244–256,  
    *see also* closures  
   coating 230, 246  
   decoration 230  
   defects 258–260  
   design 220, 222–233  
   filling 236–237  
   finish 250–253, 491

- labelling 239–240
- legislation 229–230
- manufacturing 216–218
- production line handling 227, 233
- properties 214
- quality 230–233
- recycling 229
- seals 239, 247–249, 254–256
- special containers 242
- surface treatments 213–214, 240
- terminology 257–258
- tests 260–261
- tubular 219–220, 242–245
- types (I, II, III, IV) 212–213
- testing 260–261
  - and the environment 241–242
- good laboratory practice (GLP) 48, 54, 56, 73, 148–149, 336
- good manufacturing practice (GMP) 20, 48, 54, 56, 73, 100, 105, 136, 140, 142, 145–146, 149, 199, 315, 336, 345–346, 351–352, 485, 492, 539, 550, 615, 622–627
- hazardous materials 100–101, 192, 579–580
- hazards 8–11, 216
  - biological 21–22, 565
  - chemical 27–28
  - climate 11–17, 564–565
  - contamination 17–20
  - microbiological 22–25
- head space *see* ullage
- HIBCC (Health Industry Bar Code Convention) 202
- heat sealing 118, 288–289, 303–304, 374, 377–381, 384, 389, 394, 470–472
- hot melts 387, 392
- hydrogen peroxide sterilisation 314, 397
- HVAC 551
- insects 21–22
- Institute of Quality Assurance 198, 352
- IND/NDA (Investigational New Drug Application) 54, 88–91
- inhalation device 67,
  - see also* devices
- in-process controls 140–142
- ICH (International Conference on Harmonisation) guidelines 44, 46, 52, 62–63, 76–77, 87, 312, 317, 336, 339, 345–346, 348, 365, 440, 627–628
- ISO (International Standards Organisation) 70, 512, 526
- inventory planning 551
- ISO 9000 135, 198, 199, 352
- irradiation—gamma 25–26, 302–303, 311, 314–315, 339, 341, 358–359, 397–398, 423, 474, 496, 514, 516, 549
  - electron beam 26, 311, 314, 341, 359, 397, 493, 549
- isolators 504–510, 515–516, 622
- just in time philosophies (JIT) 40
- kegs and drums 187–188
- labelling 6–7, 94, 168, 239, 411, 439, 548, 558–559, 566, 561–562
- labels 94, 152, 164–172, 178, 188, 240–247
- lacquers 384–385, 388–389
- laminate tubes 395, 405, 419, 440
- laminates 389–398, 619,
  - see also* multilayer materials
- latex end seals 421–422
- leaching 90, 500–503, 509–510
- leaflets 94, 98, 152, 172–173
- lehr 213, 215, 217–218, 230, 236, 260
- liability 62, 192, 194, 345, 515, 574
- life cycle analysis (LCA) 28, 187, 397
- lot tolerance percent defectives (LTPD) 127, 134
- lyophilised products 256, 505–506, 510, 515
- maintenance 36, 141–142
- marketing 34–35
- Marketing Authorisation Application (MAA) 82–84
- materials
  - cleaning 550, 553
  - conditioning 549–550
  - specifications 107–109
- medical device *see* device, medical
- Medicines Act 1968 78, 82
- Medicines Commission 483
- Medicines Control Agency (MCA) 197
- melt flow index (MFI) 283–284, 291, 299, 302, 369, 380, 489
- metal containers 405–406, 410, 413–417, 423–424, 427–429
  - annealing 407, 417–19
  - closures 404–406, 414–416, 418, 421, 425, 428–31
  - coatings 404–405, 407–409, 411–412, 420–422, 430, 435, 437
  - decoration 406, 411–13, 419
  - diaphragms 430–431, 434, 474–475
  - gaskets/membranes 416–418, 423–424, 428, 474–475
  - lacquering 409, 419
  - lids 416
  - recovery 435
  - sheet rolling 410
  - slugs 417, 419
  - solder 408
  - temper 408, 410
  - types 407–409
- metallisation 374, 381–382, 384, 387, 393, 399, 404, 441–42, 535–536, 583, 589, 605, 619
- micrometers 117
- Military Standards (MIL-STD105E) 109, 121, 127, 143, 150
- mix ups 204
- monobloc containers 417–418, 431
- Montreal Protocol 100
- moulding processes 304–310, 319–325, 328–329
- multilayer (combination) materials 374–383, 438–441
- multiuse injectors 509
- needle design 238–239, 245, 256, 487, 504, 508, 511, 512
- New Drug Application (NDA) 88–91
- nitrogen flushing 16
- operating characteristics (OC) 129, 132, 134–135
- optical character recognition/verification (OCR) (OCV) 115, 560–561
- orange guide 151, 351, 623, 626
- original pack dispensing (OPD) 354–355, 483–484, 524, 526, 532, 615, 618–619, 621, 623–625

- over the counter (OTC) 4, 6, 22, 33, 35, 165, 190, 200, 240, 328, 610, 615, 617
- overprint 178–180
- ozone depletion 100
- pack costs 540  
coordinator 40  
protection 9–12  
testing 560–561
- packaging  
design 37, 547–555  
development 36, 41  
ergonomics 559–562  
line processes 549–553, 560  
management 34  
rejects 551  
services 550–551  
specification 55, 262–263, 404–405  
waste 98–100  
waste directive 73
- Packaging Industries Research Association (PIRA) 576
- pallets 563, 566–567, 570–571, 576–578  
stacking 572–574  
wrapping 573
- paper 160, 164, 375–376,  
*see also* combination materials  
bleaching 154  
coatings 158–159  
conditioning 173, 204–205  
grain direction 167, 169–170  
liners 188  
manufacture 154–160  
pulping 154  
sacks 187  
sources 153–154
- parallel trading 191
- Parenteral Drug Association (PDA) 492, 511, 516
- parenteral society 492, 511, 516
- patenterals 67, 494–497
- participates 19–21, 315–316, 342–343
- permeability  
gas 379, 446–447  
water vapour (wvtr) 379, 536
- pharma codes 202–203
- pharmaceutical quality group 198, 352
- pharmacopoeias 91–93,  
*see also* EP, USP
- pillow packs 556
- plasma enhancement 384
- plastics  
additives 92, 264–267, 276, 279, 282, 293–302, 311, 330–333, 347–348, 371, 380–381  
analysis 302–303  
ancillary processes 311–312  
antioxidants 298  
coatings 270–272, 279, 282, 311, 339, 344, 372, 374–377, 381, 385–387, 399–401, 440–441, 539, 617  
container evaluation 346–353  
data sheet 283–294, 317  
decoration 329  
extractives 83–87, 93, 291, 362–363, 380
- fabrication processes 303  
fillers 296–297  
panelling 342, 362  
permeability 291–294  
preservative loss 361  
pretreatment 343, 359, 378–380  
process aids 264  
properties 266–267  
residues 273, 276, 293, 295, 300–303, 331–332, 346–347, 354, 357  
sinkage 362  
stabilisers 279, 297  
sterilisation 311, 313–315, 381, 383  
specifications 316–319, 333, 344, 352  
standards 348–350  
stage tests (1, 2, 3 and 4) 332–339  
slip additives 298, 387  
testing 283–295, 302–303, 334–335, 339–348, 352–366  
types  
Aclar 272, 331, 398, 527–528, 539, 619  
cellulosics 270–271, 376–377  
ethylene based 271  
fluoroplastics 271–272  
fluorochlorethylene 382  
ionomers (Surlyn) 272–273, 279, 381, 389, 395, 398, 439, 472, 475  
welding 311–312  
films 304, 371, 378–384,  
*see also* multilayer materials coatings 384–387, 399–401  
properties 378–380  
uses 380  
orientation 303–304, 378, 532
- polyamides 273–274, 383
- polyester 280–281, 331, 382, 398
- polyolefins 269, 275–277, 330, 380–381
- polystyrenes 277–278, 330, 382
- polysulphones 278  
Saran (PVdC) 279, 331, 373, 381–382, 384, 396, 398, 458, 527, 608  
synthetic rubbers 282–283  
vinyl polymers 278–280, 330–331, 381–387
- printing  
artwork design 37, 114, 588–591  
controls 140, 142–143  
decoration 583–585  
Desktop Publishing (DTP/DAR) 37, 591, 610, 624  
food grade inks 611  
gang printing 606  
ink hazards 611–612  
inks 591–594, 598, 601–603, 606, 611–612  
legislation 582  
office printing 610–611  
pick 584, 607  
pre treatment 607  
processes 179–180, 393–394, 588, 591, 595–606, 610–611  
rub resistance 582–583, 608  
security 606  
slip 585  
step and repeat 591  
terminology 586–588, 594  
UV drying 593–594, 598, 602, 612

- process capability 110, 116, 126, 137, 140–141
- Qualification:**  
 IQ, SQ, OQ, PQ 144–146
- Quality Assurance** 38, 56, 104–107, 142–143, 149–150, 539  
 circles 105  
 control 38, 56, 104–114, 117, 120–123, 149–150  
 costs 146  
 of conformance 105–106  
 of design 105, 327, 448, 487  
 manual 136  
 plan 136  
 procedure 113,  
*see also* SOP records 121–122, 147–148  
 standards 107–108, 110–122, 150–151,  
 quarantine areas 576–577
- radiation compatibility** 505
- random samples** *see* sampling (statistical)
- recalls** 200  
 records 121  
 recycling 29–32, 43, 242, 367–369, 442, 618–619  
 registration bar codes 555, 558, 606,  
*see also* bar codes  
 regrind 93, 279, 300–301, 306, 317, 489  
 research and development (R&D) 614–615  
 resin 333, 338–340,  
*see also* plastics  
 return on investment (ROI) 6  
 revalidation 106  
 right first time 105  
 rogue product 116, 120,  
*see also* gang printing  
 Rommelag 329, 486, 554, 557–558, 617, 620  
 Royal Pharmaceutical Society 484  
**rubber materials:**  
 additives 501–502  
 cure (vulcanisation) 501–502  
 degradation/aging 17, 500  
 formulation 498–503, 509–510  
 latex allergy 500  
 MCBT 501–502  
 natural rubber 500  
 testing 481, 486, 504, 511–513, 515  
**rubber types** 456, 459, 499  
 butyl (halobutyl) 501  
 cleanliness 513–515  
 compatibility 509–510  
 components 501  
 design 244–245, 506, 509, 557  
 fragmentation 511–512  
 liners 248–249  
 lubrication 515  
 overseals 244–245, 498, 504, 511  
 particulates 513–515  
 preservative solubility 493–499  
 seal integrity 506, 511  
 seal sterilisation 513–516  
 seal stoppers 238, 244–245, 256, 456, 486, 504–508, 511–512  
 synthetic 282–283
- teflon coating** 510, 514–515
- rules and guidance for pharmaceutical manufacturers and distributors** 151, 351, 623, 626,  
*see also* orange guide
- rules governing medicinal products in the European Community IV** 82, 144, 151,  
*see also* orange guide
- sachets** 367, 383, 389, 396–397, 488, 517, 538–539, 555
- sales** 35
- sampling (statistical)** 122–129, 143, 232, 336
- seal techniques** 467–468, 470,  
*see also* closures
- secondary pack** 174, 495, 548  
 reactions 7
- security codes** 202–203,  
*see also* pharma codes;  
 of product 188–203,  
*see also* counterfeiting
- shelf life** 2, 12, 43–46, 49–54, 64, 87, 89, 94, 96–97, 338, 354–355, 365–366, 525,  
*see also* stability testing
- shewhart charts** 141, 150
- shrink films** 368–373, 379, 381–382
- shrinkage** 191
- side effects** 2
- silicone coatings** 399–401, 539
- specifications** 38–39, 102–109, 111, 147, 262–263, 316–319,  
*see also* directives, pharmacopeias
- stability of product** 2–5, 58–59  
 testing 37, 43–6, 61–62, 69, 344–356, 516
- stage testing** (1, 2, 3 and 4 of plastics) 332–339
- stainless steel (type 304, 316)** 407
- standard operating procedures (SOP)** 54–56, 111–122, 525, 529, 561
- standards** 70, 72, 109
- statistical process controls (SPC)** 111, 121, 126, 136–137, 139, 141, 621
- statutory instruments (UK)** 95
- sterile processing** 24–27, 330, 341, 557,  
*see also* aseptic processes, autoclaving
- sterile products** *see* parenterals products leak testing 485–88
- sterilisation** 311, 313–315 375, 397–398, 311, 313–315, 397–398,  
*see also* irradiation autoclaving, gas sterilisation of materials
- sterilise in place (SIP)** 557
- storage conditions** *see* ICH
- stress cracking**, *see* environmental stress cracking
- stretch wraps** 371–373, 379
- strip packaging** 395–397, 517, 533–537, 539, 543, 554  
 packaging integrity testing 537–538
- sulphating of glass** 213
- summary of major product characteristics (SMPC)** 94–95, 98
- summary of product characteristics (SPC)** 94
- supplier rating** 51
- supplementary product tests** 357
- synthetic rubbers** 282–283,  
*see also* rubber
- syringes** 291, 503–504, 507–508, 617
- syringes testing** 504

- tampering 189–190  
 evident 42, 62, 66, 68, 74, 85, 102, 193, 368, 374, 399, 416, 418–419, 429, 434, 438, 440, 468, 474, 482, 504–506, 557, 571, 614, 622,  
*see also* child resistant closures  
 resistant 4, 22, 62, 68, 89, 327, 474
- tampon printing 329, 393, 465, 602
- tapes 367, 490
- taste recognition threshold concentration (TRTC) 332
- Technical Association for the Pulp and Paper Industry (TAPPI) 70, 109
- torque *see* closures
- traceability 69, 136, 147, 148, 351–352
- training 137, 139, 147, 561
- transit damage 241
- transit packaging 181,  
*see also* corrugated board
- transport *see* distribution
- trends 616–618
- toxicity 61, 269, 295, 301, 327, 332–334, 347–348, 380, 420, 584–585, 612
- tylenol 190, 440, 482, 618, 622
- tyvek 272, 383, 398, 497, 514
- ullage 52, 228, 241, 341, 496
- United States Pharmacopoeia (USP) 48, 89–91, 214, 291, 314–318, 333–334, 342, 347–348, 362–363, 446, 455, 493
- UV drying (inks) 593–594, 598, 602, 612
- UV sterilisation 26, 311, 314
- vacuum packing 16, 464, 466, 518  
 tests 537–538,  
*see also* closures
- validation 37, 46, 49, 53, 64, 69, 93, 126, 137, 139, 143–145, 198, 447, 485, 516, 557, 622
- valves *see* aerosols
- vapour pressure 449
- vendor rating 108
- video imaging 144–145, 621–624
- vinyl chloride monomer (VCM) 301–302, 345
- vision verification system 199, 203, 481
- wads (rubber) *see* rubber types:  
 seal stoppers
- warehouse costs 578–579  
 glass 241  
 handling 567–568, 577  
 hazards 563–566, 569, 575, 579  
 order picking 577–578  
 quality issues 568  
 space economics 575–576  
 storage 340, 351
- water for injections (WFI) 244, 251
- water vapour permeability (WVP) 69
- World Health Organisation (WHO) 44, 333, 346–347, 361–362
- woven fibres *see* Tyvek