PQS HPLC QC Run Review & Troubleshooting Checklist

Practical educational worksheet for pharmaceutical QC analysts and reviewers

Product / Material:		Method / SOP:	
Batch / Lot:		Instrument ID:	
Analyst:		Review date:	

1. Pre-run readiness

Check	Evidence / question	Status
[ ]	Current approved analytical method and specification available	[ ] OK [ ] Issue
[ ]	Instrument qualification / calibration / maintenance status acceptable as required	[ ] OK [ ] Issue
[ ]	Correct column, mobile phase, diluent, wash solution and sequence method selected	[ ] OK [ ] Issue
[ ]	Reference standard identity, lot, potency/purity and expiry/use period verified	[ ] OK [ ] Issue
[ ]	Sample identity, preparation, dilution scheme and preparation timing traceable	[ ] OK [ ] Issue
[ ]	Blank / standard / SST / sample sequence matches approved instructions	[ ] OK [ ] Issue

2. System suitability and sequence gate

SST criterion	Approved limit / requirement	Observed result	Pass?
Repeatability / %RSD			[ ] Y [ ] N
Resolution			[ ] Y [ ] N
Tailing / symmetry			[ ] Y [ ] N
Theoretical plates / efficiency			[ ] Y [ ] N
Sensitivity / S/N (if applicable)			[ ] Y [ ] N
Other method-specific criterion			[ ] Y [ ] N

Sequence check: [ ] All injections accounted for [ ] No unexplained trial/sample injections [ ] Reinjections documented and justified [ ] Aborted runs/events retained and assessed

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3. HPLC run review matrix

Evidence	What to verify	Red flag / note
Sequence / injection list	Every injection has a defined purpose and disposition.	Unexplained extra, repeated or aborted injection.
Chromatograms	Expected peaks, peak shape, baseline and unexpected peaks are evaluated.	Visible unexplained peak or ignored chromatographic event.
Integration / processing	Processing method and manual integration changes are traceable and justified.	Reintegration repeated until a preferred result appears.
Standard / sample preparation	Weights, dilutions, potency corrections and preparation records agree with calculations.	Mismatch between notebook, vial ID or CDS record.
System behavior	Pressure, retention and baseline behavior are consistent with the method/run.	Major drift, pressure event or instability without assessment.
Calculations / report	Reported result is reproduced from controlled inputs and approved formulas.	Transcription, dilution factor or potency correction discrepancy.
Audit trail / metadata	Electronic history supports sequence, acquisition, processing and final report.	Deleted data, unexplained method change or shared-user activity.

4. Data-integrity review gate

[ ]	Original electronic/raw data retained and reviewable
[ ]	Sequence creation/edits and acquisition/processing methods are traceable
[ ]	Manual integration or processing changes have documented scientific justification
[ ]	All relevant failed, repeated, aborted or unusual injections are visible and assessed
[ ]	Applicable audit trail / metadata review completed according to site procedure
[ ]	Final report is consistent with the complete electronic record

Decision point: A passing assay or passing SST does not resolve conflicting evidence from chromatograms, integration history, unexplained injections, calculations or metadata. Evaluate the impact through the applicable approved quality-system process.

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Observation	Areas to examine	Evidence to capture before action
High backpressure	Column/frit, inline filter, tubing restriction, buffer precipitation, mobile-phase viscosity.	Pressure trace, column ID/age, solvent/buffer preparation, system checks.
Low / unstable pressure	Leaks, air, pump seals/check valves, reservoir, flow delivery.	Pressure trend, leak check, flow verification, maintenance history.
Peak tailing / fronting	Column condition, pH, overload, solvent mismatch, fittings, secondary interactions.	Peak metrics, standard/sample comparison, column history, preparation details.
Split peaks	Injection solvent, column void, fitting, sample chemistry, blockage.	Blank/standard/sample comparison, injection conditions, column/system status.
Ghost / unexpected peaks	Carryover, solvents, glassware, previous injection, sample-related impurity/degradation.	Blank runs, sequence order, carryover check, sample/stability context.
Baseline noise / drift	Bubbles, detector/lamp, solvent quality, temperature, gradient mixing, contamination.	Baseline trace, detector status, mobile phase, temperature/gradient data.
Retention-time drift	Flow, mobile phase, pH, temperature, equilibration, column aging.	Retention trend, pressure/temperature data, mobile-phase preparation.
Low resolution	Column selectivity/efficiency, pH, mobile phase, gradient, flow, temperature.	Critical-pair chromatograms, Rs trend, method conditions, column history.
High %RSD	Autosampler precision, solution stability, preparation, bubbles, equilibration.	Individual injection responses, vial/solution history, system behavior.

Do not troubleshoot by changing multiple variables until the chromatogram passes. Preserve the original data, document what was observed, isolate scientifically plausible causes, and follow the approved procedure for any repeat, reinjection, method adjustment, deviation or investigation.

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5. Event / observation record

Observation or event:	
When detected:	
Affected injections / samples:	
Immediate data-preservation action:	
Evidence reviewed:	
Scientific assessment:	

6. Final disposition

[ ]	Run acceptable according to approved procedure and complete review
[ ]	Additional documented laboratory evaluation required
[ ]	Deviation / incident process required
[ ]	OOS / OOT or other investigation process required, as applicable
[ ]	Data-integrity escalation / QA assessment required
[ ]	Result not reportable pending assessment

Analyst / reviewer:		Date:	
Second reviewer / QA (if required):		Date:	

Educational resource: This checklist is a practical review aid and does not replace approved analytical methods, SOPs, pharmacopoeial requirements, regulatory filings, laboratory investigations or quality-system procedures.