GUIDEGXP SERIES · PHARMA LAB

OPERATIONAL GUIDE

ANALYTICAL INSTRUMENTATION

IN THE GMP QC LABORATORY

Selection, Qualification, Performance Verification, Troubleshooting and Lifecycle Control

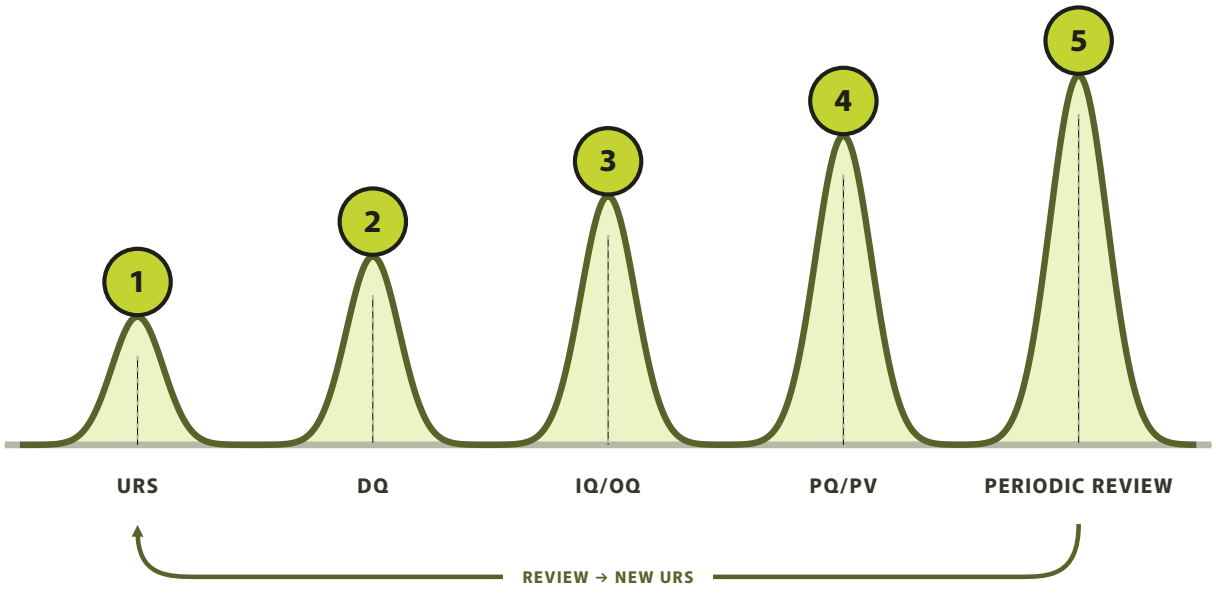
308 PAGES · 24 CHAPTERS · 6 PARTS · TOOLKIT OF 24 WORD + EXCEL TOOLS

FROM THE URS TO PERIODIC REVIEW: EVERY INSTRUMENT UNDER LIFECYCLE CONTROL

FIRST EDITION · OCTOBER 2026 · V1.0 · CUT-OFF 02/10/2026 · ENG EDITION

FREE EXCERPT

THE INSTRUMENT LIFECYCLE, READ AS A CHROMATOGRAM



GuideGxP

Practical compliance guides for Pharma professionals

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About this guide

The guide supports those who select, qualify, verify, use and govern the analytical instruments of a GMP quality control laboratory — HPLC and UHPLC, GC and headspace, UV-Vis, FTIR and Raman, LC-MS, ICP-MS, dissolution and physical testing, TOC, Karl Fischer, pH and conductivity — from the URS to periodic review. For every point it says which text governs it, with what force and in which jurisdiction, which value it gives (or does not give) and of what nature, what the laboratory has to decide and where the decision is recorded. No universal values: tolerances, calibration and requalification intervals, system suitability criteria and the number of replicates remain laboratory decisions, taken with a written criterion.

This excerpt contains, exactly as they appear in the full edition: the regulatory and technical status box and the label system; the complete table of contents; from Chapter 2 the distinction between qualification, method validation and system suitability; from Chapter 7 the HPLC→UHPLC transfer with the gradient delay volume and Case A in full; real pages of three toolkit tools; the list of what the purchase contains. First edition, October 2026, v1.0; regulatory cut-off 02/10/2026.

Regulatory and technical status

⚠ NOTICE

Regulatory and technical status as of 02/10/2026

- **EU.** EudraLex Vol. 4 CURRENT REGULATORY REQUIREMENT in the EU: Chapter 1 (since 31/01/2013), Chapter 3 (since 01/03/2015), Chapter 4 and Annex 11 (since 30/06/2011), Annex 15 (since 01/10/2015), Part II for active substances (since 01/09/2014). EU GMP, Part I, Chapter 6 'Quality Control' (revision of 28/03/2014, in operation since 01/10/2014) CURRENT REGULATORY REQUIREMENT in the EU. EU GMP Annex 19 'Reference and Retention Samples', revision C(2026) 4135, applicable from 24/09/2026 CURRENT REGULATORY REQUIREMENT in the EU. EMA GMP Q&A, "Data integrity" section: CURRENT GUIDANCE in the EU.
- **GB.** Human Medicines Regulations 2012 CURRENT REGULATORY REQUIREMENT in GB. In Great Britain GMP applies under the Human Medicines Regulations 2012 (reg. 37, B17 and C17): for the texts covered in this guide, all dated before 31/12/2020, the references coincide with those of the EU.
- **PIC/S** CURRENT GUIDANCE: PE 009-18 (adopted on 22/09/2026, in force since 24/09/2026); PI 006-4 'Recommendations on Qualification and Validation' from 01/10/2026, superseding PI 006-3 ~~SUPERSEDED~~; PI 023-2 (25/09/2007); PI 041-1 (since 01/07/2021); PI 011-3 (25/09/2007, outdated). PI 006-4, PI 023-2 and PI 041-1 are PIC/S recommendations or aide-memoires GUIDANCE: they illustrate inspection expectations but are not legal acts; they become binding only if adopted by the competent authority.
- **WHO.** WHO TRS 1052, Annex 4 'WHO good practices for pharmaceutical quality control laboratories' (2024) CURRENT GUIDANCE is the revision of WHO TRS 957, Annex 1 (2010) ~~SUPERSEDED~~. Also CURRENT GUIDANCE: TRS 1019, Annex 3 (2019), TRS 1025, Annex 4 and TRS 1033, Annex 4 (2021).
- **ICH** CURRENT GUIDANCE. ICH Q2(R2) and ICH Q14 (Step 4 of 01/11/2023, effective in the EU from 14/06/2024) concern the development and validation of analytical procedures used for release and stability testing; they are not guidelines on instrument qualification. Q9(R1) of 18/01/2023; Q10 of 04/06/2008. ICH Q4B(R1) CURRENT GUIDANCE; annexes: dissolution Annex 7(R2), disintegration Annex 5(R1), friability Annex 9(R1), uniformity of dosage units Annex 6.
- **USA.** 21 CFR 211 and Part 11 CURRENT REGULATORY REQUIREMENT in the USA. In the USA 21 CFR 211.160(b)(4) requires calibration of instruments, apparatus, gauges and recording devices at suitable intervals under a written programme with specific directions, schedules, limits for accuracy and precision and remedial action, and prohibits the use of instruments not meeting specifications REGULATORY REQUIREMENT; the text does not use the term 'qualification': qualification is the evidence demonstrating compliance with this requirement and with 211.63 and 211.68. CURRENT GUIDANCE in the USA: FDA guidance on OOS results (May 2022), mechanical calibration of dissolution apparatus (January 2010), data integrity (December 2018), Part 11 (August 2003), method validation (July 2015), Q2(R2) and Q14 (March 2024) and dissolution testing (August 1997; August 2018); the CGMP Q&A "Laboratory Controls"; CPGM 7356.002; the inspection guide for QC laboratories (July 1993: reference material for investigators, not binding). The FDA guidance 'Computer Software Assurance for Production and Quality Management System Software' (03/02/2026) GUIDANCE concerns medical device production; for pharmaceutical QC laboratories subject to 21 CFR 211, 211.68, Part 11 and the FDA data integrity Q&A (2018) remain applicable. The risk-based approach is cited here as

transferable good practice. Procedure ORA-LAB.5.5 describes how FDA laboratories manage their own instruments (ISO/IEC 17025) and is archived: it is an example of good practice, not a requirement for industry.

- **Pharmacopoeias.** As of 02/10/2026 the applicable texts are Ph. Eur. 12th Edition up to Issue 12.3 and USP–NF 2026, Issue 5 (official from 01/10/2026); Ph. Eur. Issue 13.1 has been published but applies only from 01/01/2027. Ph. Eur. texts were not consulted directly: this guide reports their number, title and status from official EDQM sources and describes the structure of the decisions; for requirements, methods and criteria the current Ph. Eur. text prevails. In the states applying the Ph. Eur. its texts have mandatory applicability through the marketing authorisation and pharmaceutical legislation COMPENDIAL REQUIREMENT. In the EU the USP is not a mandatory reference: it becomes one only through a dossier commitment or a quality system decision; the EU requirement for laboratory instruments remains EU GMP (Chapter 6, Chapter 3 and Annex 15). As of 02/10/2026 the official text of USP 〈1058〉 'Analytical Instrument Qualification' is the version official since 01/08/2017 CURRENT GUIDANCE; the revision of the chapter published as a proposal in the Pharmacopeial Forum is a proposal DRAFT and is not official text. USP 〈1058〉 is an informational chapter GUIDANCE: the obligation to qualify instruments arises from the applicable GMP regulations (in the USA 21 CFR 211.160(b)(4), 211.63 and 211.68; in the EU Chapter 6, Chapter 3 and Annex 15), not from the chapter itself. JP19 CURRENT in Japan since 10/04/2026, with a transition period from JP18 until 30/09/2027.
- **OMCL.** The OMCL guideline 'Qualification of Equipment' — Core document (PA/PH/OMCL (08) 73 R7, in force since 15/11/2023) GUIDANCE is written for the Official Medicines Control Laboratories of the European OMCL network and is not binding on industry; this guide describes its structure and parameters and does not reproduce its numerical limits: for the values, refer to the annex in the current revision published by the EDQM. Official pages read online are paraphrased and must be checked against the current text before use in a controlled document; OMCL documents were read through automated extraction of the official EDQM pages, because the files could not be downloaded: this guide reports their structure and parameters, never numerical values.
- DRAFT. Revision of EU GMP Annex 11, Chapter 4 and Chapter 1 and new Annex 22 DRAFT GUIDANCE: drafts consulted in 2025 (consultation closed); as of 02/10/2026 the final texts have not been published and the 2011 Annex 11 and Chapter 4 and the 2013 Chapter 1 remain in force CURRENT REGULATORY REQUIREMENT in the EU. The draft contents are proposals. USP 〈1058〉 (Case ID SUB-1755), 〈1225〉, 〈1029〉, 〈921〉, 〈1039〉 and 〈701〉, proposed revisions DRAFT, and the new chapter 〈1221〉, proposed DRAFT: proposals published for comment in the Pharmacopeial Forum; as of 02/10/2026 they are not official text and the current official version of the existing chapters remains applicable. Ongoing PDG revisions of Ph. Eur. 2.2.46 and 2.9.3 DRAFT.
- IN DEVELOPMENT. Revision of EU GMP Annex 15 IN DEVELOPMENT: concept paper EMA/INS/GMP/163466/2026 of 19/01/2026 proposes, among other things, extending Annex 15 to active substance manufacturers; the draft is planned for December 2026. As of 02/10/2026 the 2015 Annex 15 remains in force. In the same status: ISO/CD 17034 and the CDER guidance 'Computer Software Assurance for AI-Based Systems in Drug Manufacturing and Clinical Investigations; Supplemental Guidance', which is on the agenda and has not been published.
- **Published, not yet applicable.** Ph. Eur. Issue 13.1, published on 23/04/2026 and applicable from 01/01/2027 (2.1.7 and 2.9.1 revised); Issue 13.2, published on 01/07/2026 and applicable from 01/04/2027 (new 2.2.62 on the ELSD and four revised elemental analysis chapters: as of 02/10/2026 their numbers could not be verified on an official source); USP–NF 2026, Issue 6 official from 01/12/2026; USP–NF 2027, Issue 1 from 01/02/2027 and Issue 2 from 01/04/2027.
- ~~SUPERSEDED~~. WHO TRS 957, Annex 1 (by TRS 1052, Annex 4, 2024); OMCL Annex 9 on pH meters (withdrawn on 30/04/2020, content referred to Ph. Eur. 2.2.3); PIC/S PI 006-3 (by PI 006-4 from 01/10/2026); the 2007 version of ICH Q4B (by Q4B(R1)); ICH Q2(R1) (by Q2(R2)); ISO Guide 35:2017 (by ISO 33405:2024); ASTM E2500-20 (by E2500-25); the FDA CSA guidance of 24/09/2025 (by the version of 03/02/2026).
- CURRENT TECHNICAL STANDARD. JCGM 200:2012 (VIM), JCGM 100:2008 (GUM), ISO/IEC 17025:2017, ISO 17034:2016, ISO 33405:2024, ASTM E2503-13(2020) (recognised by CDER on 21/08/2025), E275-08(2022), E1421-99(2021), E1840-96(2022), E1655-17(2024), E2500-25; ISPE GAMP 5, 2nd ed. (July 2022) CURRENT GEP/QRM. NIST certificates and their validity: SRM 2034 valid indefinitely if stored correctly; SRM 1921b until 31/12/2027; SRM 2035b until 01/01/2027; SRM 2036 until 31/12/2028; SRM 2241 until 31/12/2026; SRM 2242a until 31/12/2029; SRM 2243 expired; SRM 930e, 1930 and 935a archive certificates only.
- **What is not there.** No regulation sets a single value for the calibration, verification and requalification intervals of instruments: the criterion and the verification interval are defined for the instrument and its intended use through a documented risk assessment that considers criticality, frequency of use, observed drift and history; the FDA Q&A on laboratory controls gives "a common frequency is once a year" as an example, referring to the auto-calibrator of balances. The same holds for instrument tolerances and for the number of replicates.

- **To be re-verified before printing or at the first update:** final texts of the 2025 drafts; the Annex 15 draft; the revision of USP 〈1058〉; Ph. Eur. 13.1 and 13.2; USP–NF 2026 Issue 6 and 2027 Issues 1 and 2; validity of NIST SRM 2241 and 2035b; the EMA page for ICH Q14 ("Step 5 - Revision 1", content not verified), the CDER guidance on AI systems and the effects of the EU "new pharmaceutical legislation"; the end of the JP18 → JP19 transition.

Document	Status	Dates not to be confused	Jurisdiction	Source
EU GMP Chapter 6	CURRENT	revision of 28/03/2014; in operation since 01/10/2014; in PIC/S since 01/01/2017	EU; PIC/S	FS-06, FS-17
USP 〈1058〉	CURRENT; revision DRAFT	official since 01/08/2017; proposal with a 2025 DOI citation	USA	FS-57, FS-58
ICH Q2(R2), ICH Q14	CURRENT	Step 4 of 01/11/2023; EU from 14/06/2024; FDA March 2024	ICH, EU, USA	FS-27, FS-28, FS-43
PIC/S PI 006-4; PI 006-3	CURRENT; ~~SUPERSEDED~~	in force since 01/10/2026	PIC/S	FS-18
Revisions of Annex 11, Chapter 4, Chapter 1	DRAFT	07/10/2025: consultation closed, not adoption	EU	FS-05, FS-08
Ph. Eur. 12.3; 13.1; 13.2	CURRENT; no status label	01/07/2026; 01/01/2027; 01/04/2027	Ph. Eur. member states	FS-81

How to read the labels

Four labels give the status of a document as of 02/10/2026, seven give the nature of a statement and one marks the examples; status comes first, then nature, with the jurisdiction outside the brackets ("CURRENT in the EU").

Label	Instrumentation example
CURRENT	USP 〈1058〉 in the text official since 01/08/2017; PIC/S PI 006-4 since 01/10/2026
DRAFT	proposed revision of USP 〈1058〉: the proposal envisages, it does not require
IN DEVELOPMENT	revision of Annex 15, for which only the concept paper exists
~~SUPERSEDED~~	OMCL Annex 9 on pH meters, withdrawn on 30/04/2020
REGULATORY REQUIREMENT	written calibration programme for QC instruments (21 CFR 211.160(b)(4)) in the USA
COMPENDIAL REQUIREMENT	chromatographic system suitability test (SST) criteria of Ph. Eur. 2.2.46 in the Ph. Eur. member states
GUIDANCE	four-stage qualification DQ, IQ, OQ, PQ (WHO TRS 1052, Annex 4, 5.27)
TECHNICAL STANDARD	NIST SRM 2034 for verifying the UV-Vis wavelength scale
SCIENTIFIC PRINCIPLE	Nernst slope ln(10)·R·T/F
GEP/QRM	verification intervals shorter than the time over which the instrument has been seen to drift
GUIDEGXP RECOMMENDATION	correspondence between OMCL levels and the DQ, IQ, OQ, PQ phases
DEMONSTRATION EXAMPLE	apparent absorbance calculated with a hypothetical stray light fraction

Edge cases: USP 〈1058〉 and Annex 11 each have a current text and a draft revision; Annex 15 is current and its revision is in development; TRS 957 and OMCL Annex 9 are superseded; Ph. Eur. 13.1 and 13.2 and the USP–NF Issues not yet official carry no status label: the text reads "published on ..., applicable from ...".

The nature of a value is not a label: it is written out in words next to the number, and it decides how the number may be used.

Nature of the value	Value and object	Document and clause	Source
requirement (no value)	calibration "at suitable intervals"	21 CFR 211.160(b)(4)	FS-39
definition	"USP Dissolution Performance Verification Standard-Prednisone RS" (salicylic acid RS discontinued since 01/12/2009)	FDA guidance of January 2010; USP 〈711〉	FS-47, FS-66
guidance	deaeration to less than 60% saturation of total dissolved gases	FDA guidance of January 2010	FS-47
certificate	holmium oxide band 9: 416.02 nm (spectral bandwidth 0.1 nm) and 416.89 nm (3 nm), U95 ±0.05 nm	NIST SRM 2034, Table 1	FS-108
convention	linear conductivity compensation at 2%/°C, for dilute salt solutions	instrument practice	FS-114, FS-116
example	"a common frequency is once a year" for the balance auto-calibrator	FDA CGMP Q&A "Laboratory Controls", Q1	FS-51
literature	deaeration adequate at ≤ 95% of saturation at 37 °C, the criterion of one study	Rohrs and Stelzer, 1995	FS-121
principle	59.159 mV/pH at 25 °C, Nernst slope	CODATA 2018 constants	FS-118

Full edition — complete table of contents: the map of the manual

The full edition comprises 24 chapters in six parts, named after the six areas of the Analytical Instrumentation hub, plus six appendices, over 308 A4 pages. Chapters 2–24 follow the same seventeen-section path: the problem and the decision; scope and boundaries; data to collect; technical principles; requirements and sources; interpretation; risk; decision; reasoned procedure; evidence; audit readiness; example (or integrated case); errors to avoid; chapter checklist; toolkit tools and related articles; the decisions the chapter produces; chapter sources. Page numbers refer to the full edition, not to this excerpt.

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CHAPTER 2

Analytical instrument qualification: lifecycle, classification and software

Excerpt from Chapter 2, exactly as it appears in the full edition: the problem and the decision, data quality in layers from the technical principles, the errors to avoid. In the full edition the chapter continues with USP 〈1058〉, WHO and OMCL, the three classifications, instrument and system, supplier tests, requirements and sources, risk, decision, example, checklist and the D-02.n decisions.

The problem and the decision

An instrument goes into use when someone signs that it is fit for its intended use: the decision is which evidence supports that signature, and how deep that evidence must go for each class of instrument. The signature is at its weakest precisely for the instrument that passes the method's system suitability test (SST) every day and has never been challenged outside those conditions: a gradient UHPLC whose gradient delay volume has never been measured, a supplier IQ/OQ package signed "for acceptance", a calculation entrusted to a spreadsheet that was left outside the system. The QC manager and laboratory QA decide, with laboratory CQV (D-02.1, D-02.2); release for use is a decision of the quality function (D-02.6), and no worksheet in the toolkit takes it in its place.

Technical principles

Data quality in layers

The quality of an analytical result rests on distinct components, each answering its own question; the literature describes this as a component model (Bansal and co-authors, 2004) SCIENTIFIC PRINCIPLE. Qualification demonstrates that the instrument is suitable for its intended use and performs within defined specifications; method validation or verification demonstrates that the analytical procedure is fit for purpose; system suitability verifies, at the time of analysis, that the complete analytical system (instrument, column, reagents, analyst) performs as required by the procedure. They are distinct and complementary levels: none replaces the others.

Level	What it verifies	Example test	Who defines it	Source
Instrument qualification	fitness of the configuration for its intended use, across the operating ranges	flow accuracy at the limits of the operating range	laboratory (CQV with the family lead); QA approval	FS-22, FS-10
Method validation or verification	fitness of the procedure for its purpose	accuracy and precision of the procedure on the sample	method development; implementing laboratory	FS-27, FS-06
System suitability	performance of the complete analytical system at the time of use	resolution of the critical pair in the sequence	analytical procedure; applicable chapter for compendial uses	FS-22, FS-28
Sample controls	control of the individual analysis	blanks, control samples	procedure; laboratory	FS-122

System suitability checks what the method exercises: a systematic error in flow, wavelength or temperature accuracy, in linearity outside the method range or in carryover at levels other than those in the sequence can remain within the SST criteria and still shift the result. The WHO ties SST to the complete system "prior to and throughout the analysis of samples" (WHO TRS 1052, Annex 4, 6.27)

CURRENT GUIDANCE; ICH Q14 CURRENT GUIDANCE places it inside the procedure: "the system suitability test (SST) which is part of the analytical procedure."

> **▲ COMMON MISTAKE**
>
> "The HPLC passed system suitability, so it is qualified": the sentence collapses two levels into one. The 1993 FDA inspection guide CURRENT GUIDANCE in the USA states that "System suitability data alone is insufficient for and does not constitute method validation."; still less does it demonstrate qualification. SST stops at the method parameters; qualification covers the configuration and the operating ranges. Both are needed, with separate records.

Errors to avoid

1. **"Validated instrument".** The instrument is qualified, the procedure is validated and the computerised system is validated as a system: three objects and three records.
2. **"〈1058〉 compliant".** The chapter is informational; the correct wording is "qualified under the qualification SOP, which cites USP 〈1058〉 as a reference".
3. **Groups A/B/C or the OMCL mapping attributed to the texts.** The Groups are concepts of 〈1058〉 and the correspondence between levels and phases is a reading of this guide; the laboratory's classes are a documented decision (D-02.1).
4. **Supplier package signed without review.** Annex 11, 3.3 and MHRA 6.19: the package is reviewed against the URS and the intended use.
5. **Software excluded from qualification.** WHO TRS 1052, 5.46 includes firmware and software; data-supporting functions are verified in OQ (D-02.5).
6. **Printout as the record of a dynamic system.** FDA DI Q&A, Q10: the printout of a dynamic record is not the original record.
7. **CSA cited for a pharmaceutical CDS.** The guidance of 03/02/2026 concerns medical devices.

PART II — HPLC & UHPLC

CHAPTER 7

Columns, mobile phase, system suitability and HPLC→UHPLC transfer

Excerpt from Chapter 7, exactly as it appears in the full edition: the problem and the decision, the HPLC→UHPLC transfer with the gradient delay volume and Case A in full. Case A is one of the five integrated cases of the book (A UHPLC fleet, B headspace GC, C ICP-MS, D dissolution, E TOC), linked to the toolkit with the same identifiers. Corvessa Pharma S.p.A. is a fictitious company: data, dates and codes are hypothetical.

The problem and the decision

Between a qualified instrument and a valid result sit the column, the mobile phase, the system suitability test (SST) and, when a method moves to another system, the gradient delay volume (dwell volume). The decision is when the analytical system is fit for use at the time of analysis, and how a gradient is moved to another system without losing the separation. The risk grows when the fleet runs the same method on systems with different dwell volumes, admitted by a protocol that does not name them. The method owner and the chromatography lead decide with laboratory QA; the regulatory classification of the change belongs to regulatory affairs.

Technical principles

Transfer

DEMONSTRATION EXAMPLE SCIENTIFIC PRINCIPLE Transfer at constant reduced velocity, total porosity assumed to be 0.68, same mobile phase and temperature:

Quantity	Original	Target	Formula	Notes
Column; L/d_p	250 × 4.6 mm, 5 µm; 50,000	100 × 2.1 mm, 1.7 µm; 58,824	L/d_p	+17.6%
Flow rate	1.000 mL/min	0.613 mL/min	$F_1 \cdot (d_{c2}/d_{c1})^2 \cdot (d_{p1}/d_{p2})$	—
Injection	20 µL	1.67 µL	V_inj1·r_V	r_V: ratio of column volumes
Gradient; run time	27.00; 45.0 min	3.672; 6.12 min	Factor $r_V \cdot F_1/F_2 = 0.1360$	%B unchanged; mobile phase 45.0 → 3.75 mL
Dwell volume	1.0 mL (V_D/V_m 0.354)	83.4 µL	V_D1·V_m2/V_m1	Same V_D/V_m

Correction for the receiving system: Δt = (target V_D − measured V_D)/F; with 50 µL, +0.054 min (initial isocratic hold); with 400 µL, −0.517 min (delayed injection). DEMONSTRATION EXAMPLE Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or parameters of a real instrument. Studies of HPLC→UHPLC transfer identify the dwell volume as the most critical factor in gradient methods (peer-reviewed articles, paraphrased).

GUIDEGXP RECOMMENDATION The gradient delay volume is a property of the individual system in its installed configuration: it is measured, recorded in the qualification report and compared with that of the originating system before a gradient method is run.

GUIDEGXP RECOMMENDATION Instrument qualification does not certify the efficiency of every column: a system for small-volume columns is selected and verified also for its extra-column dispersion.

Informational USP chapters 〈1224〉, 〈1225〉 and 〈1226〉 GUIDANCE: they set no requirements or acceptance criteria and are a reference for the US market. 〈1224〉 describes transfer as "the documented process that qualifies a laboratory (the receiving unit) to use an analytical test procedure that originated in another laboratory". USP 〈1225〉, proposed revision DRAFT: proposal published for comment in the Pharmacopeial Forum; as of 02/10/2026 it is not official text and the current official version remains applicable. For Ph. Eur. 5.26, the EDQM FAQ leaves it to the user to demonstrate suitability under their own conditions (paraphrased); qualification as a prerequisite is a reading of this guide GUIDEGXP RECOMMENDATION. ICH Q14: "Changes to parameters that are not ECs do not require regulatory communication."; this guide stops here on this point: the regulatory classification of the method change is covered in the GuideGxP ICH Q guide.

Case A — UHPLC fleet: from URS to method transfer and gradient delay volume

Scenario built for teaching purposes. Simulated case: Corvessa Pharma S.p.A. is a fictitious company; its QC laboratory and the data are hypothetical.

Context. FCV-04 announces the end of support for HPLC-CV-01/02; periodic review PR-LAB-23 launches PRJ-UHPLC-24 to replace them and to transfer MET-CV-11-AS (assay and related substances of CVP-11) to UHPLC; the method was validated on HPLC-CV-04 (reference dwell volume 1.0 mL). UHPLC-CV-03 (FCV-02, quaternary) has been in service since 2022 for CVP-14: its URS (URS-UHPLC03-21) did not ask for the dwell volume and its OQ had not measured it.

Problem. Run on UHPLC-CV-03 for capacity reasons on 09/02/2026, v2 of the method gives Rs 1.7 on the critical pair (impurities B and C, the first to elute in the gradient), outside the internal criterion of ≥ 2.0 (D-07.1).

Risk. Related substances reported with the critical pair unresolved; a protocol that admitted "the laboratory's UHPLCs" without listing them.

Decisions. D-03.1–D-03.4 (see Chapter 3; the TCO of 18/06/2024 does not indicate a winner and does not offset a mandatory requirement); D-05.1 (≥ 1,200 bar); D-06.1; D-07.1; D-07.2; D-07.3.

Activities and data. Geometry: table in the "Technical principles" section. Dwell volumes and corrections at F 0.613 mL/min and a target V_D of 83.4 µL:

System	Measured V_D (µL)	V_D/V_m (target 0.354)	t_D (min) (target 0.136)	Correction Δt (min)	Corvessa decision
UHPLC-CV-01	100 (OQ-UHPLC01-25)	0.425	0.163	−0.027	No correction: negligible effect (D-07.2)
UHPLC-CV-02	100 (OQ-UHPLC02-25)	0.425	0.163	−0.027	As UHPLC-CV-01
UHPLC-CV-03	400 (INV-CV-26-006)	1.698	0.653	−0.517	Injection delayed by 0.517 min in v3, on this system only (CC-CV-26-007)

Rs of the critical pair (convention declared in the method): HPLC-CV-04 2.6 and UHPLC-CV-01/02 2.5 (comparative testing MTP-CV-11-25); UHPLC-CV-03 1.7 with v2 and 2.5 with v3. S/N on the solution at the quantitation level: 25.1 with the RMS convention that CDS-CV applied by default to the new systems, 6.8 with the peak-to-peak convention of the validated method, subsequently aligned (D-07.3). Rs ≥ 2.0 is a Corvessa internal criterion, demonstration choice of a fictitious company: it is not a recommended or reference value. DEMONSTRATION EXAMPLE Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or parameters of a real instrument. Tool AN-TK-08 (HPLC-to-UHPLC Transfer Calculator (Scaling and Dwell Volume)) recalculates geometry, times and delay corrections and returns the same results as this case. Tool AN-TK-07 (Chromatographic System Suitability Calculator and Trending) compares the resolutions with the entered criterion: it returns

"Comparison with the entered criteria" for HPLC-CV-04, UHPLC-CV-01/02 and UHPLC-CV-03 with v3, and "Assessment required" for UHPLC-CV-03 with v2 (Rs 1.7).

Date	Event	Record	Who
20/09/2022	OQ of UHPLC-CV-03 without dwell volume	OQ-UHPLC03-22	CQV-LAB-01; QA-LAB-01
14/09/2023	End of support for HPLC-CV-01/02 announced for 31/12/2025	FCV-04 letter	—
15/11/2023	PRJ-UHPLC-24 launched	PR-LAB-23	QC-CV-01; QA-LAB-01
12/02/2024	URS-UHPLC-24 rev. 1: 52 requirements, 15 mandatory	URS-UHPLC-24	QC-CHR-01; QA-LAB-01
04/03/2024	RFP to FCV-01, FCV-02, FCV-04; request to FCV-09 for refurbished UHPLCs	RFP-UHPLC-24	PRC-CV-01
15/04/2024	Bids received	—	PRC-CV-01
28/05/2024	FCV-04 excluded: stand-alone software only	TBE-UHPLC-24	QC-CHR-01; CSV-LAB-01; QA-LAB-01
18/06/2024	Three-option TCO; bid A selected (D-03.4)	TCO-UHPLC-24	QC-CV-01; FIN-CV-01; QA-CV-01
03/07/2024	Order to FCV-01	PO-UHPLC-24	PRC-CV-01
30/10/2024	DQ approved	DQ-UHPLC-24	CQV-LAB-01; QA-LAB-01
24/01/2025	IQ of UHPLC-CV-01/02	IQ-UHPLC01-25; IQ-UHPLC02-25	CQV-LAB-01
07/02/2025	OQ including dwell volume (100 µL)	OQ-UHPLC01-25; OQ-UHPLC02-25	CQV-LAB-01; QA-LAB-01
28/03/2025	PQ and comparative testing completed; S/N aligned (D-07.3)	PQ-UHPLC-25; MTP-CV-11-25	QC-CHR-01
14/04/2025	Transfer report; v2 approved; regulatory assessment started	MTR-CV-11-25; CC-CV-25-008	QC-CHR-01; REG-CV-01; QA-LAB-01
30/06/2025	v2 effective on UHPLC-CV-01/02; protocol refers to "the laboratory's UHPLCs"	CC-CV-25-008	QA-LAB-01
30/09/2025	HPLC-CV-01/02 retired, data retained	DSM-CV-25-01; DSM-CV-25-02	QC-CV-01; CSV-LAB-01
09/02/2026	v2 on UHPLC-CV-03: Rs 1.7; sequence invalid; no results reported	DEV-CV-26-006; INV-CV-26-006	QC-AN; QC-CHR-01
17/02/2026	Dwell volume of UHPLC-CV-03: 400 µL	INV-CV-26-006	CQV-LAB-01
24/02/2026	v3; dwell volume in all gradient OQs (D-06.1); SOP-CV-QC-002 rev. 4; admitted systems listed by name	CC-CV-26-007	QA-LAB-01
26/02/2026	v3 on UHPLC-CV-03: Rs 2.5; release with a condition of use	INV-CV-26-006; DEV-CV-26-006	QA-LAB-01

Documents. URS, TBE, TCO, DQ, IQ/OQ/PQ, MTP/MTR, change control and investigation, as listed in the chronology.

Evidence. "Delay volume" tables of the OQs; sequence of 09/02/2026 retained and not used; verification of 26/02/2026; peak-to-peak processing method locked.

> ▣ **EVIDENCE EXPECTED**
>
> MET-CV-11-AS v3 (CC-CV-26-007) with the 0.517 min delayed injection restricted to UHPLC-CV-03 and the named list of admitted systems.

Outcome as of 02/10/2026. The v3 method is in use on UHPLC-CV-01/02, where it does not change the v2 parameters, and on UHPLC-CV-03 with delayed injection; dwell volume measurement is part of the OQ of every gradient system.

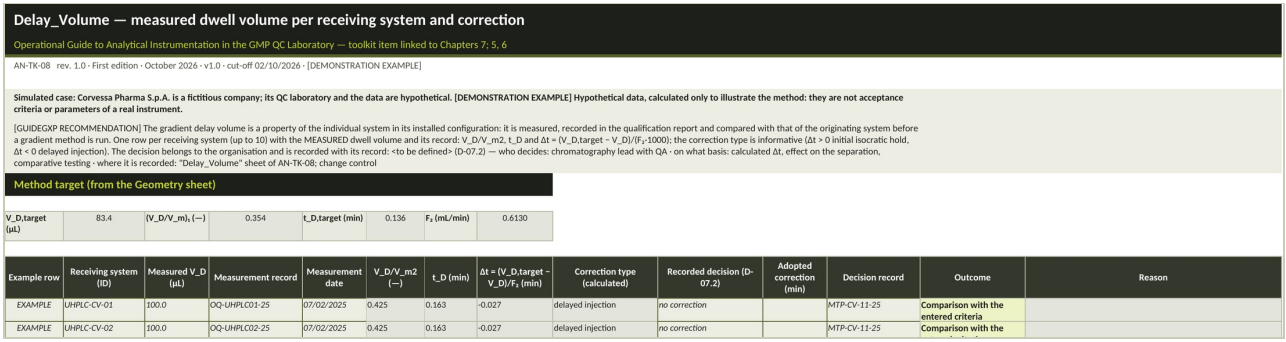
Three lessons. The dwell volume is measured on every gradient system. The protocol lists the systems by name. Conventions are locked in the processing method.

D codes. D-03.1, D-03.2, D-03.3, D-03.4, D-05.1, D-06.1, D-07.1, D-07.2, D-07.3.

Tools used. AN-TK-02 and AN-TK-03 (see Chapter 3); AN-TK-06 (see Chapter 6); AN-TK-07; AN-TK-08.

The toolkit: real pages of three tools

The images are pages of the delivered files — Corvessa filled-in examples from the 07_Examples folder, English edition — converted to PDF without retouching. In the clean templates of folders 01–06 the same sheets are empty: no criterion is preloaded and no sheet declares an instrument qualified or a result valid: the outcomes are "Comparison with the entered criteria" or "Assessment required".



Delay_Volume — measured dwell volume per receiving system and correction

Operational Guide to Analytical Instrumentation in the GMP QC Laboratory — toolkit item linked to Chapters 7; 5, 6

AN-TK-08 rev. 1.0 · First edition · October 2026 · v1.0 · cut-off 02/10/2026 · [DEMONSTRATION EXAMPLE]

Simulated case: Corvessa Pharma S.p.A. is a fictitious company; its QC laboratory and the data are hypothetical. [DEMONSTRATION EXAMPLE] Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or parameters of a real instrument.

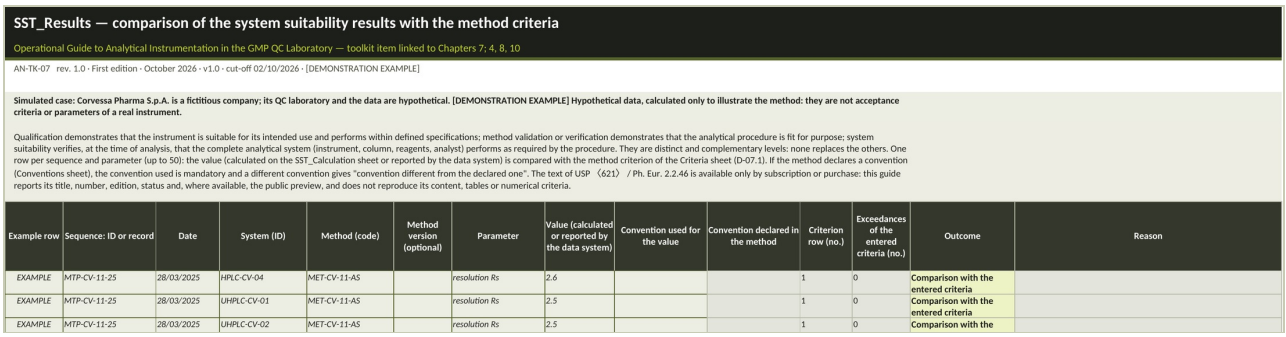
[GUIDEGXP RECOMMENDATION] The gradient delay volume is a property of the individual system in its installed configuration: it is measured, recorded in the qualification report and compared with that of the originating system before a gradient method is run. One row per receiving system (up to 10) with the MEASURED dwell volume and its record: V_D/V_m2, t_D and Δt = (V_D,target − V_D)/(F_2·1000); the correction type is informative (Δt > 0 initial isocratic hold, Δt < 0 delayed injection). The decision belongs to the organisation and is recorded with its record: <to be defined> (D-07.2) — who decides: chromatography lead with QA · on what basis: calculated Δt, effect on the separation, comparative testing · where it is recorded: "Delay_Volume" sheet of AN-TK-08; change control

Method target (from the Geometry sheet)

V_D,target (µL)	83.4	(V_D/V_m), (—)	0.354	t_D,target (min)	0.136	F_2 (mL/min)	0.6130

Example row	Receiving system (ID)	Measured V_D (µL)	Measurement record	Measurement date	V_D/V_m2 (—)	t_D (min)	Δt = (V_D,target − V_D)/F_2 (min)	Correction type (calculated)	Recorded decision (D-07.2)	Adopted correction (min)	Decision record	Outcome	Reason
EXAMPLE	UHPLC-CV-01	100.0	OQ-UHPLC01-25	07/02/2025	0.425	0.163	-0.027	delayed injection	no correction		MTP-CV-11-25	Comparison with the entered criteria	
EXAMPLE	UHPLC-CV-02	100.0	OQ-UHPLC02-25	07/02/2025	0.425	0.163	-0.027	delayed injection	no correction		MTP-CV-11-25	Comparison with the	

AN-TK-08 — HPLC-to-UHPLC Transfer Calculator (Scaling and Dwell Volume) (Excel) · measured gradient delay volume per receiving system and Δt correction



SST_Results — comparison of the system suitability results with the method criteria

Operational Guide to Analytical Instrumentation in the GMP QC Laboratory — toolkit item linked to Chapters 7; 4, 8, 10

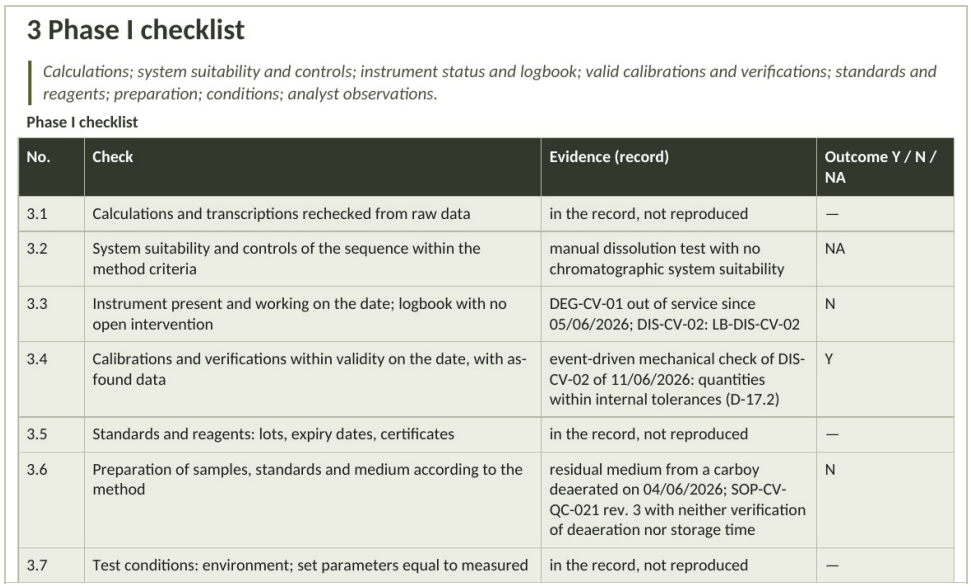
AN-TK-07 rev. 1.0 · First edition · October 2026 · v1.0 · cut-off 02/10/2026 · [DEMONSTRATION EXAMPLE]

Simulated case: Corvessa Pharma S.p.A. is a fictitious company; its QC laboratory and the data are hypothetical. [DEMONSTRATION EXAMPLE] Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or parameters of a real instrument.

Qualification demonstrates that the instrument is suitable for its intended use and performs within defined specifications; method validation or verification demonstrates that the analytical procedure is fit for purpose; system suitability verifies, at the time of analysis, that the complete analytical system (instrument, column, reagents, analyst) performs as required by the procedure. They are distinct and complementary levels: none replaces the others. One row per sequence and parameter (up to 50): the value (calculated on the SST_Calculation sheet or reported by the data system) is compared with the method criterion of the Criteria sheet (D-07.1). If the method declares a convention (Conventions sheet), the convention used is mandatory and a different convention gives "convention different from the declared one". The text of USP 〈621〉 / Ph. Eur. 2.2.46 is available only by subscription or purchase: this guide reports its title, number, edition, status and, where available, the public preview, and does not reproduce its content, tables or numerical criteria.

Example row	Sequence: ID or record	Date	System (ID)	Method (code)	Method version (optional)	Parameter	Value (calculated or reported by the data system)	Convention used for the value	Convention declared in the method	Criterion row (no.)	Exceedances of the entered criteria (no.)	Outcome	Reason
EXAMPLE	MTP-CV-11-25	28/03/2025	HPLC-CV-04	MET-CV-11-AS		resolution Rs	2.6			1	0	Comparison with the entered criteria	
EXAMPLE	MTP-CV-11-25	28/03/2025	UHPLC-CV-01	MET-CV-11-AS		resolution Rs	2.5			1	0	Comparison with the entered criteria	
EXAMPLE	MTP-CV-11-25	28/03/2025	UHPLC-CV-02	MET-CV-11-AS		resolution Rs	2.5			1	0	Comparison with the	

AN-TK-07 — Chromatographic System Suitability Calculator and Trending (Excel) · system suitability results compared with the method criteria



3 Phase I checklist

Calculations; system suitability and controls; instrument status and logbook; valid calibrations and verifications; standards and reagents; preparation; conditions; analyst observations.

Phase I checklist

No.	Check	Evidence (record)	Outcome Y / N / NA
3.1	Calculations and transcriptions rechecked from raw data	in the record, not reproduced	—
3.2	System suitability and controls of the sequence within the method criteria	manual dissolution test with no chromatographic system suitability	NA
3.3	Instrument present and working on the date; logbook with no open intervention	DEG-CV-01 out of service since 05/06/2026; DIS-CV-02: LB-DIS-CV-02	N
3.4	Calibrations and verifications within validity on the date, with as-found data	event-driven mechanical check of DIS-CV-02 of 11/06/2026: quantities within internal tolerances (D-17.2)	Y
3.5	Standards and reagents: lots, expiry dates, certificates	in the record, not reproduced	—
3.6	Preparation of samples, standards and medium according to the method	residual medium from a carboy deaerated on 04/06/2026; SOP-CV-QC-021 rev. 3 with neither verification of deaeration nor storage time	N
3.7	Test conditions: environment; set parameters equal to measured	in the record, not reproduced	—

AN-TK-20 — Phase I Investigation Form for Suspected Instrument Cause (Word) · section 3: phase I checklist of Case D

What the purchase contains

The purchase is digital: after payment you download a ZIP package with the guide and the toolkit in the language you chose. Choose one variant: **ITA - Italiano** or **ENG - English**; the two editions have the same structure, the same tools and the same codes.

- **The complete PDF guide** — 308 A4 pages, 24 chapters in six parts, five integrated cases and six appendices (ITA/ENG glossary, source matrix, chapter–toolkit–article matrix, toolkit instructions, assumptions and limitations, revision); clickable table of contents and bookmarks.
- **24 editable tools** — 12 Word templates and 12 Excel workbooks, codes AN-TK-01…24, arranged in the six folders of the parts (list below).
- **24 filled-in examples** on the simulated Corvessa Pharma laboratory, with the case datasets (folder 07_Examples).
- **Test Log and checks** of the Excel workbooks (folder 08_Verification).

Folder and group	Code	Tool	Format
01 · Analytical Qualification and Reliability	**AN-TK-01**	Instrument Inventory and Classification Register	Excel
01 · Analytical Qualification and Reliability	**AN-TK-02**	Analytical Instrument URS and Selection/DQ Checklist	Word
01 · Analytical Qualification and Reliability	**AN-TK-03**	Instrument Bid Evaluation and TCO	Excel
01 · Analytical Qualification and Reliability	**AN-TK-04**	IQ/OQ/PQ Qualification Protocol and Report	Word
01 · Analytical Qualification and Reliability	**AN-TK-05**	Calibration, Performance Verification, Maintenance and Periodic Review Planner	Excel
02 · HPLC & UHPLC	**AN-TK-06**	HPLC/UHPLC OQ/PV Calculator	Excel

Folder and group	Code	Tool	Format
02 · HPLC & UHPLC	**AN-TK-07**	Chromatographic System Suitability Calculator and Trending	Excel
02 · HPLC & UHPLC	**AN-TK-08**	HPLC-to-UHPLC Transfer Calculator (Scaling and Dwell Volume)	Excel
02 · HPLC & UHPLC	**AN-TK-09**	HPLC/UHPLC Troubleshooting Guide and Log	Word
03 · GC & Headspace	**AN-TK-10**	GC and Headspace Qualification Protocol	Word
03 · GC & Headspace	**AN-TK-11**	GC/HS Performance Calculator	Excel
03 · GC & Headspace	**AN-TK-12**	GC/HS Troubleshooting Guide	Word
04 · Spectroscopy, LC-MS & ICP-MS	**AN-TK-13**	UV-Vis Qualification Calculator	Excel
04 · Spectroscopy, LC-MS & ICP-MS	**AN-TK-14**	FTIR/Raman Qualification and Identity Library Verification Protocol	Word
04 · Spectroscopy, LC-MS & ICP-MS	**AN-TK-15**	LC-MS Qualification and Contamination Control Plan	Word
04 · Spectroscopy, LC-MS & ICP-MS	**AN-TK-16**	ICP-MS Performance Calculator	Excel
05 · Dissolution and Physical Testing	**AN-TK-17**	Dissolution Apparatus Mechanical Qualification Calculator	Excel
05 · Dissolution and Physical Testing	**AN-TK-18**	Dissolution Test Execution Checklist	Word
05 · Dissolution and Physical Testing	**AN-TK-19**	Disintegration, Friability and Breaking-Force Tester Qualification and Routine Check Protocol	Word
05 · Dissolution and Physical Testing	**AN-TK-20**	Phase I Investigation Form for Suspected Instrument Cause	Word
06 · TOC and Physicochemical Measurements	**AN-TK-21**	TOC System Suitability and Blank Calculator	Excel
06 · TOC and Physicochemical Measurements	**AN-TK-22**	Karl Fischer, pH and Conductivity Calculator	Excel
06 · TOC and Physicochemical Measurements	**AN-TK-23**	Karl Fischer Titrator Qualification Protocol	Word
06 · TOC and Physicochemical Measurements	**AN-TK-24**	pH Meter and Conductivity Meter Verification Protocol	Word

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