INTERNATIONAL STANDARD

ISO 15198

First edition
2004-07-15

Clinical laboratory medicine — *In vitro* diagnostic medical devices — Validation of user quality control procedures by the manufacturer

Laboratoires d'analyses de biologie médicale — Dispositifs médicaux de diagnostic in vitro — Validation des recommandations du fabricant pour la maîtrise de la qualité par l'utilisateur

Reference number
ISO 15198:2004(E)

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 15198 was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and* in vitro *diagnostic test systems.*

Introduction

Manufacturers of IVD medical devices often include quality control (QC) procedures in their instructions for use. These quality control procedures are intended to provide users with assurance that the device is performing within specifications, and therefore the results are suitable for their intended diagnostic use. For some devices, QC procedures can be an essential risk control measure. Depending on the design of the device, these quality control procedures can help users ensure the quality of results by:

a) verifying the suitability of analytical systems (sample, reagents, instruments, and/or users);

b) monitoring the precision and trueness of measurement results;

c) preventing false-negative and false-positive results;

d) identifying fault conditions that could lead to inaccurate results; and/or

e) troubleshooting problems that require corrective action.

In addition, manufacturers often design IVD medical devices with the ability to detect potential failures and alert users to take corrective action. Such internal control systems could potentially reduce or even eliminate the need for users to run quality control samples to monitor the performance of the device.

This International Standard is written for manufacturers of *in vitro* diagnostic (IVD) medical devices as part of their design control and risk management programs. It will also enable manufacturers to provide validated quality control procedures for users in clinical diagnostic laboratories.

This International Standard describes how manufacturers can validate quality control procedures for their devices. Validation ensures that quality control procedures will perform as intended by the manufacturers and that manufacturers' recommendations fit the needs of particular devices, such as discrete systems, products with built-in electronic controls, and products with “on board” chemical and/or biological controls. Information about the validated quality control procedures increases user's understanding of devices' overall quality assurance requirements so that informed choices regarding suitable control procedures can be made.

Although laboratory directors have the ultimate responsibility for determining appropriate quality control procedures for their laboratories, manufacturers of IVD medical devices are responsible for providing adequate information to users about performance of devices as well as a means to control risks and to verify performance within specifications. Thus, in practice, quality control is a shared responsibility of IVD medical device manufacturers and users.

No single quality control procedure can cover all IVD medical devices, neither now, nor in the future, since the devices may differ fundamentally in design, technology, function and intended use. Quality control practices that developed over the years have provided laboratories with some degree of assurance that results are valid. Although widely accepted by laboratories, government agencies and accrediting organizations, these practices originated when laboratory analyses were performed manually and laboratories prepared their own reagents. They may not always be optimal for current IVD medical devices. Therefore, when quality control procedures are required, the manufacturer has the responsibility to design and validate quality control procedures appropriate for the device.

Quality system standards for medical device manufacturers have also evolved over time. Design control and risk management requirements, for example, are included in ISO 13485:2003 as well as in most contemporary regulatory schemes. Design controls require a risk analysis of the design, and, prior to introduction to the marketplace, require that the design be validated with respect to user requirements and intended use. Quality control procedures in the instructions for use should be viewed as an integral part of the design of an IVD medical device; and thus are subject to design validation requirements.

Clinical laboratory medicine — *In vitro* diagnostic medical devices — Validation of user quality control procedures by the manufacturer

1 Scope

This International Standard describes a process for manufacturers of *in vitro* diagnostic medical devices to validate quality control procedures they recommend to their users. These quality control procedures are intended to provide users with assurance that device performance is consistent with its intended use and the manufacturers' claims. This International Standard applies to all *in vitro* diagnostic medical devices.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 3534-1, *Statistics — Vocabulary and symbols — Part 1: Probability and general statistical terms*

ISO 5725-1, *Accuracy (trueness and precision) of measurement methods and results — Part 1: General principles and definitions*

ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

ISO 14971, *Medical devices — Application of risk management to medical devices*

International vocabulary of basic and general terms in metrology (VIM). BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML, 2nd ed.

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 3534-1, ISO 5725-1, ISO 13485, ISO 14971, the VIM and the following apply. For the convenience of the user, some of the terms and definitions have been reproduced below.

3.1
accuracy
closeness of agreement between a test result and the accepted reference value

[ISO 3534-1]

NOTE The term accuracy, when applied to a set of test results, involves a combination of random error components and a common systematic error or **bias** (3.2) component. See the VIM.

3.2
bias
difference between the expectation of the test results and an accepted reference value

[ISO 5725-1]

3.3
commutability of a material
ability of a material to yield the same numerical relationships between results of measurements by a given set of measurement procedures, purporting to measure the same quantity, as those between the expectations of the relationship obtained when the same procedures are applied to other relevant types of materials

[ISO 15194]

3.4
control material
substance, material or article used to verify the performance characteristics of an *in vitro* diagnostic medical device

[EN 375]

3.5
control procedure
activities at the point of use to monitor the performance of an IVD medical device

NOTE 1 In the IVD medical device industry and in many laboratories that use IVD medical devices, these activities are commonly referred to as quality control.

NOTE 2 Quality control may monitor all or part of the measurement procedure, from the collection of samples to reporting the result of the measurement.

3.6
examination
set of operations having the object of determining the value of a property

NOTE In the IVD medical device industry and in many laboratories that use IVD medical devices, examination of an analyte in a biological sample is commonly referred to as a test, assay or analysis.

3.7
examination procedure
set of operations, described specifically, used in the performance of examinations according to a given method

NOTE In the IVD medical device industry and in many laboratories that use IVD medical devices, an examination procedure for an analyte in a biological sample is commonly referred to as an analytical method, analytical procedure or test procedure.

3.8
information supplied by the manufacturer with the medical device
all written, printed, or graphic matter on a medical device or any of its containers or wrappers, or accompanying a medical device, relating to the identification, technical description and use of the medical device, but excluding shipping documentation and promotional material

NOTE 1 Adapted from EN 1041.

NOTE 2 In some countries, information supplied by the manufacturer is called “labelling”.

3.9
instructions for use
information supplied by the manufacturer with an *in vitro* diagnostic medical device concerning the safe and proper use of the reagent or the safe and correct operation, maintenance and basic troubleshooting of the instrument

NOTE Adapted from EN 375 and EN 591.