USING EMPOWER SystemsQT QUALIFICATION TOOL FOR AGILENT 1100, 1200, AND 1260 HPLC SYSTEMS

A summary of Empower SystemsQT Qualification Tool features and benefits, with emphasis on the technical attributes of the qualification tests.

GXP[1] COMPLIANCE

Regulatory agencies continue to require documented evidence (electronic and written) that responsible companies and persons can consistently generate quality products with supporting analytical data.

Analytical systems have become more automated and generate analytical data that is managed by sophisticated software programs. While automated analytical systems require less operator involvement to produce data, it is worth noting that routine involvement of a designated responsible person(s) to ensure continued system performance is still required.

Regulated companies are constantly balancing expenses to maximize shareholder value as well as meeting product quality and regulatory compliance requirements. The constant quest for reduced expenses may target analytical system qualification (performance verification) and maintenance as means to decrease laboratory operating costs. Short cuts in such areas can result in erosion of system performance with accompanying analysis and product errors which may result in regulatory compliance problems and loss of corporate reputation.

To assist customers in meeting their regulatory requirements as well as meeting laboratory throughput and system uptime objectives, Waters® has created an extensive portfolio of regulatory compliance products and services. Empower Systems Qualification Tool (SystemsQT™), chemical test solutions kits, qualification workbooks, and Global Services are all focused on ensuring customer success.

THE EVOLUTION OF CHROMATOGRAPHY SYSTEM QUALIFICATION

As HPLC, UPLC,® and LCMS systems evolve into highly automated, computer software controlled systems, so too is the need to verify performance in an "as used" system configuration. With the growing acceptance of Waters Empower Software as the preferred chromatography laboratory platform, adding systems qualification capability extends its value and benefits to GxP regulated laboratories.

When non-automated HPLC systems were comprised of individually programmed and controlled modules, there was a need to verify the performance of each individual component. Individual component performance verification, in terms of accuracy and linearity is called OQ or Operational Qualification. Following the successful completion of module OQs, the total system performance is verified in terms of precision as vendor Performance Qualification (PQ).

Qualification data and records are still required for fully automated systems but qualification processes have needed to evolve to meet these new challenges.

Throughout all the evolutionary changes to system qualification processes, the roles of the involved participants have remained constant.

- Company (System Owner) management is still responsible for the overall use, operation and integrity of analytical systems and generated analytical data. During the process of qualifying analytical systems for use in a GxP regulated environment, owner management (Approver) is responsible for designating a qualified company individual to oversee qualification processes (Reviewer) as well as approve qualification results and the qualification Performer.
- The Reviewer is responsible for ensuring the Performer follows the company approved protocols and has completed all maintenance, qualification testing and documentation.
- The Performer is a trained and owner management approved system maintenance and qualification services specialist who can successfully complete all required qualification processes.

Traditional Paper-Based Qualification Processes

Tied to the evolution of chromatographic systems, Waters Qualification Services has kept pace with the production of Qualification Workbooks, chemical test kits, and software qualification tools.

Paper-based qualification processes, while being used successfully for many years, share many of the same problems as do manual system control and data acquisition processes.

1. Paper records present archival challenges: storage logistics, record management, and record retrieval/access issues.
2. Risk of human error in testing, calculations and documentation.
3. Metrology-type testing of modules in a non "as-used" configuration.

Please Note

While paper-based qualification processes have issues, there are and will be instances when such processes are required to complete system qualification. With the addition of specialized detectors to UPLC and HPLC systems as well the continued requirement of metrology-type testing of some physical parameters for automated systems, a paper or electronic workbook-based process may be required to supplement automated qualification processes.

Automated HPLC and UPLC Systems Qualification

Older, automated HPLC systems can continue to utilize paper-based qualification processes. But in light of today's laboratory regulatory and efficiency challenges, automated system qualification tools are receiving much more focus and acceptance.

Waters Empower SystemsQT Features and Benefits

- Built-in option to a validated chromatography control and data system, which is switched on as required, not a third-party program.
- Eliminates manual calculations and decisions to reduce human error opportunities as well as provide much faster system testing.
- Qualification processes can be managed as electronic records.
- All system control, data collection (acquisition, processing, reporting, archiving) are auditable.
- Uses validated chromatographic methods to test and verify total system performance.
- Designed to provide means to integrate metrology-type test methods where required. Manual test measurements are incorporated into Empower Software allowing electronic storage and reporting of those results through Empower SystemsQT.
- Waters Compliance Specialists are trained and certified to perform all system testing, maintenance, and documentation.

Empower SystemsQT Qualification Tool versus Paper Workbook-Based Qualification Processes

	Empower SystemsQT Processes	Paper Workbook Processes
Responsible Person	Owner management designated responsible 'approver'.	Same
Qualification Performer	Trained, certified and owner management approved qualification and system service expert.	Same
Approval/sign-off Process	Electronic record or summary page print out sign-off.	Performer initials and dates each results page. Approver signs and dates summary page.
Qualification Documents	Empower software validated projects. Waters Compliance Specialist (Performer) provides DVD-based projects and documents as required for testing. Storage binder supplied for hard copy sign-off sheets.	Comprehensive workbook containing IQ, OQ, PQ, and maintenance instructions, procedures, results logs and sign-off pages for each system module. Storage binder supplied for workbook archiving.
Qualification Test Chemicals	Ready-to-use, certified test chemicals in accordance with sample manager loading instructions.	Ready-to-use, certified test chemicals to be manually used in accordance with workbook instructions.
Calibrated Test Equipment	As required, calibrated measurement devices provided by Waters Compliance Specialist (Performer).	As required, calibrated measurement devices provided by Waters Compliance Specialist (Performer).
New System Installation Qualification (IQ)	Empower Acquisition Node provides system configuration for inserting serial number, location, purchase information for either electronic record sign-off or print out for manual sign-off and binder insertion.	Performer written insertion of system configuration, serial numbers, location, purchase information with initials and dates on workbook form pages.
Operational Qualification (OQ) and System Performance Qualification (PQ)	If required, (for specialized detector and physical parameter testing), load DVD-based protocols and follow instructions for manual procedures. For system testing, select Empower qualification project, follow system preparation instructions, load test chemicals in specified sample manager locations and run automated qualification tests. SystemsQT will analyze chromatographic results and, through the use of Boolean custom fields, provide a pass/fail decision for all test parameters. Reviewer approves qualification results. Performer and Reviewer sign-off either electronic record or hard copy of summary report. Hard-copy sign-off sheets filed in supplied storage binder.	Performer follows workbook instructions and procedures for test chemical preparation, test equipment use, individual module testing, system preparation and total system testing. Performer makes pass/fail decisions for all tests, signs and dates all result forms, and has Reviewer approve and signs-off completed document. Completed workbook chapters are inserted into storage binder.
Failed Test Result Process	SystemsQT will identify failed test. Performer will then investigate system problem, either provide repair(s) or, more likely, ensure system passes all performance diagnostics and re-run test injections and failed qualification test. Performer will log required maintenance.	Performer will stop module /system testing when an individual test fails. Performer will then investigate system problem, either provide repair(s) or, more likely, ensure system passes all performance diagnostics and re-run failed qualification test. The performer will then continue qualification testing. Performer will log required maintenance.
Pre-OQ and PQ Maintenance Processes	For existing systems, maintenance must be performed prior to running system qualification. Recommended maintenance procedures are DVD-based and are electronically transferred to owner's management location of choice. Maintenance information report is inserted into qualification binder.	For existing systems, maintenance must be performed prior to running system qualification. Individual maintenance chapters are supplied with each module's qualification workbook. Maintenance information report is inserted into qualification binder.
Archiving System Qualification and Maintenance Records	System qualification and maintenance records should be stored in a safe place that makes them easily available for inspection. SystemsQT records can be stored as electronic records or as hard copy signed-off summary reports that can be stored in the supplied binder. Empower search capabilities can be used to locate records easily.	System qualification and maintenance records should be stored in a safe place that makes them easily available for inspection. Completed and signed-off workbooks can be stored in the supplied binder.

Empower SystemsQT Pass/Fail Processes

For automated system qualification, SystemsQT employs the appropriate sample sets in Empower software to acquire data in Run Samples. Appropriate statistical analysis is applied to the results to provide standard deviation, %RSD, R^2 linearity, etc. results. Custom Boolean Fields are applied to the final results to determine test pass or fail.

Non-Standard System Qualification Tests and Processes

The development of Waters Global Compliance Services and Products included reviews and input by key experts in the USA Department of Health and Human Services (US FDA) inspection branch, international Ministries of Health experts, internationally recognized experts in CGMP/GLP validation as well as global pharmaceutical, cosmetic, insert , and food regulatory compliance groups. Customers using Waters Regulatory Compliance Products (workbooks and SystemsQT) have been achieving successful system audits for over fifteen years.

The portfolio of qualification tests utilized by Waters is designed to meet or exceed all regulatory agency requirements. Testing of parameters that are connected to a specific analytical method and not the analytical system are not included in Waters qualification processes.

If custom qualification tests and services are required, please contact your local Waters Service Management Team or Global Compliance Services Marketing.

Qualification of Agilent 1100, 1200 or 1260 Systems with VWD/MWD/DAD Detector using Empower SystemsQT Qualification Tool. An Agilent 1100, 1200 or 1260 System includes:

A binary or quaternary pump and an autosampler with or without thermostatted sample compartment with thermostatted column compartment plus detector option which can be:

- A Variable Wavelength (VWD) UV/Visible Detector, a Multiple Wavelength (MWD) UV/Visible Detector or a Diode-array (DAD) Detector

Empower SystemsQT processes for qualifying an Agilent 1100, 1200 or 1260 HPLC System containing an autosampler, column heater plus a UV detector are as follows:

Manual OQ Performed Before Running Automated SystemsQT Tests	**OQ Tests From SystemsQT Projects/Documentation DVD** 1. Autosampler temperature accuracy. 2. Thermostatted column compartment temperature accuracy. 3. Flow rate accuracy (only when system includes binary pump).	**OQ Test Methods** 1. Temperature verified using calibrated temperature probe. 2. Temperature verified using calibrated temperature probe. 3. Timing (with calibrated stopwatch) collection of fixed volume of mobile phase.
System Preparedness Test	1. Test injections.	1. Replicate test sample injections to verify system is equilibrated and ready to commence automated OQ & PQ tests.
Agilent 1100/1200/1260 UV OQ and PQ Tests	**Automated OQ and PQ Tests Running Empower Project Sample Sets** 1. System precision test. 2. (A) PDA detector wavelength accuracy test. (B) VWD or MWD detector wavelength accuracy test. 3. Detector linearity test and plate positioning test. 4. Detector noise and drift test. 5. Carryover test. 6. Injector linearity and accuracy test. 7. Flow rate linearity and accuracy test (accuracy test for quaternary pump only). 8. Compositional accuracy test (quaternary pump only).	**OQ and PQ Test Methods** 1. System precision (standard deviation and %RSD of peak retention times, peak areas and heights) is verified by making replicate injections of test sample. 2. (A) Wavelength accuracy is determined by scanning spectra and verifying lambda maximums of well characterized compound falls within specifications. (B) Wavelength accuracy is determined by the wavelength of highest peak from several injections of well characterized compound. 3. Detector linearity is determined by using a fixed injection volume of varying sample concentrations to generate a plot of peak height and area versus sample amount. Proper function of autosampler plate positioning is verified during linearity test by injecting from vials in different plate locations. 4. Data for noise and drift is collected for 15 minutes. The average peak to peak noise (equivalent to ASTM 685-79) is calculated for 30-second intervals from 3 to 15 minutes. Detector drift is is calculated for the 3 to 15 minute interval. 5. Carryover is determined by injecting a high concentration challenge sample and measuring the amount of that sample seen in the post challenge blank injections. 6. Injector linearity is determined by plotting the response from variable injection volumes of a fixed sample concentration. Accuracy is determined from the X intercept of injection volume. 7. Flow rate linearity is determined by plotting the inverse of peak retention time versus the flow rates. Flow rate accuracy is determined from the X intercept of the plot. 8. Compositional accuracy is determined by the %RSD of peak retention times from replicate injections run with mobile phase generated by varying proportions of solvents.

Qualification of Agilent 1100, 1200 or 1260 Systems with Agilent Refractive Index using Empower SystemsQT Qualification Tool. An Agilent 1100, 1200 or 1260 System includes:

A binary or quaternary pump and an autosampler with or without thermostatted sample compartment with thermostatted column compartment plus detector option which can be:

- An Agilent Refractive Index (RID) Detector

Empower SystemsQT processes for qualifying an Agilent 1100, 1200 or 1260 HPLC Systems containing an autosampler, column heater plus a RI detector are as follows:

Manual OQ Tests Performed Before Running Automated SystemsQT Tests	**OQ Tests From SystemsQT Projects/Documentation DVD**	**OQ Test Methods**
	1. Autosampler temperature accuracy.	1. Temperatures verified using calibrated temperature probe.
	2. Thermostatted column compartment temperature accuracy.	2. Temperatures verified using calibrated temperature probe.
	3. Flow rate accuracy (only when system includes a binary pump).	3. Timing (with calibrated stopwatch) collection of fixed volume of mobile phase.
System Preparedness Test	1. Test injections.	1. Replicate test sample injections to verify system is equilibrated and ready to commence automated OQ and PQ tests.
Agilent 1100/1200/1260 RI OQ and PQ Tests	**Automated OQ and PQ Tests Running Empower Project Sample Sets**	**OQ and PQ Test Methods**
	1. System precision test.	1. System precision (standard deviation and %RSD of peak retention times, peak areas, and heights) is verified by making replicate injections of test sample.
	2. Detector linearity test and plate positioning test.	2. Detector linearity is determined by using a fixed injection volume of varying sample concentrations and plotting peak area and height versus sample amount. Proper function of autosampler plate positioning is verified during linearity test by injecting from vials in different plate locations.
	3. Injector linearity and accuracy test.	3. Injector linearity is determined by plotting the response from variable injection volumes of a fixed sample concentration. Accuracy is determined from the X intercept of injection volume.
	4. Detector noise and drift test.	4. Data for noise and drift is collected for 15 minutes. The average peak to peak noise (equivalent to ASTM 685-79) is calculated for 30-second intervals from 3 to 15 minutes. Detector drift is is calculated for the 3 to 15 minute interval.
	5. Carryover test.	5. Carryover is determined by injecting a high concentration challenge sample and measuring the amount of that sample seen in the post challenge blank injections.
	6. Flow rate linearity and accuracy test.	6. Flow rate linearity is determined by plotting the inverse of peak retention time versus the flow rates. Flow rate accuracy is determined from the X intercept of the plot.

Qualification of Agilent 1100, 1200 or 1260 Systems with Fluorescence Detector using Empower SystemsQT Qualification Tool. An Agilent 1100, 1200 or 1260 system includes:

A binary or quaternary pump and an autosampler with or without thermostatted sample compartment with thermostatted column compartment plus detector option which can be:

- Agilent Fluorescence (FLD) Detector

Empower SystemsQT processes for qualifying an Agilent 1100, 1200 or 1260 HPLC Systems containing an autosampler, column heater plus a FLD detector are as follows:

Manual OQ Tests Performed Before Running Automated SystemsQT Tests	**OQ Tests From SystemsQT Projects/Documentation DVD**	**OQ Test Methods**
	1. Autosampler temperature accuracy.	1. Temperatures verified using calibrated temperature probe.
	2. Thermostatted column compartment temperature accuracy.	2. Temperatures verified using calibrated temperature probe.
	3. Flow rate accuracy.	3. Timing (with calibrated stopwatch) collection of fixed volume of mobile phase.
System Preparedness Test	1. Test injections.	1. Replicate test sample injections to verify system is equilibrated and ready to commence automated OQ and PQ tests.
Agilent 1100/1200/1260 RI OQ and PQ Tests	**Automated OQ and PQ Tests Running Empower Project Sample Sets**	
	1. System precision test.	1. System precision (standard deviation and %RSD of peak retention times, peak areas and heights) is verified by making replicate injections of test sample.
	2. Signal-to-noise test.	2. Using water Raman band, average peak-to-peak signal to baseline noise ratio is reported.
	3. Emission wavelength accuracy test.	3. Emision wavelength accuracy is determined by verifying lambda maximum of well characterized compound falls within specifications.
	4. Excitation wavelength accuracy test.	4. Excitation wavelength accuracy is determined by verifying lambda maximums of well characterized compound falls within specifications.
	5. Carryover test.	5. Carryover is determined by injecting a high concentration challenge sample and measuring the amount of that sample seen in the post challenge blank injections.
	6. Detector linearity test and plate positioning test.	6. Detector linearity is determined by using a fixed injection volume of varying sample concentrations and plotting peak height versus sample amount. Proper function of autosampler plate positioning is verified during linearity test by injecting from vials in different plate locations.
	7. Injector linearity and accuracy test.	7. Injector linearity is determined by plotting the response from variable injection volumes of a fixed sample concentration. Accuracy is determined from the X intercept of injection volume.
	8. Compositional accuracy test (quaternary pump only).	8. Compositional accuracy is determined by the %RSD of peak retention times from replicate injections run with mobile phase generated by varying proportions of solvents.

References

1. GxP refers to all government required good laboratory operating practices including, Current Good Laboratory Practices (CGLP), Current Good Manufacturing Practices (CGMP), Current Good Automated Laboratory Practices (CGALP), Current Good Clinical Practices (CGCP) as well as other regulatory agency required practices.

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