The National Ribat University

Faculty of Graduate Studies and Scientific Research

Instrument Qualification of Analytical Laboratory

A Review Submitted in Partial Fulfillment of the Requirements for Master Degree in Drug Quality Control

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بسم الله الرحمن الرحيم

{ وَقُلِ اعْمَلُواْ فَسَيَرَى اللّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ وَسَتُرَدُّونَ إِلَى عَالِمِ الْغَيْبِ وَالشَّهَادَةِ فَيُنَبِّئُكُم بِمَا كُنتُمْ تَعْمَلُونَ}

صدق الله العظيم

سورة التوبة (105)

Dedication

Affectionately dedicated to:

My dearest father and mother …

To those my heart always remember them…

To my husband and sisters whose affection and

encouragement make me able to get success...

To my sweet and loving son...

To all people who told me that nothing is impossible…

Acknowledgement

The realization of this work was only possible due to the several people's collaboration, to who I desire to express my gratefulness. First and foremost, I would like to express my sincere gratitude and my heartfelt thanks to my supervisor:

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Abstract

Analytical equipment are used for a specific analysis. So regular performance verifications are made to ensure that the equipment to be used is suitable for its intended application. All equipment used in the production of products shall be properly validated and calibrated.

Equipment qualification is one of the important steps in achieving and maintaining the quality of final products.

The article gives an introduction and general overview on equipment qualification of analytical laboratory.

Qualification is an ideal step for analytical equipment validation.

This review also gives the individual steps of qualification such as design qualification DQ, installation qualification IQ, operational qualification OQ, and performance qualification PQ. These steps are done in order to qualify the equipment.

This review describes the development of guidance for the equipment qualification EQ of analytical equipment and examines the need for equipment qualification, the various approaches and steps involved, and other pertinent considerations.

المستخلص

الاجهزة التحليلية تستخدم لنوع محدد من العمليات التحليلية، لذلك يتم التحقق من أداء هذة الأجهزة التحليلية بإنتظام للتأكد من أن الاجهزة المستخدمة مناسبة للتطبيق المقصود. جميع الأجهزة المستخدمة في إنتاج المنتجات يجب التحقق من صحتها ومعايرتها بشكل صحيح.

يعتبر تأهيل الاجهزة أحد الخطوات الهامة في تحقيق والحفاظ على جودة المنتجات النهائية.

هذا المقال يعطي مقدمة ونظرة عامة على تأهيل أجهزة المعامل التحليلة.

التأهيل هو خطوة مثالية للتحقق من المعدات التحليلية.

كما يقدم هذا المقال ايضا" الخطوات الفردية للتأهيل مثل تأهيل التصميم، تاهيل التركيب، تأهيل التشغيل، وتأهيل الآداء. تتم هذة الخطوات من أجل تأهيل المعدات التحليلية.

يصف هذا المقال تطوير الإرشادات المتبعة لتأهيل المعدات التحليلية ويدرس الحوجة إلى تأهيل المعدات ، والنهج والخطوات المختلفة المعنية ، وغيرها من الاعتبارات ذات الصلة.

Introduction:

The reliability of analytical data generated from chemical and physical analyses is critically dependent on the validity of the analytical methods used, the reliability of the instruments used for the experiments, and proper training of the analysts, these three factors, linked together by cGMPs (current Good Manufacturing Practices), provide the fundamental assurance to the quality of the data [1].

Non reliable instruments can be a major source of error in all analyses. Analytical data generated from instruments that are not properly qualified or not calibrated with traceable standards are questionable and hence will be challenged [2].

Regulatory agencies in most countries demand the use of calibrated instruments for data generation. The International Organization for Standardization ISO and International Conference of Harmonization ICH have similar requirements [1].

Qualifications:

Instrument qualification is required to establish the functional capability and reliability of a system for its intended use in a suitable environment. Instrument qualification can be divided into design, installation, operation, and performance qualifications, a qualification protocol that provides details about the system, the scope and constraints of the qualification, qualification tests, test procedures, and acceptance criteria should be available for review and approval before qualification begins, a protocol should also contain an exception log to record any out of specification results, investigation, and problem resolution [1].

Validation:

Validation of an analytical procedure is the process by which it is established, by laboratory studies, that the performance characteristics of the procedure meet the requirements for the intended analytical applications [2].

Analytical Instrument Qualification:

Analytical Instrument Qualification AIQ Is documented evidence that an instrument performs suitably for its intended purpose and that it is properly maintained and calibrated [3].

The benefits of Equipment Qualification to the analysts:

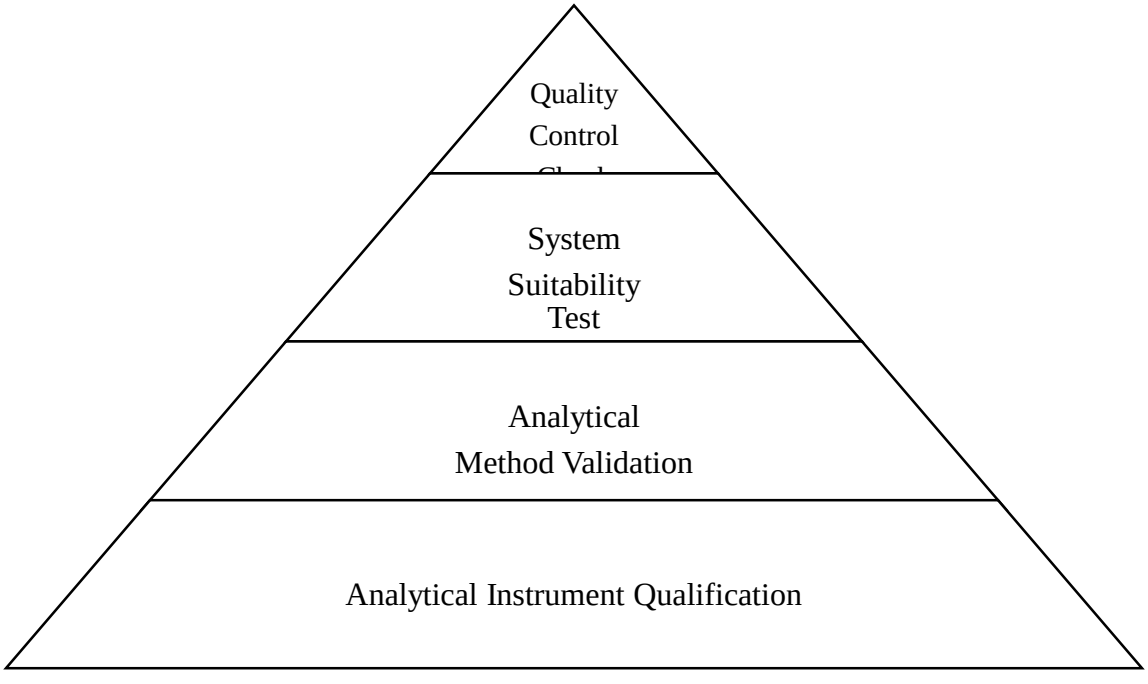
Fully defining all of the required characteristics of the measuring system assure that new equipment is fit for its intended purpose, proving that the selected equipment meets these requirements before using it for analysis, reduced probability of incorrect test results, and it is a template for troubleshooting any problem that may occur whilst the instrument is in service [4].

The components of data quality:

Analytical instrument qualification helps justify the continued use of equipment, but it alone does not ensure the quality of data. Analytical instrument qualification is one of the four critical components of data quality. Analytical Instrument Qualification forms the base for generating quality data [5].

The other essential components for generating quality data are the Analytical Methods Validation, System Suitability Tests, and Quality Control Checks as indicated in figure (1) [5].

Figure (1): The Components of Data Quality



a. Analytical Instrument Qualification:

The AIQ is documented evidence that an instrument performs suitably for its intended purpose and that it is properly maintained and calibrated [1].

b. Analytical Methods Validation:

Analytical methods validation is documented evidence that an analytical method does what it purports to do and delivers the required attributes. Use of a validated method should instill confidence that the method can generate test data of acceptable quality, some common parameters of method validations are accuracy, precision, sensitivity, specificity, repeatability, linearity, and analyte stability [1].

c. System Suitability Tests:

System suitability tests assure that the system works according to the performance expectations and criteria set forth in the method, assuring that at the time of the test the system met an acceptable performance standard [5].

d. Quality Control Checks:

Analyses are performed using reference or calibration standards. Single or multipoint calibration or standardization correlates instrument response with a known analyte quantity or quality. Calibrators/standards are generally prepared from certified materials suitable for the test. Besides calibration or standardization, some analyses also require the inclusion of quality control check samples, which provide an in-process assurance of the test's performance suitability [5].

The AIQ and analytical method validation assure the quality of analysis before conducting the tests. System suitability tests and quality control checks assure the high quality of analytical results immediately before or during sample analysis [5].

Requirement of qualification process:

Qualification is using an efficient and science based approach to provide documented evidence that the instrument is work as its intended purpose. This not only serves to meet the FDA requirements, which call for companies to establish procedures to ensure fitness for use of instruments that generate data which support product testing, but also enables the everyday lab objective of consistently obtaining reliable and valid data to be satisfied [6].

In order to fulfill these requirements, a process is developed and followed, and documented. It is of critical importance to stay focused on the scientific value of the process and not get lost in producing documentation, a way to stay focused, and to keep the documentation simple, is to create an instrument history file, take a folder, label it, and add the relevant documentation. Include purchase orders, repair records, calibration records, and maintenance records. The file helps to track and categorize the different types of instruments, and eventually serves as the foundation of the qualification [6].

The Master Plan:

Equipment qualification is begin by developing a MP. This is a high-level document that generally discusses the company, the lab site, its operations, and internal processes, the MP states the basic process for qualification, including a general discussion of development, execution, review, and approval. A list of instruments required resources, and a timeline for the different phases of completion are included. Since the instrument list and timeline are dynamic, ensure the MP is flexible to allow for constant changes. Evaluate this overall program periodically to ensure that current regulations and requirements are met and excessive or inefficient practices are eliminated [6].

Qualification phases:

Qualification of instruments is not a single, continuous process but instead results from many discrete activities. For convenience, these activities have been grouped into four phases of qualification. These phases are DQ, IQ, OQ and PQ [4].

The program must contain provisions for the qualification, maintenance, and documentation of failures of all equipment used to collect data for regulatory submissions. This is usually accomplished by using a standard operating procedure (SOP) that describes the overall program [7].

a. Design Qualification:

It is a familiar process that all companies complete before purchasing an item. The DQ ensures the process has the right people involved, covers all aspects related to the instrument to make sure the correct one is purchased, and documents the activities. The goal is to ensure the selected instrument is fit for its intended purpose [5].

Before investigating what instrument to purchase, identify the instrument type. A document called the User and Functional Specifications (UFS) is developed to capture what the user needs the equipment to do [6].

In the UFS, the basic functional requirements outlining the key features are defined. Such things as the environment it will reside in, the operating range it will cover, how often it will be used, type of analysis technique, the types of materials it will test, local/federal regulations it must satisfy, safety and utility requirements, procedures for operation, maintenance, calibration, computer interaction, and user interface friendliness are captured [4].

Instrument Selection process is the most important step in design qualification, instrument selection is done by selecting a number of vendors who manufacture the type of instrument defined [6].

Besides ensuring the vendor has an instrument that meets the UFRS, ensure they have the necessary quality systems in place to develop, manufacture, and test the equipment. Assuring the vendor has the quality systems in place will ensure the equipment you receive works properly. Once the instrument design is accepted, then develop a test protocol with the vendor to ensure all company requirements are met, this protocol that is executed with the vendor at their site is commonly referred to as the Factory Acceptance Test (FAT) [6].

Once everything is approved and in order, instrument delivery is scheduled, prepare the area in your facility for delivery and installation. Ensure the physical dimensions of the instrument can be accommodated, and the correct utilities and support systems are available. Once the instrument arrives, basic checks can be performed to ensure nothing happened during shipping and the equipment is what was ordered. This is commonly referred to as the Site Acceptance Test (SAT) for custom built systems [6].

As the instrument arrives on-site, create the instrument history file and add it to the instrument tracking database. Ensure the equipment is assigned an ID number via the instrument identification system and a corresponding logbook [7].

b. Installation qualification:

Installation Qualification is a documented collection of activities needed to install an instrument in the user's environment. IQ applies to a new, pre-owned or an existing onsite but not previously qualified instrument [4].

The activities of IQ are to provide a description of the instrument, including its manufacturer, model, serial number, and software version. Also insure that the instrument, software, manuals, supplies, and any other accessories arrive with the instrument as the purchase order specifies and that they are undamaged. Other activities of IQ are to assure that the installation site satisfactorily meets vendor specified environmental requirements. Some analytical systems require users to provide network connections and data storage capabilities at the installation site, so they must connect the instrument to the network and check its functionality [6].

The final activities of IQ are assemble and install the instrument and perform any initial diagnostics and testing. Assembly and installation of a complex instrument are best done by the vendor or specialized engineers, whereas users can assemble and install simple ones [5].

c. Operational qualification:

After a successful IQ the instrument is ready for OQ testing. The OQ phase may consist of testing the fixed parameters to measure the instrument's non-changing [4].

The fixed parameters such as length, height, and weight, they do not change over the life of the instrument and therefore never need predetermining. Secure data handling, such as storage, backup, and archiving should be tested at the user site according to written procedures [5].

The OQ consist of testing the important instrument functions to assure that the instrument operates as intended by the manufacturer and required by the user. The user should select important instrument parameters for testing according to the instrument's intended use [6].

The OQ tests can be modular or holistic. Modular testing of individual components of a system may facilitate interchange of such components without requalification and should be done whenever possible. Having successfully completed OQ testing, the instrument is qualified for use in regulated samples testing [5].

d. Performance qualification:

After the (IQ) and (OQ) have been performed, the instrument's continued suitability for its intended use is proved through performance qualification. It's performed by Set up a test or series of tests to verify an acceptable performance of the instrument for its intended purpose. The PQ tests are performed routinely on a working instrument, not just on a new instrument at installation [5].

The frequency of PQ depends on the ruggedness of the instrument and criticality of the tests performed. Testing may be unscheduled for example, each time the instrument is used. Or it may be scheduled to occur at regular intervals; e.g., weekly, monthly, yearly. Experience with the instrument can influence this decision. Generally, the same PQ tests are repeated each time so that a history of the instrument's performance can be compiled [5].

Timing, Applicability, and Activities for Each Phase of Analytical Instrument Qualification:

Instrument Qualification activities under each phase are usually performed as indicated in the table (1) [5].

Table (1): The timing, applicability, and activities for each phase of AIQ

	Design qualification (DQ)	Installation qualification (IQ)	Operation qualification (OQ)	Performance qualification (PQ)
Timing& Applicability	Prior to purchase of a new type of instrument.	At installation of each instrument (new, old, or existing unqualified).	After installation or major repair of each instrument.	Periodically at specified intervals for each instrument.
Activities	Assurance of vendor's DQ. Assurance of adequate support availability from manufacturer. Instrument's fitness for use in laboratory.	System description. Instrument delivery. Utilities/facility/environment. Network and data storage. Assembly and installation. Installation verification.	Fixed parameters. Secure data storage, backup, and archive. Instrument functions tests.	Preventive maintenance and repairs. SOPs – operation, calibration, and Performance checks.

Classification of laboratory instruments:

There are numerous types of laboratory instrumentation, they are classified to determine the extent of qualification [5].

Based on the level of qualification needed, it is convenient to categorize instruments into three groups:

a. Group (A) Instruments:

Conformance of Group (A) instruments to user requirements is determined by visual observation. It's not used for making measurements or with minimal influence on measurements, no independent qualification process is required. Just ensuring they are correctly used, maintained, and are suitable for the testing and their environment usually suffices [6].

Example instruments in this group include light microscopes, magnetic stirrers, mortars and pestles, nitrogen evaporators, ovens, spatulas, and vortex mixers [5].

b. Group (B) Instruments:

Conformance of Group (B) instruments to user requirements is performed according to the instruments' standard operating procedures. Their conformity assessments are generally unambiguous. Installation of Group B instruments is relatively simple and causes of their failure readily discernable by simple observations [6].

Example instruments in this group include balances, incubators, infrared

spectrometers, melting point apparatus, muffle furnaces, pH meters, pipettes, refractometers, refrigerator-freezers, thermocouples, thermometers, titrators, vacuum ovens, and viscometers [5].

c. Group (C) Instruments:

Conformance of Group (C) instruments to user requirements is highly method specific, and the conformity bounds are determined by their application. Installing these instruments can be a complicated undertaking and may require the assistance of specialists. A full-qualification process should apply to these instruments [6].

Example instruments in this group might include the atomic absorption spectrometers, differential scanning calorimeters, densitometers, diode-array detectors, electron microscopes, elemental analyzers, flame absorption spectrometers, gas chromatographs, and high-pressure liquid chromatographs [5].

Additional Support to equipment qualification:

a. Training:

Training ensures proper instrument operation and that the process for producing quality data is always followed. Training associated with the protocol, the setup and operation, maintenance, cleaning, and laboratory practices are all critical, for both employees and vendors. Records are maintained and only trained personnel are allowed to interact with the instrument [6].

b. Preventative Maintenance:

A strong Preventive Maintenance PM program sets the frequency of maintenance conducted to ensure the equipment does not encounter unnecessary breakdowns or stoppages while sustaining the life expectancy of the instrument. Maintenance intervals are defined, documented, and an integral part of the qualification life cycle [6].

When PQ tests fail to meet specifications, the instrument requires maintenance or repair. For many instruments a periodic preventive maintenance may also be recommended. Relevant PQ tests should be repeated after the needed maintenance or repair to ensure that the instrument remains qualified [5].

Some OQ testing should be performed following equipment maintenance. The testing should be limited to the operational functions that are affected by

the specific maintenance procedure. This usually involves repeating the OQ tests that evaluate the component that has been repaired or replaced. Components that are subject to wear and require routine replacement are best handled with a PM program. The PM intervals should be defined, be documented, and be an integral part of the qualification life cycle. Intervals can be defined or adjusted on the basis of the actual equipment qualification or maintenance history [7].

Preventive maintenance is performed mainly for business reasons because it represents the most cost-effective method of maintaining equipment that requires frequent service [7].

c. Calibration:

Calibration is defined as an operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication [8].

Calibration of an instrument ensures when a setting is selected, it produces an outcome meeting that setting. With-out this data, validity is

questionable. The program for defining frequencies, intervals, document requirements, identification, and operation must be defined [6].

d. Deviations:

Proper training, maintenance, testing, and utilizing templates are ways of preventing deviations, but error does exist. Deviations add to the timeline so it is important to define them properly. Minor typographical errors, wording issues, cut and paste errors, etc. should be separated from those deviations that could truly pose a critical negative impact to the instrument. Ensuring only the latter types of deviations are investigated will save time and resources without affecting the quality of the qualification [6].

e. Auditing:

Auditing the vendors is important. It does not stop there though. The only way to ensure you have a strong qualification program is to perform audits at defined intervals to ensure it is being followed and kept current [6].

Roles and responsibilities in the qualification process:

a. Users:

Users are ultimately responsible for the instrument operations and data quality. Users group includes analysts, their supervisors, and the organizational management. They are should be adequately trained in the instrument's use, and their training records should be maintained as required by the regulations [5].

Users should be responsible for qualifying their instruments. Their training and expertise in the use of instruments make them the best qualified group to design the instrument tests and specifications necessary for successful AIQ. Consultants, validation specialists, and quality assurance personnel can advise and assist as needed, but the final responsibility for qualifying instruments lies with the users. The users must also maintain the instrument in a qualified state by routinely performing PQ [5].

b. Quality Assurance:

The quality assurance QA role in AIQ remains as it is in any other regulated study. QA personnel should understand the instrument qualification process, and they should learn the instrument's application by working with the users [5].

They should review the AIQ process to determine whether it meets regulatory requirements and that the users attest to its scientific validity [5].

c. Manufacturer:

The manufacturer is responsible for DQ when designing the instrument. It is also responsible for validating relevant processes for manufacturing and assembly of the hardware and for validating software associated with the instrument as well as the stand-alone software used in analytical work. The manufacturer should test the assembled instrument prior to shipping to the user [5].

The manufacturer should make available to the users a summary of its validation efforts and also the results of final instrument and software tests. It should provide the critical functional test scripts used to qualify the instrument and software at the user site. For instance, the manufacturer can provide a large database and scripts for functional testing of the network's bandwidth for laboratory information management system LIMS software.

Finally, the manufacturer should notify all known users about hardware or software defects discovered after a product's release, offer user training and installation support, and invite user audits as necessary [5].

Conclusion:

- The purpose of the use of analytical instruments is to generate reliable

data. Instrument qualification helps fulfill this purpose.

- A systematic approach to managing the entire life cycle of laboratory instrumentation, from procurement to decommissioning, is a good business practice for smooth laboratory operation.
- Doing things right the first time will help save time, money, and resources and avoid preventable instrument failures.
- A systematic approach conveys confidence to auditors during laboratory inspections.
- Most important, a systematic approach to make sure an instrument is functioning properly and adequately according to the intended requirements is one of the most important factors in ensuring the quality and reliability of data generated by the instrument.

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