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# M.Pharm Practical Notes

## Pharmaceutical Quality Assurance Practicals II

Semester 2

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# Organic-Contaminant Residues by HPLC

Practical 1 - Bench practical

## Aim

To measure an organic contaminant residue using a selective, suitably sensitive chromatographic method.

## Principle

An analyte distributes between a stationary phase and flowing mobile phase. Retention and separation depend on the column chemistry, mobile-phase composition, flow, temperature and analyte ionisation.

A detector response is related to concentration using a qualified calibration or comparison with a reference preparation. Retention agreement supports identification but needs the selectivity evidence required for the intended use.

## Materials and Requirements

- HPLC system with suitable column and detector
- Method-specified mobile phase and diluent
- Reference material, blank and placebo
- Qualified filters, vials and volumetric glassware

## Procedure

1. Record the column identity, mobile-phase composition, flow, temperature, detector settings, injection volume and method version.
2. Prepare mobile phase and solutions using compatible grades and the adopted filtration and degassing process. Record solution stability and reference potency.
3. Check the system for leaks and equilibrate using the instrument procedure. Establish a stable baseline before the analytical sequence.
4. Run a blank, reference preparations and system-suitability injections. Evaluate retention, resolution, peak shape and repeatability against predefined method criteria.
5. Inject independently prepared test solutions bracketed by appropriate check standards. Include a blank after high concentrations when carryover is a concern.
6. Review peak identification and integration consistently. Retain the original chromatograms and document any justified integration changes.
7. Calculate concentration or assay, reverse dilutions and review the complete sequence before reporting. Preserve audit-trail and processing information.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Injection | Retention time (min) | Area / area ratio | Resolution or comment |
|---|---|---|---|
| Blank | Record | Record | Interference / carryover |
| Reference replicates | Record | Record | Suitability |
| Test preparation 1 | Record | Record | Assay |
| Test preparation 2 | Record | Record | Preparation precision |

## Calculations

• Resolution, Rs = 2(tR2 - tR1) / (w1 + w2), using baseline peak widths
• Theoretical plates, N = 16(tR / w)^2, using baseline width
• For matched dilutions in a valid external-standard comparison: assay (%) = test area / standard area x reference concentration / nominal test concentration x reference potency (%)

### Worked Example

Illustrative adjacent peaks: retention times 5.00 and 5.40 min; baseline widths 0.20 and 0.24 min.

Rs = 2(0.40) / 0.44 = 1.82. The first peak gives N = 16(5.00/0.20)^2 = 10000.

For equal nominal concentrations, test and standard areas of 49000 and 50000 with reference potency 99.7% give assay = 49000/50000 x 99.7 = 97.706%.

These values illustrate calculations; use the adopted method criteria to decide whether a sequence is acceptable.

### Residue calculation

• Report blank response, extraction recovery, quantitation limit and the mass or surface-area basis.
• For a measured extract concentration of 0.020 micrograms/mL in 10.0 mL, recovered residue is 0.200 micrograms before any justified recovery correction.

## Result and Interpretation

• Report assay or concentration together with the observed suitability results.
• A resolved, reproducible peak must also be shown to be specific for the intended analysis.
• Investigate failed suitability or carryover before using affected test results.

## Precautions

• Use compatible solvents and the column pressure and temperature limits.
• Collect solvent waste in designated containers and keep incompatible wastes separate.
• Prevent particles and bubbles entering the flow path.
• Avoid selective reintegration or reinjection to obtain a preferred result.

## Viva Questions and Answers

### Why equilibrate the column?

A stable stationary-phase environment improves retention and response reproducibility.

### Does a single retention time prove identity?

No; coelution is possible and identity requires the intended method evidence.

### Why bracket test injections?

Check standards can reveal response drift during the run.

# Metallic-Contaminant Estimation

Practical 2 - Practical study

## Aim

To compare flame-emission and atomic-absorption measurements for specified metals.

## Principle

Flame photometry measures emitted radiation, whereas AAS measures absorption of element-specific radiation. Calibration, matrix effects, atomisation conditions and interferences must be controlled separately for the selected element and technique.

## Materials and Requirements

- Approved metal reference, blank and matrix check
- Qualified flame-emission or AAS instrument
- Validated digestion or dilution record and gas-system controls
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Choose the element, wavelength, atomisation system and validated preparation for the actual matrix.
3. Prepare calibration, blank and an independent check; verify background and interference controls.
4. Have trained staff operate the specified instrument and assess calibration and replicate readings.
5. Calculate metal content with all dilution and preparation factors and compare technique selectivity and limitations.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Preparation | Technique / wavelength | Response / concentration | Metal content |
|---|---|---|---|
| Blank | Specify | Measure | Evaluate |
| Reference check | Specify | Measure | Recovery |
| Test digest | Specify | Measure | Calculate |

## Calculations

- Metal content (mg/kg) = concentration (mg/L) x final digest volume (L) x dilution / test mass (kg)

### Worked Example

Illustrative digest contains 0.40 mg/L metal in 0.050 L from 0.0020 kg material: content = 10 mg/kg.
This is an arithmetic example; use the actual element-specific specification to assess it.

## Result and Interpretation

• State the element, method, blank, recovery and quantitation limits.

## Precautions

• Use trained gas and flame operation.
• Prevent metal contamination.
• Do not assume identical matrix effects across elements.

## Viva Questions and Answers

### What does AAS measure?

Absorption of radiation by atomised analyte species.

### Why analyse a blank?

Preparation and reagents may introduce the metal.

### Why use a matrix check?

The preparation matrix can change analytical response.

# Antibiotic-Residue Identification by TLC

Practical 3 - Bench practical

## Aim

To identify a specified antibiotic residue by validated TLC comparison.

## Principle

TLC compares migration and detection behaviour against a suitable reference under matched conditions. A matching Rf alone is presumptive and may require a confirmatory method.

## Materials and Requirements

- HPLC system with suitable column and detector
- Method-specified mobile phase and diluent
- Reference material, blank and placebo
- Qualified filters, vials and volumetric glassware

## Procedure

1. Select the antibiotic, matrix and validated extraction and TLC method; document its detection capability.
2. Prepare a matrix blank, fortified recovery control, reference and test extract.
3. Apply comparable bands or spots, develop in the specified chamber and detect by the adopted procedure.
4. Measure migration, examine blank interferences and recovery, and record confirmation needs.
5. Report identity evidence and any limit or quantitation claim only when supported by method validation.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Injection | Retention time (min) | Area / area ratio | Resolution or comment |
|---|---|---|---|
| Blank | Record | Record | Interference / carryover |
| Reference replicates | Record | Record | Suitability |
| Test preparation 1 | Record | Record | Assay |
| Test preparation 2 | Record | Record | Preparation precision |

## Calculations

- Rf = distance travelled by analyte zone / distance travelled by solvent front

### Worked Example

Illustrative reference and test zones travel 30 and 31 mm while the front travels 60 mm: Rf values are 0.50 and 0.52. Similar migration is not definitive identification.

### Food-matrix preparation

- Choose the method for the specified colour class; compare retention and spectra against suitable standards and assess matrix selectivity.
- Include extraction recovery, matrix blank where available, a suitable calibration and reporting on the stated food-mass basis.

• If the extract contains 2.00 micrograms/mL in 25.0 mL from a 5.00 g portion with no further dilution, content is 10.0 micrograms/g before a justified recovery correction.

## Result and Interpretation

• Report assay or concentration together with the observed suitability results.
• A resolved, reproducible peak must also be shown to be specific for the intended analysis.
• Investigate failed suitability or carryover before using affected test results.

## Precautions

• Use compatible solvents and the column pressure and temperature limits.
• Collect solvent waste in designated containers and keep incompatible wastes separate.
• Prevent particles and bubbles entering the flow path.
• Avoid selective reintegration or reinjection to obtain a preferred result.

## Viva Questions and Answers

### Why equilibrate the column?

A stable stationary-phase environment improves retention and response reproducibility.

### Does a single retention time prove identity?

No; coelution is possible and identity requires the intended method evidence.

### Why bracket test injections?

Check standards can reveal response drift during the run.

# Hydrogen Sulphide in Air - Sampling Records and Calculation

Practical 4 - Air-sampling data practical

## Aim

To interpret a validated workplace-air sampling and analytical dataset for the specified gas.

## Principle

An occupational-air result relates collected analyte mass to a defined sampled air volume. Collection medium, flow, breakthrough, recovery, analytical selectivity and reporting conditions are method specific. This exercise uses supplied or certified closed-system data and does not generate hazardous gas.

## Materials and Requirements

- Selected current validated sampling method and safety assessment
- Supplied pump calibration, field blank and analytical records
- Gas-specific calibration and recovery data
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Identify the gas, applicable method, sampling medium, flow range, duration and required correction conventions.
3. Review pre- and post-sampling flow, field blanks, storage, holding time and breakthrough checks.
4. For the colour or instrument assay assess blank correction, calibration, interference and recovery evidence.
5. Calculate air concentration, document temperature/pressure conventions and compare only with the relevant current occupational limit and averaging period.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Sampling / assay item | Raw value | Correction basis | Reported result |
|---|---|---|---|
| Flow / duration | Enter L/min and min | Volume convention | Calculate |
| Field blank / test | Enter micrograms | Blank correction | Calculate |
| Recovery / breakthrough | Record | Method rule | Evaluate |

## Calculations

- Sampled volume (m^3) = flow (L/min) x duration (min) / 1000
- Concentration (mg/m^3) = blank-corrected analyte mass (mg) / sampled volume (m^3)

### Worked Example

Illustrative flow 0.20 L/min for 60 min gives 0.012 m^3. Net analyte mass 6.0 micrograms = 0.0060 mg; concentration = 0.50 mg/m^3.

Apply recovery and air-volume corrections only as prescribed; the example assigns no exposure limit.

### Hydrogen sulphide method record

• Use the selected gas-specific validated sampling and assay method. Record collection chemistry, analytical selectivity and interferences explicitly.

• For a colorimetric method retain wavelength, colour-development conditions and the calibration worksheet; do not substitute another gas method.

## Result and Interpretation

• Report method, gas identity, blank, sampled volume, uncertainty and any invalidating sampling condition.

## Precautions

• Do not generate or deliberately expose anyone to the gas.

• Use only supplied data or a professionally controlled certified system.

• Do not compare a short sample with a time-weighted limit without the proper averaging basis.

## Viva Questions and Answers

### Why analyse field blanks?

They reveal contamination introduced by media, handling and transport.

### What is breakthrough?

Analyte passes beyond the collecting section, potentially biasing recovery.

### Why specify averaging time?

Exposure limits refer to defined time bases.

# Chlorine in Workplace Air - Sampling Records and Calculation

Practical 5 - Air-sampling data practical

## Aim

To interpret a validated workplace-air sampling and analytical dataset for the specified gas.

## Principle

An occupational-air result relates collected analyte mass to a defined sampled air volume. Collection medium, flow, breakthrough, recovery, analytical selectivity and reporting conditions are method specific. This exercise uses supplied or certified closed-system data and does not generate hazardous gas.

## Materials and Requirements

- Selected current validated sampling method and safety assessment
- Supplied pump calibration, field blank and analytical records
- Gas-specific calibration and recovery data
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Identify the gas, applicable method, sampling medium, flow range, duration and required correction conventions.
3. Review pre- and post-sampling flow, field blanks, storage, holding time and breakthrough checks.
4. For the colour or instrument assay assess blank correction, calibration, interference and recovery evidence.
5. Calculate air concentration, document temperature/pressure conventions and compare only with the relevant current occupational limit and averaging period.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Sampling / assay item | Raw value | Correction basis | Reported result |
|---|---|---|---|
| Flow / duration | Enter L/min and min | Volume convention | Calculate |
| Field blank / test | Enter micrograms | Blank correction | Calculate |
| Recovery / breakthrough | Record | Method rule | Evaluate |

## Calculations

- Sampled volume (m^3) = flow (L/min) x duration (min) / 1000
- Concentration (mg/m^3) = blank-corrected analyte mass (mg) / sampled volume (m^3)

### Worked Example

Illustrative flow 0.20 L/min for 60 min gives 0.012 m^3. Net analyte mass 6.0 micrograms = 0.0060 mg; concentration = 0.50 mg/m^3.

Apply recovery and air-volume corrections only as prescribed; the example assigns no exposure limit.

### Chlorine method record

• Use the selected gas-specific validated sampling and assay method. Record collection chemistry, analytical selectivity and interferences explicitly.

• For a colorimetric method retain wavelength, colour-development conditions and the calibration worksheet; do not substitute another gas method.

## Result and Interpretation

• Report method, gas identity, blank, sampled volume, uncertainty and any invalidating sampling condition.

## Precautions

• Do not generate or deliberately expose anyone to the gas.

• Use only supplied data or a professionally controlled certified system.

• Do not compare a short sample with a time-weighted limit without the proper averaging basis.

## Viva Questions and Answers

### Why analyse field blanks?

They reveal contamination introduced by media, handling and transport.

### What is breakthrough?

Analyte passes beyond the collecting section, potentially biasing recovery.

### Why specify averaging time?

Exposure limits refer to defined time bases.

# Sulphur Dioxide by Colorimetric Analysis

Practical 6 - Air-sampling data practical

## Aim

To interpret a validated workplace-air sampling and analytical dataset for the specified gas.

## Principle

An occupational-air result relates collected analyte mass to a defined sampled air volume. Collection medium, flow, breakthrough, recovery, analytical selectivity and reporting conditions are method specific. This exercise uses supplied or certified closed-system data and does not generate hazardous gas.

## Materials and Requirements

- Selected current validated sampling method and safety assessment
- Supplied pump calibration, field blank and analytical records
- Gas-specific calibration and recovery data
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Identify the gas, applicable method, sampling medium, flow range, duration and required correction conventions.
3. Review pre- and post-sampling flow, field blanks, storage, holding time and breakthrough checks.
4. For the colour or instrument assay assess blank correction, calibration, interference and recovery evidence.
5. Calculate air concentration, document temperature/pressure conventions and compare only with the relevant current occupational limit and averaging period.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Sampling / assay item | Raw value | Correction basis | Reported result |
|---|---|---|---|
| Flow / duration | Enter L/min and min | Volume convention | Calculate |
| Field blank / test | Enter micrograms | Blank correction | Calculate |
| Recovery / breakthrough | Record | Method rule | Evaluate |

## Calculations

- Sampled volume (m^3) = flow (L/min) x duration (min) / 1000
- Concentration (mg/m^3) = blank-corrected analyte mass (mg) / sampled volume (m^3)

### Worked Example

Illustrative flow 0.20 L/min for 60 min gives 0.012 m^3. Net analyte mass 6.0 micrograms = 0.0060 mg; concentration = 0.50 mg/m^3.

Apply recovery and air-volume corrections only as prescribed; the example assigns no exposure limit.

### Sulphur dioxide method record

• Use the selected gas-specific validated sampling and assay method. Record collection chemistry, analytical selectivity and interferences explicitly.
• For a colorimetric method retain wavelength, colour-development conditions and the calibration worksheet; do not substitute another gas method.

## Result and Interpretation

• Report method, gas identity, blank, sampled volume, uncertainty and any invalidating sampling condition.

## Precautions

• Do not generate or deliberately expose anyone to the gas.
• Use only supplied data or a professionally controlled certified system.
• Do not compare a short sample with a time-weighted limit without the proper averaging basis.

## Viva Questions and Answers

### Why analyse field blanks?

They reveal contamination introduced by media, handling and transport.

### What is breakthrough?

Analyte passes beyond the collecting section, potentially biasing recovery.

### Why specify averaging time?

Exposure limits refer to defined time bases.

# Autoclave Qualification

Practical 7 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a steam steriliser.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Chamber and load mapping, air removal where applicable, calibrated temperature/pressure sensors and defined load configurations.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. Review heat distribution, heat penetration, exposure records and biological-indicator evidence where specified. A display temperature alone does not qualify the load.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- For a moist-heat model: F0 = sum[10^((T - 121.1)/z) x interval], with T in degrees C, interval in minutes and the stated z value.

### Worked Example

Illustrative constant 121.1 degrees C for 10 min with z = 10 degrees C contributes F0 = 10 min. This is a lethality calculation, not a universal sterilisation cycle.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Hot-Air Oven Qualification

Practical 8 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a hot-air oven.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Calibrated air and load temperature mapping, recovery, airflow and defined loading patterns.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. Review cold/hot positions, exposure consistency and load-specific sterilisation or depyrogenation evidence. The intended claim determines the qualification tests.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- Temperature deviation = observed temperature - target temperature.

### Worked Example

Illustrative target 160 degrees C and mapped point 157 degrees C give -3 degrees C. Compare with the approved tolerance; this observation alone establishes neither sterilisation nor depyrogenation.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Dry-Powder Mixer Qualification

Practical 9 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a dry-powder mixer.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Installation, rotation controls, load range, mixing time, sampling design and assay capability.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. Evaluate representative locations and blend uniformity without relying on a single composite; assess segregation during discharge.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- RSD (%) = sample standard deviation / mean x 100.

### Worked Example

Illustrative location results 98, 100 and 102 units give mean 100 and sample SD 2; RSD = 2.0%. A three-point example is not a validated sampling plan.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Tablet Compression Machine Qualification

Practical 10 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a tablet compression machine.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Guards/interlocks, force and speed settings, feeder and tooling identification, and operating ranges.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. At defined load and speed settings assess mass, dimensions, strength, friability, disintegration or dissolution as appropriate; connect changes to force and feed behaviour.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- Percentage mass difference = (mean observed mass - target mass)/target mass x 100.

### Worked Example

Illustrative target 400 mg and mean 396 mg give -1.0%. Use the approved product and machine qualification criteria for disposition.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Analytical Method Validation

Practical 11 - Protocol and data-analysis practical

## Aim

To design and evaluate a fit-for-purpose analytical method-validation study.

## Principle

Validation provides evidence that a procedure meets its intended analytical purpose over a defined reportable range. Relevant characteristics depend on whether the method measures identity, assay, impurities or another attribute.

A predefined protocol connects the analytical target and acceptance criteria to specificity, response behaviour, accuracy, precision and other required performance characteristics. Method development and risk assessment inform the validation design.

## Materials and Requirements

- Written analytical procedure and target
- Suitable reference, placebo, impurity or challenge materials
- Predefined protocol and qualified measurement system
- Data-analysis worksheet

## Procedure

1. Define the analyte, matrix, purpose, reportable range and performance requirements before generating validation results.
2. Identify the characteristics required for that use and explain the study design, levels, replicates and independent preparations.
3. Evaluate selectivity with appropriate blanks, placebo, relevant impurities or other justified challenges.
4. Assess response behaviour, accuracy and precision across the intended range. Include quantitation capability when required by the purpose.
5. Use development knowledge and deliberate small changes to understand relevant robustness factors; define operational controls.
6. Assess solution and preparation stability as needed and document handling conditions.
7. Review every result against the protocol and issue a report explaining deviations, limitations and the supported method use.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Characteristic | Study design | Result | Predefined criterion and conclusion |
|---|---|---|---|
| Selectivity | Record challenges | Record | Evaluate |
| Accuracy | Levels and independent preparations | Record | Evaluate |
| Precision | Replicates / conditions | Record | Evaluate |
| Range and response | Model and residuals | Record | Evaluate |

| Characteristic | Study design | Result | Predefined criterion and conclusion |
|---|---|---|---|
| Other relevant characteristics | Justify | Record | Evaluate |

## Calculations

- Recovery (%) = measured added amount / known added amount x 100
- RSD (%) = standard deviation / mean x 100
- Bias (%) = (mean measured - nominal) / nominal x 100

### Worked Example

Illustrative replicate assay results are 99.2, 100.0 and 100.8%. Mean = 100.0%, sample standard deviation = 0.8 percentage point and RSD = 0.80%.

For an independently added 10.0 mg amount recovered as 9.85 mg after valid native-content correction, recovery is 98.5%.

Interpretation uses the prespecified method-purpose criteria; there is no one universal recovery or RSD limit for every analytical use.

## Result and Interpretation

- Conclude on the defined method purpose and range, with specific limitations and required controls.
- Do not substitute a high calibration R-squared value for validation.

## Precautions

- Set criteria before viewing study results.
- Use independent preparations where the characteristic requires them.
- Keep failed and repeated results with justified investigations.
- Separate reference-material uncertainty from test-preparation variability.

## Viva Questions and Answers

### Why define the intended purpose first?

The necessary performance depends on what the method must measure.

### Is linearity alone validation?

No; it does not establish selectivity, accuracy or precision.

### Where is robustness knowledge useful?

It helps identify critical method parameters and practical operational controls.

# Processing-Area Qualification and Validation

Practical 12 - Facility-record practical

## Aim

To evaluate processing-area qualification and its connection to process validation.

## Principle

Facility qualification addresses the intended environmental and utility conditions. Process validation assesses the manufacturing process; a qualified room alone does not validate a product process.

## Materials and Requirements

- Fictional facility plan and area classification rationale
- HVAC qualification and environmental records
- Personnel/material flow and cleaning procedures
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Define intended operations, contamination risks, cleanroom requirements where applicable and adjacent areas.
3. Review air handling, filters, airflow direction, pressure differences and recovery or other relevant qualified tests.
4. Map personnel, material, waste and equipment movements; assess cleaning, monitoring locations and environmental trends.
5. Connect facility evidence to the process-control strategy and identify gaps, deviations and requalification needs.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Area / function | Required condition | Qualification evidence | Gap / action |
|---|---|---|---|
| Dispensing | Define | Review | Assess |
| Processing | Define | Review | Assess |
| Transfer route | Define | Review | Assess |

## Calculations

- Pressure difference = pressure in the defined room - pressure in the stated reference room

### Worked Example

Illustrative room pressure +15 Pa and adjacent reference +5 Pa give a +10 Pa difference relative to that space. The required direction and acceptable range must come from the facility contamination-control strategy.

## Result and Interpretation

• Provide a flow diagram and requirement-to-evidence matrix with an authorised-use recommendation.

## Precautions

• Do not infer cleanroom class from pressure alone.
• Distinguish at-rest and operational conditions.
• Use qualified personnel for facility challenges.

## Viva Questions and Answers

### What does positive pressure imply?

A pressure relationship; airflow and contamination control still need evaluation.

### Why map flows?

Crossing routes can create contamination or mix-up risks.

### Does room qualification validate a process?

The process requires its own lifecycle evidence.

# Qualification of an HPLC System

Practical 13 - Bench practical

## Aim

To qualify HPLC performance through prescribed checks of the pump, injector, detector and analytical response.

## Principle

An analyte distributes between a stationary phase and flowing mobile phase. Retention and separation depend on the column chemistry, mobile-phase composition, flow, temperature and analyte ionisation.

A detector response is related to concentration using a qualified calibration or comparison with a reference preparation. Retention agreement supports identification but needs the selectivity evidence required for the intended use.

## Materials and Requirements

- HPLC system with suitable column and detector
- Method-specified mobile phase and diluent
- Reference material, blank and placebo
- Qualified filters, vials and volumetric glassware

## Procedure

1. Record the column identity, mobile-phase composition, flow, temperature, detector settings, injection volume and method version.
2. Prepare mobile phase and solutions using compatible grades and the adopted filtration and degassing process. Record solution stability and reference potency.
3. Check the system for leaks and equilibrate using the instrument procedure. Establish a stable baseline before the analytical sequence.
4. Run a blank, reference preparations and system-suitability injections. Evaluate retention, resolution, peak shape and repeatability against predefined method criteria.
5. Inject independently prepared test solutions bracketed by appropriate check standards. Include a blank after high concentrations when carryover is a concern.
6. Review peak identification and integration consistently. Retain the original chromatograms and document any justified integration changes.
7. Calculate concentration or assay, reverse dilutions and review the complete sequence before reporting. Preserve audit-trail and processing information.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Injection | Retention time (min) | Area / area ratio | Resolution or comment |
|---|---|---|---|
| Blank | Record | Record | Interference / carryover |
| Reference replicates | Record | Record | Suitability |
| Test preparation 1 | Record | Record | Assay |

| Injection | Retention time (min) | Area / area ratio | Resolution or comment |
|---|---|---|---|
| Test preparation 2 | Record | Record | Preparation precision |

## Calculations

- Resolution, Rs = 2(tR2 - tR1) / (w1 + w2), using baseline peak widths
- Theoretical plates, N = 16(tR / w)^2, using baseline width
- For matched dilutions in a valid external-standard comparison: assay (%) = test area / standard area x reference concentration / nominal test concentration x reference potency (%)

### Worked Example

Illustrative adjacent peaks: retention times 5.00 and 5.40 min; baseline widths 0.20 and 0.24 min.

Rs = 2(0.40) / 0.44 = 1.82. The first peak gives N = 16(5.00/0.20)^2 = 10000.

For equal nominal concentrations, test and standard areas of 49000 and 50000 with reference potency 99.7% give assay = 49000/50000 x 99.7 = 97.706%.

These values illustrate calculations; use the adopted method criteria to decide whether a sequence is acceptable.

### Qualification record

- Include flow verification, injector repeatability, carryover, detector wavelength or response checks and temperature checks where required.
- State how each measured result is linked to a traceable standard and its predefined acceptance criterion.

## Result and Interpretation

- Report assay or concentration together with the observed suitability results.
- A resolved, reproducible peak must also be shown to be specific for the intended analysis.
- Investigate failed suitability or carryover before using affected test results.

## Precautions

- Use compatible solvents and the column pressure and temperature limits.
- Collect solvent waste in designated containers and keep incompatible wastes separate.
- Prevent particles and bubbles entering the flow path.
- Avoid selective reintegration or reinjection to obtain a preferred result.

## Viva Questions and Answers

### Why equilibrate the column?

A stable stationary-phase environment improves retention and response reproducibility.

### Does a single retention time prove identity?

No; coelution is possible and identity requires the intended method evidence.

### Why bracket test injections?

Check standards can reveal response drift during the run.

# Qualification of a UV-Visible Spectrophotometer

Practical 14 - Bench practical

## Aim

To evaluate wavelength, photometric and other relevant performance characteristics of a UV-visible spectrophotometer.

## Principle

Instrument qualification uses appropriate traceable materials to test performance characteristics separately. A wavelength check concerns the location of spectral features; a photometric check concerns the accuracy of measured absorbance or transmittance.

The required materials, conditions and tolerances depend on the instrument, intended use and adopted compendial or laboratory procedure. A single absorbance reading cannot establish complete instrument qualification.

## Materials and Requirements

- Identified UV-visible instrument and cells
- Suitable certified wavelength and photometric reference materials
- Method-required blanks and stray-light materials
- Qualification protocol and controlled raw-data forms

## Procedure

1. Define the intended spectral range and the performance tests required for that application.
2. Record instrument configuration, software version, reference certificates, cell path length and environmental conditions.
3. Perform baseline and readiness checks before qualification measurements.
4. Measure certified spectral features under their specified conditions and calculate wavelength differences.
5. Assess photometric performance at the specified levels and, where required, linearity, resolution, stray light and repeatability.
6. Compare each result with the applicable criterion and investigate failures by an approved process.
7. Issue a qualification report linking raw data to each test, conclusion and next review condition.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Test | Assigned value | Observed value | Error / conclusion |
|---|---|---|---|
| Wavelength feature | Certificate value | Record | Calculate difference |
| Photometric level | Certificate value | Record | Calculate difference |
| Repeatability | Protocol criterion | Record | Calculate variation |
| Other required test | Protocol criterion | Record | Evaluate |

## Calculations

- Wavelength error = observed wavelength - assigned wavelength
- Photometric error = observed absorbance - assigned absorbance

• RSD (%) = standard deviation / mean x 100

### Worked Example

Illustrative wavelength feature: assigned 287.50 nm, observed 287.70 nm; error = +0.20 nm.

Illustrative photometric level: assigned absorbance 0.500, observed 0.503; error = +0.003.

The certificate uncertainty and adopted tolerance are part of the assessment. These illustrative values are not universal acceptance limits.

## Result and Interpretation

• Report results by characteristic, rather than giving a single unsupported pass statement.
• Include any restriction on the qualified range or operating mode.
• Confirm suitability after relevant repair, relocation or configuration change according to the quality system.

## Precautions

• Use the certificate conditions for each reference material.
• Keep cell orientation and cleanliness controlled.
• Avoid treating a calibration solution as a general-purpose reference outside its certified conditions.
• Preserve failed results and the investigation record.

## Viva Questions and Answers

### Are wavelength and absorbance accuracy the same?

No; they are different instrument characteristics.

### Why assess stray light?

Unwanted light can bias high-absorbance measurements.

### What must a qualification conclusion identify?

The tested configuration, range, criteria and supporting results.

# Equipment Cleaning Validation

Practical 15 - Validation-record practical

## Aim

To evaluate cleaning effectiveness using a justified residue limit and a qualified recovery method.

## Principle

Cleaning validation links the product and equipment risks to a predefined cleaning process and evidence that relevant residues are controlled. Sampling location, recovery, analytical capability and dirty and clean hold conditions affect the conclusion.

A residue result must be compared with a scientifically justified limit appropriate to the product and equipment context. A convenient historical rule alone is not a sufficient toxicological justification.

## Materials and Requirements

- Equipment map and approved cleaning procedure
- Justified residue and microbial requirements where relevant
- Qualified swab or rinse recovery procedure
- Selective analytical method and sampling records

## Procedure

1. Define the equipment train, product sequence, worst-case rationale and the residue limits established through the approved assessment.
2. Identify difficult-to-clean locations, contact surfaces and the intended swab or rinse approach.
3. Demonstrate recovery at relevant levels on suitable representative surfaces or through the justified sampling model.
4. Perform the approved cleaning process and collect identified blanks, controls and samples at the prescribed locations.
5. Analyse using a method with adequate quantitation capability and review any recovery correction or uncorrected conservative reporting convention.
6. Calculate residue per area or other defined basis and compare all locations with the justified limits.
7. Issue a report covering process records, sampling recovery, results, deviations and the supported cleaning conditions.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Location / area | Raw residue amount | Recovery convention | Reported residue and limit |
|---|---|---|---|
| Sampling blank | Record | State | Evaluate |
| Recovery control | Record | Calculate | Evaluate |
| Worst-case location | Record | Apply justified convention | Compare |
| Additional location | Record | Apply justified convention | Compare |

## Calculations

• Residue per area = measured recovered residue / sampled area
• If validated and prescribed: recovery-corrected residue = measured recovered residue / recovery fraction

### Worked Example

Illustrative measured residue is 2.0 micrograms from a 25 cm^2 area. Uncorrected result = 0.080 micrograms/cm^2.
For a validated recovery fraction of 0.80 and a protocol requiring correction, corrected residue is 2.5 micrograms, or 0.100 micrograms/cm^2.
Compare with the limit from the approved assessment; the example supplies no universal acceptable limit.

## Result and Interpretation

• State recovery convention, analytical capability and each location result. A result below quantitation is interpreted with the method limit and reporting rule.

## Precautions

• Select limits before generating validation data.
• Prevent contamination of blanks and swabs.
• Document actual sampled area and surface identity.
• Do not average a failing difficult-to-clean location into a passing overall mean.

## Viva Questions and Answers

### Why choose worst-case locations?

They challenge the cleaning process at relevant difficult points.

### Why qualify recovery?

Sampling may collect only a fraction of the actual residue.

### Does a low analytical value alone validate cleaning?

The process, sampling, method capability and justified limits must all be considered.

# Dissolution Apparatus Qualification

Practical 16 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a dissolution apparatus.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Vessel and shaft geometry, centring, verticality, wobble, speed, temperature and relevant performance testing.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. Record each position and distinguish mechanical qualification from the applicable performance-verification requirements.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- Speed error (%) = (measured speed - set speed)/set speed x 100.

### Worked Example

Illustrative setting 50 rpm and measured 49.5 rpm give -1.0% error. This is not a universal tolerance.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Friability Apparatus Qualification

Practical 17 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a friability tester.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Drum identity and dimensions, rotation count, speed, timer and loading procedure.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. Verify the specified rotation programme and evaluate a suitable model tablet batch using pre- and post-test dedusted masses.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- Mass loss (%) = (initial mass - final mass)/initial mass x 100.

### Worked Example

Illustrative initial 6.000 g and final 5.970 g give 0.50% loss. Apply the relevant method and product requirements.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Disintegration Tester Qualification

Practical 18 - Equipment qualification practical

## Aim

To evaluate qualification evidence for a disintegration tester.

## Principle

Qualification demonstrates fitness for an intended use. User requirements and risk assessment define the installation checks, operational challenges and performance evidence. Calibration of one sensor is only part of this evidence.

## Materials and Requirements

- Equipment specification, user requirements and approved protocol
- Calibration, installation and maintenance records
- Supplied qualification readings and deviation forms
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Trace user requirements to design and installation checks, utilities, materials, safety systems and document availability.
3. Basket/tube/disc configuration, stroke, frequency, temperature, timing and endpoint observation.
4. Challenge the justified operating range with calibrated independent measurements and retain actual readings.
5. Verify physical operating parameters and apply the selected dosage-form method, including disc requirements and individual-unit records.
6. Assess performance with representative or worst-case loads or materials under the approved protocol.
7. Review deviations, acceptance criteria, requalification triggers and authorised release for the intended use.
8. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Requirement / test | Method / challenge | Actual result | Criterion and decision |
|---|---|---|---|
| Installation | Specify | Record | Evaluate |
| Operating range | Specify | Record | Evaluate |
| Performance / load | Specify | Record | Evaluate |

## Calculations

- Timing error = indicated duration - reference duration.

### Worked Example

Illustrative indicated 600 s and reference 598 s give +2 s. This check is distinct from a dosage-form disintegration result.

## Result and Interpretation

- Provide a requirement-to-evidence matrix and a qualified-use statement with unresolved restrictions.

## Precautions

- Use independent calibrated measurements.
- Set criteria before testing.
- Never bypass interlocks to perform a teaching challenge.

## Viva Questions and Answers

### What is IQ?

Documented verification of installation against requirements.

### What distinguishes OQ and PQ?

OQ challenges operating functions; PQ demonstrates intended performance under justified use conditions.

### When is requalification considered?

After relevant change, adverse trend or the approved periodic review.

# Bulk Pharmaceutical Chemical Vendor Checklist

Practical 19 - Audit case-study practical

## Aim

To create and apply an evidence-based audit checklist for the specified facility or supplier.

## Principle

An audit evaluates objective evidence against defined criteria and scope. A checklist supports consistent coverage but does not replace risk-based sampling, interviews and corroboration of actual practice.

## Materials and Requirements

- Fictional site profile, applicable current requirements and SOPs
- Audit plan, checklist and finding templates
- Selected records and interview notes
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Define purpose, scope, products, jurisdictions, auditor roles and sampling rationale.
3. For each question specify the requirement, objective evidence and record to inspect; trace one selected batch or transaction end to end.
4. Classify each observation using the approved system and describe the evidence, requirement and gap without speculation.
5. Prepare an exit summary and proposed action follow-up with responsibility, due dates and effectiveness evidence.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Audit question / criterion | Evidence sampled | Finding / risk | Action / verification |
|---|---|---|---|
| Governance / scope | Identify records | Assess | Assign |
| Selected process | Trace evidence | Assess | Assign |
| Follow-up | Review closure | Assess | Verify |

## Calculations

- Closure completion (%) = verified closed actions / actions due for closure x 100

### Worked Example

Illustrative 8 actions are due and 6 have verified closure: completion = 75%.
The two remaining actions must be evaluated by risk; the percentage does not itself establish site compliance.

### Audit scope: Bulk pharmaceutical chemical supplier

• Supplier authorisation and material traceability; change notification; impurity and contamination controls; laboratory data integrity; transport and complaint handling.
• For each listed area record the criterion, selected evidence, actual observation, risk and follow-up.

## Result and Interpretation

• Deliver a traceable checklist, factual finding statements and a risk-based follow-up plan.

## Precautions

• Avoid patient or commercial identifiers in teaching records.
• Do not confuse absence of evidence with proof of conformity.
• Do not claim an audit is a regulatory certification.

## Viva Questions and Answers

### What makes a finding defensible?

A clear criterion, objective evidence and a described gap.

### Why sample records?

A reasoned sample examines actual implementation within the audit scope.

### Is an action closed when promised?

Closure requires verified implementation and, where relevant, effectiveness.

# Tableting-Production Audit Checklist

Practical 20 - Audit case-study practical

## Aim

To create and apply an evidence-based audit checklist for the specified facility or supplier.

## Principle

An audit evaluates objective evidence against defined criteria and scope. A checklist supports consistent coverage but does not replace risk-based sampling, interviews and corroboration of actual practice.

## Materials and Requirements

- Fictional site profile, applicable current requirements and SOPs
- Audit plan, checklist and finding templates
- Selected records and interview notes
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Define purpose, scope, products, jurisdictions, auditor roles and sampling rationale.
3. For each question specify the requirement, objective evidence and record to inspect; trace one selected batch or transaction end to end.
4. Classify each observation using the approved system and describe the evidence, requirement and gap without speculation.
5. Prepare an exit summary and proposed action follow-up with responsibility, due dates and effectiveness evidence.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Audit question / criterion | Evidence sampled | Finding / risk | Action / verification |
|---|---|---|---|
| Governance / scope | Identify records | Assess | Assign |
| Selected process | Trace evidence | Assess | Assign |
| Follow-up | Review closure | Assess | Verify |

## Calculations

- Closure completion (%) = verified closed actions / actions due for closure x 100

### Worked Example

Illustrative 8 actions are due and 6 have verified closure: completion = 75%.
The two remaining actions must be evaluated by risk; the percentage does not itself establish site compliance.

### Audit scope: Tableting production

• Line clearance and cleaning; dispensing checks; granulation and drying records; blend sampling; compression controls; reconciliation and status segregation.
• For each listed area record the criterion, selected evidence, actual observation, risk and follow-up.

## Result and Interpretation

• Deliver a traceable checklist, factual finding statements and a risk-based follow-up plan.

## Precautions

• Avoid patient or commercial identifiers in teaching records.
• Do not confuse absence of evidence with proof of conformity.
• Do not claim an audit is a regulatory certification.

## Viva Questions and Answers

### What makes a finding defensible?

A clear criterion, objective evidence and a described gap.

### Why sample records?

A reasoned sample examines actual implementation within the audit scope.

### Is an action closed when promised?

Closure requires verified implementation and, where relevant, effectiveness.

# Sterile-Production Area Audit Checklist

Practical 21 - Audit case-study practical

## Aim

To create and apply an evidence-based audit checklist for the specified facility or supplier.

## Principle

An audit evaluates objective evidence against defined criteria and scope. A checklist supports consistent coverage but does not replace risk-based sampling, interviews and corroboration of actual practice.

## Materials and Requirements

- Fictional site profile, applicable current requirements and SOPs
- Audit plan, checklist and finding templates
- Selected records and interview notes
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Define purpose, scope, products, jurisdictions, auditor roles and sampling rationale.
3. For each question specify the requirement, objective evidence and record to inspect; trace one selected batch or transaction end to end.
4. Classify each observation using the approved system and describe the evidence, requirement and gap without speculation.
5. Prepare an exit summary and proposed action follow-up with responsibility, due dates and effectiveness evidence.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Audit question / criterion | Evidence sampled | Finding / risk | Action / verification |
|---|---|---|---|
| Governance / scope | Identify records | Assess | Assign |
| Selected process | Trace evidence | Assess | Assign |
| Follow-up | Review closure | Assess | Verify |

## Calculations

- Closure completion (%) = verified closed actions / actions due for closure x 100

### Worked Example

Illustrative 8 actions are due and 6 have verified closure: completion = 75%.
The two remaining actions must be evaluated by risk; the percentage does not itself establish site compliance.

### Audit scope: Sterile production

• Contamination-control strategy; facility and personnel qualification; environmental monitoring; aseptic-process simulation where applicable; sterilisation and integrity evidence; interventions and investigations.
• For each listed area record the criterion, selected evidence, actual observation, risk and follow-up.

## Result and Interpretation

• Deliver a traceable checklist, factual finding statements and a risk-based follow-up plan.

## Precautions

• Avoid patient or commercial identifiers in teaching records.
• Do not confuse absence of evidence with proof of conformity.
• Do not claim an audit is a regulatory certification.

## Viva Questions and Answers

### What makes a finding defensible?

A clear criterion, objective evidence and a described gap.

### Why sample records?

A reasoned sample examines actual implementation within the audit scope.

### Is an action closed when promised?

Closure requires verified implementation and, where relevant, effectiveness.

# Water-for-Injection System Audit Checklist

Practical 22 - Audit case-study practical

## Aim

To create and apply an evidence-based audit checklist for the specified facility or supplier.

## Principle

An audit evaluates objective evidence against defined criteria and scope. A checklist supports consistent coverage but does not replace risk-based sampling, interviews and corroboration of actual practice.

## Materials and Requirements

- Fictional site profile, applicable current requirements and SOPs
- Audit plan, checklist and finding templates
- Selected records and interview notes
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Define purpose, scope, products, jurisdictions, auditor roles and sampling rationale.
3. For each question specify the requirement, objective evidence and record to inspect; trace one selected batch or transaction end to end.
4. Classify each observation using the approved system and describe the evidence, requirement and gap without speculation.
5. Prepare an exit summary and proposed action follow-up with responsibility, due dates and effectiveness evidence.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Audit question / criterion | Evidence sampled | Finding / risk | Action / verification |
|---|---|---|---|
| Governance / scope | Identify records | Assess | Assign |
| Selected process | Trace evidence | Assess | Assign |
| Follow-up | Review closure | Assess | Verify |

## Calculations

- Closure completion (%) = verified closed actions / actions due for closure x 100

### Worked Example

Illustrative 8 actions are due and 6 have verified closure: completion = 75%.
The two remaining actions must be evaluated by risk; the percentage does not itself establish site compliance.

### Audit scope: Water-for-injection system

• System design and materials; generation and distribution qualification; sanitisation; sampling representativeness; microbial and endotoxin trends; alarms, maintenance and excursion response.
• For each listed area record the criterion, selected evidence, actual observation, risk and follow-up.

## Result and Interpretation

• Deliver a traceable checklist, factual finding statements and a risk-based follow-up plan.

## Precautions

• Avoid patient or commercial identifiers in teaching records.
• Do not confuse absence of evidence with proof of conformity.
• Do not claim an audit is a regulatory certification.

## Viva Questions and Answers

### What makes a finding defensible?

A clear criterion, objective evidence and a described gap.

### Why sample records?

A reasoned sample examines actual implementation within the audit scope.

### Is an action closed when promised?

Closure requires verified implementation and, where relevant, effectiveness.

# Sterile and Non-Sterile Plant Layouts

Practical 23 - Facility-record practical

## Aim

To design and assess sterile and non-sterile pharmaceutical plant layouts.

## Principle

Facility qualification addresses the intended environmental and utility conditions. Process validation assesses the manufacturing process; a qualified room alone does not validate a product process.

## Materials and Requirements

- Fictional facility plan and area classification rationale
- HVAC qualification and environmental records
- Personnel/material flow and cleaning procedures
- Approved method or teaching-data pack and a dated record sheet

## Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Define intended operations, contamination risks, cleanroom requirements where applicable and adjacent areas.
3. Review air handling, filters, airflow direction, pressure differences and recovery or other relevant qualified tests.
4. Map personnel, material, waste and equipment movements; assess cleaning, monitoring locations and environmental trends.
5. Connect facility evidence to the process-control strategy and identify gaps, deviations and requalification needs.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Area / function | Required condition | Qualification evidence | Gap / action |
|---|---|---|---|
| Dispensing | Define | Review | Assess |
| Processing | Define | Review | Assess |
| Transfer route | Define | Review | Assess |

## Calculations

- Pressure difference = pressure in the defined room - pressure in the stated reference room

### Worked Example

Illustrative room pressure +15 Pa and adjacent reference +5 Pa give a +10 Pa difference relative to that space. The required direction and acceptable range must come from the facility contamination-control strategy.

### Layout drawing requirements

• Draw separately labelled personnel, material, product and waste routes for both layouts. Show receipt, quarantine, released storage, dispensing, processing, packaging, laboratories and support spaces.
• For the sterile layout include the justified segregation, transfers, gowning, utilities and contamination-control concept. For the non-sterile layout consider dust, cross-contamination and campaign or dedicated-area needs.
• Use arrows, area functions and pressure relationships where justified; do not invent room classifications without a process-risk basis.

## Result and Interpretation

• Provide a flow diagram and requirement-to-evidence matrix with an authorised-use recommendation.

## Precautions

• Do not infer cleanroom class from pressure alone.
• Distinguish at-rest and operational conditions.
• Use qualified personnel for facility challenges.

## Viva Questions and Answers

### What does positive pressure imply?

A pressure relationship; airflow and contamination control still need evaluation.

### Why map flows?

Crossing routes can create contamination or mix-up risks.

### Does room qualification validate a process?

The process requires its own lifecycle evidence.

# Quality-by-Design Case Study

Practical 24 - Software and data-analysis practical

## Aim

To prepare a quality-by-design case linking a product target, risks, experiments and a control strategy.

## Principle

Quality by design begins with the intended product performance and uses scientific understanding and risk management to identify important quality attributes, material attributes and process parameters. Experimental evidence supports the control strategy; a risk table alone is not a design space.

Keep the supplied data, transformations, software version, analysis settings and complete output together. Record units explicitly and distinguish assumptions from observations.

## Materials and Requirements

- Defined target product profile and product-use context
- Material and process knowledge
- Risk assessment, experiment plan and control-strategy template
- Spreadsheet or institution-approved analysis software
- Raw-data dictionary and analysis worksheet

## Procedure

1. Define the analysis question and the variables, units, identifiers and missing-data conventions in the dataset.
2. Import a working copy and check values against the original file. Inspect ranges, duplicates, timing and unit consistency.
3. State the intended route, dosage form, strength and relevant performance targets in the quality target product profile.
4. Identify critical quality attributes and explain how each relates to patient or product performance.
5. Map potentially influential material attributes and process parameters and assess the available knowledge and uncertainty.
6. Plan experiments and measurements that address important uncertainties and interactions.
7. Use the resulting evidence to propose justified operating controls, material controls and monitoring. Update the risk assessment with new knowledge.
8. Retain diagnostics, intermediate calculations and the selected analysis settings. Explain exclusions and sensitivity checks.
9. Write a conclusion that addresses the stated question and the limitations of the design rather than relying on one fitted statistic.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Target / attribute | Risk and rationale | Evidence or study | Proposed control |
|---|---|---|---|
| Drug release | Record | Record | Propose |
| Content uniformity | Record | Record | Propose |

| Target / attribute | Risk and rationale | Evidence or study | Proposed control |
|---|---|---|---|
| Relevant impurity or stability attribute | Record | Record | Propose |
| Manufacturing attribute | Record | Record | Propose |

## Calculations

• For a declared classroom FMEA, risk-priority number = severity x occurrence x detectability. Define each scoring scale; this is one prioritisation tool, not a universal regulatory requirement.

### Worked Example

Illustrative binder-level risk has severity 4, occurrence 3 and detectability 2 on the specified five-point classroom scales.

RPN = 24. A control proposal should explain the underlying risk and evidence, rather than simply targeting a smaller number.

Independent confirmation of a proposed formulation setting supports the decision more than an unverified optimisation output.

## Result and Interpretation

• Show a traceable connection from the product target to the proposed controls and remaining uncertainty.

## Precautions

• Keep risk-scoring definitions consistent.
• Use scientific evidence for the control strategy.
• Avoid presenting an unvalidated acceptable region as an established regulatory design space.
• Preserve the original dataset and a reproducible record of the analysis.

## Viva Questions and Answers

### What is a critical quality attribute?

An attribute that needs appropriate control to support the intended product quality.

### Is an RPN a universal acceptance criterion?

No; it depends on the selected risk tool and context.

### What makes a control strategy credible?

A justified link to product and process understanding and appropriate evidence.

# Process Analytical Technology Case Study

Practical 25 - Software and data-analysis practical

## Aim

To prepare a process-analytical-technology case linking measurements to a process decision.

## Principle

Quality by design begins with the intended product performance and uses scientific understanding and risk management to identify important quality attributes, material attributes and process parameters. Experimental evidence supports the control strategy; a risk table alone is not a design space.

Keep the supplied data, transformations, software version, analysis settings and complete output together. Record units explicitly and distinguish assumptions from observations.

## Materials and Requirements

- Defined target product profile and product-use context
- Material and process knowledge
- Risk assessment, experiment plan and control-strategy template
- Spreadsheet or institution-approved analysis software
- Raw-data dictionary and analysis worksheet

## Procedure

1. Define the analysis question and the variables, units, identifiers and missing-data conventions in the dataset.
2. Import a working copy and check values against the original file. Inspect ranges, duplicates, timing and unit consistency.
3. State the intended route, dosage form, strength and relevant performance targets in the quality target product profile.
4. Identify critical quality attributes and explain how each relates to patient or product performance.
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6. Plan experiments and measurements that address important uncertainties and interactions.
7. Use the resulting evidence to propose justified operating controls, material controls and monitoring. Update the risk assessment with new knowledge.
8. Retain diagnostics, intermediate calculations and the selected analysis settings. Explain exclusions and sensitivity checks.
9. Write a conclusion that addresses the stated question and the limitations of the design rather than relying on one fitted statistic.

## Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

| Target / attribute | Risk and rationale | Evidence or study | Proposed control |
|---|---|---|---|
| Drug release | Record | Record | Propose |
| Content uniformity | Record | Record | Propose |

| Target / attribute | Risk and rationale | Evidence or study | Proposed control |
|---|---|---|---|
| Relevant impurity or stability attribute | Record | Record | Propose |
| Manufacturing attribute | Record | Record | Propose |

## Calculations

• For a declared classroom FMEA, risk-priority number = severity x occurrence x detectability. Define each scoring scale; this is one prioritisation tool, not a universal regulatory requirement.

### Worked Example

Illustrative binder-level risk has severity 4, occurrence 3 and detectability 2 on the specified five-point classroom scales.

RPN = 24. A control proposal should explain the underlying risk and evidence, rather than simply targeting a smaller number.

Independent confirmation of a proposed formulation setting supports the decision more than an unverified optimisation output.

### PAT case

• Example: monitor a blending or drying process with a qualified measurement strategy, such as an appropriate spectral model supported by reference measurements.

• Define the measurand, sampling representativeness, calibration domain, model validation, decision rule and handling of out-of-domain results.

• A fast or in-line sensor does not by itself establish real-time release. The complete analytical and process control approach requires appropriate evidence.

## Result and Interpretation

• Show a traceable connection from the product target to the proposed controls and remaining uncertainty.

## Precautions

• Keep risk-scoring definitions consistent.
• Use scientific evidence for the control strategy.
• Avoid presenting an unvalidated acceptable region as an established regulatory design space.
• Preserve the original dataset and a reproducible record of the analysis.

## Viva Questions and Answers

### What is a critical quality attribute?

An attribute that needs appropriate control to support the intended product quality.

### Is an RPN a universal acceptance criterion?

No; it depends on the selected risk tool and context.

### What makes a control strategy credible?

A justified link to product and process understanding and appropriate evidence.

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