Jordanian Accreditation System
نظام الاعتماد الأردني
Accreditation Unit

ACCREDITATION UNIT

POLICY FOR METHOD VALIDATION IN MEDICAL LABORATORIES

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Purpose

The Accreditation Unit (AU) has set this document to ensure consistency in applying validation-testing procedures as a requirement for accreditation of medical testing laboratories.
In addition, the policy is intended to provide AU assessors a tool for assessing laboratory performance related to the quality of results they generate and reports they issue.

Scope:

This document addresses the following subjects:

- Identification of methods which require validation.
- AU requirements concerning validation data.
- This document provides general guidance to laboratories, accreditation bodies and regulatory authorities on validation steps that laboratories should follow to ensure acceptable performance of testing methods and consequently the quality of results generated.
- Validation of computer software.
- Validation of any other elements involved affecting the testing process
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Authorship

This publication has been written by the Technical Committee, and approved by the Accreditation Director.

Official language

The text may be translated into other languages as required. The English language version remains the definitive version.

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Further information

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This document is also available at our web site where you can check updates directly.

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1. Introduction

Millions of tests, measurements and examinations are made every day in thousands of laboratories around the world. The cost of carrying out these measurements is high and additional costs may arise from decisions made on the basis of the results.

Method validation is an important practice in the field of medical tests, it help to demonstrate that methods used are fit for its purpose. Clause 5.5.1.1 in the international standard ISO 15189:2012 indicates that the laboratory ***shall*** select examination procedures which have been validated for their intended use. In addition, clause 5.5.1.2 indicates Validated examination procedures used without modification ***shall*** be subject to independent verification by the laboratory before being introduced into routine use.

Users of this policy should note that although there are many publications and methods on the validation and verification of different laboratory methods and systems, no one method is universally agreed upon. The recommendations on the specimens/replicates needed to study method characteristics and the definitions of some of the terms used in method validation do vary across references, thus, it is an AU requirement that the definitions and terms used by laboratories should adhere to those used in this policy whenever applicable.

2. Definitions

The definitions used in this document are based on international vocabulary of Metrology (VIM), 3rd Edition : 2012, and other documents listed in the references section:

(2.44 – VIM :2012) Provision of objective evidence that a given item fulfils specified requirements.

NOTES:

1- When applicable, measurement uncertainty should be taken into consideration.

2- The item may be, e.g. a process, measurement procedure, material, compound, or measuring system.

3- The specified requirements may be, e.g. that a manufacturer's specifications are met.

4- Verification should not be confused with calibration.

5- In chemistry, verification of the identity of the entity involved, or of activity, requires a description of the structure or properties of that entity or activity.

Verification:

provision of objective evidence that a given item fulfils specified requirements.

Validation:

verification, where the specified requirements are adequate for an intended use.

3. Responsibility

a- It is the responsibility of AU assessors to evaluate the compliance of the laboratories with this Policy.
b- Laboratory Director are responsible for ensuring compliance with this policy.

4. Policy

4.1 Validation:

The stated purpose of validation is to confirm that a method is fit for its intended use. As a result, the validation shall be as extensive as necessary to meet the need of the given application. Validation must cover all aspects of the method and recruit adequate number of samples as recommended in the published and adopted validation protocol.

The laboratory shall validate examination procedures derived from the following sources:

a) non-standard methods;
b) laboratory designed or developed methods;
c) standard methods used outside their intended scope;
d) validated methods subsequently modified. Modification may include modification of: equipment and software, reagents, diluents and matrix, reference materials and standards, media, control parameters such as time and temperature, test environment, addition or omission of steps, modification in sample handling, changes in calculations etc.

The laboratory shall document the protocol/procedure used for the validation, the raw data and records of the results obtained from validation studies must be kept on file, and a statement as to whether the method is fit for the intended use or not shall be written in the validation report. This data shall be available on request for the Accreditation Body, which has to be checked during a assessment Visit or on request.

Once a method is modified, updated or introduced as a new method within the given scope, it must be validated before it can be considered as being included in the scope of accreditation.

The laboratory director or designee should review the validation protocol, raw data, findings and the conclusion of whether validation is acceptable or not.

An authorized staff should take the responsibility for modification, development and implementation of new or revised methods and under the supervision of the laboratory director.

Assessors must be able to judge whether the applied procedures provide the results needed to ensure the quality of an individual method in view of its field of application and the kind of products tested.

The responsible staff (including those responsible for quality management) shall regularly review the modified, revised or newly developed methods. Procedures and responsibilities linked to the development or revision of validated methods shall be reviewed periodically by the responsible management taking into account the results of internal and external quality control. Records of these review activities must be available to the Accreditation Body.

4.2 Performance characteristics evaluated during method validation

The extent required should be assessed based on sound scientific data and/or rational. The laboratory shall document the rational for omission and inclusion of the specific validation characteristic of the entire spectrum of characteristics. Characteristic to be validated in a quantitative analytical method may include some or all the listed performance parameters; which are applicable:

- Trueness
- Accuracy
- Precision (repeatability & reproducibility)
- Recovery
- Specificity & Selectivity
- Linear and working range
- Limit of detection
- Limit of quantification
- Sensitivity
- Robustness/Rigidness
- Interferences
- Carry over

- Or any other relevant performance characteristic

4.3 Verification:

The intended purpose of verification is to confirm, through obtaining objective evidence that the performance claims for the examination procedure have been met and can thus be put into service for its intended use. The performance claims for the examination procedure confirmed during the verification process shall be those relevant to the intended use of the examination results.

The laboratory shall verify the performance of Validated examination procedures if there is an important change such as a new but similar instrument, relocation of equipment etc.

Commercially available standard methods from reputable manufacturers or those adopted from reputable technical organizations may not need to be validated when used without any changes affecting the test results. Such methods are usually well validated by the manufacturer and were subjected to approval by regulatory bodies such as FDA or CE or Validated procedures implanted from an accredited expert laboratory.

However verification for such methods is needed and on condition that the original protocols are used exactly as described; any change of conditions (eg, reduction or reagent volumes) would invalidate the performance criteria and lead to a need for validation and remains the responsibility of the testing laboratory.

The laboratory should show that the characteristics set by the manufacturer are achieved when the test is performed in the laboratory.

As a minimum, the testing laboratory should provide evidence that key parameters of the method including accuracy, precision, analytical measuring range, limits of detection/quantification, linearity and reference limits are verified. Reportable range should also be defined. Although it is preferred that testing laboratories verify parameters such as specificity and interferences, manufacturer published data may be acceptable.

Data on precision and bias is also needed for the estimation of the method uncertainty.

Validation/verification material used should cover all applicable matrices such as serum, urine, CSF etc.

4.4 In the context of this document, the intended use may be interpreted as below:

- A method intended to demonstrate absence of a given measurand/analyte should be validated for LOD (Limit of Detection) and does not require studies such as linearity.

- Under optimal conditions, such as in cases of introduction of a new laboratory method, validation should be designed and performed prospectively (prior to introduction of the method for use to provide client with test results).
  It should be emphasized that validation prior to use of the method is recommended as the first step however, one should repeat this validation as an on-going activity periodically as defined in laboratory policies to confirm the link between the ongoing performance of the laboratory and the initial validation results.

4.5 Non-validated method that has been used in the past should be subjected to validation. This validation should be based on past relevant data, provided the data is judged to be scientifically valid, relevant and all method changes throughout the period from which the data has been derived from are fully traceable. Regardless of the type of validation, a protocol and associated approved report are obligatory.

4.6 With regards to number of repeated testing (independent replicates) required for the study of validation characteristic, The laboratory must decide on this, on the basis of their experience and performance requirements; it is the duty of the laboratory to provide evidence that the tests provided are reliable, and that the performance claims are correct.

4.7 Instead of a validation study, AU shall accept scientific data generated by a laboratory during the routine conduct of statistical quality control tests (control charts data) and other laboratory Control Testing Program data. Such data, when presented in an un-ambiguous and comprehensive manner and addresses validation parameters of interest, shall be considered as satisfying AU validation requirement provided that the Test Method is identical to the procedure which otherwise would be required to be validated. Laboratories engaged in planning these activities should consider validation issues so as to avoid redundant work. This should not be applied in routine testing and may be applied in specific circumstances where obtaining validation samples is extremely difficult.

4.8 The laboratory shall document and follow their validation and verification procedures. As a minimum, re-verification is required when:

- The results of the validation do not conform to its pre-determined acceptance criteria.
- Once changes are made to validated non-standard methods.
- Upon testing site change, including equipment, or a major environmental change.
- Methods, which are not used on a routine basis, including standard methods.
- Key parameters such as linearity, limit of detection etc. should be verified every six months.
- Introducing of new lot/batch of a reference standard

4.9 In order to assure that a validated method remains in a controlled state, the laboratory shall implement periodic re-verification plan or observe and control the method in an “ongoing" fashion by the usage of appropriate techniques.

4.10 For method associated with software validation; ISO15189:2012 .AU requires that computer software, developed by the user & used in the performance of a laboratory method subject to validation, must be sufficiently documented so as to provide evidence that it is suitably validated as being adequate for use for its intended purpose.

AU shall consider commercial off the shelf software in general use within their designed application range to be sufficiently validated however verification is still needed. When interfacing laboratory instruments to information system, the laboratory must validate the data transfer process and ensure accurate transfer of results.

Whether or not a method by itself is required to be validated, laboratory software re-configuration and modification should be validated.

4.11 Laboratories engaged in a validation study should use well-characterized Standard Reference Material, which are maintained and used in accordance with written instructions. The material should be traceable to a national or internationally recognized Reference Material or non-certified with known target values when available or Reference Standard (as per ISO Guide 34) with a certificate of analysis (CoA).

4.12 Validation may be contracted out, provided it is followed by verification by the laboratory to ensure that the methods fit their intended use on site.

4.13 Verification cannot be contracted out –it must be conducted on site, under the responsibility of the laboratory, which intends to run the test under routine use and by the personnel intended to run the test method routinely. The lab shall use the same equipment, the same materials and in the same environmental conditions

4.14 The test method subject to the validation study shall be documented and approved. The method shall not be changed throughout the validation study or after otherwise the method considered void and will require revalidation / revivification , however such changes should be documented.

4.15 Validation should be designed as planned. A detailed validation protocol should include the acceptance criteria for approval by the laboratories' authorized personnel.

4.16 Personnel engaged in the validation procedures should undergo a thorough training. Such training should be documented.

4.17 The validation report should include individual test results in addition to other numerical expressions as needed.

4.18 All raw data should be secured and should include all of the results, including those out of acceptable limits.

4.19 Validation report and related raw data shall be kept by the lab and be readily available for assessment purposes as long as the test method is used in the lab and 5 years after its withdraw from use.

5. References :

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6. Harmonized guidelines for single Laboratory validation of methods of analysis. (IUPAC Technical Report), 2002, Pure Appl. Chem, Vol:74, No 5, pp:835-855.
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10. NATA Technical Note 17 - Guidelines for the validation and verification of quantitative and qualitative test methods, 2013.
11. European Medicines Agency, Guideline on bioanalytical method validation, 2011.