GPAT Pharmaceutics

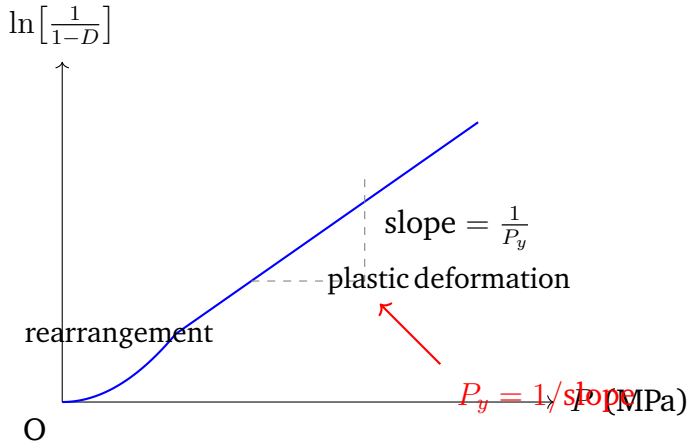
Sample Paper – 2

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 Technology, Stability, Parenteral Preparations, Pharmacokinetics, Rheology.**
- 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. In tablet compression, consider the Heckel plot shown below where $\ln\left[\frac{1}{1-D}\right]$ (D = relative density) is plotted against applied pressure P.



The linear slope of the Heckel plot represents which property

of the powder?

(A) Elastic modulus of the compact

(B) Reciprocal of mean yield pressure P_y (plasticity index)

(C) Carr's compressibility index

(D) Tensile strength of the tablet

Q2. Which mechanism **primarily** explains the action of sodium starch glycolate (Explotab®) as a superdisintegrant in tablet formulations?

(A) Rapid water uptake causing particle swelling up to 200–300 times original volume

(B) Capillary action drawing water through tablet pores via wicking

(C) Gas evolution from an effervescent acid–base reaction

(D) Enzymatic degradation of the starch backbone

Q3. Which loss-on-drying (LOD) range is generally considered acceptable for dried granules intended for tablet manufacture?

(A) $< 0.1\%$

(B) 5–8%

(C) 1–3%

(D) 10–15%

Q4. During aqueous film coating of tablets in a perforated pan, the inlet air temperature is set excessively high. Which coating defect is **most likely** to occur?

(A) Blistering due to rapid moisture uptake by the core

(B) Orange-peel texture from insufficient plasticiser concentration

(C) Twinning caused by tablets sticking together

(D) Spray drying of droplets before they reach the tablet surface, leading to roughness and logo bridging

Q5. Which type of material is **suitable** as a fill for soft gelatin capsules?

(A) Non-aqueous liquids such as vegetable oils or PEG 400

(B) Aqueous drug solutions at neutral pH

(C) Strongly alkaline solutions (pH > 10)

(D) Dry powder blends containing high proportions of water-soluble excipients

Q6. The Arrhenius equation $k = A\,e^{-E_a/RT}$ is fundamental to accelerated stability studies. If the rate constant at $40\,^{\circ}\text{C}$ is k_1 and at $50\,^{\circ}\text{C}$ is k_2, which expression correctly gives the activation energy E_a?

(A) $E_a = R\ln(k_2/k_1)$

(B) $E_a = \dfrac{R\ln(k_2/k_1)}{\left(\dfrac{1}{T_1} - \dfrac{1}{T_2}\right)}$

(C) $E_a = \dfrac{k_2 - k_1}{T_2 - T_1}$

(D) $E_a = \dfrac{\ln(k_1/k_2)}{R(T_2 - T_1)}$

Q7. A pharmaceutical solution degrades by first-order kinetics with a rate constant $k = 0.007\,\text{month}^{-1}$. What is the shelf life t_{90} (time for potency to fall to 90% of label claim)?

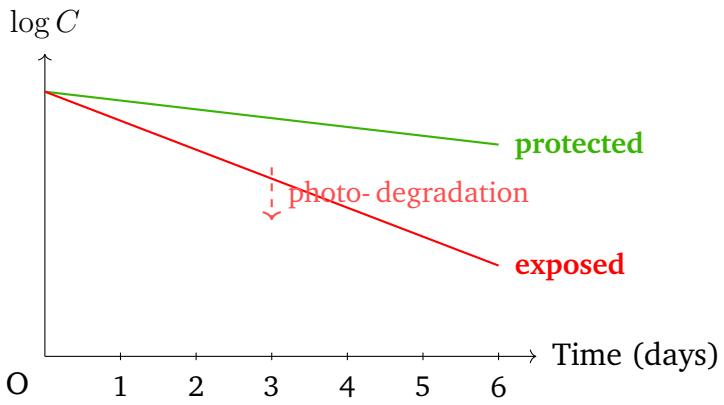
(A) ≈ 99 months

(B) ≈ 7 months

(C) ≈ 15 months

(D) ≈ 30 months

Q8. The graph below shows semi-logarithmic concentration–time profiles for a drug stored under two conditions.



Which statement **correctly** describes the ICH Q1B photostability testing conditions specified for drug substances?

(A) Exposure to a minimum of $200\,\text{Wh/m}^2$ UV from a xenon arc lamp only

(B) Storage at $40\,^{\circ}\text{C}/75\%$ RH for 6 months under dark conditions

(C) Exposure to 1.2×10^6 lux hours of cool-white fluorescent light **and** $200\,\text{Wh/m}^2$ of near-UV light

(D) Exposure to a minimum of 1.2×10^6 lux hours of cool-white fluorescent light **and** not less than $200\,\text{Wh/m}^2$ of near-UV fluorescent light (Option 1 or Option 2 per ICH Q1B)

Q9. An acetate buffer is prepared using acetic acid ($\text{p}K_a = 4.76$) and sodium acetate in a ratio $[\text{Ac}^-]/[\text{AcH}] = 2.5$. Using the Henderson–Hasselbalch equation, what is the pH of the buffer?

(A) 5.16

(B) 4.76

(C) 4.36

(D) 5.56

Q10. Which statement **correctly** compares the Limulus Amebocyte Lysate (LAL) test with the rabbit pyrogen test for endotoxin detection in parenteral preparations?

(A) The rabbit test is more sensitive and is the preferred pharmacopoeial method

(B) The LAL test detects endotoxin at picogram-per-mL levels and is the preferred pharmacopoeial method; the rabbit test detects non-endotoxin pyrogens but is less sensitive

(C) Both tests are equally sensitive and interchangeable without validation

(D) The LAL test requires living animals and is subject to the same animal welfare restrictions as the rabbit test

Q11. In the lyophilization (freeze-drying) process, what is **primarily** removed during the *secondary drying* stage?

(A) Free (unbound) water removed by sublimation under vacuum

(B) Ice crystals formed during the freezing stage

(C) Bound (adsorbed) water removed by desorption at slightly elevated shelf temperature

(D) Residual organic solvents trapped in the amorphous cake

Q12. A drug is administered by constant-rate IV infusion at $R_0 = 20\,\text{mg/h}$. The total body clearance is $\text{CL} = 5\,\text{L/h}$. What is the steady-state plasma concentration C_{ss}?

(A) $1\,\text{mg/L}$

(B) $2\,\text{mg/L}$

(C) $100\,\text{mg/L}$

(D) $4\,\text{mg/L}$

Q13. A drug is completely absorbed from the gastrointestinal tract. Its hepatic extraction ratio (ER) is 0.85. Which calculation **correctly** gives its oral bioavailability F?

(A) $F = 1 - 0.85 = 0.15\ (15\%)$

(B) $F = 0.85\ (85\%)$

(C) $F = 1/0.85 \approx 1.18\ (118\%)$

(D) $F = 0.85 \times 0.85 = 0.72\ (72\%)$

Q14. Which drug class **commonly** exhibits Michaelis–Menten (saturable, dose-dependent) pharmacokinetics at therapeutic plasma concentrations?

(A) Penicillin antibiotics

(B) Antiepileptics such as phenytoin

(C) Angiotensin-converting enzyme (ACE) inhibitors

(D) Thiazide diuretics

Q15. What is the FDA acceptance criterion for the 90% confidence interval (CI) of the geometric mean AUC ratio (Test/Reference) in an oral bioequivalence study?

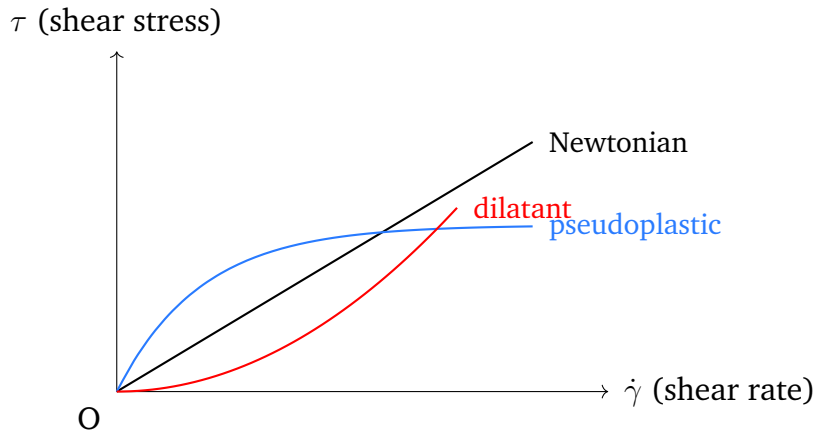
(A) 70.00–143.00%

(B) 75.00–133.33%

(C) 80.00–125.00%

(D) 85.00–118.00%

Q16. The graph below shows flow curves (shear stress τ vs shear rate $\dot{\gamma}$) for three different pharmaceutical systems.



Which flow behaviour is exhibited by a system in which the **apparent viscosity decreases** with increasing shear rate?

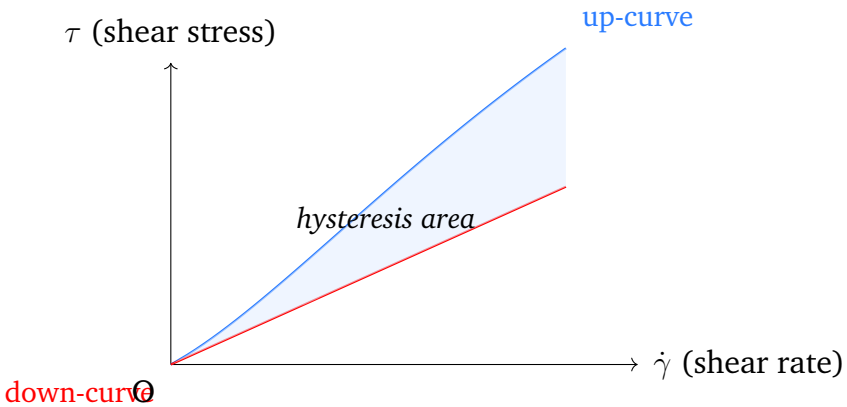
(A) Newtonian

(B) Dilatant (shear-thickening)

(C) Plastic (Bingham)

(D) Pseudoplastic (shear-thinning)

Q17. The flow diagram below was recorded for a pharmaceutical gel using a rotational viscometer (shear rate ramped up then back down).



Which observation **confirms** thixotropic behaviour in a pharmaceutical suspension?

(A) A hysteresis loop is formed between the up-curve and down-curve of the flow diagram, indicating time-dependent, reversible structure breakdown

(B) The apparent viscosity is constant regardless of shear rate

(C) The system shows an infinite viscosity below a yield stress value

(D) Viscosity increases irreversibly after high shear

Q18. A pharmacist needs to prepare 500 mL of a 2% w/v solution from a 10% w/v stock solution. How many mL of the stock solution are required?

(A) 50 mL

(B) 100 mL

(C) 200 mL

(D) 250 mL

Q19. What is the normality of a 0.5 M sulfuric acid (H_2SO_4) solution? (Assume complete ionisation; n-factor $= 2$.)

(A) 0.25 N

(B) 0.5 N

(C) 1 N

(D) 2 N

Q20. Which NaCl equivalent concentration range is generally considered acceptable for ophthalmic preparations to avoid eye

irritation due to hypertonicity or hypotonicity?

(A) 0.1–0.3% NaCl equivalent

(B) 0.3–0.6% NaCl equivalent

(C) 1.5–3.0% NaCl equivalent

(D) 0.6–2.0% NaCl equivalent

Q21. Which system involves **complex coacervation** for microencapsulation?

(A) Gelatin and gum arabic at a pH below the isoelectric point of gelatin, forming an oppositely charged polymer pair

(B) Ethyl cellulose with acetone as the single polymer desolvated by a non-solvent

(C) Sodium alginate cross-linked with calcium chloride solution

(D) Poly(lactic-co-glycolic acid) precipitated from an organic solvent into water

Q22. How does PLGA (poly(lactic-co-glycolic acid)) predominantly degrade to release encapsulated drug from microspheres?

(A) Surface erosion: hydrolysis proceeds exclusively at the outer surface giving zero-order release

(B) Bulk erosion: hydrolysis of ester bonds occurs throughout the matrix simultaneously, producing an initial lag phase followed by a sigmoidal release profile

(C) Enzymatic degradation: specific lipases cleave the polymer backbone only at elevated temperatures

(D) Photochemical degradation: UV exposure breaks ester bonds causing drug release

Q23. Which factor **most significantly** limits the residence time of a drug solution administered intranasally?

(A) Low aqueous solubility of the drug substance

(B) High molecular weight preventing mucosal absorption

(C) Mucociliary clearance: cilia beating at 10–20 Hz transport particles and mucus to the nasopharynx within 15–30 min

(D) Nasal pH incompatibility causing drug precipitation

Q24. What are the **critical temperature** and **critical pressure** of CO_2 used in supercritical fluid-based particle engineering processes such as RESS (Rapid Expansion of Supercritical Solution)?

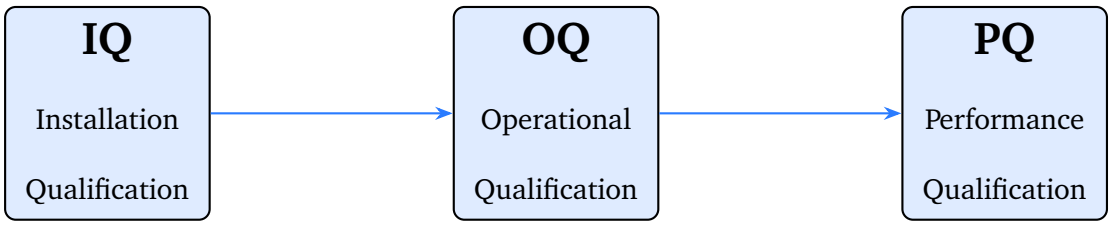
(A) $T_c = 100\,^\circ\text{C}, \quad P_c = 220\,\text{bar}$

(B) $T_c = 50\,^\circ\text{C}, \quad P_c = 50\,\text{bar}$

(C) $T_c = 20\,^\circ\text{C}, \quad P_c = 100\,\text{bar}$

(D) $T_c = 31.1\,^\circ\text{C}, \quad P_c = 73.8\,\text{bar}$

Q25. The diagram below represents the validation sequence for pharmaceutical manufacturing equipment.



Which validation protocol sequence is **correct** for qualifying pharmaceutical manufacturing equipment?

(A) IQ $\rightarrow$ OQ $\rightarrow$ PQ

(B) OQ $\rightarrow$ IQ $\rightarrow$ PQ

(C) PQ $\rightarrow$ OQ $\rightarrow$ IQ

(D) IQ $\rightarrow$ PQ $\rightarrow$ OQ

Detailed Solutions

Q1.

Solution

Concept — Heckel Analysis (Tablet Compression): The Heckel equation $\ln\left[\frac{1}{1-D}\right] = kP + A$ linearises the densification of a powder compact during compression. In the linear region, k is the slope and equals $1/P_y$, where P_y is the *mean yield pressure* — the pressure at which 50% of the particles undergo plastic deformation.

Step 1 — Identify the slope: In the Heckel plot, the slope of the linear (plastic deformation) region is $k = \frac{\Delta[\ln(1/(1-D))]}{\Delta P}$.

Step 2 — Relate slope to P_y: By definition, $k = 1/P_y$, so the slope represents the **reciprocal of the mean yield pressure**. A steeper slope $\Rightarrow$ lower P_y $\Rightarrow$ greater plasticity.

Why other options are wrong:

- Option A: Elastic modulus relates stress to strain in the elastic regime; it is *not* the Heckel slope.
- Option B: **Correct.** Slope $= 1/P_y$, the reciprocal of mean yield pressure.
- Option C: Carr's compressibility index $= ((\rho_{\text{tap}} - \rho_{\text{bulk}})/\rho_{\text{tap}}) \times 100$ — unrelated to the Heckel slope.
- Option D: Tensile strength is measured by diametral compression (Brazilian) test, not from the Heckel plot.

Final Answer: Slope of Heckel plot $= k = 1/P_y \Rightarrow \boxed{\text{B}}$

Answer: (B) Go Back to Q1

Q2.

Solution

Concept — Superdisintegrant Mechanisms: Superdisintegrants accelerate tablet disintegration by one or more mechanisms: swelling, wicking (capillary action), or deformation recovery. Sodium starch glycolate (SSG) acts *primarily* by swelling.

Step 1 — Mechanism of SSG: SSG is a cross-linked, carboxymethylated starch derivative. The cross-linking prevents dissolution while the carboxymethyl groups are hydrophilic. Upon water contact, SSG granules swell isotropically by 200–300

times, generating internal pressure that ruptures the tablet.

Step 2 — Distinguish from other mechanisms: Croscarmellose sodium also swells but additionally relies on wicking. Crospovidone works mainly by wicking/deformation recovery with minimal swelling. Effervescent pairs (citric acid + $NaHCO_3$) use gas evolution.

Why other options are wrong:

- Option A: **Correct.** Rapid swelling (200–300×) is the primary mechanism of SSG.
- Option B: Wicking (capillary action) is the primary mechanism of croscarmellose sodium, not SSG.
- Option C: Gas evolution is the mechanism of effervescent disintegrants, not SSG.
- Option D: SSG is not an enzyme; enzymatic degradation is not a superdisintegrant mechanism.

Final Answer: Rapid particle swelling by water uptake $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q2

Q3.

Solution

Concept — Loss on Drying (LOD) in Wet Granulation: LOD measures the moisture content of granules after the drying step. Optimal LOD ensures good flow, compressibility, and chemical stability without being so dry that granule brittleness becomes problematic.

Step 1 — Industry standard range: For most tablet formulations, a final granule LOD of **1–3%** is acceptable. Below 1%, granules may be too brittle and generate excessive fines; above 3%, sticking/picking and microbial growth become concerns.

Step 2 — Specific formulation adjustments: Moisture-sensitive drugs (e.g., aspirin, effervescents) require LOD $< 1\%$, while hygroscopic drugs may tolerate up to 3.5% with appropriate packaging.

Why other options are wrong:

- Option A: $< 0.1\%$ is excessively dry, causing brittle granules and poor compaction.

- Option B: 5–8% is too moist; promotes microbial contamination and poor flow.
- Option C: **Correct.** 1–3% LOD is the generally accepted target for dried granules.
- Option D: 10–15% would be unacceptable for most oral solid dosage forms.

Final Answer: Acceptable LOD range is 1–3% $\Rightarrow$ C

Answer: (C) Go Back to Q3

Q4.

Solution

Concept — Film Coating Defects and Inlet Air Temperature: In perforated pan film coating, the atomised coating dispersion must reach the tablet surface as a droplet (not as a dry particle) so that it can spread and coalesce into a continuous film. Inlet air temperature governs the evaporation rate.

Step 1 — Effect of excessive temperature: If inlet temperature is too high, the solvent (water in aqueous coating) evaporates from droplets *before* they contact the tablet. The dried polymer particles deposit without coalescence, producing a rough, powdery surface — described as *spray drying* on the tablet.

Step 2 — Consequences: Logo bridging (coating fills in embossing), roughness, and poor gloss result. The coating may also peel because adhesion to the core is poor.

Why other options are wrong:

- Option A: Blistering is caused by solvent (moisture) trapped in a thermoplastic film at high temperature, not by spray drying.
- Option B: Orange-peel texture results from *low* plasticiser or *high* spray rate, not high inlet temperature.
- Option C: Twinning/sticking is caused by excessive spray rate or insufficient pan speed, not high temperature.
- Option D: **Correct.** Excessive inlet temperature causes spray drying of droplets before contact, leading to roughness and logo bridging.

Final Answer: Spray drying of droplets before reaching tablet surface $\Rightarrow$ D

Answer: (D) Go Back to Q4

Q5.

Solution

Concept — Soft Gelatin Capsule Fill Requirements: The shell of a soft gelatin capsule is composed of gelatin, a plasticiser (glycerin/sorbitol), and water. The fill material must be compatible with this shell — aqueous fills dissolve the shell, while strongly alkaline or acidic fills degrade the gelatin.

Step 1 — Suitable fill criteria:

- Non-aqueous or anhydrous: vegetable oils (soybean, olive), medium-chain triglycerides, PEG 400, propylene glycol.
- pH 2.5–7.5 (to avoid gelatin hydrolysis at extremes).
- Not strongly reactive with gelatin or plasticiser.

Step 2 — Why non-aqueous: Aqueous solutions migrate into the shell, plasticise it excessively and cause dissolution/leakage. PEG 400 is miscible with water but is used at controlled water activity.

Why other options are wrong:

- Option A: **Correct.** Non-aqueous liquids (oils, PEG 400) are the standard fill materials.
- Option B: Aqueous drug solutions dissolve the gelatin shell; incompatible.
- Option C: Strongly alkaline solutions (pH > 10) hydrolyse gelatin; prohibited.
- Option D: Dry powder blends are used in hard gelatin capsules, not soft gelatin capsules (which require liquid/semi-liquid fills).

Final Answer: Non-aqueous liquids such as vegetable oils or PEG 400 $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q5

Q6.

Solution

Concept — Arrhenius Equation and Activation Energy: The Arrhenius equation relates the rate constant k to temperature T:

$$k = A\, e^{-E_a/RT}$$

Taking the natural logarithm:

$$\ln k = \ln A - \frac{E_a}{RT}$$

Step 1 — Two-temperature form: At temperatures T_1 and T_2:

$$\ln k_1 = \ln A - \frac{E_a}{RT_1}, \qquad \ln k_2 = \ln A - \frac{E_a}{RT_2}$$

Subtracting: $\ln\left(\frac{k_2}{k_1}\right) = \frac{E_a}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$

Step 2 — Solve for E_a:

$$E_a = \frac{R\ln(k_2/k_1)}{\left(\frac{1}{T_1} - \frac{1}{T_2}\right)}$$

This is Option B. Note $T_1 = 313\,\text{K}$ ($40\,^\circ\text{C}$) and $T_2 = 323\,\text{K}$ ($50\,^\circ\text{C}$); since $T_2 > T_1$, $k_2 > k_1$ for an exothermic degradation.

Why other options are wrong:

- Option A: Missing the temperature difference denominator; dimensionally incorrect.
- Option B: **Correct.** Standard two-point Arrhenius rearrangement.
- Option C: Dividing Δk by ΔT gives a linear approximation, not the Arrhenius expression.
- Option D: Inverted ratio and wrong arrangement of terms.

Final Answer: $E_a = R\ln(k_2/k_1)/\left(\frac{1}{T_1} - \frac{1}{T_2}\right) \Rightarrow \boxed{\text{B}}$

Answer: (B) Go Back to Q6

Q7.

Solution

Concept — Shelf Life t_{90} for First-Order Degradation: For a first-order reaction, the time for the concentration to fall to 90% of the initial value is:

$$t_{90} = \frac{\ln(100/90)}{k} = \frac{\ln(10/9)}{k} \approx \frac{0.1054}{k}$$

Commonly approximated as $t_{90} \approx 0.105/k$.

Step 1 — Substitute values:

$$t_{90} = \frac{0.105}{0.007\,\text{month}^{-1}} = 15\,\text{months}$$

Step 2 — Verify: $k \times t_{90} = 0.007 \times 15 = 0.105 \approx \ln(10/9)$. ✓

Why other options are wrong:

- Option A: 99 months would result from $t_{90} = 0.693/k$ (half-life formula), incorrect for t_{90}.
- Option B: 7 months uses k value directly as time; dimensional error.
- Option C: **Correct.** $t_{90} = 0.105/0.007 = 15$ months.
- Option D: 30 months corresponds to t_{50} (half-life) when $k = 0.023\,\text{month}^{-1}$; not applicable here.

Final Answer: $t_{90} = 0.105/0.007 = 15$ months $\Rightarrow$ C

Answer: (C) Go Back to Q7

Q8.

Solution

Concept — ICH Q1B Photostability Testing: ICH Q1B (Stability Testing: Photostability Testing of New Drug Substances and Products) specifies two options for light sources and minimum exposure levels for confirmatory photostability studies.

Step 1 — ICH Q1B Option 1 and Option 2:

- **Option 1**: A combination source that emits both visible (cool-white fluorescent, $\geq 1.2 \times 10^6$ lux h) and near-UV ($\geq 200\,\text{Wh/m}^2$, 320–400 nm) light.
- **Option 2**: A xenon lamp or metal-halide lamp covering both UV and visible ranges with equivalent integrated output.

Step 2 — Interpret the graph: The graph shows faster degradation in the exposed sample vs. the protected (light-shielded) sample, demonstrating photodegradation. ICH Q1B quantifies this by comparing degraded vs. protected samples after the minimum specified fluence.

Why other options are wrong:

- Option A: 200 Wh/m^2 is the *UV* requirement; the visible requirement (1.2×10^6 lux h) is omitted, and xenon arc is not the only permitted source.

- Option B: 40 °C/75% RH dark storage describes the ICH Q1A long-term stressed condition, not photostability.
- Option C: Lists both components but states them as a single combined requirement without noting Option 1 vs. Option 2 flexibility; partially correct but incomplete.
- Option D: **Correct.** Specifies $\geq 1.2 \times 10^6$ lux h visible *and* ≥ 200 Wh/m^2 near-UV, per ICH Q1B Option 1.

Final Answer: $\geq 1.2 \times 10^6$ lux h visible + ≥ 200 Wh/m^2 near-UV (ICH Q1B) $\Rightarrow$ D

Answer: (D) Go Back to Q8

Q9.

Solution

Concept — Henderson–Hasselbalch Equation: For a weak acid buffer:

$$\text{pH} = \text{p}K_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

Step 1 — Substitute given values:

$$\text{pH} = 4.76 + \log(2.5)$$

Step 2 — Calculate:

$$\log(2.5) = \log\left(\frac{5}{2}\right) = \log 5 - \log 2 = 0.699 - 0.301 = 0.398 \approx 0.40$$

$$\text{pH} = 4.76 + 0.40 = \mathbf{5.16}$$

Why other options are wrong:

- Option A: **Correct.** pH $= 4.76 + 0.40 = 5.16$.
- Option B: 4.76 corresponds to pH when $[\text{Ac}^-]/[\text{AcH}] = 1$ (equal concentrations); not the case here.
- Option C: 4.36 would arise from $\log(2.5) = -0.40$ (wrong sign; would require $[\text{AcH}]/[\text{Ac}^-] = 2.5$).
- Option D: 5.56 would require $\log([\text{Ac}^-]/[\text{AcH}]) = 0.80$, i.e., a ratio of ≈ 6.3; incorrect.

Final Answer: pH $= 4.76 + \log(2.5) = 5.16 \Rightarrow$ A

Answer: (A) Go Back to Q9

Q10.

Solution

Concept — Pyrogen Testing: LAL vs. Rabbit Test: Parenteral preparations must be tested for pyrogens. Two major methods are (i) the Rabbit Pyrogen Test (RPT) and (ii) the Limulus Amebocyte Lysate (LAL) test.

Step 1 — LAL test characteristics:

- Detects *endotoxins* (lipopolysaccharide from Gram-negative bacteria) at pg/mL concentrations.
- In vitro assay; faster, more reproducible, less ethical concern vs. animal test.
- USP ⟨85⟩, BP, and EP preferred method for endotoxin detection.

Step 2 — Rabbit test characteristics:

- Detects a broader spectrum of pyrogens (including non-endotoxin pyrogens).
- Less sensitive (ng/mL range for endotoxins).
- Still used for products where LAL is not validated or for non-endotoxin pyrogens.

Why other options are wrong:

- Option A: Incorrect — the rabbit test is less sensitive and not the preferred pharmacopoeial method for endotoxins.
- Option B: **Correct.** LAL is more sensitive (pg/mL) and the preferred pharmacopoeial method; rabbit test detects non-endotoxin pyrogens.
- Option C: They are not equally sensitive and not interchangeable without validation.
- Option D: LAL is an *in vitro* test; no living animals are used.

Final Answer: LAL is more sensitive and preferred; rabbit test detects non-endotoxin pyrogens $\Rightarrow$ B

Answer: (B) Go Back to Q10

Q11.

Solution

Concept — Lyophilization Stages: Freeze-drying has three stages: (1) Freezing, (2) Primary drying (sublimation), and (3) Secondary drying (desorption).

Step 1 — Primary drying: The shelf temperature is kept below the product's collapse temperature and chamber pressure is reduced. *Free (bulk) ice* sublimes directly to vapour. Approximately 95% of total water is removed at this stage.

Step 2 — Secondary drying: After all bulk ice is removed, the shelf temperature is *raised* (commonly to $+20$–$+40\,^{\circ}$C) under continued vacuum. This provides energy to break the hydrogen bonds between water molecules and polar groups of the cake (protein, sugar). *Bound water* (adsorbed water) is removed by **desorption**. Residual moisture falls to $\leq 1\%$.

Why other options are wrong:

- Option A: Free water removed by sublimation describes *primary* drying, not secondary.
- Option B: Ice crystals are removed during *primary* drying (sublimation).
- Option C: **Correct.** Bound water removed by desorption at elevated shelf temperature = secondary drying.
- Option D: Organic solvent removal requires validated drying cycles; secondary drying targets water, not organic solvents.

Final Answer: Bound (adsorbed) water removed by desorption $\Rightarrow$ C

Answer: (C) Go Back to Q11

Q12.

Solution

Concept — Steady-State Concentration During IV Infusion: At steady state, the rate of drug input equals the rate of elimination:

$$C_{ss} = \frac{R_0}{\text{CL}}$$

where R_0 is the zero-order infusion rate (mg/h) and CL is total body clearance (L/h).

Step 1 — Substitute values:

$$C_{ss} = \frac{20\,\text{mg/h}}{5\,\text{L/h}} = 4\,\text{mg/L}$$

Step 2 — Units check: $\frac{\text{mg/h}}{\text{L/h}} = \frac{\text{mg}}{\text{L}}$ ✓. Steady state is reached after approximately 4–5 half-lives regardless of infusion rate.

Why other options are wrong:

- Option A: 1 mg/L would result from CL = 20 L/h (too high).
- Option B: 2 mg/L would result from CL = 10 L/h.
- Option C: 100 mg/L would result from CL = 0.2 L/h (unrealistically low).
- Option D: **Correct.** $C_{ss} = 20/5 = 4$ mg/L.

Final Answer: $C_{ss} = R_0/\text{CL} = 20/5 = 4\,\text{mg/L} \Rightarrow \boxed{\text{D}}$

Answer: (D) Go Back to Q12

Q13.

Solution

Concept — Hepatic First-Pass Effect and Oral Bioavailability: When a drug is absorbed from the GI tract, it travels via the portal vein to the liver before reaching systemic circulation. The liver extracts a fraction (ER) on each pass. Oral bioavailability accounting for hepatic first-pass:

$$F = F_a \times F_h = F_a \times (1 - \text{ER})$$

where F_a = fraction absorbed from GI tract (given as 1.0 = complete absorption) and $F_h = 1 - \text{ER}$.

Step 1 — Apply the formula:

$$F = 1.0 \times (1 - 0.85) = 0.15 = 15\%$$

Step 2 — Interpretation: With ER = 0.85 (high extraction drug), 85% of the absorbed dose is removed on first pass through the liver. Only 15% reaches systemic circulation. Such drugs (e.g., lidocaine, propranolol, morphine) often require much higher oral doses than IV doses.

Why other options are wrong:

- Option A: **Correct.** $F = 1 - 0.85 = 0.15 = 15\%$.
- Option B: $F = 0.85 = 85\%$ confuses ER (fraction extracted) with bioavailability.
- Option C: $F > 1$ is physically impossible.
- Option D: Squaring ER (0.85^2) has no pharmacokinetic basis.

Final Answer: $F = 1 - \text{ER} = 1 - 0.85 = 15\% \Rightarrow$ A

Answer: (A) Go Back to Q13

Q14.

Solution

Concept — Michaelis–Menten (Nonlinear) Pharmacokinetics: Most drugs follow first-order elimination (rate $\propto C$). However, when an elimination pathway (usually hepatic oxidation via CYP450) becomes saturated, kinetics become *dose-dependent* (nonlinear): at high concentrations ($C \gg K_m$), the rate approaches V_{max} (zero-order); at low concentrations ($C \ll K_m$), it is effectively first-order.

$$v = \frac{V_{max} \cdot C}{K_m + C}$$

Step 1 — Phenytoin as the classic example: Phenytoin (an antiepileptic) is metabolised by CYP2C9/CYP2C19, which saturates near therapeutic plasma concentrations (10–20 μg/mL). Small dose increments cause disproportionately large rises in plasma level — a hallmark of Michaelis–Menten kinetics.

Step 2 — Other drugs with Michaelis–Menten kinetics: Salicylates (high dose), ethanol, and some antivirals (e.g., acyclovir at high doses). But phenytoin is the *prototype* GPAT example.

Why other options are wrong:

- Option A: Penicillins are renally excreted by active tubular secretion which saturates, but this is not the classical teaching example of Michaelis–Menten PK.
- Option B: **Correct.** Phenytoin is the standard example of dose-dependent pharmacokinetics due to saturable CYP metabolism.
- Option C: ACE inhibitors follow first-order kinetics at therapeutic doses.
- Option D: Thiazide diuretics follow linear (first-order) pharmacokinetics.

Final Answer: Antiepileptics such as phenytoin $\Rightarrow$ B

Answer: (B) Go Back to Q14

Q15.

Solution

Concept — FDA Bioequivalence Acceptance Criterion: FDA's guidance on bioequivalence requires a two-period, two-sequence, crossover study. Statistical equivalence is demonstrated if the 90% CI of the geometric mean ratio (Test/Reference) for both AUC_{0-t} and C_{max} falls within the predefined limits.

Step 1 — Standard limits: The FDA acceptance criterion is **80.00–125.00%**. These limits are symmetric on a log scale: $\ln(0.80) = -0.2231$ and $\ln(1.25) = +0.2231$.

Step 2 — Rationale for 80–125%: The limits correspond to a $\pm 20\%$ difference on a ratio scale. The upper limit is the reciprocal of the lower ($1/0.80 = 1.25$), maintaining symmetry on the log scale as required by the log-normal distribution assumption.

Why other options are wrong:

- Option A: 70–143% is wider than FDA requires; used in some special cases (e.g., highly variable drugs with expanded limits) but not the standard.
- Option B: 75–133.33% is not the FDA standard criterion.
- Option C: **Correct.** 80.00–125.00% is the FDA standard BE acceptance criterion for AUC and C_{max}.
- Option D: 85–118% is more restrictive; applied to narrow therapeutic index drugs in some jurisdictions, not the general standard.

Final Answer: 90% CI must fall within 80.00–$125.00\% \Rightarrow$ C

Answer: (C) Go Back to Q15

Q16.

Solution

Concept — Rheological Flow Behaviour Classification: The relationship between shear stress (τ) and shear rate ($\dot{\gamma}$) defines the flow type:

- **Newtonian**: $\tau = \eta\dot{\gamma}$ (linear, constant viscosity).
- **Pseudoplastic (shear-thinning)**: apparent viscosity $\eta_{app} = \tau/\dot{\gamma}$ *decreases* with increasing $\dot{\gamma}$ (concave curve).
- **Dilatant (shear-thickening)**: η_{app} *increases* with increasing $\dot{\gamma}$ (convex curve).
- **Plastic (Bingham)**: requires a yield stress before flow begins.

Step 1 — Identify pseudoplastic: The curve that rises steeply at low $\dot{\gamma}$ then flattens (concave) represents pseudoplastic flow. As $\dot{\gamma}$ increases, the ratio $\tau/\dot{\gamma}$ decreases $\Rightarrow$ decreasing η_{app}.

Step 2 — Pharmaceutical examples: Polymer solutions (CMC, HPMC), suspensions with flocculated particles, and many gels are pseudoplastic. This is beneficial in formulation: low viscosity during pouring/injection, high viscosity at rest.

Why other options are wrong:

- Option A: Newtonian systems have constant viscosity regardless of shear rate (e.g., water, dilute solutions).
- Option B: Dilatant systems show *increasing* viscosity with shear rate (e.g., dense starch suspensions).
- Option C: Plastic (Bingham) flow requires a yield stress; once flowing, may behave nearly Newtonian.
- Option D: **Correct.** Pseudoplastic (shear-thinning) flow: η_{app} decreases with increasing $\dot{\gamma}$.

Final Answer: Pseudoplastic (shear-thinning) behaviour $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q16

Q17.

Solution

Concept — Thixotropy: Thixotropy is a time-dependent, reversible decrease in viscosity (or apparent viscosity) upon application of shear, with recovery of structure on standing. It is distinct from purely shear-rate-dependent pseudoplasticity.

Step 1 — Hysteresis loop as diagnostic: In a rotational viscometry experiment, the shear rate is ramped *up* from 0 to a maximum and then ramped *down* back to 0. A thixotropic material exhibits a **hysteresis loop**: the up-curve (structure intact) lies *above* the down-curve (structure partially broken down). The enclosed area represents the energy per unit volume dissipated in structure breakdown — the *thixotropic coefficient*.

Step 2 — Pharmaceutical significance: Thixotropic suspensions (e.g., bentonite, sodium carboxymethylcellulose gels) are desirable: they flow easily when shaken (low viscosity), then reform a gel-like network at rest (preventing sedimentation).

Why other options are wrong:

- Option A: **Correct.** Hysteresis loop between up-curve and down-curve con-

firms thixotropy.

- Option B: Constant viscosity regardless of shear rate is Newtonian behaviour.
- Option C: Infinite viscosity below yield stress is the definition of a Bingham plastic, not thixotropy.
- Option D: Irreversible viscosity increase after shear describes rheopexy or structural damage, not thixotropy (which is reversible).

Final Answer: Hysteresis loop in the flow diagram confirms thixotropy $\Rightarrow$ A

Answer: (A) Go Back to Q17

Q18.

Solution

Concept — Dilution Calculation ($C_1V_1 = C_2V_2$): For dilution of a solution, the amount of solute is conserved:

$$C_1V_1 = C_2V_2$$

Step 1 — Identify knowns:

$$C_1 = 10\%\,\text{w/v}, \quad C_2 = 2\%\,\text{w/v}, \quad V_2 = 500\,\text{mL}, \quad V_1 = ?$$

Step 2 — Solve for V_1:

$$V_1 = \frac{C_2 \times V_2}{C_1} = \frac{2\% \times 500\,\text{mL}}{10\%} = \frac{1000}{10} = 100\,\text{mL}$$

Take 100 mL of the 10% stock and make up to 500 mL with solvent.

Why other options are wrong:

- Option A: $50\,\text{mL}$ would give $50 \times 10 = 500\,\text{mg}$ total drug in $500\,\text{mL} = 0.1\%\,\text{w/v}$; incorrect.
- Option B: **Correct.** $V_1 = 100\,\text{mL}$ (verified: $100 \times 10\% = 1000\,\text{mg};\ 1000\,\text{mg}/500\,\text{mL} = 2\%$).
- Option C: $200\,\text{mL}$ would give $200 \times 10 = 2000\,\text{mg}/500\,\text{mL} = 4\%$; too concentrated.
- Option D: $250\,\text{mL}$ would give $250 \times 10 = 2500\,\text{mg}/500\,\text{mL} = 5\%$; too concentrated.

Final Answer: $V_1 = C_2V_2/C_1 = 100\,\text{mL} \Rightarrow$ B

Answer: (B) Go Back to Q18

Q19.

Solution

Concept — Normality and n-factor: Normality (N) relates to the number of equivalents per litre:

$$\text{Normality} = \text{Molarity} \times n\text{-factor}$$

The n-factor for an acid = number of replaceable H^+ ions per molecule.

Step 1 — n-factor of H_2SO_4: Sulfuric acid is diprotic: it can donate 2 protons per molecule. Therefore $n = 2$.

Step 2 — Calculate normality:

$$\text{Normality} = 0.5\,\text{M} \times 2 = 1\,\text{N}$$

Why other options are wrong:

- Option A: $0.25\,\text{N}$ would require $n = 0.5$; impossible.
- Option B: $0.5\,\text{N}$ treats H_2SO_4 as monoprotic (like HCl); incorrect.
- Option C: **Correct.** $0.5\,\text{M} \times 2 = 1\,\text{N}$.
- Option D: $2\,\text{N}$ would require Molarity $= 1\,\text{M}$ with $n = 2$; not the given concentration.

Final Answer: Normality $= 0.5 \times 2 = 1\,\text{N} \Rightarrow$ C

Answer: (C) Go Back to Q19

Q20.

Solution

Concept — Isotonicity of Ophthalmic Preparations: Human lachrymal fluid is isotonic with 0.9% NaCl (osmolality $\approx 290\,\text{mOsmol/kg}$). Ophthalmic preparations that deviate significantly from this cause discomfort (stinging, lacrimation).

Step 1 — Acceptable range: The generally accepted NaCl equivalent (isotonicity) range for ophthalmic preparations is **0.6–2.0% NaCl equivalent**. Within this range, the eye can tolerate the osmotic difference without significant discomfort; the lacrimal fluid dilutes or concentrates the preparation rapidly.

Step 2 — Extremes: Solutions below $\approx 0.6\%$ NaCl equivalent are strongly hypotonic and cause cell swelling; above $\approx 2.0\%$ are strongly hypertonic and cause cell shrinkage and pain.

Why other options are wrong:

- Option A: 0.1–0.3% NaCl equivalent is far too hypotonic and would cause significant ocular discomfort.
- Option B: 0.3–0.6% is below the lower limit of tolerance.
- Option C: 1.5–3.0% extends into hypertonic territory beyond the accepted upper limit.
- Option D: **Correct.** 0.6–2.0% NaCl equivalent is the pharmacopoeially recognised acceptable range.

Final Answer: Acceptable range: 0.6–2.0% NaCl equivalent $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q20

Q21.

Solution

Concept — Coacervation Microencapsulation: Coacervation is a phase separation technique to form microcapsules. Two types exist:

- **Simple coacervation**: one polymer + desolvating agent (e.g., addition of electrolyte or non-solvent).
- **Complex coacervation**: two *oppositely charged* polymers combine and phase-separate due to electrostatic attraction.

Step 1 — Gelatin + gum arabic system: Gelatin is amphoteric; at pH below its isoelectric point (pI $\approx$ 8–9 for Type A gelatin), it carries a net positive charge. Gum arabic is anionic at this pH. The electrostatic attraction between cationic gelatin and anionic gum arabic drives complex coacervation, forming a coacervate phase that deposits around the core material.

Step 2 — Process conditions: pH is adjusted to ≈ 4 (below gelatin pI), at which point complex coacervate forms; temperature lowering then solidifies the shell.

Why other options are wrong:

- Option A: **Correct.** Gelatin + gum arabic at pH below gelatin pI = classic complex coacervation.

- Option B: Single polymer (ethyl cellulose) desolvated by a non-solvent = *simple* coacervation.
- Option C: Sodium alginate + $CaCl_2$ = ionotropic gelation (not coacervation).
- Option D: PLGA precipitation = solvent evaporation / nanoprecipitation (not coacervation).

Final Answer: Gelatin + gum arabic below gelatin pI (complex coacervation) $\Rightarrow$ A

Answer: (A) Go Back to Q21

Q22.

Solution

Concept — PLGA Degradation Mechanism: PLGA (poly(lactic-co-glycolic acid)) is a biodegradable polyester used widely in controlled-release microspheres and implants. Its degradation mode determines the drug release pattern.

Step 1 — Bulk erosion mechanism: PLGA undergoes **bulk erosion** (also called homogeneous erosion): water penetrates the entire matrix, and ester bonds are hydrolysed throughout the bulk simultaneously. This differs from surface erosion, where degradation proceeds only from the exterior (e.g., polyanhydrides).

Step 2 — Release profile consequence: Because the interior and surface degrade simultaneously, drug release follows a *triphasic pattern*: (i) initial burst (surface drug), (ii) lag phase (matrix intact), (iii) accelerated release (bulk erosion and autocatalysis by acidic degradation products – lactic and glycolic acids).

Why other options are wrong:

- Option A: Surface erosion giving zero-order release is characteristic of polyanhydrides (e.g., Gliadel wafers), not PLGA.
- Option B: **Correct.** Bulk erosion via ester hydrolysis throughout the matrix, producing triphasic/sigmoidal release.
- Option C: PLGA degradation is hydrolytic (chemical), not enzymatic.
- Option D: PLGA does not degrade by UV/photochemical mechanisms.

Final Answer: Bulk erosion: hydrolysis throughout matrix $\Rightarrow$ B

Answer: (B) Go Back to Q22

Q23.

Solution

Concept — Nasal Drug Delivery and Mucociliary Clearance: The nasal cavity is lined with ciliated epithelium covered by a mucus layer. The mucociliary escalator continuously moves mucus and trapped particles posteriorly toward the nasopharynx, where they are swallowed.

Step 1 — Mucociliary clearance rate: Nasal cilia beat at **10–20 Hz**, propelling the mucus layer at $\approx$ 5–6 mm/min. Drug deposited in the nasal cavity is cleared within **15–30 minutes**. This severely limits drug residence time and, hence, absorption window.

Step 2 — Impact on nasal formulation: To overcome mucociliary clearance, formulators use: mucoadhesive polymers (HPMC, chitosan), viscosity enhancers, ciliary inhibitors, or nasal powder formulations (slower clearance than solutions).

Why other options are wrong:

- Option A: Low solubility limits dissolution rate but is secondary to the clearance issue for solution formulations.
- Option B: High MW limits transmucosal absorption but does not directly limit residence time.
- Option C: **Correct.** Mucociliary clearance (cilia at 10–20 Hz, 15–30 min clearance) is the primary factor limiting nasal residence time.
- Option D: Nasal pH ($\approx$ 5.5–6.5) can affect ionisation but is not the dominant factor limiting residence time.

Final Answer: Mucociliary clearance (cilia 10–20 Hz, clearance in 15–30 min) $\Rightarrow$ C

Answer: (C) Go Back to Q23

Q24.

Solution

Concept — Supercritical CO_2 in Pharmaceutical Particle Engineering: A supercritical fluid exists above its critical temperature (T_c) and critical pressure (P_c). CO_2 is the most widely used supercritical fluid in pharmaceutics because of its mild critical conditions and non-toxicity.

Step 1 — Critical constants of CO_2:

$$T_c = 31.1\,^{\circ}\text{C} \qquad P_c = 73.8\,\text{bar}\,(7.38\,\text{MPa})$$

These mild conditions allow processing of thermolabile drugs without thermal degradation.

Step 2 — Applications: Supercritical CO_2 is used in RESS (Rapid Expansion of Supercritical Solutions) and SAS/SEDS (Supercritical Anti-Solvent / Solution Enhanced Dispersion by Supercritical fluids) to produce micronised or nano-sized drug particles without organic solvent residues.

Why other options are wrong:

- Option A: $T_c = 100\,^\circ$C, $P_c = 220$ bar are approximately the critical constants of water; not CO_2.
- Option B: $T_c = 50\,^\circ$C, $P_c = 50$ bar are not the correct values for any common supercritical fluid.
- Option C: $T_c = 20\,^\circ$C, $P_c = 100$ bar are incorrect; CO_2 has $T_c > 25\,^\circ$C at room temperature.
- Option D: **Correct.** $T_c = 31.1\,^\circ$C, $P_c = 73.8$ bar for CO_2.

Final Answer: $T_c = 31.1\,^\circ$C, $P_c = 73.8$ bar $\Rightarrow$ D

Answer: (D) Go Back to Q24

Q25.

Solution

Concept — Equipment Validation Sequence (IQ/OQ/PQ): Pharmaceutical equipment qualification follows a defined three-stage protocol mandated by GMP guidelines (ICH Q7, FDA 21 CFR Part 211, EU GMP Annex 15):

Step 1 — Definitions:

- **IQ (Installation Qualification)**: Verifies that equipment is installed correctly according to design specifications (utilities, hardware, software, documentation).
- **OQ (Operational Qualification)**: Verifies that equipment operates as intended across its design range (temperature, speed, pressure limits) under simulated or actual conditions.
- **PQ (Performance Qualification)**: Verifies that the equipment consistently performs to specification under actual production conditions using the intended product or surrogate.

Step 2 — Correct sequence: Each stage builds on the previous. You cannot confirm operational performance (OQ) before verifying correct installation (IQ),

and you cannot confirm process performance (PQ) before confirming operational capability (OQ). Hence: **IQ** $\rightarrow$ **OQ** $\rightarrow$ **PQ**.

Why other options are wrong:

- Option A: **Correct.** IQ$\rightarrow$OQ$\rightarrow$PQ is the universally accepted GMP sequence.
- Option B: OQ$\rightarrow$IQ$\rightarrow$PQ skips installation verification before operational testing; non-compliant.
- Option C: PQ$\rightarrow$OQ$\rightarrow$IQ reverses the entire sequence; fundamentally incorrect.
- Option D: IQ$\rightarrow$PQ$\rightarrow$OQ skips OQ before PQ; a non-compliant sequence under GMP.

Final Answer: IQ $\rightarrow$ OQ $\rightarrow$ PQ $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q25

Answer Key

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