

Title: Analytical Instrument Qualification and Facility Equipment Maintenance

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Reference: USP <1058>: Analytical Instrument Qualification
SOP 220: Change Control
SOP 2160: Laboratory Data Review and Generation of Reports

<u>Rev. No.</u>	<u>Effective Date</u>	<u>Revision Summary</u>
1.	3-19-98	Original Version
2.	12-19-00	3.2, 3.4, 4.0 Copy of IQ/OQ to QA 4.7 GCMS OQ for calibrated flows and oven temp 4.8 generalized to ICP and GFAA systems
3.	2-01-02	Section 1.0: Added statement for facility equipment. Section 2.3: Added section to define facility equipment. Sections 4.0, 5.0: Included statement for completion of deviation/corrective action form. Section 5.0: New for facility equipment. Appendix II: Added deviation/corrective action form.
4.	02-17-03	Sec. 2.1: Clarified move to another location. Sec.s 4.3-4.5: Added IC to list. Sec.'s 4.0, 5.1: Clarified instrument repair, removed deviation/corrective action form verbiage and added reference to SOP 220. Removed Deviation/Corrective Action form.
5.	05-02-07	2.1, 3.2, 4.5: Added copy of data given to QA to file with approved protocol/report package. Added section on generating IQ and/or OQ protocol/report package. Renumbered starting at the IQ section. 5.0: Added remove or tag equipment out of service if fail IQ and/or OQ. 5.2, 5.7, Appendix 2: Added oven temperature OQ worksheet. 5.10: Added statement for Part 11 compliant software OQ. 6.2: Changed from QA to maintenance personnel.
6.	08-18-09	Revised throughout to comply with current SOP 101 and USP <1058>.

<u>Rev. No.</u>	<u>Effective Date</u>	<u>Revision Summary</u>
7.	NOV 17 2010	Sec. 2.0, 3.3, 5.1, Appendix II, III, IV: Added. Sec. 3.0, 5.12: Expanded. Rewording and expansion throughout.

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<u>Prepared by</u>	<u>Date</u>	<u>Technical Review</u>	<u>Date</u>
	10/07/10		10-12-10

QA Approval/Date: Christina M Garcia 11/17/10

1.0 SCOPE AND APPLICATION

- 1.1 This SOP pertains to the qualification of analytical instrumentation and equipment used in testing of clients samples. It does not cover ancillary equipment used in the lab not directly involved in producing test results. This includes standard equipment with no measurement capability or usual requirement for calibration, where the manufacturer's specification of basic functionality is accepted as user requirements. Conformance of this equipment with user requirements is verified through visual observation of its operation with each use.
- 1.2 Instrument qualification is not a single continuous process, but instead results from several discrete activities. These activities can be grouped into four phases: design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ). The purpose of qualification activities is to demonstrate that the analytical equipment is suitable for its intended purpose. It may also provide standardization, so that results produced in this lab will be comparable to results from other labs. For example, if an HPLC method is developed using a flow rate of 1.0 mL/min or a GC oven temperature of 200°C, a qualification of those parameters establishes confidence that the method is transferable and capable of producing similar results elsewhere.
 - 1.2.1 Design Qualification (DQ) is the documented collection of activities that define the functional and operational specifications of the instrument and criteria for selection of the vendor, based on the intended purpose of the instrument. Functional and operational specifications of the instrument are typically developed and tested by the instrument manufacturer. Criteria for selection of the vendor and instrument are included as part of the justification process for capital expenditures (controlled by corporate procedure EXOVA SP05), and beyond the scope of this SOP.
 - 1.2.2 Installation Qualification (IQ) is the documented collection of activities necessary to establish that an instrument is delivered as designed and specified and is properly installed in the selected environment. It assures that the environment is suitable for the instrument. Testing of fixed parameters that do not change over the life of the instrument (voltage inputs, acceptable pressures, and loads) may be included in IQ activities.
 - 1.2.3 Operational Qualification (OQ) is the documented collection of activities necessary to demonstrate that an instrument will function according to its intended use in the selected environment. Where appropriate, performance of individual instrument components may be documented or a holistic approach may be taken. Requalification occurs when an instrument is moved to another location or undergoes major repairs or modifications. A holistic Performance Verification is performed on each instrument on an annual or semi-annual basis.

1.2.4 Performance Qualification (PQ) is the documented collection of activities necessary to demonstrate that an instrument consistently performs according to the specifications required during use of the testing equipment. PQ activities are covered by various test method SOPs that describe the manner in which demonstration of system suitability are documented. As a contract laboratory, our test equipment is used for several different methods and for a large variety of applications; each method SOP should contain pertinent suitability criteria or quality control parameters. In addition, method development and validation activities contracted by the client may determine appropriate system suitability specifications for a particular test in a specific matrix.

1.3 The procedure and documentation pertaining to facility equipment maintenance and repair is also outlined in this SOP.

1.4 Method validations are a client driven process, therefore method validations are not included in the Master Validation Plan.

2.0 MASTER VALIDATION PLAN

2.1 Approved equipment qualification protocols, software validation protocols, requalification and recalibration schedules, and the master equipment list comprise the Master Validation Plan.

2.2 Calibration and qualification dates are entered into the master equipment list maintained by QA. The master equipment list includes equipment location, unique identifier, frequency of requalification/recalibration, GMP status, the dates of the last requalification/recalibration, and when the next requalification/recalibration is due. The list is reviewed monthly to determine upcoming due dates for the following month.

2.2.1 A job number is assigned to the requalification and entered into Job Tracking as an outstanding job.

2.2.2 A timeframe of thirty days is given for completion. The qualification is tracked weekly at the staff meetings until completed.

2.2.3 If the recalibration or requalification is not performed before the expiration date, the equipment will be marked "Non-GMP" or removed from service until requalified/recalibrated. Examples of the stickers used to indicate qualification status are given in Appendix III.

3.0 PROTOCOLS AND REPORTS

3.1 Prior to the qualification or requalification of instruments, a protocol is written and approved by the appropriate Department Manager or Technical Director and additionally approved by Quality Assurance (QA). Initial IQ/OQ of new equipment may be performed by the instrument manufacturer (or their qualified designee) in accordance with their pre-approved protocols. This qualification may be supplemented with an abbreviated OQ protocol specific for the intended use of the instrument, if deemed necessary by the Department Manager, Technical Director, or Quality Assurance (QA). The approved protocol masters will be maintained in the QA Office in the Master Validation Plan binder.

3.1.1 The instrument parameters to be tested and the choice to use a modular vs. a holistic approach to qualification will be determined by the Department Manager in consultation with the Technical Director and will be subject to approval by QA. A modular approach may be preferred to allow the movement, replacement, or repair of individual system components or auxiliary equipment without the need for complete system requalification (only the component or auxiliary equipment will need to be requalified).

3.1.2 Specifications are set based on the intended use of the instrument and in accordance with equipment requirements described by test methods, typical client specifications, manufacturer's recommendations, regulatory guidances, SOPs, or the current USP/NF.

3.2 An operational qualification/performance verification protocol consists of the following components:

3.2.1 Title page to document the instrument or equipment identification, type, issuance of the protocol, and the final approval of the executed protocol by the Department Manager or Technical Director and QA.

3.2.2 Protocol Approval section.

3.2.3 Qualification Index.

3.2.4 Objective and Scope of the protocol.

3.2.5 Identification of the Instrument or Equipment, including the location within the facility where the equipment can be found and a brief description of the system.

3.2.6 System Description, including a list of the various components that will be qualified.

3.2.7 References, including any manufacturer's procedures or technical literature.

3.2.8 Procedures for execution of the qualification.

3.2.9 Acceptance criteria.

3.2.10 Description and instructions for the Qualification Tests to be performed.

3.2.11 Qualification Documentation for the results of the qualification tests. This includes a table to document the names of those who executed the tests and the qualification and a table to document the equipment and/or reagents used in the qualification.

3.2.12 Deviations/Exceptions documentation.

3.2.13 Appendix for the raw data.

3.3 QA will issue the protocol as follows:

3.3.1 QA and the Department Manager should review the previously executed protocol, if applicable, to determine if any changes are needed to the protocol.

3.3.2 QA will make requested revisions to the master protocol, if necessary, and route the protocol for approval.

3.3.3 Once approved, QA will issue a working copy of the protocol to the Department Manager, and refile the master in the Master Validation Plan binder. Dispose of the obsolete master protocol, as any executed protocols will be on file in the instrument binders.

3.3.4 Make a new line entry into the protocol issuance spreadsheet (Appendix IV) as follows:

Protocol Type
Equipment #
Issued By
Date Issued

3.3.5 After the protocol has been executed and submitted to QA for approval, update the protocol issuance spreadsheet with the returned date.

3.3.6 Complete remaining fields, as applicable.

3.4 The executed protocol and the raw data package are reviewed by the Department Manager or Technical Director and the technical review section of the title page of the executed protocol is signed and dated. Any deviations or exceptions occurring during the execution of the protocol must be either corrected or justified.

- 3.5 The executed protocol and all attachments (including raw data), whether performed by the instrument manufacturer or internally, will then be given to QA for review. The approval signatures on the executed protocol must not be the same as the executor's signatures.
 - 3.6 Following QA approval of the executed protocol, the instrument will be labeled, indicating the current qualification status and assigning a date for requalification. Sample labeling stickers are found in Appendix III.
 - 3.7 Once final review of the executed protocol has been completed, QA will change the job status in Job Tracking to "COMP" (complete) and submit the Job Envelope to Client Services.
 - 3.8 The presence of Technical Review and QA Review signatures on the front page of the executed protocol documents the conclusion that the system has been accepted as qualified for its intended use.
 - 3.9 Approved qualification packages are filed by instrument ID and maintained by QA.
- 4.0 INSTALLATION QUALIFICATION (IQ)
- 4.1 When new equipment arrives in the laboratory, it will either be quarantined in the QA office until the equipment has been uniquely identified, labeled with a calibration due date, and is deemed qualified for use (timers, viscometers, thermometers, and other small portable equipment) or labeled with an Out-of-Service tag (Appendix II) pending qualification (analytical instrumentation). New equipment and its calibration due date (if applicable) is entered into the master equipment list by QA upon receipt.
 - 4.2 The Department Manager and QA will review the installation instructions and manufacturer's IQ/OQ protocol (if applicable) prior to execution.
 - 4.3 Document the adequacy of the utility supplies (electricity, ventilation, cooling water, space, etc.) Compared to the manufacturer's requirements using the form in Appendix I (or equivalent form provided by the manufacturer).
 - 4.4 Retain copies of the test data performed by the installation engineer or analyst. Keep all the raw data, protocols, specifications and installation instructions with this data package.
 - 4.5 Use a normal signature page for the data package (per SOP 2160) to document the Department Manager review.
 - 4.6 Submit the executed IQ/OQ protocol and raw data to QA for review.

5.0 OPERATIONAL QUALIFICATION OR PERFORMANCE VERIFICATION

- 5.1 Prior to executing a requalification protocol, appropriate preventative maintenance of the instrument should be performed, as defined in the instrument SOP.
- 5.2 Qualification Tests should be documented in the instrument logbook and a data package produced with signatures as is normally done with all work.
- 5.3 Requalification of major analytical instrumentation is performed annually (at a minimum), whenever an instrument is moved off a physical surface, or whenever a component has been repaired or modified and this action may affect calibration or the qualified state of the instrument, as determined by QA during the change control process. (Refer to SOP 220)
- 5.4 Any instrument that no longer meets qualification specifications must be tagged as “out of service” (Appendix II) until a decision is made to either repair the instrument or remove it from the area for disposal. Out-of-Service tags may be placed on equipment by any employee observing that the equipment is no longer in a qualified state, however they may only be removed by QA.
- 5.5 Gas Chromatograph qualification consists of (at a minimum):
 - 5.5.1 Demonstration of the accuracy of the gas carrier system.
 - 5.5.2 Demonstration of injector and autosampler precision and accuracy (if applicable).
 - 5.5.3 Demonstration of the precision of the automated headspace sampler or purge and trap unit (if applicable).
 - 5.5.4 Demonstration of detector accuracy, sensitivity, linearity, and precision.
 - 5.5.5 Demonstration of oven temperature programming accuracy and stability.
- 5.6 Liquid Chromatograph and Ion Chromatograph qualification consists of (at a minimum):
 - 5.6.1 Demonstration of the eluent carrier system accuracy, including gradient (if applicable).
 - 5.6.2 Demonstration of injector and autosampler precision and accuracy.
 - 5.6.3 Demonstration of detector accuracy, sensitivity, linearity, and precision.
 - 5.6.4 Demonstration of column compartment and/or autosampler tray temperature programming accuracy (if applicable).
 - 5.6.5 Demonstration of the precision of the autosampler (if applicable).

5.7 ICPMS, ICPOES qualification consists of (at a minimum):

- 5.7.1 Demonstration of the sensitivity, stability, and acceptable tuning of the instrument.
- 5.7.2 Demonstration of the accuracy, precision, and linearity of the detector.
- 5.7.3 Demonstration of the accuracy of the autosampler.

5.8 FTIR instrument qualification consists of (at a minimum):

- 5.8.1 Demonstration that the detector signal differential meets manufacturer's specifications.
- 5.8.2 Demonstration that the accuracy of the peak spectra of a reference standard meets the specifications programmed in the instrument.

5.9 UV-Vis Spectrometer and Fluorometer qualification consists of, at a minimum, demonstration of the accuracy, precision, and linearity of the detector.

5.10 Polarimeter qualification consists of (at a minimum):

- 5.10.1 Documentation of the trough and bulb alignment
- 5.10.2 Documentation of the dark sample threshold
- 5.10.3 Documentation of the quartz calibration plate (QCP) integrity and accuracy
- 5.10.4 Determination of measurement accuracy and repeatability
- 5.10.5 Documentation of zero stability
- 5.10.6 Documenting the accuracy of the temperature control system

5.11 Elemental Analyzer qualification consists of (at a minimum):

- 5.11.1 Documentation of the helium pressure adequacy.
- 5.11.2 Documentation of zero reading stability.
- 5.11.3 Documentation of the precision and accuracy of standards within the range of use.
- 5.11.4 Determination of measurement accuracy and repeatability.
- 5.11.5 Documenting the accuracy of the temperature control system.

5.12 NMR qualification consists of (at a minimum):

5.12.1 Documentation of the lineshape for ^1H , ^{13}C , ^{15}N , ^{19}F , ^{31}P , and ^{109}Ag (as appropriate) for each probe.

5.12.2 Documentation of the resolution for ^1H , ^{13}C , ^{15}N , ^{19}F , ^{31}P , and ^{109}Ag (as appropriate) for each probe.

5.12.3 Documentation of the sensitivity for ^1H , ^{13}C , ^{15}N , ^{19}F , ^{31}P , and ^{109}Ag (as appropriate) for each probe.

5.12.4 Demonstration of acceptable quality of a two-dimensional gradient enhanced HMBC spectrum for the most common isotopes analyzed.

5.12.5 Demonstration of acceptable sample temperature control.

5.13 Lab Ovens: Lab ovens and muffle furnaces are calibrated annually by an ISO 17025 certified vendor. Mapping is performed for larger ovens.

5.14 Refer to the following SOPs for calibration of other equipment:

- SOP 2110 for calibration of balances
- SOP 2170 for calibration of pipettes
- SOP 2140 for calibration of thermometers
- SOP 2290 for calibration of pH meters
- SOP 7830 for calibration of the sample preparation microwave
- SOP 8100 for calibration of Karl Fisher titrators
- SOP 8180 for calibration of the conductivity meter
- SOP 8260 for calibration of the turbidity meter
- SOP 8360 for calibration of the melting point apparatus
- SOP 8370 for calibration of automatic titrators.
- SOP 8540 for calibration of the Halogen Moisture Analyzer

5.15 Timers will be replaced when they reach the manufacturer's initial calibration expiration date.

5.16 The Brookfield Viscometer is calibrated at the time of use with a suitable standard.

5.17 The Gel Permeation Chromatography unit is calibrated for flow rate with each use.

6.0 FACILITY EQUIPMENT

- 6.1 When it has been determined that either maintenance or repair is required, a Change Control form is completed and given to QA. Refer to SOP 220 for procedure and form.
- 6.2 Facility maintenance personnel will maintain all records of repair for facility equipment, such as air conditioners, blowers, safety hoods, etc.
- 6.3 Facility equipment pertains to equipment which are used to maintain a suitable working environment during business hours, such as air conditioners, exhaust hoods, etc. This includes utilities, such as potable water systems.
- 6.4 Units used for controlled temperature storage will be mapped per a qualification protocol prior to being placed into use and annually thereafter. Refer to SOP 1510 for temperature monitoring.
- 6.5 Water systems - Refer to SOP 2200 for qualification of water systems.

7.0 SOFTWARE VALIDATION

- 7.1 Computerized analytical instruments contain integrated chips with low-level software, known as firmware. Such instruments will not function without properly operating firmware, and users generally cannot alter firmware design or function. Firmware is therefore considered a component of the instrument itself and the qualification of hardware is not possible without operating it via its firmware. Operational Qualification, which involves the entire instrument and software system, qualifies the firmware holistically. Firmware upgrades are managed per the Change Control system (SOP 220).
- 7.2 The manufacturer performs DQ, validates the software, and will provide a summary of validation when the instrument is installed. Operational Qualification, which involves the entire instrument and software system, qualifies the instrument control, data acquisition, and processing software holistically.

7.3 The security of data storage, backup, and archiving for GMP analytical instrumentation is demonstrated by executing a Data Integrity Protocol. An abbreviated protocol will be executed at a minimum of every three years or when a change in software is made that has the potential to affect data integrity (refer to SOP 220: Change Control). This software validation process includes:

- 7.3.1 Documenting Microsoft Windows and instrumentation software users and their permission levels.
- 7.3.2 Demonstration of the individual security levels built into and maintained by the software, including ExovaGuard (where applicable), a proprietary software component that provides a secure interface for instrument operation.
- 7.3.3 Demonstration of system lock out.
- 7.3.4 Documentation of the system for raw data acquisition, storage, backup, and restoration.
- 7.3.5 Documentation of processed data storage, back up, and versioning.
- 7.3.6 Verification of data integrity features which protect raw and meta data.
- 7.3.7 Documentation of audit trails associated with raw and processed data.

APPENDIX I

INSTALLATION QUALIFICATION FORM

Instrument Manufacturer _____ Model _____

Location _____ Software Version: _____

The system consists of the following components:

Component	Model	Serial number

IQ Parameters:

Parameter	N/A	Required	Supplied	Adequate?
Space	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
Clearance	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
Electrical	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
Ventilation	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
Coolant	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
Pneumatics/gases	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
Computer system/network	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No

Manuals and appropriate accessories provided? Yes No _____

Performed By/Date _____ QA Review/Date _____

APPENDIX II

TEMPLATE FOR OUT-OF-SERVICE TAG

EQUIPMENT OUT-OF-SERVICE

- Pending Service/Repair
- Pending Qualification

Change control: C- _____

THIS TAG MAY BE REMOVED ONLY BY QA

Returned to service by QA

Initials: _____ Date: _____

File with the change control

APPENDIX III

EXAMPLES OF QUALIFICATION STICKERS

GMP

Compliant through:

10 / 11 AS
MM / YY QA

IC-5
System ID

GMP

Certified as part of

IC-5
System ID

**NON
GMP**

IC-5 AS
QUAL : 10/15/10
DUE : 10/2011

APPENDIX IV

F:\NONINSTRUMENT CAL & QUAL PROTOCOL ISSUANCE SHEET.123												
Issued Protocol												
A	B	C	D	E	F	G	H	I	J	K	L	M
Equipment ID (entered by issuer)	Hardware or Software	Protocol Type (entered by issuer)	Issued By	Date Issued	Reviewed (entered by reviewer)	Stecker Updated (entered by reviewer)	Update Schedule (entered by reviewer)	Approve in JT (entered by reviewer)	Pull JE (entered by QA Asst.)	Documents (entered by QA Asst.)		
112	RSR	320 JY/TIS model	C Garcia	09/16/2010	09/21/2010	09/21/2010	09/21/2010	09/21/2010	09/21/2010	09/21/2010		
113	FT7	320 JY/TIS model	C Garcia	09/21/2010	10/06/2010	09/21/2010	10/06/2010	09/21/2010	10/06/2010	09/21/2010		
114	RMR	320 JY/TIS model	C Garcia	09/21/2010	09/28/2010	09/28/2010	09/28/2010	09/28/2010	09/28/2010	09/28/2010		
115	ICONS-42	320 JY/TIS	C Garcia	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010		
116	ICONS-4	320 JY/TIS	C Garcia	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010		
117	ICONS-16	320 JY/TIS	C Garcia	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010	09/27/2010		
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