

**In vitro diagnostik – Krav avseende självtestning
vid peroral trombosförebyggande behandling
(ISO 17593:2007, IDT)**

**Clinical laboratory testing and in vitro medical
devices – Requirements for in vitro monitoring
systems for self-testing of oral anticoagulant
therapy (ISO 17593:2007, IDT)**

Den internationella standarden ISO 17593:2007 gäller som svensk standard. Detta dokument innehåller den officiella engelska versionen av ISO 17593:2007.

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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.

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 17593 was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems*.

Introduction

Oral-anticoagulation monitoring systems are *in vitro* diagnostic medical devices that measure prothrombin time in fresh, unmodified human blood samples. Prothrombin time is an indicator of the ability of blood to clot. *In vitro* diagnostic 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. 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 International Standard 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 users to achieve acceptable performance, and to specify procedures for manufacturers and other interested parties to demonstrate conformance of such systems to this standard.

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 [68], [69]. 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 users. 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 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, that the device will be properly maintained, 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 maintenance, 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 International Standard. General requirements that apply to all *in vitro* diagnostic medical devices and are covered by other standards (e.g., IEC 61010, ISO 13485, ISO 14971 and ISO 18113) are incorporated by reference, where appropriate. In addition, national regulations may apply.

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

1 Scope

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

This International Standard pertains solely to prothrombin time measuring systems used by individuals for monitoring their own vitamin-K antagonist therapy, and which report results as international normalized ratios (INR).

This International Standard 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 International Standard does not

- pertain to *in vitro* measuring systems for coagulation quantities assessing vitamin-K antagonist therapy used by physicians or healthcare providers,
- provide a comprehensive evaluation of all possible factors that could affect the performance of these systems, or
- address the medical aspects of oral-anticoagulation therapy.

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 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 — Measurement of quantities in biological samples — Metrological traceability of values assigned to calibrators and control materials*

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ISO 18113-1:—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:—¹⁾, *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:—¹⁾, *Clinical laboratory testing and in vitro diagnostic medical systems — Information supplied by the manufacturer (labelling) — Part 5: In vitro diagnostic instruments for self-testing*

IEC 60068-2-64:1993, *Environmental testing — Part 2: Test methods — Test Fh: Vibration, broad-band random (digital control) and guidance*

IEC 61010-1:2001, *Safety requirements for electrical equipment for measurement, control and laboratory use — Part 1: General requirements*

IEC 61010-2-101:2002, *Safety requirements for electrical equipment for measurement, control and laboratory use — Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment*

IEC 61000-4-2, *Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test*

IEC 61000-4-3, *Electromagnetic compatibility (EMC) — Part 4-3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test*

IEC 61326, *Electrical equipment for measurement, control and laboratory use — EMC requirements*

EN 13532:2002, *General requirements for in vitro diagnostic medical devices for self-testing*

EN 13612, *Performance evaluation of in vitro diagnostic medical devices*

EN 13640, *Stability testing of in vitro diagnostic reagents*

WHO Technical Report Series, No. 889, 1999, *Annex 3 — Guidelines for thromboplastins and plasma used to control oral-anticoagulant therapy*

3 Terms and definitions

For the purposes of this document, the terms and definitions in ISO 18113-1 and the following apply.

3.1

accuracy of measurement

closeness of agreement between a measurement result and the accepted reference value

NOTE 1 The term “measurement accuracy”, when applied to a set of test results, involves a combination of random components and a common systematic error or bias component. (VIM:1993)

NOTE 2 For oral-anticoagulation monitoring systems, accuracy is measured by the extent to which measurements of blood samples from different patients agree with INR values traceable to a thromboplastin International Reference Preparation (IRP).

NOTE 3 Adapted from ISO 3534-1:2006, 3.11.

1) To be published.

3.2

bias of measurement

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

[ISO 5725-1:1994, 3.8]

NOTE Bias is a measure of trueness. [VIM:1993]

3.3

blood

circulating intravascular tissue of the body, consisting of suspended formed elements and fluid plasma and suspended formed elements

NOTE In this International Standard, the term refers to fresh, nonanticoagulated blood.

3.4

capillary blood sample

blood collected after puncturing minute vessels that connect the arterioles and venules

NOTE Often obtained by pricking a fingertip; capillary blood is usually collected without additives, such as anticoagulants or preservatives. Therefore, it is inherently unstable.

3.5

control material

substance, material or article intended by the manufacturer to be used to verify the performance characteristics of an *in vitro* diagnostic medical device

NOTE 1 Adapted from EN 375:2001, 3.5.

NOTE 2 Control materials for anticoagulation monitoring may be reactive or nonreactive. A reactive control material participates in a reaction with the reagent components. A nonreactive control does not react with the reagent components, but may provide control functionality through other means, e.g., a simulation of the reaction (see physical control).

3.6

control interval

statistically justified values specified as acceptable measured values obtained using a given control material

3.7

healthcare provider

individual authorized to deliver health care to a patient

NOTE In this International Standard, a healthcare provider is an individual, such as a doctor, nurse, technician, technical specialist or appropriate assistant, that provides instruction to a self-testing patient.

3.8

integrated functional control

control material that is inherent in a reagent component of a measuring system, intended by the manufacturer to verify the performance of the measuring system

NOTE The integrated functional control is run concurrently with a patient measurement, includes a reactive component and provides a functional check of the measurement procedure. The integrated control results must be within a predefined measurement interval for the measured value to be displayed.

3.9

international normalized ratio

INR

patient's prothrombin time measurement result, which has been standardized for the potency of the thromboplastin used in the measurement procedure and expressed relative to a normal population average

NOTE For a discussion of the use of INR, see Poller, et al. [30].

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3.10 international reference preparation IRP

reference calibrator maintained by the World Health Organization

NOTE The IRP for thromboplastin is directly calibrated for potency against the original British comparative thromboplastin preparations used in the establishment of the INR system.

3.11 intermediate precision of measurement

measurement precision under conditions intermediate between reproducibility conditions and repeatability conditions

NOTE 1 The concept of intermediate levels of precision is described in ISO 5725-3:1994^[5].

NOTE 2 Quantitative measures of intermediate precision depend on the stipulated conditions.

NOTE 3 Intermediate precision provides an indication of the variability that will be experienced by a user during typical use.

3.12 intermediate precision conditions

conditions where independent measurement results are obtained with the same measurement method on identical samples in the same location, but where other variables, such as operators, equipment, calibration, environmental conditions and/or time intervals, differ

3.13 international sensitivity index ISI

factor that allows the conversion of a patient's prothrombin time measurement result to international normalized ratio values

NOTE For a discussion of the use of ISI and INR, see Poller, et al. ^[30].

3.14 lay person

individual without formal training in a relevant field or discipline

NOTE 1 Adapted from the definition of "lay user" in EN 376:2002.

NOTE 2 For the purposes of this International Standard, a lay person is a user of an oral-anticoagulation monitoring device who does not have specific medical, scientific or technical knowledge related to oral-anticoagulation monitoring.

3.15 manufacturer's working calibrator

working measurement standard
standard that is used routinely at the manufacturer's laboratory to calibrate or check material measures, measuring instruments or reference materials

NOTE 1 Adapted from ISO 17511:2003.

NOTE 2 This applies to a thromboplastin preparation used by the manufacturer during the preparation of a PT reagent mixture.

NOTE 3 The assigned value of the manufacturer's working calibrator is metrologically traceable to that of the IRP.

3.16 manufacturer's selected measurement procedure

measurement procedure that is calibrated by one or more primary or secondary calibrators and validated for its intended use

NOTE ISO 17511:2003, 4.2.2 f), shows the manufacturer's selected measurement procedure in the traceability chain.

3.17

manufacturer's standing measurement procedure

measurement procedure that is calibrated by one or more of the manufacturer's working calibrators or higher types of calibrator and validated for its intended use

NOTE ISO 17511:2003, 4.2.2 h) shows the manufacturer's standing measurement procedure in the traceability chain.

3.18

measurement procedure

set of operations, described specifically, used in the performance of particular measurements according to a given method

[VIM:1993, 2.5]

3.19

measuring interval

set of values of measurands for which the bias and imprecision are intended to lie within specified limits

NOTE 1 This represents the interval of examination results over which the performance characteristics have been validated by the manufacturer.

NOTE 2 Adapted from VIM:1993, 5.4.

3.20

metrological traceability

property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties

[VIM:1993, 6.10]

3.21

physical control system

control device that does not include chemically reactive components and that is intended by the manufacturer to verify the performance of the instrument

NOTE 1 The physical control system may be in the form of an electronic device that provides a simulated reaction.

NOTE 2 The physical control result must be within predefined limits, in order for the measuring system to be considered properly functional.

3.22

precision of measurement

closeness of agreement between independent measurement results obtained under stipulated conditions

NOTE 1 Adapted from ISO 3534-2:2006.

NOTE 2 The degree of precision is expressed numerically by the statistical measures of imprecision of measurements, such as standard deviation and coefficient of variation, that are inversely related to precision. Quantitative measures of precision depend on the stipulated conditions.

NOTE 3 Precision of a given measurement procedure is subdivided according to the specified precision conditions. Particular sets of extreme conditions are termed "repeatability" (3.26) and "reproducibility" (3.28).

3.23

prothrombin time

PT

time required to clot a blood sample once exposed to a thromboplastin reagent material