METHOD VALIDATION

# Eurachem guidance on validating analytical methods

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## Abstract

Eurachem is a network of organisations within Europe that focuses on promoting the reliability of measurement results in analytical sciences and fostering good laboratory practices. To this aim, Eurachem brings together expert working groups to identify needs, pool expertise and propose authoritative guidance in the form of short information leaflets and guides. It also organises workshops to promote the exchange of experience and views among the analytical community. The validation of test methods is a key issue in ensuring the quality of analytical results, and as such is specifically addressed in standards underpinning the requirements for testing and calibration laboratories. Recently, Eurachem released a second edition of its Guide on method validation, devised to help laboratories demonstrating the fitness-for-purpose of test methods, taking into account developments in terminology, standards and analytical practice. This paper summarises this Guide and the work of Eurachem.

## Keywords

- Analyses
- Eurachem
- Guidance
- Methods
- Validation

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# METHOD VALIDATION

## Introduction

Eurachem (www.eurachem.org) is a network of organisations within Europe designed to (i) establish a system for the international traceability of chemical measurements and (ii) promote good quality practices in analytical sciences. Currently represented in 32 European countries, Eurachem aims to provide a forum for analytical scientists, laboratory staff and those interested in using the results of analytical measurements, to discuss common problems and develop informed and considered approaches to both technical and policy issues. Eurachem members and stakeholders meet once a year at the Eurachem General Assembly. An Executive Committee and several topical Working Groups continue pursue the organisation's stated goals throughout the year, often in cooperation with other organisations. Participation is open and channelled through the national representatives. Eurachem's main production is the development of new guidance documents, promoted through dedicated events which are also designed to provide opportunities to collect feedback. Beside the Guides, Eurachem develops information leaflets, short briefing documents on specific topics usually intended to inform a wide audience, including laboratory staff, managers and laboratory customers.

## The revised Eurachem guide on method validation

Laboratory staff is well aware of the importance of validating test methods in order to demonstrate that the test results are fit for their intended use. However, what exactly should be done, why and when, is not always clear. A Eurachem Guide on method validation was first issued in 1998 and has since proven very popular. Over the years, and following the introduction of formal requirements on the competence of testing and calibration laboratories [ISO/IEC 17025, 2005], a growing body of experience has developed, leading to several changes in terminology, working practices, reference documents and requirements. Acknowledging these changes, Eurachem set up a working group on method validation to thoroughly revise the Guide [Eurachem, 2014]. This second edition accommodates the main changes in international standards and working practices, and includes notes on certain aspects of validation that are specific to qualitative test methods. While a number of field-specific guides exist, and even legal requirements on how to perform a validation study in certain areas, the Guide aims to provide a more general approach to method validation. This approach therefore supports the view expressed in ISO/IEC 17025, *i.e.* that the same requirements on competence apply to all types of testing and calibration laboratories. To this aim, the Guide includes both elements of the rationale behind validation and practical details on how to plan, perform, evaluate and make the most of such studies in the laboratories. Last, but not least, the Guide includes a substantial bibliography, listing over 80 useful sources of information. To further support method validation, the Working Group provides input for the Eurachem "Reading list", an annually updated bibliography of documents relating to several quality aspects of tests and measurements, available from the Eurachem website.

## The concept of method validation

In ISO/IEC 17025, validation is defined as "confirmation, by examination and provision of objective evidence, that the particular requirements for a specific intended use have been fulfilled". From this statement, the method validation process can be designed as a sequence of steps, starting from the definition of the particular requirements for the intended use of the test result. This is the basis upon which performance requirements for specific characteristics

# METHOD VALIDATION

of the method—such as selectivity, limit of detection and limit of quantification, working range, analytical sensitivity, trueness, precision, measurement uncertainty and ruggedness—can be set. To provide evidence that these requirements are fulfilled, the laboratory shall plan and perform a series of experiments to determine the values of these characteristics and compare them with the stated requirements. The successful outcome of such a comparison provides a statement of "fitness for purpose" for the method under scrutiny. A wealth of information is produced during a validation study. It is essential that this is properly recorded and reported to best support the fitness-for-purpose statement. Furthermore, the validation study is the best source of information on which to base the ongoing monitoring of the method's performance in routine use, thus supporting continuous adequate performance and suitable quality of the analytical results reported to customers.

## Setting requirements

The purpose of method validation is to demonstrate that the test results are fit for their intended use. The first step in the process therefore entails clearly stating the analytical requirements needed to achieve this goal. The analyst has the task of translating the customer's stated or implied needs into analytical requirements. For example, if the customer's request is to determine the cadmium content in chocolate so as to state compliance with existing legal limits, it is the analyst's responsibility to assess the maximum allowable measurement uncertainty that can be associated with the measurement results and other related analytical requirements. When no other guidance exists, analysts may base their judgement on available data concerning the capabilities of the technique being used and the results of proficiency tests or other inter-laboratory studies on similar test items. Authoritative guidance on how to set requirements on target measurement uncertainty in any analytical field where this is not set by legislation or the customer is provided in another Eurachem document [Eurachem, 2015] and includes a discussion on the setting of target uncertainty for process development in addition to applied or fundamental research. Once analytical requirements have been set, the analyst can consider whether any current method can satisfy them, whether any substantial modification is needed or whether a completely new procedure has to be developed. These choices will then affect the extent of validation required.

## Practical aspects of assessing method performance

The extent of validation work varies depending on the scope of the method (broad, narrow), the analytical application (qualitative, quantitative, trace or major level etc.) and measurement quality requirements such as target uncertainty. The availability of information on method performance is also a driving force in defining the extent of the experiment plan. A limited number of tests are required, for example, when introducing into a laboratory a new standard method for which performance data have already been published. In this case, the tests are designed to show that the laboratory achieves the stated precision and to check bias over the method's working range. In general, however, it is necessary to investigate several more characteristics of a test method. The limit of quantification, precision and bias (a measure of trueness) will almost always be required. The Guide provides the reader with the key definitions and rationale behind determining the various characteristics, and includes "quick reference tables" to help put this knowledge to work. Each quick reference table suggests simple experiments and provides the necessary statistical calculations for evaluating and reporting each performance characteristic. Particular attention is given to revisiting the definition and calculations to be ap-

plied to determine the limit of detection and limit of quantification. The concept and evaluation of measurement uncertainty is treated only briefly in this Guide, since Eurachem has provided comprehensive guidance on this subject elsewhere [Eurachem, 2012].

## Follow-up of method validation

No matter how well the validation study is performed, important information may be lost, misused or disregarded if not recorded properly and in a way that identifies the key parameters to be kept under control when performing the test. To this aim, the Eurachem Guide includes recommendations on what and how data should be reported, along with a template for the documentation of validated methods.

Special attention is given to the use of performance data to plan internal quality controls (IQC). With reference to the Nordtest Guide on IQC [Hovind *et al.*, 2011], the method's performance can be monitored through the regular analysis of control samples, and the outcome recorded in control charts. Typically, the control value (a result obtained with a control sample) or the differences between replicates are recorded (X-charts or R- and r% charts). In both cases, the performance data on the method's precision (intermediate precision or repeatability) will form the most reliable basis for setting up the warning and action limits of the respective charts. The Eurachem Guide on method validation helps analysts make the best use of these data.

## Conclusion

Nowadays, there are various guidance documents that address the validation of test methods in specific sectors. Eurachem has revised its own Guide to address changes in terminology, requirements and current practice. The Guide is intended to provide analytical laboratories with general and practical guidance on how to plan, perform and record validation studies. It also addresses the use of these data for the ongoing monitoring of method performance in routine use. The Guide is freely available from the Eurachem website.

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