Analytical Method Validation Checklist

Aligned with USP <1225> Validation of Compendial Procedures, ICH Q2(R2), and USP <1224> Transfer/Verification — for chromatographic and other quantitative procedures in a GMP QC environment.

1. Scope & Reference Standards

- ■ Confirm the compendial monograph / in-house procedure version is current and the checklist applies to the correct dosage form and matrix.
- ■ Verify reference standards (potency, water content, assignment) and reagent/apparatus suitability before starting.
- ■ Define acceptance criteria for each validation characteristic up front, per USP <1225> and ICH Q2(R2).

2. Specificity / Selectivity

- ■ Demonstrate no interference from placebo, excipients, degradants, or impurities at the analyte retention time / wavelength.
- ■ Peak purity (PDA/MS) across the analyte peak; force-degradation mass balance where applicable.
- ■ For assay vs. content uniformity vs. dissolution, confirm each procedure is specific for its intended use.

3. Linearity & Range

- ■ Minimum 5 concentration levels across the specified range (assay: typically 80–120% of test concentration).
- ■ Report regression slope, intercept, correlation coefficient (r) or r2; residual plots reviewed for curvature.
- ■ Range covered: from LOQ (or reporting level) up to 120% (assay) or ±20–50% (impurities) of specification.

4. Accuracy (Recovery)

- ■ Spike recovery at 3 levels, typically 80/100/120% (assay) or 50/100/150% of specification (impurities).
- ■ Report % recovery and %RSD against pre-set acceptance (e.g. 98.0–102.0% for assay).
- ■ For matrix-rich samples, compare standard-addition or placebo-spiked results to neat standards.

5. Precision

- ■ Repeatability: n=6 replicate preparations at 100% level; %RSD typically ≤2.0% (assay).
- ■ Intermediate precision: different analyst, day, instrument, or column; analyze combined data vs. acceptance.
- ■ For impurities at low levels, evaluate precision against signal-to-noise-based criteria, not %RSD alone.

6. Detection & Quantitation Limits (impurity procedures)

- ■ DL: S/N ≥ 3 or calibration-based; QL: S/N ≥ 10 with precision and accuracy demonstrated at the QL level.
- ■ Verify LOQ recovery and repeatability (e.g. 80–120% recovery, RSD ≤10%) at the reporting threshold.
- ■ Confirm the reporting threshold and identification threshold used match the filing / monograph requirements.

7. Robustness

- Deliberate small variations: flow rate, column temperature, pH/mobile phase ratio, wavelength, injection volume.
- Document effects on resolution, tailing, and result; define which parameters are critical and must be controlled.
- Column lot/brand substitution evaluated where relevant (especially for compendial methods).

8. System Suitability

- SSE/tailing/plate count/resolution limits set from method development data and justified per USP <621>.
- SIST / system suitability mixture prepared and acceptance verified at the start of each run sequence.
- Define actions when system suitability fails before any sample results are reported.

9. Solution Stability & Handling

- Demonstrate analyte and standard solution stability (bench-top and autosampler) for the full run duration.
- Confirm storage conditions, diluent compatibility, and light sensitivity where applicable.

10. Documentation & Compliance

- Validation protocol and report approved (author, reviewer, QA); deviations and OOS handled per SOP.
- Raw data, audit trails, and reprocessing records comply with data integrity expectations (ALCOA+, 21 CFR Part 11 / Annex 11).
- Method transferred to QC with training records, or transfer/verification performed per USP <1224>.
- Periodic review trigger set: revalidation upon change to synthesis, manufacturer, or specification changes.

Prepared by Murali Jujjavarapu — Analytical Sciences & Quality Control Leader · muralijujjavarapu.lovable.app · This checklist is a practical planning aid, not a substitute for your approved SOPs, current USP/ICH texts, or regulatory guidance.