GPAT Pharmaceutics

Sample Paper – 6

Duration: 36 Minutes **Maximum Marks: 100**

Instructions

- This paper contains **25** Multiple Choice Questions (Single Correct Answer), modelled on the Pharmaceutics portion of **GPAT** entrance.
- Each correct answer carries **+4 marks**. There is **a penalty of −1 mark** for each incorrect answer. Unattempted questions carry no marks.
- Only **one** option is correct per question.
- Syllabus: **GPAT Pharmaceutics — Tablet Manufacturing, Dosage Form Technology, Coating, and Pharmaceutical Process Control.**
- Personal calculators, mobile phones, and electronic gadgets are strictly prohibited. A simple on-screen calculator is provided in the CBT interface; rough sheets are supplied at the centre.

Q1. A moisture-sensitive drug degrades rapidly on contact with water. A formulation scientist considers roller compaction (dry granulation) instead of high-shear wet granulation. Which statement **BEST** describes the PRIMARY advantage of roller compaction for this drug?

(A) Roller compaction always produces granules with a larger median particle size than wet granulation, improving dissolution rate

(B) No liquid water or aqueous binder is used in roller compaction, eliminating hydrolytic exposure and preserving chemical integrity of the moisture-sensitive drug

(C) Roller compaction inherently produces harder tablets with lower friability because the ribbon is more uniformly compressed than a wet granule bed

(D) Roller compaction eliminates the need for any disintegrant in the final tablet formulation

Q2. A drug substance is processed by spray drying from an aqueous feed solution. Compared with granules produced by high-shear wet granulation, spray-dried particles typically exhibit which **characteristic** morphological and flow property?

(A) Dense, irregular shards with high bulk density and poor flowability
(B) Elongated needles with high aspect ratio that improve tablet compressibility
(C) Hollow spherical particles (cenospheres) with low bulk density and improved powder flowability
(D) Highly crystalline compact particles with narrow particle size distribution requiring no additional milling

Q3. An amorphous solid dispersion (ASD) of a poorly water-soluble drug in HPMC-AS has a glass transition temperature $T_g = 115°\text{C}$. To ensure long-term physical stability and prevent drug recrystallisation, the ASD should be stored below which **maximum** temperature? (Apply the rule: $T_{\text{storage}} < T_g - 50°\text{C}$)

(A) Not more than $115°\text{C}$ (at the T_g itself)
(B) Not more than $90°\text{C}$ ($T_g - 25°\text{C}$)
(C) Not more than $75°\text{C}$ ($T_g - 40°\text{C}$)
(D) Not more than $65°\text{C}$ ($T_g - 50°\text{C}$)

Q4. Hot melt extrusion (HME) is used to prepare amorphous solid dispersions. The schematic below shows the key process steps.

HME requires a polymer that is thermoplastic (processable above its T_g by heat and shear), has a T_g amenable to extrusion at 120–$160°\text{C}$, and offers high drug miscibility. Which polymer is **MOST** suitable?

(A) Kollidon VA 64 (copovidone/PVP-VA 64), $T_g \approx 105^\circ$C, thermoplastic and highly miscible with many drugs

(B) Hydroxyethylcellulose (HEC), which is water-soluble but lacks thermoplastic behaviour above 180°C

(C) Hydroxypropyl methylcellulose (HPMC E5), which degrades before softening and is unsuitable for melt extrusion without plasticiser

(D) Calcium carbonate, used as a filler to lower T_g of the extrudate below 60°C

Q5. During tablet compression, a tacky wet granule fraction adheres to the upper punch face, pulling material away from the tablet surface on ejection (a defect called *picking*). Which punch tip treatment is **MOST** commonly employed to minimise this sticking problem?

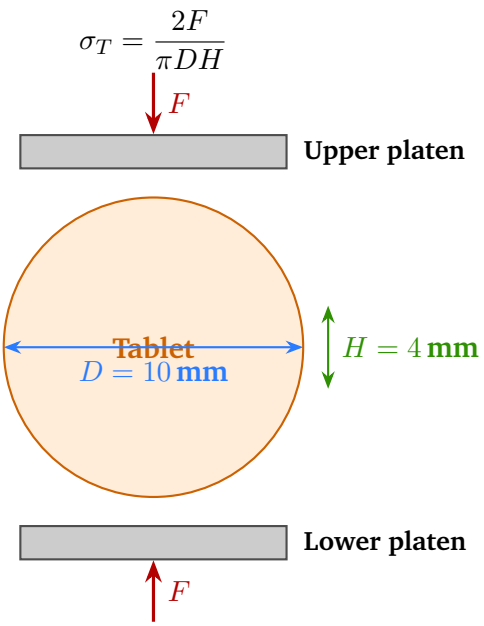
(A) Hard chrome plating over a nickel undercoat applied to the punch shank only

(B) Coating punch faces with PTFE (polytetrafluoroethylene), which provides a non-stick low-friction surface

(C) Spraying a dilute sodium lauryl sulfate solution onto punch faces before each compression cycle

(D) Diamond-turned mirror-polished stainless steel punch faces without any additional surface treatment

Q6. Tablet tensile strength is measured by the diametral (indirect) compression test. A flat-faced tablet is placed on its side between two flat platens and a compressive force F is applied until the tablet fractures. The diagram below shows the test geometry.



A tablet with diameter $D = 10\,\text{mm}$ and height $H = 4\,\text{mm}$ fractures at a diametral compressive force of $F = 107\,\text{N}$. The tensile strength σ_T is:

(A) $0.85\,\text{MPa}$
(B) $1.07\,\text{MPa}$
(C) $1.70\,\text{MPa}$
(D) $3.40\,\text{MPa}$

Q7. USP $\langle 905 \rangle$ Content Uniformity of Dosage Units specifies an Acceptance Value (AV) as the criterion for passing the test. What does the AV calculation **incorporate**?

(A) Only the relative standard deviation (RSD %) of the 30 individual assay results, with no correction for mean bias
(B) The absolute difference between the target label claim and the sample mean content only, ignoring within-sample variability
(C) The arithmetic mean of the 30 individual assay values expressed as % of label claim
(D) Both the absolute mean deviation $|M - \bar{X}|$ and the variability term $k \cdot s$ (where k is a constant and s is the sample standard deviation)

Q8. A BCS Class II drug (low solubility, high permeability) shows poor correlation between its in-vitro dissolution in simple pH buffers and in-vivo

oral absorption. Which dissolution medium is **MOST** likely to provide a meaningful IVIVC (Level A) for this compound?

(A) FaSSIF (Fasted State Simulated Intestinal Fluid, pH 6.5) containing sodium taurocholate and lecithin to mimic intestinal bile and phospholipid content
(B) 0.1 N HCl (pH 1.2) simulated gastric fluid without pepsin
(C) pH 6.8 phosphate buffer without bile salts or lecithin
(D) Purified water (pH 7.0) without added buffer capacity or solubilising agents

Q9. Triethyl citrate (TEC) is routinely incorporated at 15–20% w/w (based on polymer weight) into HPMC-based aqueous film coating suspensions. What is the **PRIMARY** function of TEC in this context?

(A) Acts as a pore former in the deposited polymer film, creating channels that accelerate drug diffusion across the coat
(B) Lowers the glass transition temperature (T_g) of the HPMC film by plasticising the polymer chains, imparting flexibility and preventing film cracking
(C) Increases the viscosity of the coating suspension, ensuring a more uniform spray droplet size and coat thickness
(D) Prevents aggregation of film-coated tablets during pan coating by acting as an anti-tack agent on newly coated surfaces

Q10. Conventional sugar coating involves a defined sequence of stages applied to compressed tablet cores. What is the **PRIMARY** purpose of the *sealing coat* applied in the **first stage**?

(A) To apply a uniform colour layer for aesthetic product identification
(B) To build up coating bulk and round off sharp tablet edges before the syruping stage
(C) To seal the tablet core from moisture ingress, protecting a moisture-sensitive drug during the subsequent aqueous sugar-syrup coating stages

(D) To deposit a final wax polish that provides pharmaceutical elegance and smooth packaging-line performance

Q11. Aquacoat ECD is a 30% w/w aqueous pseudolatex dispersion of ethylcellulose used for extended-release coating. It requires coalescence of discrete polymer spheres into a continuous water-insoluble film during the drying step. Which process parameter is **MOST** critical in determining whether coalescence occurs?

(A) Inlet air temperature of the coating pan
(B) Tablet core hardness measured by diametral compression before coating
(C) Concentration of ethylcellulose solids in the Aquacoat dispersion (% w/w)
(D) Curing temperature relative to the minimum film-forming temperature (MFT) of the ethylcellulose dispersion

Q12. Cellulose acetate phthalate (CAP) is used as an enteric coating polymer. Above which approximate pH does CAP dissolve due to ionisation of its phthalyl carboxylate groups (p$K_a \approx 5.7$)?

(A) pH > 6.0
(B) pH > 5.0
(C) pH > 7.0
(D) pH > 4.5

Q13. Croscarmellose sodium (CCS) is classified as a superdisintegrant due to its exceptionally rapid tablet disintegration action. Which mechanism **PRINCIPALLY** accounts for its superior performance compared with conventional starch?

(A) CCS dissolves rapidly on contact with water, creating a localised osmotic gradient that draws dissolution medium into the tablet matrix
(B) The cross-linked carboxymethylcellulose network of CCS absorbs water and swells 10–20 fold in volume, generating hydrostatic pres-

sure that ruptures the tablet structure

(C) CCS functions as an effervescent agent by releasing CO_2 gas on contact with saliva, physically disrupting the tablet

(D) CCS forms a soluble inclusion complex with the drug, increasing drug solubility and thereby accelerating release

Q14. Sieve analysis characterises granule particle size distribution. Which **US mesh** sieve number corresponds to an aperture of approximately $250\,\mu$m?

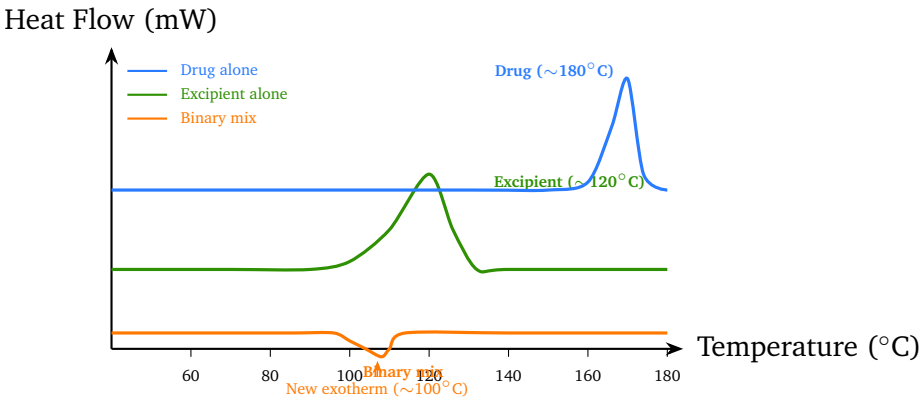
(A) US mesh 20 (aperture $\approx 841\,\mu$m)

(B) US mesh 40 (aperture $\approx 420\,\mu$m)

(C) US mesh 60 (aperture $\approx 250\,\mu$m)

(D) US mesh 120 (aperture $\approx 125\,\mu$m)

Q15. DSC is widely used for binary drug–excipient compatibility screening. Three DSC traces are overlaid in the figure below.



Which observation in the DSC binary mixture trace **MOST** strongly indicates drug–excipient incompatibility?

(A) The melting endotherm of the drug in the binary mix shifts to a higher temperature compared to pure drug alone

(B) The drug melting endotherm in the binary mix is sharper and taller than in pure drug

(C) The DSC trace of the binary mix is superimposable on the arithmetic sum of the individual component traces

(D) A new exothermic peak appears in the binary mix at a temperature lower than either individual component's thermal event

Q16. In a PAT-enabled blending operation, near-infrared (NIR) spectroscopy monitors blend uniformity of a tablet formulation in real time. The Moving Block Standard Deviation (MBSD) method tracks spectral variability across successive spectra. Which observation **INDICATES** that the blend endpoint has been reached?

(A) The MBSD of the NIR signal reaches a minimum value and remains stationary (plateau), indicating no further change in composition heterogeneity
(B) The NIR absorbance at the principal drug wavelength reaches its theoretical maximum, confirming complete drug dispersion
(C) The relative standard deviation (RSD %) of the blend assay result exceeds 5%, triggering auto-stop
(D) The inlet-air temperature of the bin blender drops to ambient, signalling that mixing energy has been fully dissipated

Q17. ICH Q8(R2) introduces a Quality-by-Design (QbD) framework for pharmaceutical development. According to ICH Q8(R2), a *"design space"* is defined as:

(A) The set of raw material specifications (particle size distribution, moisture content) guaranteed by the API supplier
(B) The multidimensional combination of input material attributes and process parameters that has been demonstrated to provide assurance of quality
(C) The full range of all equipment settings permitted by cGMP regulations regardless of their demonstrated effect on critical quality attributes
(D) A single optimal process description (one batch formula and one set of parameters) submitted in the dossier as the approved process

Q18. Failure Mode and Effects Analysis (FMEA) is a prospective risk assess-

ment tool recommended under ICH Q9 for pharmaceutical process evaluation. In a pharmaceutical FMEA, the Risk Priority Number (RPN) is calculated as the product of which three risk factors?

(A) Severity $\times$ Probability of hazard exposure $\times$ Patient population size
(B) Frequency of failure $\times$ Cost of correction $\times$ Regulatory impact score
(C) Severity $\times$ Occurrence (probability of failure) $\times$ Detectability (likelihood of non-detection)
(D) Severity $\times$ Number of affected patients $\times$ Time to corrective action

Q19. In pharmaceutical cleaning validation, a Maximum Allowable Carryover (MACO) value is calculated for each drug product manufactured on shared equipment. The primary purpose of the MACO calculation is to ensure what?

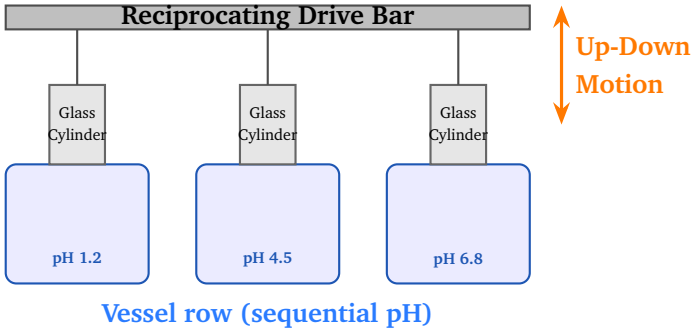
(A) The minimum batch size of the next product is economically viable given the cleaning cost
(B) The maximum allowable campaign length (number of batches) before mandatory equipment cleaning
(C) The microbiological acceptance limit for bioburden on cleaned equipment surfaces
(D) Residual drug from a previous product does not carry over into any single dose of the next product at a level that would be therapeutically active or toxic

Q20. Pharmaceutical change control ensures that modifications to approved processes, equipment, or materials are evaluated, validated if necessary, and approved before implementation. Which of the following changes would **ALWAYS** require initiation of a formal change control process?

(A) Replacing the approved active pharmaceutical ingredient (API) supplier with a different vendor
(B) Changing the font size of a section heading within an internal SOP
(C) Replacing a broken thermocouple with an identical model from the same approved manufacturer

(D) Rearranging office furniture in the administrative area adjacent to the production floor

Q21. The figure below shows a schematic of a USP Dissolution Apparatus.



USP Dissolution Apparatus 3 (reciprocating cylinder) is **PARTICULARLY** suited for testing which type of dosage form?

(A) Immediate-release hard gelatin capsules requiring mechanical agitation to overcome capsule buoyancy

(B) Delayed-release and extended-release pellets or beads where sequential pH changes along the gastrointestinal tract must be simulated

(C) Topical semisolid preparations (creams, gels) where drug release is measured across a synthetic membrane

(D) Enteric-coated tablets requiring only a single pH switch from 1.2 to 6.8

Q22. During high-shear wet granulation, the granulation endpoint must be identified to avoid over-wetting (agglomeration) or under-wetting (poor granule strength). Which in-process test is the **STANDARD** method used to determine when the granulation endpoint has been reached?

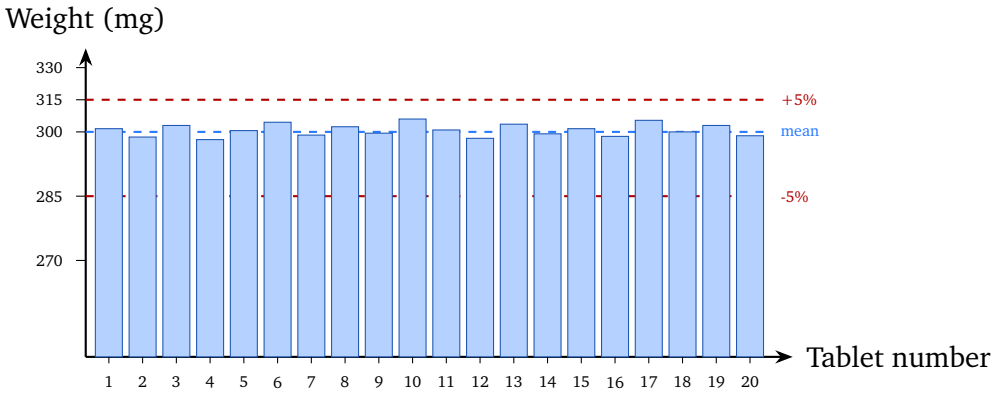
(A) An increase in impeller power consumption (torque) to a pre-set maximum value

(B) Visual inspection of granule size distribution using an inline particle imaging probe

(C) Loss on drying (LOD), measuring granule moisture content by offline moisture analyser or inline NIR spectroscopy

(D) Bulk density measurement using a tapped-density instrument at fixed intervals during mixing

Q23. USP ⟨2091⟩ Weight Variation requires that 20 uncoated tablets are weighed individually. The bar chart below represents individual tablet weights for a batch with average weight of 300 mg.



For this 300 mg uncoated tablet, USP ⟨2091⟩ specifies that individual tablet weights must not deviate from the average by more than:

(A) $\pm 10\%$ of the average weight
(B) $\pm 7.5\%$ of the average weight
(C) $\pm 2.5\%$ of the average weight
(D) $\pm 5\%$ of the average weight

Q24. According to 21 CFR 211.188 (US cGMP regulations for finished pharmaceuticals), which document must be completed and reviewed by the quality unit **before every batch** is released for distribution?

(A) The Batch Production and Control Record (executed master batch record for the specific batch, including weights, process steps, in-process results, and operator signatures)
(B) The Process Validation Report for that product
(C) The Annual Product Review (APR/PQR) covering all batches manufactured in the preceding twelve months
(D) The Equipment Qualification Report (IQ/OQ/PQ) for all manufacturing equipment used in the batch

Q25. ICH Q2(R1) describes several validation characteristics for analytical methods. Which ICH Q2(R1) validation characteristic is defined as the *"capacity of the method to remain unaffected by small, deliberate variations in method parameters"* and is evaluated by intentional perturbation of variables such as pH, column temperature, or mobile-phase composition?

(A) Specificity — the ability to measure the analyte unequivocally in the presence of all expected impurities
(B) Robustness — the capacity of the method to remain unaffected by small, deliberate variations in method parameters
(C) Repeatability — the closeness of agreement between individual results obtained under the same prescribed conditions within a short time period
(D) Linearity — the ability of the method to obtain results directly proportional to analyte concentration within a defined range

Detailed Solutions

Q1.

Solution

Concept — Roller Compaction (Dry Granulation) for Moisture-Sensitive Drugs: Roller compaction compacts dry powder blends between counter-rotating rolls under high pressure to form dense ribbons, which are then milled into granules. The entire process is conducted in the absence of water or any granulating liquid, making it the method of choice when the drug substance is susceptible to hydrolytic degradation on contact with moisture.

Step 1 — Compare process conditions: Wet granulation: granulating liquid (water, ethanol, or aqueous binder solution) is added to powder; drying step required. Exposure to water at elevated temperature during drying poses a degradation risk for moisture-sensitive drugs.

Step 2 — Identify the primary advantage of roller compaction: Roller compaction uses no solvent. The powder is consolidated solely by mechanical pressure (compaction force on rolls). Chemical integrity of the drug is preserved because no aqueous exposure occurs. This is the defining advantage over wet granulation for moisture-sensitive APIs.

Why other options are wrong:

- Option A: Roller compaction does not universally produce larger granules that improve bioavailability; granule size is controlled by milling and roll force.
- Option B: Absence of liquid water prevents hydrolytic degradation of the moisture-sensitive drug. **Correct.**
- Option C: Roller compacted granules can be less plastic than wet granules; tablet hardness is not automatically superior.
- Option D: Roller compacted tablets still require disintegrants; dry granulation does not eliminate this need.

Final Answer: Roller compaction avoids all water exposure $\Rightarrow$ chemical integrity of moisture-sensitive drug is preserved $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q1

Q2.

Solution

Concept — Spray-Dried Particle Morphology: In spray drying, the feed solution is atomised into fine droplets. As the droplets travel through the hot drying chamber, rapid evaporation of solvent from the droplet surface creates a shell while the interior remains liquid briefly. Continued drying produces a hollow sphere (cenosphere). This distinct morphology confers low bulk density (high porosity) and improved powder flow due to the spherical shape reducing inter-particle friction.

Step 1 — Explain hollow sphere formation: Rapid surface drying locks the outer shell before the interior fully dries, trapping residual gas and forming a hollow centre. The resulting particles are approximately spherical with smooth surfaces, which minimises contact points between particles and improves flowability.

Step 2 — Compare with wet granulation output: Wet granules are typically irregular, denser, and less spherical, with lower flowability unless spheronised or coated. Spray-dried particles have the opposite characteristics.

Why other options are wrong:

- Option A: Dense, irregular shards describe milled material, not spray-dried particles.
- Option B: Elongated needles describe certain crystallisation products or milled fibre-like materials, not spray-dried output.
- Option C: Hollow spheres with low bulk density and good flowability accurately describe spray-dried particles. **Correct.**
- Option D: Spray drying typically produces amorphous material with broader PSD; additional milling is not the defining feature.

Final Answer: Spray drying produces hollow spherical cenospheres with low bulk density and improved flowability $\Rightarrow$ C

Answer: (C) Go Back to Q2

Q3.

Solution

Concept — Physical Stability of Amorphous Solid Dispersions and T_g: The physical stability of an amorphous solid dispersion (ASD) is governed by molecular mobility in the amorphous matrix. Below T_g, the system is in a kinetically frozen, glassy state with very low molecular mobility, minimising nucleation and crystal growth. The empirical $T_g - 50°C$ rule provides a conservative safety margin: storage at $T \leq T_g - 50°C$ ensures mobility is suppressed and recrystallisation is negligible on pharmaceutical shelf-life timescales.

Step 1 — Apply the stability rule: $T_{\text{max,storage}} = T_g - 50°C = 115°C - 50°C = 65°C$.

Step 2 — Evaluate each option: $115°C$: at T_g itself — glass transition zone, mobility increasing rapidly, unacceptable.
$90°C$: only $25°C$ below T_g — insufficient margin; mobility significant.
$75°C$: $40°C$ below T_g — borderline; standard guideline demands $50°C$ margin.
$65°C$: exactly $T_g - 50°C$ — satisfies the stability rule. **Correct.**

Why other options are wrong:

- Option A: Storage at T_g provides no thermal safety margin; the ASD would be at its glass transition, where relaxation and crystallisation are facile.
- Option B: $T_g - 25°C$ is insufficient; conventional practice requires at least $50°C$ margin below T_g.
- Option C: $T_g - 40°C$ is a common intermediate rule but does not satisfy the stringent $50°C$ criterion.
- Option D: $T_g - 50°C = 65°C$ satisfies the standard stability guideline for ASDs. **Correct.**

Final Answer: $T_{\text{max}} = 115 - 50 = 65°C \Rightarrow$ D

Answer: (D) Go Back to Q3

Q4.

Solution

Concept — Polymer Selection for Hot Melt Extrusion: HME requires a polymer that (i) is thermoplastic: it softens and flows under heat and shear above its T_g without degrading, (ii) has a T_g amenable to processing (typically $80–160°C$), and (iii) provides good drug miscibility to inhibit drug recrystallisation in the solid dispersion. Kollidon VA 64 (copovidone: vinylpyrrolidone–vinyl acetate 60:40 copolymer) has $T_g \approx 105°C$, is thermoplastic, and is highly miscible with many

small-molecule drugs through hydrogen bonding.

Step 1 — Evaluate Kollidon VA 64: $T_g \approx 105°$C; extrusion temperature 120–160°C (well above T_g, within thermal stability window). Strong hydrogen-bond acceptor/donor sites promote drug–polymer miscibility. Widely validated in HME for amorphous solid dispersions.

Step 2 — Eliminate other options: HEC: cellulosic ether with no thermoplastic behaviour; does not soften homogeneously for extrusion.
HPMC E5: also cellulosic, high degradation temperature ($> 200°$C), poor thermoplasticity without added plasticiser; generally unsuitable for standard HME.
Calcium carbonate: inorganic filler with no polymer properties; cannot form a thermoplastic melt.

Why other options are wrong:

- Option A: Kollidon VA 64 is thermoplastic, with $T_g \approx 105°$C and excellent drug miscibility. **Correct.**
- Option B: HEC lacks thermoplastic flow below its degradation temperature.
- Option C: HPMC E5 degrades before adequate softening; requires significant plasticiser addition.
- Option D: Calcium carbonate is not a polymer and does not contribute thermoplastic behaviour.

Final Answer: Kollidon VA 64 ($T_g \approx 105°$C, thermoplastic, high drug miscibility) is the optimal HME polymer $\Rightarrow$ A

Answer: (A) Go Back to Q4

Q5.

Solution

Concept — Punch Tip Surface Treatment to Prevent Picking/Sticking: Picking and sticking occur when tablet mass adheres to the punch face and is removed from the tablet surface on punch withdrawal. This arises from excessive adhesion between the formulation and the punch metal (often stainless steel). PTFE (polytetrafluoroethylene) coating provides an extremely low surface energy, non-stick surface. Its coefficient of friction ($\mu \approx 0.04$) is among the lowest of any solid material, dramatically reducing adhesion and the tendency for material to plate onto punch faces.

Step 1 — Why PTFE is preferred: PTFE's low surface energy prevents strong adhesive bonds between the punch face and the polar functional groups of excip-

ients (cellulose, lactose). The electropolished PTFE surface leaves no microscopic surface irregularities for material to anchor in.

Step 2 — Evaluate other options: Chrome plating on the shank only does not protect the punch face where contact occurs.
Sodium lauryl sulfate spray is not a documented anti-sticking punch treatment and would introduce a variable process step.
Mirror polishing reduces but does not eliminate sticking; PTFE coating is far more effective.

Why other options are wrong:

- Option A: Chrome plating of the punch shank does not address face sticking.
- Option B: PTFE coating of punch faces provides the lowest surface energy and best anti-stick performance. **Correct.**
- Option C: SLS spray is not a standard or validated anti-sticking punch treatment.
- Option D: Mirror polishing alone is insufficient; formulations with high tack still stick to polished steel.

Final Answer: PTFE-coated punch faces minimise adhesion and picking during tablet compression $\Rightarrow$ B

Answer: (B) Go Back to Q5

Q6.

Solution

Concept — Diametral Tensile Strength of Tablets: The diametral (indirect) tensile strength test applies a compressive load across the diameter of a tablet placed on its side. At fracture, the tensile stress developed perpendicular to the loading axis is calculated by:

$$\sigma_T = \frac{2F}{\pi D H}$$

where F is the fracture force (N), D is the tablet diameter (m), and H is the tablet height (m). The result is in Pa; divide by 10^6 to convert to MPa.

Step 1 — Convert units: $F = 107\,\text{N}$; $D = 10\,\text{mm} = 0.010\,\text{m}$; $H = 4\,\text{mm} = 0.004\,\text{m}$.

Step 2 — Calculate σ_T:

$$\sigma_T = \frac{2 \times 107}{\pi \times 0.010 \times 0.004} = \frac{214}{1.2566 \times 10^{-4}} = 1.703 \times 10^6\,\text{Pa} \approx 1.70\,\text{MPa}$$

Why other options are wrong:

- Option A: 0.85 MPa would result from $F \approx 53$ N, not 107 N.
- Option B: 1.07 MPa would require an arithmetic error (e.g., omitting the factor of 2 in the numerator would give $107/(\pi \times 0.010 \times 0.004) \approx 0.85$ MPa, not 1.07).
- Option C: $\sigma_T = 2 \times 107/(\pi \times 0.010 \times 0.004) \approx 1.70$ MPa. **Correct.**
- Option D: 3.40 MPa would result from $F \approx 214$ N (double the given value).

Final Answer: $\sigma_T = 2 \times 107/(\pi \times 0.010 \times 0.004) \approx 1.70$ MPa $\Rightarrow$ C

Answer: (C) Go Back to Q6

Q7.

Solution

Concept — USP ⟨905⟩ Acceptance Value (AV): USP ⟨905⟩ Content Uniformity uses the Acceptance Value (AV) as the decision criterion. The AV combines two components: the absolute mean deviation (distance of the sample mean $\bar{X}$ from the reference value M) and the product of a coverage factor k with the sample standard deviation s (a measure of spread). Together these capture both bias and variability:

$$\text{AV} = |M - \bar{X}| + k \cdot s$$

The acceptance criterion is AV $\leq$ L1 (15.0%) at the first stage (10 units); if AV $>$ L1 but $\leq$ L2 (25.0%), a second stage of 20 additional units is tested.

Step 1 — Understand the two-component structure of AV: $|M - \bar{X}|$ penalises formulations whose mean deviates from the label claim.
$k \cdot s$ penalises formulations with high content variability (poor uniformity).

Step 2 — Distinguish from simpler criteria: RSD alone (Option A) does not account for mean bias. Mean alone (Option C) ignores variability. AV uniquely combines both, as stated in Option D.

Why other options are wrong:

- Option A: RSD alone ignores mean bias; a batch could have low RSD but biased mean, yet still fail AV.
- Option B: Mean deviation alone ignores within-batch variability, which is central to content uniformity.
- Option C: The arithmetic mean does not assess uniformity; it only confirms average potency.

- Option D: AV $= |M - \bar{X}| + k \cdot s$ incorporates both mean deviation and variability. **Correct.**

Final Answer: AV combines absolute mean deviation $|M - \bar{X}|$ and variability $k \cdot s$ $\Rightarrow$ D

Answer: (D) Go Back to Q7

Q8.

Solution

Concept — Biorelevant Dissolution Media for BCS Class II Drugs: BCS Class II drugs have low aqueous solubility but high permeability; their oral absorption is dissolution-rate limited. In simple pH buffers, their solubility is often under-predicted because bile salts and phospholipids present in intestinal fluid significantly enhance solubility via mixed micelle formation. FaSSIF (Fasted State Simulated Intestinal Fluid) contains sodium taurocholate (3 mM), lecithin (0.75 mM) and NaH_2PO_4/NaOH buffer at pH 6.5, closely mimicking the solubilising capacity of human fasted intestinal contents.

Step 1 — Mechanism of FaSSIF enhancement: Bile salt/lecithin mixed micelles solubilise lipophilic BCS Class II drugs far above their intrinsic aqueous solubility. This better captures in-vivo dissolution conditions, enabling a Level A IVIVC where changes in dissolution directly predict changes in bioavailability.

Step 2 — Eliminate other media: 0.1 N HCl mimics only gastric conditions; no bile salt present.
pH 6.8 phosphate buffer lacks the surfactant component essential for lipophilic drug solubilisation.
Purified water has no buffer capacity or solubilising agent; it severely underestimates in-vivo conditions.

Why other options are wrong:

- Option A: FaSSIF (pH 6.5 with bile salts and lecithin) best mimics fasted small intestinal fluid and enables IVIVC for BCS Class II drugs. **Correct.**
- Option B: 0.1 N HCl models only gastric conditions without intestinal solubilising components.
- Option C: Plain phosphate buffer (pH 6.8) lacks bile salts; drug solubility is under-predicted.
- Option D: Purified water is the least biorelevant medium for poorly soluble compounds.

Final Answer: FaSSIF (pH 6.5, bile salts + lecithin) best mimics in-vivo intestinal conditions for BCS Class II $\Rightarrow$ A

Answer: (A) Go Back to Q8

Q9.

Solution

Concept — Plasticiser Function in HPMC Film Coating: Triethyl citrate (TEC) is a non-volatile, water-miscible ester plasticiser. Its small molecules insert between HPMC polymer chains, reducing intermolecular cohesion and increasing free volume. This lowers the glass transition temperature (T_g) of the polymer film. A lower T_g means the film becomes rubbery (flexible) at the tablet coating temperature, preventing the brittle fracture (cracking) that would otherwise occur in an unplasticised, glassy film during pan coating, tablet handling, or packaging.

Step 1 — Mechanism of plasticisation: TEC disrupts hydrogen bonding and Van der Waals interactions between HPMC chains. The resulting increase in chain mobility lowers T_g from approximately $175°$C (pure HPMC) to below $100°$C at 15–20% TEC, keeping the film above its T_g during ambient storage (flexible, not brittle).

Step 2 — Impact on elongation at break: Plasticised HPMC films have substantially greater elongation at break and lower tensile modulus, allowing the film to deform elastically under mechanical stress without cracking.

Why other options are wrong:

- Option A: Pore forming is the role of water-soluble excipients like PEG, not a hydrophobic ester like TEC in an immediate-release HPMC film.
- Option B: Lowering T_g of HPMC to impart flexibility and prevent cracking is the primary function of TEC. **Correct.**
- Option C: Suspension viscosity is controlled by polymer concentration and processing parameters, not by plasticiser addition.
- Option D: Anti-tack action is provided by talc or colloidal silicon dioxide, not by TEC.

Final Answer: TEC plasticises HPMC by lowering T_g $\Rightarrow$ flexible film, prevents cracking $\Rightarrow$ B

Answer: (B) Go Back to Q9

Q10.

Solution

Concept — Sugar Coating Stages: Sealing Coat: The conventional sugar coating process follows a defined sequence: (1) Sealing coat, (2) Subcoating, (3) Syruping/smoothing, (4) Colouring, (5) Polishing. The sealing coat (Stage 1) is applied as a solution of a hydrophobic material such as shellac (zein or HPMC are modern alternatives) dissolved in alcohol or applied as an aqueous dispersion. Its sole purpose is to form a water-impermeable barrier around the tablet core before subsequent aqueous sucrose syrup coating stages, which involve large volumes of water.

Step 1 — Purpose of sealing: Without sealing, the aqueous sucrose syrup applied during subcoating would penetrate the unprotected core, dissolving the binder, softening the core, and causing chemical degradation of moisture-sensitive drugs. The sealant film prevents water ingress throughout all remaining stages.

Step 2 — Distinguish sealing from other stages: Colouring (Stage 4) and polishing (Stage 5) occur much later in the sequence.
Subcoating (Stage 2) builds tablet roundness; it occurs after sealing.
Polishing (Stage 5) applies wax for gloss; occurs last.

Why other options are wrong:

- Option A: Colour application is Stage 4, not Stage 1 (sealing).
- Option B: Building up bulk and rounding edges is the function of the subcoating stage (Stage 2), not the sealing stage.
- Option C: The sealing coat protects the core from moisture during subsequent aqueous coating stages. **Correct.**
- Option D: Wax polishing is the final (Stage 5) step, not Stage 1.

Final Answer: Sealing coat forms a moisture barrier protecting the core during aqueous sugar coating stages $\Rightarrow$ C

Answer: (C) Go Back to Q10

Q11.

Solution

Concept — Aquacoat ECD Film Formation and Minimum Film-Forming Temperature (MFT): Aquacoat ECD is a 30% w/w aqueous pseudolatex of ethylcellulose (EC) spheres stabilised by sodium lauryl sulfate and cetyl alcohol. On drying after pan coating, the discrete EC latex particles must coalesce into a continuous, coherent, water-insoluble film. Coalescence only occurs when the drying/curing temperature exceeds the minimum film-forming temperature (MFT) of the dispersion. Below MFT, particles remain discrete and the "film" is powdery and discontinuous, offering no barrier function. Plasticisers (e.g., dibutyl sebacate, triethyl citrate) lower the MFT to $\leq 60^{\circ}$C, making the film formation achievable under practical coating conditions.

Step 1 — Identify the critical parameter: MFT is the minimum temperature at which EC latex particles deform and coalesce into a continuous film. If the pan or curing temperature is below MFT, no coalescence occurs regardless of spray rate or other parameters. This makes curing temperature relative to MFT the critical parameter.

Step 2 — Consequence of under-curing: If the coating pan dries the coat below MFT, particle packing occurs but no fusion; the film is porous and non-functional for controlled release. Post-coating curing at $\geq$MFT resolves this.

Why other options are wrong:

- Option A: Inlet air temperature influences drying efficiency but not directly the coalescence threshold; MFT of the polymer itself is the governing parameter.
- Option B: Tablet core hardness does not affect polymer film coalescence.
- Option C: Solids concentration affects coat weight build-up, not polymer chain mobility or coalescence.
- Option D: Curing temperature relative to MFT determines whether coalescence into a continuous film occurs. **Correct.**

Final Answer: Curing temperature $\geq$ MFT of Aquacoat ECD is essential for continuous film formation $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q11

Q12.

Solution

Concept — Cellulose Acetate Phthalate (CAP) Enteric Dissolution pH: CAP is an enteric coating polymer formed by esterification of cellulose acetate with phthalic anhydride. The phthalyl half-ester carboxylate groups ($-$COOH, p$K_a \approx 5.7$) remain protonated and the polymer is insoluble at gastric pH (≤ 2). As the pH rises in the proximal small intestine, the carboxylate groups ionise (deprotonate) above pH 6.0, the polymer chains become hydrophilic and soluble, and the enteric coat dissolves. This pH threshold ensures gastric protection while providing complete release in the duodenum/jejunum.

Step 1 — Ionisation of phthalyl groups: p$K_a \approx 5.7$. At pH 6.0 (one pH unit above pK_a), ionised fraction $\approx 95\%$. The cumulative hydrophilicity at pH > 6.0 exceeds the threshold for macroscopic polymer dissolution.

Step 2 — Comparison with other enteric polymers: HPMCP HP-55 dissolves at pH > 5.5; Eudragit L 100 at pH > 6.0; Eudragit S 100 at pH > 7.0. CAP and Eudragit L 100 share the pH > 6.0 threshold.

Why other options are wrong:

- Option A: pH > 6.0 is the correct dissolution threshold for CAP. **Correct.**
- Option B: pH > 5.0 is below CAP's threshold; CAP remains insoluble at pH 5.0 to 6.0.
- Option C: pH > 7.0 is the dissolution threshold for Eudragit S 100, not CAP.
- Option D: pH > 4.5 would describe a more rapidly dissolving polymer; CAP requires pH > 6.0.

Final Answer: CAP dissolves at pH > 6.0 due to ionisation of phthalyl carboxylate groups $\Rightarrow$ A

Answer: (A) Go Back to Q12

Q13.

Solution

Concept — Mechanism of Croscarmellose Sodium (CCS) as Superdisintegrant: Croscarmellose sodium is a cross-linked sodium carboxymethylcellulose. The cross-links prevent dissolution while the highly hydrophilic carboxymethyl groups wick water into the particle with extraordinary speed. The absorbed water causes the CCS particle to swell 10–20 times its dry volume. This enormous volumetric expansion generates hydrostatic swelling pressure within the compact that

exceeds the tensile strength of the tablet matrix, rupturing it rapidly. This swelling mechanism distinguishes superdisintegrants from conventional starch (which primarily wicks but swells only $\sim$2–3$\times$).

Step 1 — Quantify swelling capacity: CCS swells to $\sim$10–20$\times$ original volume in water. Comparison: sodium starch glycolate $\sim$10$\times$; crospovidone acts mainly by wicking/deformation recovery; unmodified starch $\sim$2–3$\times$.

Step 2 — Distinguish from other mechanisms: CCS is not water-soluble (cross-linked), so osmotic dissolution pressure is not the mechanism.
CCS does not produce gas; effervescent mechanisms require acid–base pairs.
CCS does not form drug inclusion complexes.

Why other options are wrong:

- Option A: CCS is cross-linked and does not dissolve; osmotic pressure from CCS dissolution is not the mechanism.
- Option B: Volumetric swelling 10–20$\times$ generating hydrostatic pressure is the correct mechanism. **Correct.**
- Option C: Effervescence requires CO_2 generation from acid–base reaction; CCS has no such chemistry.
- Option D: CCS does not form inclusion complexes with drugs; this is a cyclodextrin property.

Final Answer: CCS swells 10–20$\times$ in volume $\Rightarrow$ hydrostatic pressure ruptures tablet matrix $\Rightarrow$ B

Answer: (B) Go Back to Q13

Q14.

Solution

Concept — US Mesh Sieve Numbers and Aperture Sizes: The US mesh number indicates the number of square openings per linear inch. Higher mesh numbers correspond to finer sieves (smaller apertures). Standard aperture sizes for key mesh numbers:

US Mesh	Aperture (μm)
10	2000
20	841
40	420
60	250
80	177
120	125
200	74

Step 1 — Identify US mesh 60: US mesh 60 = 250 μm aperture. This is a commonly used sieve for classifying granules used in tablet manufacturing ($<250\,\mu$m fraction = fines; $>250\,\mu$m = coarse granules in many specifications).

Why other options are wrong:

- Option A: US mesh 20 has aperture $\approx 841\,\mu$m (much coarser).
- Option B: US mesh 40 has aperture $\approx 420\,\mu$m (intermediate).
- Option C: US mesh 60 has aperture $\approx 250\,\mu$m. **Correct.**
- Option D: US mesh 120 has aperture $\approx 125\,\mu$m (much finer).

Final Answer: US mesh 60 $\approx 250\,\mu$m aperture $\Rightarrow$ C

Answer: (C) Go Back to Q14

Q15.

Solution

Concept — DSC-Based Excipient Compatibility Screening: In DSC binary mix studies, the thermal event of the drug (typically a sharp melting endotherm) and the excipient are compared in their pure forms and in a 1:1 (or other ratio) physical mixture. Absence of interaction: the binary mix thermogram approximates the sum of both individual traces (superimposable). Drug–excipient incompatibility is most reliably indicated by the appearance of a new thermal event (especially an exothermic peak) at a temperature different from either individual component, or by complete disappearance/major shift of the drug melting endotherm.

Step 1 — Interpret the figure: Orange trace (binary mix): new exothermic peak at ~100°C, lower than both the excipient endotherm (~120°C) and the drug endotherm (~180°C). This exotherm indicates an energetically favourable intermolecular interaction (e.g., eutectic formation, solid-state reaction, or co-crystal formation) between drug and excipient — a clear sign of incompatibility.

Step 2 — Why new exotherm at lower temperature is diagnostic: A lower-temperature exotherm indicates the drug–excipient pair undergoes a spontaneous, exothermic reaction below the melting/decomposition temperatures of the individual components. In stability terms this means the two materials react under storage conditions, compromising drug potency, purity, or stability.

Why other options are wrong:

- Option A: A shift to higher temperature would suggest enhanced crystallinity or stabilisation, not incompatibility.
- Option B: A sharper, taller melting endotherm would indicate increased crystallinity or crystal perfection, not incompatibility.
- Option C: Superimposable traces indicate no interaction (compatibility).
- Option D: A new exothermic peak at lower temperature is the definitive DSC indicator of drug–excipient incompatibility. **Correct.**

Final Answer: New exothermic peak in binary mix $<$ either component's thermal event $\Rightarrow$ drug–excipient incompatibility $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q15

Q16.

Solution

Concept — NIR PAT Blend Monitoring and MBSD Endpoint: Near-infrared spectroscopy measures the spectral composition of the blend in real time. As mixing proceeds, the composition of the blend at the probe location becomes progressively more uniform. The Moving Block Standard Deviation (MBSD) calculates the standard deviation of a set of consecutive NIR spectra in a sliding window. When blending is incomplete, spectra vary substantially (high MBSD). As the blend approaches uniformity, spectral variation decreases. The endpoint is defined as the point at which MBSD reaches a minimum value and remains stationary (plateau) — indicating that no further compositional change is occurring and a homogeneous blend has been achieved.

Step 1 — Interpret MBSD behaviour: High initial MBSD: heterogeneous blend, spectra changing rapidly.
Decreasing MBSD: blend becoming progressively more uniform.
Plateau MBSD: blend uniformity is stable $\Rightarrow$ endpoint reached.

Step 2 — USP ⟨1120⟩ PAT guidance: USP ⟨1120⟩ supports MBSD plateau as a scientifically sound endpoint criterion for blend uniformity monitoring. It replaces

time-based blending endpoints with outcome-based determination.

Why other options are wrong:

- Option A: MBSD reaching a stationary minimum plateau indicates blend endpoint. **Correct.**
- Option B: NIR absorbance does not reach a "theoretical maximum" at the endpoint; the signal reaches a stable, uniform value.
- Option C: RSD exceeding 5% indicates poor uniformity (non-compliance), not endpoint.
- Option D: Blender temperature drop is unrelated to blend uniformity; it is not a PAT endpoint indicator.

Final Answer: MBSD reaches a minimum plateau $\Rightarrow$ blend is homogeneous $\Rightarrow$ endpoint reached $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept — ICH Q8(R2) Design Space Definition: ICH Q8(R2) *Pharmaceutical Development* introduces the concept of design space as a formal element of Quality-by-Design (QbD). The design space is defined as: *"The multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality."* Working within the design space is not considered a change from the approved submission; movement outside the design space requires a regulatory change notification.

Step 1 — Key elements of the ICH Q8 definition: (i) Multidimensional: encompasses multiple critical material attributes (CMAs) and critical process parameters (CPPs) simultaneously.
(ii) Demonstrated: supported by experimental evidence (DoE, mechanistic models).
(iii) Assurance of quality: all critical quality attributes (CQAs) meet specifications within the space.

Step 2 — Distinguish design space from other concepts: Raw material specifications (Option A) are part of CMAs but not the full design space.
Regulatory equipment settings (Option C) do not constitute a design space without quality demonstration.
A single optimal process (Option D) is a control strategy, not a multidimensional

space.

Why other options are wrong:

- Option A: Raw material specifications are one input dimension, not the entire multidimensional design space.
- Option B: Multidimensional combination of CMAs and CPPs demonstrated to assure quality. **Correct; verbatim ICH Q8 definition.**
- Option C: Equipment settings without demonstrated quality assurance are not a design space.
- Option D: A single optimal formula is a point, not a multidimensional space.

Final Answer: Design space = multidimensional CMAs $\times$ CPPs demonstrated to provide quality assurance $\Rightarrow$ B

Answer: (B) Go Back to Q17

Q18.

Solution

Concept — FMEA Risk Priority Number (RPN): Failure Mode and Effects Analysis (FMEA) is a bottom-up, prospective risk assessment tool listed in ICH Q9. For each identified failure mode, three risk factors are assessed on numerical scales (typically 1–10):

- **Severity (S)**: how serious are the consequences of the failure?
- **Occurrence (O)**: how frequently does the failure mode arise?
- **Detectability (D)**: what is the likelihood of failing to detect the failure before it reaches the patient? (Low detectability = high D-score)

The Risk Priority Number is:

$$\text{RPN} = S \times O \times D$$

High RPN values flag process steps or material interactions requiring risk mitigation or enhanced controls.

Step 1 — Role of Detectability in RPN: Detectability score is inverted: a score of 10 means the failure is nearly undetectable. An undetectable, severe, frequent failure would have the highest possible RPN, demanding immediate corrective action.

Why other options are wrong:

- Option A: "Probability of hazard exposure" is not a standard FMEA factor; the three factors are Severity, Occurrence, Detectability.
- Option B: Cost and regulatory impact are not FMEA risk scoring parameters.
- Option C: RPN $=$ Severity $\times$ Occurrence $\times$ Detectability is the correct ICH Q9 FMEA formula. **Correct.**
- Option D: Number of affected patients and time to correction are not standard FMEA parameters.

Final Answer: RPN $=$ Severity $\times$ Occurrence $\times$ Detectability $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q18

Q19.

Solution

Concept — Cleaning Validation MACO Calculation: When the same equipment is used to manufacture different drug products in sequence (campaign manufacturing), residual drug from the preceding product may contaminate the next product. The Maximum Allowable Carryover (MACO) calculation determines the maximum mass of residual drug that may remain on equipment after cleaning without posing a safety or therapeutic concern to patients receiving the next product.

Step 1 — MACO calculation rationale: The most common approach ensures that the residual does not contribute more than 1/1000th of the minimum therapeutic dose of the preceding product to the maximum daily dose of the next product. Alternatively, the MACO is based on the No-Observed-Effect Level (NOEL) or the Acceptable Daily Intake (ADI) of the residue. The patient safety criterion is paramount: no carryover at a level that is pharmacologically active or toxic.

Step 2 — Practical criterion (10-ppm or 0.1% dose): In practice: residue per dose of next product $\leq 0.001\times$ minimum therapeutic dose of residue drug, or ≤ 10 ppm in next product. Both approaches share the same patient-protective intent.

Why other options are wrong:

- Option A: Economic viability of batch size is irrelevant to MACO; MACO is a patient safety parameter.
- Option B: Campaign length between cleaning events is set by a separate campaign policy, not by MACO.
- Option C: Microbiological bioburden limits are set by environmental monitoring standards, not MACO.

- Option D: Ensuring no therapeutic/toxic residue dose reaches the patient via the next product is the MACO objective. **Correct.**

Final Answer: MACO ensures residual drug cannot reach a pharmacologically active or toxic dose in the next product $\Rightarrow$ D

Answer: (D) Go Back to Q19

Q20.

Solution

Concept — Change Control in Pharmaceutical Manufacturing: Change control is a formal system mandated by GMP (21 CFR 211, ICH Q10) that ensures all modifications to approved processes, specifications, materials, equipment, or facilities are documented, assessed for potential impact on product quality and regulatory compliance, validated or verified as necessary, approved before implementation, and reported to regulatory authorities when required. A change to the API supplier is a significant change that could affect drug substance purity, polymorphic form, particle size, impurity profile, and ultimately product CQAs. It requires full change control, compatibility testing, potentially new validation batches, and a regulatory filing.

Step 1 — Evaluate each option: Replacing an API supplier: changes the material being introduced into the product — high potential impact on quality. Always requires formal change control.
Font change in SOP: administrative change with no quality impact; typically requires document control, not formal change control.
Identical replacement thermocouple: like-for-like replacement; managed via maintenance records, not formal change control.
Office furniture rearrangement: no GMP relevance.

Why other options are wrong:

- Option A: Replacing the API supplier requires formal change control; different vendors have different manufacturing processes, impurity profiles, and material attributes. **Correct.**
- Option B: Changing font size in a heading of an SOP is an administrative document control action, not a quality-impact change requiring full change control.
- Option C: A like-for-like replacement of an identical instrument model from the same manufacturer is a routine maintenance action, not a GMP change.
- Option D: Office furniture has no GMP impact; change control is reserved

for quality-relevant changes.

Final Answer: API supplier change has potential quality/regulatory impact ⇒ always requires formal change control ⇒ A

Answer: (A) Go Back to Q20

Q21.

Solution

Concept — USP Dissolution Apparatus 3 (Reciprocating Cylinder): USP Apparatus 3 consists of a row of glass vessels (typically 3 or 6 per row) containing different dissolution media (e.g., pH 1.2, 4.5, 6.8) at controlled temperatures. Glass cylinders containing the dosage form are attached to a reciprocating drive bar that moves them up and down repeatedly into successive pH-staged vessels. This reciprocating motion simulates peristaltic movement and the progressive pH change along the gastrointestinal tract. Apparatus 3 is uniquely suited for extended-release beads, pellets, mini-tablets, and delayed-release systems where the pH-change kinetics critically influence drug release.

Step 1 — Unique features of Apparatus 3: Sequential pH exposure in the same run mimics the pH gradient from stomach (pH 1.2) through duodenum/jejunum (pH 4.5–6.8) to ileum/colon. This is not possible with Apparatus 1 or 2 without manual media changes.

Step 2 — Compare with other apparatus: Apparatus 1 (basket) and 2 (paddle): single-compartment, single medium; suited for IR and simple extended-release tablets.
Apparatus 4 (flow-through cell): for very low-solubility compounds.
Apparatus 3: specifically intended for multiparticulate and delayed-release forms with complex pH-dependent release.

Why other options are wrong:

- Option A: Immediate-release capsules are best tested with Apparatus 1 or 2; reciprocating cylinder is over-specified.
- Option B: Pellets and beads requiring sequential pH simulation for delayed/extended release. **Correct.**
- Option C: Topical semisolids use Apparatus 4 or Franz diffusion cells, not Apparatus 3.
- Option D: Enteric-coated tablets requiring only a single pH switch are well served by Apparatus 1 or 2 with medium change; Apparatus 3 is not required.

Final Answer: Apparatus 3 simulates sequential GI pH changes ⇒ optimal for extended-release pellets/beads ⇒ B

Answer: (B) Go Back to Q21

Q22.

Solution

Concept — In-Process LOD Measurement as Wet Granulation Endpoint: In wet granulation, the granulation endpoint is the point at which the granule has the correct moisture content, particle size, and mechanical properties for subsequent drying and compression. Loss on drying (LOD) measures the mass of water removed from a granule sample when dried to constant weight, expressed as % of original weight. LOD values are:

- Too high (>6%): granules over-wetted; agglomeration and slow drying likely.
- Optimal (≈2–4%): granules have adequate binder bridges; good compression.
- Too low (<1%): insufficient liquid; granules lack strength; excessive fines.

LOD is measured offline using a halogen/infrared moisture analyser or inline using NIR (Process Analytical Technology), providing real-time endpoint determination.

Step 1 — Distinguish LOD from torque/impeller power: Torque/power consumption (Option A) is an indirect method sensitive to bowl load and rheology changes; LOD is more specific and quantitative. LOD is the ICH/USP-recognized standard endpoint parameter.

Step 2 — NIR as inline LOD method: NIR quantifies water via O-H overtone/combination bands in the 1400–2000 nm region. It provides real-time, non-destructive LOD measurement without sampling, directly measuring the moisture driving force for granule drying endpoint.

Why other options are wrong:

- Option A: Impeller torque/power is a supplementary endpoint indicator, not the primary standard method.
- Option B: Inline particle imaging provides particle size but not moisture content; size changes can be misleading in overwet granulations.
- Option C: LOD by moisture analyser or inline NIR is the standard, direct in-process endpoint measurement. **Correct.**

- Option D: Bulk/tapped density is a post-drying characterisation parameter, not an endpoint indicator during granulation.

Final Answer: LOD (moisture content by moisture analyser or inline NIR) is the standard wet granulation endpoint parameter $\Rightarrow$ C

Answer: (C) Go Back to Q22

Q23.

Solution

Concept — USP ⟨2091⟩ Weight Variation Acceptance Limit: USP ⟨2091⟩ Weight Variation for uncoated tablets specifies the maximum allowable percentage deviation of individual tablet weights from the average weight. The limits depend on tablet weight:

Average tablet weight	Maximum allowed deviation
< 80 mg	$\pm 10\%$
80 mg to < 250 mg	$\pm 7.5\%$
≥ 250 mg	$\pm 5\%$

Not more than 2 tablets out of 20 may deviate beyond the specified percentage, and no tablet may deviate by more than twice the percentage.

Step 1 — Identify the relevant weight category: Average weight $= 300$ mg. This falls in the ≥ 250 mg category.
Applicable limit: $\pm 5\%$.

Step 2 — Calculate acceptable weight range: 5% of 300 mg $= 15$ mg. Acceptable individual weight: 285–315 mg.

Why other options are wrong:

- Option A: $\pm 10\%$ applies only to tablets weighing < 80 mg.
- Option B: $\pm 7.5\%$ applies to tablets weighing 80–249 mg.
- Option C: $\pm 2.5\%$ is not a pharmacopoeial weight variation limit.
- Option D: $\pm 5\%$ is correct for tablets ≥ 250 mg (including 300 mg). **Correct.**

Final Answer: 300 mg tablet ≥ 250 mg $\Rightarrow$ USP ⟨2091⟩ limit $= \pm 5\% \Rightarrow$ D

Answer: (D) Go Back to Q23

Q24.

Solution

Concept — Batch Production and Control Records (21 CFR 211): 21 CFR 211.188 requires that a batch production and control record be prepared for each batch of drug product. This record, executed from the master batch record, must include: the complete list of ingredients, actual weights and measures of each component, identification of all equipment used, each significant step in manufacture, in-process and laboratory control results, the date and signature of persons performing and/or supervising each step, and results of examinations performed. This document must be reviewed and approved by the quality unit before the batch is released for distribution.

Step 1 — Purpose of batch record review: The quality unit's review verifies that the batch was manufactured and controlled in compliance with the approved procedure and meets all specifications before any product reaches patients.

Step 2 — Distinguish from other documents: Process Validation Reports are executed once per validated process, not for every batch.
APR/PQR covers historical trends; it is not prepared or reviewed before each batch release.
Equipment qualification reports are one-time documents for equipment commissioning, not batch-specific.

Why other options are wrong:

- Option A: The executed batch production and control record is prepared and reviewed before every batch release per 21 CFR 211.188. **Correct.**
- Option B: Process Validation Report is prepared per validated process, not per individual batch.
- Option C: APR/PQR is an annual document; it is not batch-specific nor a pre-release requirement.
- Option D: Equipment qualification reports are static documents completed at equipment commissioning, not reviewed per batch.

Final Answer: The Batch Production and Control Record (21 CFR 211.188) must be completed and reviewed before every batch is released $\Rightarrow$ A

Answer: (A) Go Back to Q24

Q25.

Solution

Concept — ICH Q2(R1) Analytical Method Validation — Robustness: ICH Q2(R1) defines robustness as: *"A measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage."* Robustness is evaluated by intentionally perturbing method parameters and measuring the effect on analytical results. Typical variables explored include: mobile phase pH (± 0.2 units), column temperature ($\pm 5^{\circ}$C), mobile phase composition ($\pm 5\%$), flow rate (± 0.1 mL/min), and column lot/supplier. Robustness differs from ruggedness (reproducibility across laboratories) and from repeatability (within-run precision).

Step 1 — Distinguish robustness from related characteristics: Specificity: ability to measure the analyte unequivocally in the presence of interferences.
Repeatability: within-run precision (same analyst, same day).
Linearity: proportional response across concentration range.
Robustness: stability of results under small, deliberate parameter changes.

Step 2 — Why robustness testing is critical: Real-world laboratories operate slightly different instruments, columns, and reagent batches. A robust method produces acceptable results across this natural variability. Robustness testing prevalidates this tolerance before the method is transferred.

Why other options are wrong:

- Option A: Specificity (selectivity) is the ability to measure the analyte in the presence of interferences, not robustness.
- Option B: Robustness: capacity to remain unaffected by small, deliberate variations in method parameters. **Correct; verbatim ICH Q2(R1) definition.**
- Option C: Repeatability (intra-assay precision) measures agreement under identical conditions, not under varied conditions.
- Option D: Linearity quantifies the proportional response range, not method parameter tolerance.

Final Answer: Robustness = capacity of method to remain unaffected by small, deliberate parameter variations (ICH Q2(R1)) $\Rightarrow$ B

Answer: (B) Go Back to Q25

Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	B	2	C	3	D	4	A	5	B
6	C	7	D	8	A	9	B	10	C
11	D	12	A	13	B	14	C	15	D
16	A	17	B	18	C	19	D	20	A
21	B	22	C	23	D	24	A	25	B