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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.

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*

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.

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1)   To be published.