EQUIPMENT QUALIFICATION PLAN

Agilent CrossLab Compliance Services

EQP Name: AgilentRecommended

Service Type: OQ

Company Name: ___________________________

Customer Name/Title: ___________________________

EQP Filename: ICPMS.02.56.eqp

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Scope and Purpose

Overview

An Equipment Qualification Plan (EQP) documents the work performed during qualification services provided using the Agilent Automated Compliance Engine (ACE) software. The EQP must be approved before the work is performed (see customer responsibilities) and the results are reported in an Equipment Qualification Report (EQR), which documents the following.

-Tests performed during the qualification work
-Setpoints used (for example, wavelength, temperature, and flow settings, as applicable)
-Limits (acceptance criteria) applied to tests and setpoints
-Test descriptions and rationales for tests performed (these and test parameters are also reported EQR)
-Traceability of the Agilent qualification protocol

EQP PDF review documents support customer review and approval and are digitally produced directly from the electronic EQP contained within ACE. Two different EQP approval formats can be created.

-Concise: standard format, typically used for Agilent-recommended EQPs
-Tabular: expanded format, typically used for configured EQPs

Many customers approve the Agilent-recommended EQP in the concise format. The tests, setpoints, and limits applied are typically organized in a concise table format (see information below and the Operational Qualification (OQ) test suite). The table can also display which qualification tests can be configured, which Agilent designates as variance (see Glossary).

In a concise EQP approval document used for Agilent-recommended EQPs, the test, setpoints and parameters, and limits (as applicable) are displayed in a concise abbreviated format as shown below.

NOTE This section is used by all ACE techniques, but only LC examples are provided for illustrative purposes.

Key:	Fixed HPLC setpoints/limits	UHPLC setpoints (primary module)	Variance allowed

Test	Setpoints and Parameters	Limits
CDS Logon Verification	N/A	Evidence of logon used to collect qualification data
Pump Flow Accuracy and Precision (Pump)	Flow Rate 1: 0.500 ml/minute Flow Rate 2: 5.000 ml/minute Flow Rate 2: 2.000 ml/minute (G4220B) Flow Rate 2: 1.500 ml/minute (with ULD kit)	Accuracy Ò3.00% Precision RSD Ò0.50%

By design, ACE EQPs can be configured to align the qualification work to laboratory use of the system and / or satisfy user requirements such as range of use for parameter settings (for example, HPLC flow). This requires close collaboration with Agilent to align the configured EQP with laboratory requirements and may include additional optional tests and/or changes to test setpoints and limits. With configured EQPs, an expanded tabular test format is used. Changes from the Agilent-recommended EQP are displayed at the individual test level (so the test section of a tabular EQP document is longer). The electronic EQP file used to create the customer configured EQP is displayed on front page of the EQP. When the qualification work is complete, the results will be reported in the Equipment Qualification Report (EQR) for review and approval.

Understanding the Test Specification Section in Tabular Review Documents

Tabular formatted EQP PDF review documents are typically used for configured EQPs (or if this format is requested by customers). When this EQP approval format is used, which applies to hardware qualifications only, tests are displayed in an expanded tabular arrangement, where the setpoints and limits are explicitly displayed for each test. Agilent-recommended setpoints and limits and the range of allowable values are designated as L (for low) and H (for high). Changes are noted relative to these limits é W (changes within the Agilent range) and O (changes outside the Agilent range). Where dual reporting limits are enables, these are designated as DW (within the Agilent limits) and DO (outside the Agilent limits). Optional tests that are enabled are included and marked as such. Additionally, any required tests that are disabled at customer request are included and marked as such. The EQP documents changes that are within the Agilent variance range as well as any out of variance range tests (see Glossary).

Note: (1) Agilent is NOT responsible for test failures for O (out of range) setpoints and limits. (2) Limit ranges must be more tightly managed than setpoint ranges because they often reflect physical measurement limits and are directly linked to the testing method. Therefore *within range* user limits are subject to best effort repairs if they cannot be met. In particular, Agilent is not be responsible for test failures for limits tighter (more demanding or challenging) than the recommended values. (3) Changes from the Agilent-recommended EQP are also displayed in the Test Summary section of the EQR. (4) For hyphenated systems (for example, LC-LCMS), an EQP for each system needs to be approved.

In a tabular EQP approval document, the test, setpoints and parameters, and limits are typically displayed in the following representative format.

Pump Flow Accuracy

Flow 1

Analytical Agilent and non-Agilent pump

	Setpoint:	0.500	mL/min		L:	0.100	H:	5.000
W	Setpoint:	0.200	mL/min					
	Limit:	<=	5.00	%	L:	5.00	H:	10.00

Injection Precision Additional FLD

This optional test is enabled for this EQP.

Agilent or non-Agilent injector with FLD detector							
Vial verification performed?	No						
Injection Volume on Column:	5	uL		L:	1	H:	5
Area RSD Limit:	<=	1.00	%	L:	1.00	H:	5.00
Height RSD Limit:	<=	1.00	%	L:	1.00	H:	5.00

Column Temperature Accuracy

This standard default test is disabled for this EQP.

Customer Responsibilities

To perform ACE instrument qualification services, requirements associated with instrument control and use of ACE software on site need to be understood and satisfied.

- Instrument control to perform the qualification tests.
- ACE software access by the field service engineer (FSE) to load the electronic EQP, run the qualification workflow, and publish the EQR.

ACE is designed to satisfy ALCOA+ data integrity requirements and provide qualification tests that are independent of the instrument control software. This Agilent qualification design philosophy facilitates a harmonized approach to analytical instrument qualification and ensures consistent application of validated algorithms (such as those used to perform gradient pump HPLC testing), independent of instrument and software manufacturer. Additional documentation is available to provide further information on these subjects.

Agilent recommends that the software routinely used in the lab to control the instrument is used by the FSE to perform qualification tests. Therefore, appropriate access to the instrument control software, such as the customer data system (CDS), needs to be set up for the Agilent representative before they arrive on site. For ACE software access on site, Agilent recommends installation of Network ACE to load the electronic EQP, run the qualification workflow, and publish the EQR.

Customers need to address the following responsibilities.

- EQP review
  - Review the EQP supplied (standard or configured).
  - Request changes to the EQP if required (to meet user requirements such as testing range of use) or approve the supplied EQP (that satisfies user requirements).
  - Return an electronic copy of the EQP to Agilent prior to qualification delivery.

- Agree and set up instrument control access to perform the work (provide a CDS logon for the FSE).
- Agree and approve ACE usage on site (Network ACE).
- For configured EQPs, maintain change control and revision history of the specific approved EQP.
- Safely store and archive an approved copy of this EQP.
- Review and sign the EQR when the qualification work is complete and reported.

NOTE: If Agilent representatives use customer software such as a CDS account to acquire test data during the qualification, they log off from the CDS account at the end of test acquisition. Account credentials created for FSE CDS access are a customer responsibility (that is, some labs disable the account when the work is complete).

Agilent Responsibilities

Agilent representatives follow an approved structured training process, which is represented by the training certificates included in the EQR. Additionally, any customer-specific training that is required to perform the work should be specified and complete before the work is scheduled and can be optionally added as a PDF attachment to an EQR, if required. Agilent representatives do the following.

- Deliver the approved services following the test programs described in the approved EQP;
- Provide a locked and e-signed EQR upon completion of the service;
- If requested, provide an optional ink-signed EQR CD to the customer.

Statement of Intent

The qualification is delivered according to the approved EQP. The standard EQP is followed unless a configured EQP has been requested and approved. If a configured EQP has been created and approved, Agilent defines variances as changes to the default recommended values (stated in the standard EQP) that fall within a well-defined range. These changes are considered to be within the intended use range of the system under test.

Customizations are (a) values that subject the system to limits that exceed the typical operational range or (b) additional tests that are not considered part of the core program required for completion of the selected service. Because user-defined setpoints and limits may exceed the operational envelope of the equipment, Agilent reserves the right to warrant conformance only to the closest variance value. The user is notified of this stipulation at EQP setup time and the qualification report (EQR) reflects this situation.

The service is delivered according to the terms and conditions stated in the corresponding service exhibit. After approval, it is recommended that this EQP be archived with the electronic EQP file.

General Statements on the Testing Program

The hardware OQ tests described within this EQP are designed to satisfy analytical instrument qualification (AIQ) requirements for regulated laboratories. The laboratory is responsible for documenting that analytical instruments are suitable for the analytical procedures they use and the decisions they make on the reportable values / quality attributes being measured. Diligent application of an instrument life cycle framework such as USP <1058> help define and satisfy this requirement.

Agilent-recommended EQPs are derived from Agilent's interpretation of the analytical instrument life-cycle framework defined in USP <1058> and authoritative literature requirements from sources such as ISO9001, FDA, GAMPÉ, PIC/S, ASTM 2500, and others. User requirements and intended use can vary from laboratory to laboratory. Therefore, it is recommended that prior to EQP approval, laboratories determine if additional set points and/or optional additional tests are required to test their user requirements. Additional charges may apply to any changes. This can be accommodated in a configured or customized EQP. In line with the USP <1058> requirements, Agilent qualification services include Installation Qualification (IQ) and Operational Qualification (OQ). Typically, the range of instrument use should be tested in the OQ. Laboratories are responsible for addressing PQ requirements of the USP <1058> life cycle.

Agilent CrossLab Compliance uses a balanced selection of direct metrology and chemical-based tests to directly determine the performance of the systems without unnecessary reliance on graphical extrapolation, interpolation, inferred or derived results. For example, for HPLC qualification, direct metrology measurements are used to test pump flow rate accuracy and precision, and thermal-controlled column compartment and autosampler modules. Holistic chemical testing is used for the evaluation of the following critical instrument characteristics: linearity, precision, signal to noise, and carry over.

EQP Revision History

ACE qualification protocols follow a standardized software development life cycle within Agilent. The electronic EQP files used by ACE are managed under change control within this life cycle. Changes to the core electronic EQP are recorded in the Agilent EQP Revision History and are available on request. Change control processes vary between organizations; therefore, although Agilent maintains a revision history for electronic EQPs contained within ACE, it is recommended that, for configured EQPs, laboratories maintain EQP-independent revision history information appropriate to their own policies and procedural requirements.

CDS Software Pre-requisites for Hardware Qualifications

The software used to control instruments during hardware qualification needs to be suitable. Agilent recommends that software used during the qualification has been qualified within the qualification period specified by the customer s software qualification SOP.

Glossary

Agilent EQP

ACE:

Agilent Automated Compliance Engine or Agilent software used to provide qualification services

EQP:

Equipment Qualification Plan that documents qualification work to be performed

EQR:

Equipment Qualification Report that documents qualification results

CDS:

Customer data system

Network ACE:

ACE is installed on a network node within the laboratory LAN infrastructure

Local ACE:

ACE resides on an independent external drive connected to the LAN infrastructure

Alternative Method:

ACE is installed and run from a PC not connected to the laboratory network

Standard EQP:

EQP pre-defined by Agilent that includes default tests, setpoints, and limits

Configured EQP:

EQP that has been changed based on user requirements

Variance, Range:

The range of operating values for a test parameter within ACE (flow, temperature, and so on) that were defined and tested when the test was first developed and set up

Variance, W:

Change to a test parameter that is within the Agilent variance range

Variance, O:

Change to a test parameter that is outside the Agilent variance range

Variance, DW:

Dual reporting limits within the Agilent supported range

Variance, DO:

Dual reporting limits outside the Agilent supported range

Optional Test:

An optional additional test that is not included in the standard EQP

Additional Setpoint:

Additional measurement value for a test parameter (flow, temperature, and so on)

Qualification Life Cycle Stages

URS:

User Requirement Specification that documents intended instrument use

DQ:

Design Qualification that documents suitability of instrument for intended use

IQ:

Installation Qualification that documents the installation of the instrument

OQ:

Operational Qualification that tests the range of use

PQ:

Performance Qualification that tests the system under conditions of use

RQ:

Repair Qualification that tests the instrument after an instrument repair

PM:

Planned Maintenance for scheduled preventive maintenance

Reference Sources

ASTM:

American Society for Testing and Materials

FDA:

United States Food and Drug Administration

GAMPÉ:

Good Automated Manufacturing Practice

ISO:

International Organization for Standardization

ISO9001:	ISO Standard for Quality Management Systems
PIC/S:	Pharmaceutical Inspection Cooperation Scheme
USP:	United States Pharmacopeia

HOW AGILENT CROSSLAB COMPLIANCE SERVICES INTEGRATE WITH QUALITY SYSTEMS AND REGULATIONS

Agilent CrossLab Compliance Services

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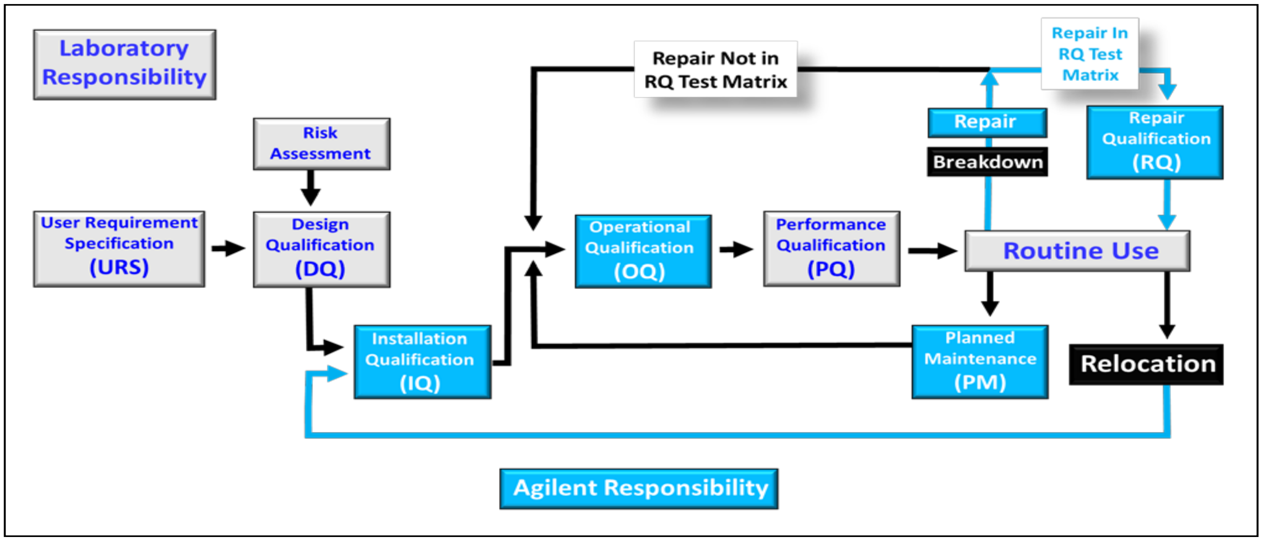
Agilent CrossLab Compliance Services

Agilent CrossLab Compliance Services are designed to seamlessly integrate with traditional quality systems used by firms and recognized by regulatory agencies worldwide. Analytical instruments must be suitable for their intended use. This requirement is good science in all laboratories and a regulatory requirement in pharma and biopharma laboratories. A life-cycle process for documenting and testing the suitability of laboratory instruments should be followed and Agilent recommends the life cycle framework defined in USP General Chapter <1058> on Analytical Instrument Qualification (AIQ). USP <1058> defines the governing framework and requirements that need to be satisfied, but the laboratory is responsible for how they satisfy these requirements.

- The United States Pharmacopoeia (USP) is the only major pharmacopeia with a general chapter dedicated to analytical instrument qualification, making <1058> an important global regulatory reference. The information is provided in a scientific, risk-based approach to analytical instrument qualification (AIQ). However, the life-cycle framework contained within USP <1058> is not prescriptive in its implementation, making the embedded scientific and risk-based principles flexible and universally applicable.
- The scientific process followed by CrossLab uses the Agilent's Automated Compliance Engine (ACE) to deliver paperless electronic qualification. The life-cycle stages Agilent perform are highlighted in the life-cycle diagram below. As part of this life-cycle, Agilent can configure the qualification tests performed to align with user requirements.


Laboratory Responsibility
Repair Not in RQ Test Matrix
Repair In RQ Test Matrix
Risk Assessment
Repair
Breakdown
Repair Qualification (RQ)
User Requirement Specification (URS)
Design Qualification (DQ)
Operational Qualification (OQ)
Performance Qualification (PQ)
Routine Use
Installation Qualification (IQ)
Planned Maintenance (PM)
Relocation
Agilent Responsibility

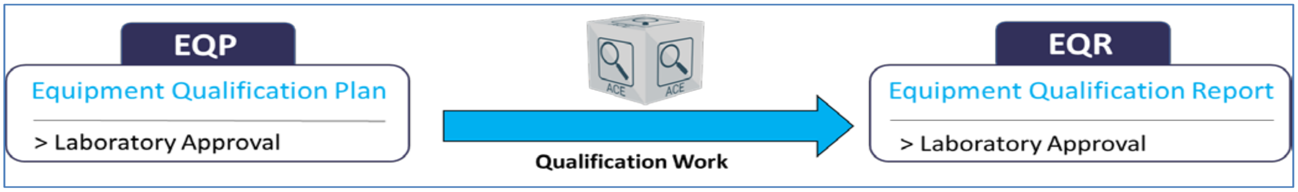
USP <1058> AIQ Framework

***NOTE**: RQ services, described later in this document, can be added to standard qualification services.*

ACE Workflow and Equipment Qualification Plans (EQPs)

Overview

Within the ACE workflow, the qualification tests, setpoints, and limits are defined in an EQP that can be configured to ensure that testing satisfies user requirements. When the qualification work is complete, an Equipment Qualification Report (EQR) is issued. The electronic workflow used within ACE has significant data integrity advantages over traditional paper or Excel-based qualification protocols, as validated calculations can be performed directly using electronic data such as chromatograms and metrology test values. Several of the instrument life-cycle stages are the responsibility of the laboratory, Agilent can provide compliance consultancy services and documentation which can help customers satisfy these requirements. These additional services are not included in our typical qualification offering.



High-level ACE Qualification Workflow

Standard and User-defined Limits

(Hardware qualifications only)

EQPs are available for download and approval as standard documents with Agilent recommended tests, setpoints, and limits, or they can be electronically configured by approved personnel to align with user requirements and intended range of use requirements. The degree of configuration depends on the analytical technology, but most EQPs can be configured to some degree, and one feature that can typically be changed is test limits.

EQPs are designed to be configurable (dependent on the analytical technology and standard requirements), but including additional tests or setpoints can impact the qualification time and associated cost. If a test limit is changed, ACE includes the capability to report results against the Agilent approved limit and any customer required limits (that is, both can be reported simultaneously).

If a user-defined test limit is more stringent than an Agilent recommended limit, Agilent makes no guarantee or obligation regarding the instrument passing the tighter test specification requirements. It is important to appreciate that tests performed under conditions of use (that is, to satisfy pharmaceutical monograph and application requirements) can have different limits than those defined in the OQ. It is the continuum of the combined OQ, PQ, and any point of use testing performed each time the instrument is used that together satisfy regulatory requirements.

User Requirements Specification (URS)

The purpose of user requirements is to document the intended use of the instrument within the life-cycle process and quality management system (QMS) being followed. Therefore, the URS is a customer / laboratory responsibility. Defining user requirements is often used to guide the customer in instrument selection and is stated as the first activity that should be followed in <1058>. The URS is important for two main reasons.

- It is a regulatory requirement for FDA and EU GMP that the intended use of the instrument and any software must be specified.
- Investment protection perspective means getting the right instrument for the right job.

Qualification protocols should test the instrument against any limits or specifications listed in the URS, which should document the intended range of use. Depending on the instrument complexity and how it is classified, a separate URS document may not be needed, but the URS requirements of the <1058> framework must be satisfied. A separate URS is almost always recommended for computerized systems.

An instrument performance specification is a product of the instrument development process by the supplier. It typically documents the performance the instrument can achieve. The URS should be based on intended use of the instrument and not the instrument specification. Additionally, if the intended use of a system changes, this may trigger a need to review the URS and associated qualification testing (for example, to ensure range of use is tested if used with a new analytical procedure).

Agilent offers compliance consultation services and documentation that can help customers address URS requirements.

Design Qualification (DQ)

The main function of the DQ stage of the laboratory instrument life-cycle process is to document why the selected instrument is suitable. Typically, this includes consideration of the instrument specification, how the instrument will be qualified, and the QMS followed by the instrument manufacturer. All together, these confirm that instrument performance is capable of satisfying user requirements. Depending on laboratory instrument life-cycle policy or SOPs being followed, instrument requirements and the relationship between the URS and DQ stages may vary – but as long as the <1058> framework principles are satisfied, this is not a problem, as it is left to each laboratory to justify and document its specific approaches.

The responsibility for satisfying DQ requirements primarily lies with the laboratory, with support from the supplier.

Agilent's approach to satisfying DQ requirements of USP <1058> includes the following.

- All Agilent hardware and software laboratory products, including the ACE software used to deliver qualification services, are designed, manufactured, and tested according to Agilent internal quality life-cycle development procedures.
- Certificates of Agilent testing, validation, and conformance to standards are provided with new Agilent instruments and similar certification can be provided for ACE software.
- Agilent is capable of installation, support, preventive maintenance, on-going qualification, and re-qualification after repair and user training worldwide.

Agilent offers a compliance consultation service that can help customers with DQ documentation.

Installation Qualification (IQ)

The main functions of the IQ stage are to document that laboratory is suitable (for example, critical systems typically include a site inspection / checklist), that the instrument is installed correctly in the environment, and IQ checks such as module start up are completed. IQ is provided and automated by ACE, which collects, checks, and tests Agilent hardware and software products for the following.

1. Purchase Order Details: Allows the customer to verify that the instrument being qualified matches their design requirements (if available) and purchase order.
2. Preparation and Installation Details: Gathers and records information about preparation and installation documents.
3. Documentation: Gathers and records information about reference and user manuals for initial installations.
4. Product Quality Assurance Details: Collects and records certificates and other forms that verify that the vendor has developed and built the product according to internal standards.
5. Startup: Verifies that all modules/components start up properly.
6. Installation Verification (software only): Verifies the correctness of all installation-related files.

Operational Qualification (OQ)

The main function of the OQ stage is to evaluate and document instrument performance at the intended operational range of use. OQ protocols should include a mix of metrology, functional, and operational tests. ACE qualification protocols include information about the test description and rational, setpoints, and the limits (acceptance criteria) for each technique, category, and instrument configuration.

OQ is provided and automated by ACE. ACE checks and tests for Agilent hardware and software products include the following.

- Metrological tests such as flow, temperature, pressure, and so on that ensure that the system is performing within Agilent (or user) specifications.
- Qualification results are reported in the EQR, which can include details of all test certificates, standards, and training information for the engineer performing the work. (Note that the EQR can be configured to customer requirements.)
- System or “holistic” tests verify the combined functions of the various system components
- The qualification testing can be configured to ensure URS requirements, such as range of use are tested.

For software qualification, the OQ consists of automated diagnostics regression testing and verification of the software installation. This supports continued use of the software in regulated environments (at install and as part of supporting periodic review).

In line with regulatory requirements, the EQPs should be approved before work is performed and the EQR should be reviewed and approved when the work is complete (as illustrated in Figure 2). The EQR contains all the raw data, results, and relevant information and attachments for complete compliance and traceability.

Mechanical Qualification (MQ)

(Dissolution systems only)

The main function of the MQ stage is to document that the mechanical performance of the instrument meets specifications and is functioning properly.

Performance Qualification (PQ)

The main function of the PQ stage is to document that the instrument is fit for purpose under conditions of intended use and to create an approved framework that ensures the instrument continues to perform as required. Because instrument range of use is tested within the OQ stage, it is usually not necessary to test this during PQ. It should be noted that requirements for instrument maintenance and repair fall within the PQ life cycle stage within the USP <1058> framework, as they are components of ensuring the continued performance of the instrument.

The customer is responsible for satisfying PQ requirements. (NOTE: Agilent can provide a PQ for Dissolution systems only.)

It is important to note that PQ is a lifecycle activity and not a one-time event. PQ tests may include activities such as method validation or system suitability tests (SST), but in Agilent’s opinion, SSTs contribute towards ensuring continued performance of the instrument (that is, PQ testing), but do may not fully satisfy <1058> PQ requirements.

Repair Qualification (RQ)

After an instrument is repaired, tests should be performed to evaluate the effectiveness of the repair and document that repaired instrument satisfies performance requirements. Agilent offers a service called Repair Qualification (RQ), which refers to the requalification of laboratory instrument hardware after a repair. For some laboratory systems, to document the performance after repair may require a full OQ. However, for some modular or component-based systems, such as HPLC and GC for example, partial qualification testing can be justified. This is accomplished by performing the qualification tests that are applicable to only the module or system component related to the repair, reducing the time the instrument is out of service. Re-qualifying the instrument after repair is a regulatory requirement defined in USP <1058>.

Agilent offers service contracts to repair and requalify an instrument during the period between scheduled annual OQs.

The level of retesting is prescribed in the RQ section of ACE: a form is displayed for the operator showing all types of repairs possible and the retesting required. Part of an example form for an LC system is shown below.

Re-Qualification After Repair		
Pump Strategies		
Repair/Replace Strategy	Modules	OQ Testing
Internal pump head parts, active inlet valve (or AIV cartridge), (parts of) check valves, reference valves, inlet manifold or pump drive, or taking pump head apart to clean (versus repair)	Any pump	Flow Accuracy & Precision
Pulse damper, pressure transducer	Any pump	Flow Accuracy & Precision
Multi-channel gradient valve	Quaternary	Flow Accuracy & Precision Gradient Composition

The full list of RQ repair and retest guidance is available for customer review.

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SERVICE DELIVERY METHODS

CUSTOMER APPROVAL OF ALTERNATIVE METHOD AND EQR STORAGE

Agilent CrossLab Compliance Services

Agilent CrossLab
From Insight to Outcome

Overview

Agilent recommends use of **Network ACE** for CrossLab qualification services that are enabled using the Agilent Automated Compliance Engine (ACE) software. Network ACE and Local ACE both access data directly (default methods) and are considered equivalent from a data integrity and data traceability perspective (see below). To provide additional flexibility in qualification service delivery, an alternative method is also available that accesses data indirectly. Use of the alternative method requires customer pre-approval using this form.

Available Methods

Method	Definition
Network ACE (Agilent recommended)	ACE software is installed on a network node within the laboratory LAN infrastructure. Raw data locations are always captured in the equipment qualification report (EQR), which provides end to end traceability and a fully characterized data workflow in the delivery. This method requires collaboration with the customer to load ACE behind the customer firewall.
Local ACE	ACE software resides on an independent external drive that can be driven from the system controller, where the customer data system (CDS) resides. Because the external drive is connected to the CDS, the data integrity of this method is equivalent to that of the Network ACE delivery method. Raw data is imported directly into ACE by the Data Manager tool, with the data paths always captured in the report, which provides data traceability assurance.
Alternative (Requires pre-approval)	This method requires customer pre-approval due to data integrity implications. Only choose this option in scenarios like the following: • ACE software is not run from a PC directly connected to the customer CDS, such as the FSE's laptop. System data files are transferred indirectly from the CDS to the FSE laptop instead of directly as done with Network and Local ACE methods. • Data is acquired using a CDS on the FSE's laptop and transferred directly to ACE. The CDS used in this method is qualified for data collection purposes.

EQR Storage

Select the checkbox below to authorize Agilent to store copies of the EQRs generated by ACE for Agilent internal assessments. The intention of the assessment is to evaluate the delivery of the qualification service, with a focus to improve delivery and assess the appropriateness of data integrity measures. The storage is exclusively for the internal assessment by Agilent and is not shared with other organizations. It is not to be considered a backup for the EQR provided at qualification delivery.

Customer Approval of Alternative Method and EQR Storage

Authorize Agilent to use the alternative method (check for approval): ☐

Authorize Agilent to store EQRs for their internal assessment (check for approval): ☐

Approved By/Title:	
Date Approved:	
Comments:	

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AGILENT CROSSLAB QUALIFICATION SERVICES

USE CASES FOR SERVICE DELIVERY

Agilent CrossLab Compliance Services

Introduction

With heightened scrutiny of data integrity, the Agilent Automated Compliance Engine (ACE) software must be able to access instrument-generated raw data files one of two ways: directly, using the connection between network nodes or with the server; and indirectly, through storage in a secure transfer location. (In this document, data integrity refers to the who, what, and where of data used in generating an ACE equipment qualification report, or EQR.)

ACE includes three main service delivery methods that address data integrity requirements; the rest of this document provides details to determine which one best fits a customer's needs.

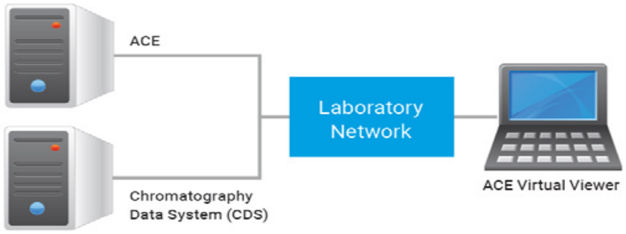
Regardless of the delivery method, ACE features and delivery procedures are compatible.

Network ACE (Agilent Recommended)

Overview

ACE software is installed on a network node within the laboratory LAN infrastructure, which requires collaboration with the customer to load ACE behind their firewall. Raw data locations are always captured in the EQR, which provides end-to-end traceability and a fully characterized data workflow in the delivery.

Details



Typical Network ACE installation diagram

Installing ACE in a separate node (a.k.a. the host PC) on the same network as the system controller offers data traceability that is equivalent to an installation on the system controller itself. The system controller (where the CDS resides) and the ACE host PC are identified and seen by the server and subject to the customer's data access controls and general IT policies. The CDS's audit trail records data movements between nodes or between the client and server, and ACE's data traceability features identify the original data directory and therefore ensures end-to-end data traceability

The ACE host PC has a separate/partitioned drive for ACE software. During ACE's installation, two services are setup on the operating system (OS): one for security and the other as a watchdog. Because the ACE host PC sits on the network as a shared drive, engineers access ACE through the networked drive: ACE is not installed on ACE Virtual Viewer PCs.

Requirements

Installation

- Install on a host PC with a separate drive (different from that of the OS)
- Attach to a network that clients can access
- 500 GB
- NTFS format
- User has local administration rights
- Customer installation instruction document is available

Operational

- User has an ACE node logon with a minimum of power user rights permissions; user also has a personal ACE account and password added through the ACE licensing tool
- Up to 5 users with 3 open sessions each can access the NDA simultaneously
- Exception to ports 11121-11141 on ACE node, clients, and switch's/Smart Hubs to be open on the network

Local ACE

Overview

ACE software resides on an independent drive that can be driven from the system controller, where the CDS resides. Because the drive is connected to the CDS, this method's data integrity is equivalent to preferred 1 method's. Raw data is imported directly into ACE by ACE's Data Manager tool, and data paths are captured in reports to provide data traceability.

ACE software resides on an independent drive that can be driven from the system controller, where the CDS resides. Because the drive is connected to the CDS, this method's data integrity is equivalent to the Network ACE method. Raw data is imported directly into ACE by ACE's Data Manager tool, and data paths are captured in reports to provide data traceability.

Details

ACE is designed to run from a dedicated drive, without leaving a footprint on the host PC. Therefore, it can be connected directly to the system controller (where the CDS resides) without altering the system's qualification status. For additional protection, the drive can be driven by another host PC on the same network; also, the drive can remain on site with the customer for use by the Agilent Field Service Engineer (FSE) during service deliveries only.

Alternative Method

This method requires customer pre-approval due to data integrity implications and only applies in scenarios like the following:

- ACE software is not run from a PC directly connected to the customer CDS, such as the FSE's laptop. System data files are transferred indirectly from the CDS to the FSE laptop instead of directly as done with Network and Local ACE methods.
- Data is acquired using a CDS on the FSE's laptop and transferred directly to ACE. The CDS used in this method is qualified for data collection purposes.

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INDUCTIVELY COUPLED PLASMA – MASS SPECTROMETER AGILENT SYSTEMS

OPERATIONAL QUALIFICATION

Agilent CrossLab Compliance Services

Agilent CrossLab
From Insight to Outcome

Introduction

This document describes tests for qualifying the ICP-MS systems, and the following tables lists all OQ tests.

Note: Injection Precision (No Gas Mode) is NOT INCLUDED in the standard OQ for ICP-MS but can be ordered as an EXTRA COST TEST.

Optional OQ Tests

Select the checkbox on the right and attach this document to your OQ EQP documentation for a record of qualification conditions.

Test / Mode	Parameters	Limits (Allowable Range)	Include
Injection Precision / No Gas Mode	Functional ICP-MS/HPLC connection	Precision RSD ≤ 10.00% (1.00 – 15.00)	☐

OQ Test Suite

General Tests

Test
CDS Logon Verification
Evidence of logon used to collect qualification data
Autosampler Operation*
Autosampler successfully moves to location(s) specified in software
Switching Valve Operation*
Automated test results are within acceptance criteria OR visual inspection confirms pump and valve function.
Autodilutor Operation*
Automated test results are within acceptance criteria

** Scheduled if the applicable module is part of the configuration*

SQ Tests

			Limits					
Setpoint / Mode	**Unit**	**^{mass}Ion**	**7700e**	**7700s**	**7700x**	**7800/7850**	**7900#100**	**7900#200**
Autotune								
** Hydrogen option only*								
Peak Width / No Gas	Amu range @10% height	^{7}Li, ^{89}Y, ^{205}Tl	0.65 to 0.80					
Mass Axis / No Gas	Amu range	^{7}Li, ^{89}Y, ^{205}Tl	± 0.1					
Doubly-charged Species / No Gas	%	^{70}Ce^{2+}/^{140}Ce+	≤ 3.45	≤ 6.9	≤ 2.0	≤ 2.0	≤ 2.0	≤ 6.9
Oxide Species / No Gas	%	^{156}CeO+/^{140}Ce+	≤ 2.3	≤ 3.45	≤ 1.38	≤ 1.38	≤ 1.38	≤ 3.45
Sensitivity / No Gas	Mcps/ppm	^{7}Li	≥ 17	≥ 42.5	≥ 25.5	≥ 25.5	≥ 25.5	≥ 42.5
		^{89}Y	≥ 68	≥ 204	≥ 85	≥ 85	≥127.5	≥297.5

			Limits					
Setpoint / Mode	**Unit**	**^{mass}Ion**	**7700e**	**7700s**	**7700x**	**7800/7850**	**7900#100**	**7900#200**
		^{205}Tl	≥ 34	≥ 102	≥ 51	≥ 51	≥ 76.5	≥ 110.5
Sensitivity / He	Mcps/ppm	^{59}Co	≥ 20.4	≥ 34	≥ 20.4	≥ 20.4	≥ 23.8	≥ 34
Sensitivity / H_2	Mcps/ppm	^{89}Y	N/A	≥ 85	≥ 51*	≥ 51*	≥ 68*	≥ 85
Background (No Gas Mode)								
Background	cps	^{7}Li	≤ 10				≤ 6.9	≤ 5.2
		^{89}Y	≤ 10				≤ 4.6	≤ 3.5
		^{205}Tl	≤ 30				≤ 11.5	≤ 11.5
Background (Gas Modes)								
** Hydrogen option only*								
Background / He	cps	^{78}Se	≤ 115	≤ 230	≤ 460	≤ 115	≤ 115	≤ 230
Background / H_2			N/A	≤ 11.5	≤ 4.6*	≤ 4.6*	≤ 4.6*	≤ 11.5
20-Minute Stability (No Gas Mode)								
Stability / No Gas	%RSD	^{7}Li, ^{89}Y, ^{205}Ti	≤ 3.45			≤ 2.3	≤ 2.3	≤ 3.45

QQQ Tests

			Limits							
Setpoint / Mode	**Unit**	**^{mass}Ion**	**8800 #100**	**8800 #200**	**8900 #080 G3665A**	**8900 #100 G3665A**	**8900 #200 G3665A**	**8900 #080 N3665A**	**8900 #100 N3665A**	**8900 #200 N3665A**
Autotune										
Q1 - Peak Width / No Gas	Amu range @10% height	^{7}Li, ^{89}Y, ^{205}Tl	0.60 to 0.80							
Q2 - Peak Width / No Gas	Amu range @10% height	^{7}Li, ^{89}Y, ^{205}Tl	0.60 to 0.80							
Q1 - Mass Axis / No Gas	Amu range	^{7}Li, ^{89}Y, ^{205}Tl	± 0.15							
Q2 - Mass Axis / No Gas	Amu range	^{7}Li, ^{89}Y, ^{205}Tl	± 0.16							
Doubly-charged Species / No Gas	%	$^{70}Ce^{2+}/^{140}Ce^{+}$	≤ 2.3	≤ 6.9	≤ 3.45	≤ 3.45	≤ 9.2	≤ 3.45	≤ 3.45	≤ 9.2
Oxide Species / No Gas	%	$^{156}CeO^{+}/^{140}Ce^{+}$	≤ 1.38	≤ 3.45	≤ 1.38	≤ 1.38	≤ 3.45	≤ 1.38	≤ 1.38	≤ 3.45
Sensitivity / No Gas	Mcps/ppm	^{7}Li	≥ 28.9	≥ 85	≥ 32.3	≥ 42.5	≥ 170	≥ 32.3	≥ 42.5	≥ 170
		^{89}Y	≥ 110.5	≥ 595	≥ 119	≥ 161.5	≥ 1020	≥ 119	≥ 161.5	≥ 1020
		^{205}Tl	≥ 40.8	≥ 212.5	≥ 45.05	≥ 59.5	≥ 382.5	≥ 45.05	≥ 59.5	≥ 382.5
Sensitivity / He	Mcps/ppm	^{59}Co	≥ 12.75	≥ 46.75	≥ 18.7	≥ 25.5	≥ 76.5	≥ 18.7	≥ 25.5	≥ 76.5
Sensitivity / H_2	Mcps/ppm	^{89}Y	≥ 76.5	≥ 127.5	≥ 85	≥ 119	≥ 136	≥ 85	≥ 119	≥ 136
Sensitivity / O_2	Mcps/ppm	^{89}Y (^{105}YO)	≥ 59.5	≥ 297.5	≥ 68	≥ 136	≥ 408	≥ 68	≥ 136	≥ 408
Background (No Gas Mode)										
Background	cps	^{205}Tl	N/A					≤ 1.0		
		^{9}Be	≤ 1.0							
		^{238}U						N/A		
Background (Gas Modes)										
Background / He	cps	^{78}Se	≤ 13.8	≤ 345	≤ 460	≤ 460	≤ 920	≤ 460	≤ 460	≤ 920
20-Minute Stability (No Gas Mode)										
Stability / No Gas	%RSD	^{7}Li, ^{89}Y, ^{205}Ti	≤ 3.45							

Test Design and Rationale

Overview

Many GMP/GLP enforcement agency inspectors now ask firms to provide a risk assessment of their equipment and computer systems plus a science-based rationale for subsequent validation and qualification testing.

GENERAL RISK STATEMENT: Any laboratory chemical system used for raw material testing or final drug product / medical device testing in GMP or used in formal GLP studies will likely fall into a HIGH RISK category. This risk assessment will imply the need for IQ & OQ & on-going qualification. ANY USER SPECIFIC RISK ANALYSIS SUPERCEDES THIS GENERAL RISK STATEMENT.

The rest of this section outlines the science-based rationale for each test in the Agilent hardware OQ plus a brief test design and procedure description.

The recommended set of hardware OQ tests described in this EQP derives from Agilent's interpretation of FDA, USP, and GAMP guidelines and other authoritative expert literature.

OQ test design incorporates both modular and holistic testing, which is a proven and regulatory acceptable approach. When applicable, direct metrology is used to test pump flow rates and thermal-controlled column compartments, for example. Holistic chemical testing is used to evaluate critical instrument characteristics.

When applicable, certified reference standards and calibrated equipment are used.

Considering the number of setpoints, parameters, and conditions of each recommended OQ test, the proven concepts of worst case, range, and representative have been applied. If a property or characteristic is known to have its worst performance at one end of a range of use, this is the setpoint that should be tested and other setpoints are not required. If a property or characteristic has no known worst case, testing at the high and low points of the range of use is required. If there are too many possible use cases and conditions to realistically test (and none is a worst case), a representative sample for test is the best approach.

The OQ procedure is intended to ensure that the ICP-MS equipment performs in accordance with recently published standards. The procedure is a standardized test protocol designed to ensure the ICP-MS system functions as intended by the manufacturer and as required by the end user. Only certified reference standards are used.

CDS Logon Verification

Description: To satisfy the attributable requirement of ALCOA+, evidence of the logon used to collect data must be provided.

Procedure: The test uses a screen capture to document who is logged on to the software that controls the instrument being qualified. The capture is automatically included with this test in the EQR.

Autosampler Operation

Description: This test is only scheduled when an autosampler is part of the configuration. It demonstrates that the module is correctly installed and connected; it does not test instrument performance.

Procedure: The instrument is power cycled, and a command to move the probe is executed. The test passes if the self test and manual command complete successfully.

Switching Valve Operation

Description: This test is only scheduled when a switching valve is part of the configuration. This test verifies the functional operation of the installed switching valve.

Procedure (ISIS): From the instrument software, commands to rotate the pump and, for ISIS3 only, operate the valve are executed and visually confirmed. When the tests are completed, results are recorded in ACE.

Procedure (AVS): From the instrument software, run the automated switching valve test and follow the prompts. When the tests are completed, the software generates a report with the results and a pass or fail is recorded in ACE.

Autodilutor Operation

Description: This test is only scheduled when an autosampler is part of the configuration. It verifies the functional operation of the installed autodilutor, which is connected to the ICP-MS instrument via an autosampler and switching valve. A known standard is injected into the system and diluted by a specific factor. The resulting diluted standard is measured by the instrument and its concentration, multiplied by the dilution factor, is then compared to the undiluted standard concentration to verify accuracy.

Procedure: From the instrument software, run the automated autodilutor test and follow the prompts. When the tests are completed, the software generates a report with the results and a pass or fail is recorded in ACE.

Autotune

Description: This test uses traceable checkout standards to run a software-executed autotune in all modes that generates a tune report.

Procedure: The tune report displays values for the peak width, mass axis, sensitivity, oxide species, and doubly-charged species sub-tests. The report values are entered in ACE and compared to limits to determine a pass/fail.

Background (No Gas Mode)

SQ

Description: This test examines the no gas/Off Mass mode background of the ICP-MS by monitoring ions during an autotune.

Procedure: No gas/Off Mass mode background signals (^{7}Li, ^{89}Y, and ^{205}Tl) are captured in ACE from the Autotune test's Tune Report. Average counts are used and recorded in ACE and then compared to limits to determine a pass/fail.

QQQ

Description: This test examines the no gas/Off Mass mode background of the ICP-MS in no gas mode by monitoring ions during a blank run using DI water.

Procedure: No gas/Off Mass mode background signals (^{9}Be and ^{205}Tl or ^{238}U) are measured during the blank run. Signals are collected for 20 cycles using an integration time of 1.0 second. Average counts are calculated and captured in ACE and then compared to limits to determine a pass/fail.

Background (Gas Modes)

Description: This test examines the background of the ICP-MS in the relevant gas modes by monitoring ions during a blank run using DI water.

Procedure: For He and, as applicable, H_2 gas modes, the background signal (^{78}Se) is collected for 20 cycles using an integration time of 1.0 second. Average counts are calculated and captured in ACE and then compared to limits to determine a pass/fail.

20-Minute Stability (No Gas Mode): Acquisition Parameters

Description: This test monitors the abundance of ions present in the checkout standard over a 20-minute period using the acquisition parameters below.

Procedure: The average spectrum/mass is calculated by the instrument, displayed in a report, entered in ACE, and compared to %RSD limits to determine a pass/fail.

Parameters	SQ	QQQ
Mode	Spectrum	Spectrum
Masses	7, 9, 59, 89, 140, 205	7, 56, 59, 89, 140, 205
Integration Time	9.99 seconds	9.99 seconds
Peak Pattern	3 points/peak	3 points/peak
Replicates	20	20
Sweeps/Replicate	100	100

Injection Precision (No Gas Mode)

Description: This optional test is unique to the hyphenated HPLC/ICP-MS configuration and is not equivalent to the LC Injection Precision, nor does it constitute a full OQ of the HPLC modules. If ordered, this test should be scheduled last of all the hardware OQ tests. It uses a series of constant volume injections of an Agilent ICP-MS calibration solution to prove a functional connection between the HPLC and the ICP-MS.

Procedure: Data is directly imported into the Data Manager within ACE. ACE then integrates the traces and reports the peak areas only. (Manual data entry of pre-integrated peak areas is also possible.) The mean peak area for the six runs is calculated, as well as the standard deviation and %RSD of the peak areas for the sequence. Results are compared to limits to determine a pass/fail.

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Report and Delivery Options

This list below includes options selected for inclusion in the EQR. By default, repeated run logs and transaction logs are always included; all other options can be included or excluded.

(For hyphenated system types only) If different options are chosen for the primary and supported system types, the primary system options are used for both techniques.

- Show chromatograms
- Show header and footer on cover
- Include repeated run logs
- Include Transaction logs

Selected Signature Options

Status: EQP is not locked

- Reporting variance is allowed in this EQP

Customer Approval

Name:
Title:
Date:
Signature:

Name:
Title:
Date:
Signature:

Name:
Title:
Date:
Signature:

Name:
Title:
Date:
Signature:

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-Product Description / Specification
-Life Cycle Phases / Transition Approval
-Quality Assurance / Testing
-Documentation and Change Management
-Source Code

Validation certificates for the ACE software and associated protocols are generated automatically as part of the life cycle process, prior to software release, and are available on request. The certificate includes a declaration of intent of interest statement, including Annex 11 and 21 CFR Part 11, and is representative of the life cycle process followed.

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