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**Clinical laboratory testing and in vitro  
medical devices — Requirements for  
in vitro monitoring systems for self-  
testing of oral anticoagulant therapy**

*Laboratoires d'analyses de biologie médicale et dispositifs  
médicaux de diagnostic in vitro — Exigences relatives aux systèmes  
d'autosurveillance des traitements par anti-coagulant oraux*



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## 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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see [www.iso.org/directives](http://www.iso.org/directives)).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see [www.iso.org/patents](http://www.iso.org/patents)).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see [www.iso.org/iso/foreword.html](http://www.iso.org/iso/foreword.html).

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

This second edition cancels and replaces the first edition (ISO 17593:2007), which has been technically revised.

The main changes are as follows:

- Updated with more current state of the art information that has evolved over several years.
- [Subclause 8.4](#) Validation of measurement precision: added a more robust study design.
- [Subclause 8.5.8.2](#) and [8.5.8.3](#): updated examples were added to reflect changes in criteria.
- [Subclause 8.6](#) Minimum acceptable system accuracy : Updated requirements/performance criteria.
- [Clause 9](#) Lay person performance evaluation: added clarity, revised performance criteria and increased sample size.
- Removed Annex F listing of publications.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at [www.iso.org/members.html](http://www.iso.org/members.html).

## Introduction

Oral-anticoagulation monitoring systems are in vitro diagnostic (IVD) medical devices that measure prothrombin time in fresh, untreated human blood specimens. Prothrombin time is an indicator of the ability of blood to clot. IVD medical devices for self-testing of oral-anticoagulation therapy are used predominantly by individuals who have heart valve replacements, or who are suffering from atrial fibrillation or deep vein thrombosis and are receiving oral anticoagulant therapy with vitamin K antagonist medicines (e.g. warfarin). Patients must maintain the level of anticoagulant in the blood high enough to reduce thrombin formation, yet low enough to avoid excessive bleeding. An oral-anticoagulation monitoring system allows the user to monitor anticoagulation therapy and take action to control the level of anticoagulant present in the blood. This document applies to oral-anticoagulation monitoring systems to be used by lay persons. The primary objectives are to establish requirements for oral-anticoagulation monitoring systems that will enable lay persons to achieve acceptable performance, and to specify procedures for manufacturers and other interested parties to demonstrate conformance of such systems to the requirements stated in this document.

Performance criteria for oral-anticoagulation monitoring systems were established, based on the state-of-the-art, which has been shown to offer significant benefit to patients [31]. The criteria are given in terms of “system accuracy”, because metrological terms commonly used in International Standards (e.g. trueness and measurement uncertainty) would not be familiar to lay persons. System accuracy, which is affected by systematic bias and random effects (and is inversely related to measurement uncertainty), describes the degree to which the individual results produced by an oral-anticoagulation monitoring system agree with correct international normalized ratio (INR) values when the system is used as intended by lay persons. In setting the performance criteria, it is assumed that users will be properly selected and will receive the necessary training and that operating and control procedures will be followed in accordance with the manufacturer’s instructions for use. It is also assumed that manufacturers will anticipate and mitigate the effects of reasonably foreseeable misuse, including reasonably foreseeable deviations from recommended operating and control procedures by the intended users.

Requirements that are unique to self-testing with oral anticoagulation monitoring systems, including specific content of information supplied by the manufacturer, are addressed in this document. General requirements that apply to all IVD medical devices and which are covered by other standards (e.g. IEC 61010-1, IEC 61010-2-101, ISO 13485, ISO 14971, ISO 23640 and ISO 18113-1, ISO 18113-4, ISO 18113-5) are incorporated by reference, when appropriate. While the goal is to standardize these requirements, it is also recognized that current national and regional usage by patients and regulatory authorities should be taken into consideration.

# Clinical laboratory testing and in vitro medical devices — Requirements for in vitro monitoring systems for self-testing of oral anticoagulant therapy

## 1 Scope

This document specifies requirements for in vitro measuring systems for self-monitoring of vitamin-K antagonist oral anticoagulation therapy, including performance, quality assurance and user training and procedures for the validation of performance by the intended users under actual and simulated conditions of use.

This document applies solely to prothrombin time measuring systems used by lay persons for monitoring their own vitamin-K antagonist oral anticoagulation therapy, and which report results as international normalized ratios (INR).

This document is applicable to manufacturers of such systems and those other organizations (e.g. regulatory authorities and conformity assessment bodies) having the responsibility for assessing the performance of these systems.

This document is not applicable to:

- in vitro measuring systems for coagulation quantities assessing vitamin-K antagonist oral anticoagulation therapy used by physicians or healthcare providers;
- non-vitamin-K antagonist oral anticoagulation therapy (e.g. dabigatran);
- a comprehensive evaluation of all possible factors that can affect the performance of these systems;
- the medical aspects of oral-anticoagulation therapy.

## 2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

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

ISO 15198, *Clinical laboratory medicine — In vitro diagnostic medical devices — Validation of user quality control procedures by the manufacturer*

ISO 17511, *In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples*

ISO 18113-1, *Clinical laboratory testing and in vitro diagnostic medical systems — Information supplied by the manufacturer (labelling) — Part 1: Terms, definitions and general requirements*

ISO 18113-4, *Clinical laboratory testing and in vitro diagnostic medical systems — Information supplied by the manufacturer (labelling) — Part 4: In vitro diagnostic reagents for self-testing*

ISO 18113-5, *Clinical laboratory testing and in vitro diagnostic medical systems — Information supplied by the manufacturer (labelling) — Part 5: In vitro diagnostic instruments for self-testing*