INTERNATIONAL STANDARD

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In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) —

Part 2: *In vitro* diagnostic reagents for professional use

Dispositifs médicaux de diagnostic in vitro — Informations fournies par le fabricant (étiquetage) —

Partie 2: Réactifs de diagnostic in vitro à usage professionnel

Reference number
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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 18113-2 was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and* in vitro *diagnostic test systems*.

ISO 18113 consists of the following parts, under the general title In vitro *diagnostic medical devices — Information supplied by the manufacturer (labelling)*:

— *Part 1: Terms, definitions and general requirements*

— *Part 2:* In vitro *diagnostic reagents for professional use*

— *Part 3*: In vitro *diagnostic instruments for professional use*

— *Part 4:* In vitro *diagnostic reagents for self-testing*

— *Part 5:* In vitro *diagnostic instruments for self-testing*

Introduction

Manufacturers of *in vitro* diagnostic (IVD) reagents for professional use supply users with information to enable their safe use and the expected performance of their devices. The type and level of detail varies according to the intended uses and country-specific regulations.

The Global Harmonization Task Force (GHTF) encourages convergence of the evolution of regulatory systems for medical devices at the global level. Eliminating differences among regulatory jurisdictions could allow patients earlier access to new technologies and treatments. See Reference [9]. This part of ISO 18113 provides a basis for harmonization of labelling requirements for IVD reagents for professional use.

This part of ISO 18113 is concerned solely with information supplied with IVD reagents, calibrators and control materials intended for professional use. It is intended to be used in conjunction with ISO 18113-1, which contains the general requirements for information supplied by the manufacturer and definitions of general labelling concepts.

This part of ISO 18113 is based on EN 375:2001[5]. The text has been modified to conform to Part 2 of the ISO/IEC Directives[4], but the requirements, including those in ISO 18113-1, are substantially equivalent to the original European harmonized standard. This part of ISO 18113 is intended to support the essential labelling requirements of all the GHTF partners, as well as other countries that have or plan to enact labelling regulations for IVD medical devices.

For IVD reagents, calibrators and/or control materials that are intended to be used as a system with an instrument provided by the same manufacturer, this part of ISO 18113 is also intended to be used together with ISO 18113-1 and ISO 18113-3[2].

In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) —

Part 2: *In vitro* diagnostic reagents for professional use

1 Scope

This part of ISO 18113 specifies requirements for information supplied by the manufacturer of IVD reagents for professional use.

This part of ISO 18113 also applies to information supplied by the manufacturer with calibrators and control materials intended for use with IVD medical devices for professional use.

This part of ISO 18113 can also be applied to accessories.

This part of ISO 18113 applies to the labels for outer and immediate containers and to the instructions for use.

This part of ISO 18113 does not apply to

a) IVD instruments or equipment,

b) IVD reagents for self-testing.

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 8601, *Data elements and interchange formats — Information interchange — Representation of dates and times*

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

ISO 15223-1, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*

ISO 18113-1:—, In vitro *diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 1: Terms, definitions and general requirements*

EN 980, *Symbols for use in the labelling of medical devices*

3 Terms and definitions

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

4 General

4.1 Essential requirements

The requirements of ISO 18113-1 apply.

For the use of symbols, the requirements of ISO 15223-1 and EN 980 apply.

4.2 Identification of kit components

In the case of a kit, each component shall be identified by name, letter, number, symbol, colour or graphics in the same manner on all labels and in the instructions for use.

5 Content of the outer container label

5.1 Manufacturer

The name and address of the manufacturer shall be given.

NOTE In the European Union, the name and address of the manufacturer's "EC Authorized Representative" is required on the outer container label or in the instructions for use, if the legal manufacturer is not located within the EU. See Reference [8].

5.2 Identification of the IVD reagent

5.2.1 IVD reagent name

The name of the IVD reagent shall be given.

When the name does not uniquely identify the IVD reagent, an additional means of identification shall also be given.

EXAMPLES Catalogue number, commodity number.

5.2.2 Batch code

A batch code shall be given.

If a kit contains different components bearing different batch codes, the batch code indicated on the outer container shall enable the individual batch code of each component to be traced from the manufacturer's production record.

5.3 Contents

The mass, volume, volume after reconstitution and/or the number of examinations shall be indicated.

5.4 Intended use

If the intended use is not indicated by the name of the IVD reagent, then an abbreviated intended use statement shall be given or included in the instructions for use.

EXAMPLE For measurement of plasma glucose concentration.

5.5 *In vitro* diagnostic use

The *in vitro* diagnostic use of the reagent shall be indicated.

EXAMPLES "For *in vitro* diagnostic use" or graphical symbol: "*in vitro* diagnostic medical device".

5.6 Storage and handling conditions

The storage conditions necessary to maintain the stability of the reagents, calibrators and control materials in the unopened state shall be indicated.

EXAMPLE 1 2 °C to 8 °C or 2…8 °C or graphical symbol;

−18 °C or below or $\leqslant$ −18 °C or graphical symbol.

Other conditions that affect stability shall be indicated.

EXAMPLE 2 Light, humidity.

Any other conditions that affect the handling or storage of the reagents, calibrators and control materials shall be specified.

EXAMPLE 3 Fragile.

5.7 Expiry date

An expiry date based upon the stated storage instructions shall be indicated.

Expiry dates shall be expressed as the year, the month and, where relevant, the day. The requirements of ISO 8601 apply.

EXAMPLES "YYYY-MM-DD" or "YYYY-MM".

If only the year and month are given, the expiry date shall be the last day of the month indicated.

The label of the outer container shall indicate the expiry date of the component having the earliest expiry date, or an earlier date, where appropriate.

5.8 Warnings and precautions

If an IVD reagent is considered hazardous, the outer container label shall include the appropriate danger wording or symbol(s).

EXAMPLES Chemical, radioactive and biological hazards.

In the case of chemical hazards, if the IVD reagent is not accompanied by instructions for use containing the appropriate risk and safety statements, these statements shall be given on the label of the outer container.

Statements or warning symbols for specific hazards may be required by local, national or regional regulations.

6 Content of the immediate container label

6.1 General provisions

6.1.1 Single container

If the immediate container is the outer container, the requirements specified in Clause 5 apply.

6.1.2 Small label

If the available space on the immediate container label is too small to include all of the information listed below, the information about contents (6.4), *in vitro* diagnostic use (6.5), and storage and handling conditions (6.6) may be abbreviated or eliminated.

Local, national or regional regulations may apply.

6.2 Manufacturer

The manufacturer shall be identified. The name of the manufacturer or an unequivocal trade name or logo is sufficient.

6.3 Identification of the IVD reagent

6.3.1 IVD reagent or component name

The name shall ensure proper identification to the user of the IVD reagent or component.

6.3.2 Batch code

A batch code shall be given.

6.4 Contents

If not indicated by another means, the contents shall be specified.

EXAMPLES Mass, volume, volume after reconstitution and/or the number of examinations.

6.5 *In vitro* diagnostic use

The *in vitro* diagnostic use of the reagent shall be stated.

EXAMPLES "For *in vitro* diagnostic use" or graphical symbol: "*in vitro* diagnostic medical device".

6.6 Storage and handling conditions

The storage conditions necessary to maintain stability of the reagents, calibrators and control materials in the unopened state shall be indicated.

Any other conditions that affect the handling or storage of the reagents, calibrators and control materials shall be given, if different from those given on the outer container.

EXAMPLE Fragile.

6.7 Expiry date

An expiry date based upon the stated storage instructions shall be expressed as specified in 5.7.

6.8 Warnings and precautions

If an IVD reagent is considered hazardous, the immediate container label shall include the appropriate danger wording or symbol(s).

EXAMPLES Chemical, radioactive and biological hazards.

In the case of chemical hazards, if the IVD reagent is not accompanied by instructions for use containing the appropriate risk and safety statements, these statements shall be given on the label of the immediate container.

Statements or warning symbols for specific hazards may be required by local, national or regional regulations.

7 Content of the instructions for use

7.1 Manufacturer

The name and address of the manufacturer shall be given.

NOTE In the European Union, the name and address of the manufacturer's "EC Authorized Representative" is required on the outer container label or in the instructions for use, if the legal manufacturer is not located within the EU. See Reference [8].

7.2 Identification of the IVD reagent

The name of the IVD reagent shall be indicated.

If the name does not uniquely identify the IVD reagent, an additional means of identification shall also be provided.

EXAMPLES Catalogue number, commodity number.

7.3 Intended use

The intended use shall be described in appropriate detail, including the measurand, primary sample type and, where appropriate, patient population, whether the device is used for qualitative, semi-quantitative or quantitative examinations and whether it is used for monitoring, screening and/or diagnosis.

Benefits and limitations of the IVD medical device with respect to the intended use shall be described, where appropriate.

Medical use may be described, where appropriate.

EXAMPLES

— Measurement of sodium ion concentration in serum, plasma or urine;

— measurement of the concentration of thyroid stimulating hormone (TSH) in serum to aid in the diagnosis of thyroid disease;

— measurement of the concentration of prostate-specific antigen in serum of males older than 50 years of age to aid in the diagnosis of prostate cancer;

— measurement of the concentration of IgM antibodies to *Borrelia Burgdorferi* in blood plasma.

7.4 Principles of the examination method

The principle of the examination method shall be described, including the type of reaction (e.g., chemical, microbiological or immunochemical), the indicator or detection system and/or other relevant details.

7.5 Traceability of values assigned to calibrators and trueness-control materials

The metrological traceability of values assigned to calibrators and trueness-control materials shall be described including identification of applicable reference materials and/or reference measurement procedures.

NOTE ISO 17511[1] and ISO 18153[3] describe the traceability of values assigned to calibrators and trueness-control materials, to reference materials and/or to reference measurement procedures of higher order.

References to relevant scientific literature or other available documentation of the reference measurement procedure or reference material should be provided.

Local, national or regional regulations may apply.

7.6 Components

The nature, number, amount, concentration or content of the reactive ingredients shall be given.

EXAMPLE 1 Antibody.

Information concerning other ingredients that may influence the examination procedure shall be given.

EXAMPLE 2 Phosphate buffer 10 mM.

7.7 Additional required equipment

Any special equipment required for proper performance and safe use but not provided by the manufacturer shall be listed.

Information necessary to enable special equipment to be identified and connected for proper use shall be given.

7.8 Reagent preparation

All steps required for the preparation of the reagent(s) shall be described.

EXAMPLES Reconstitution, mixing, incubation, dilution.

7.9 Storage and shelf life after first opening

The storage conditions and shelf life following the first opening of the immediate container shall be given if different from the storage conditions and shelf life given on the container label.

The storage conditions and stability of working reagents, calibrators and control materials shall be given.

7.10 Warnings and precautions

If an IVD reagent is considered hazardous, the instructions for use shall include the appropriate danger wording or symbol(s).

If a hazard is associated with storage, use or disposal of the IVD reagent, including reasonably foreseeable misuse, information that enables the user to reduce the risk shall be given.

EXAMPLES Chemical, radioactive and biological hazard.

Local, national or regional regulations may apply.

The requirements of ISO 14971 pertaining to information for safety apply.

NOTE Information that enables users to reduce a risk is called “information for safety”. See ISO 14971.

If an IVD reagent includes substances of human or animal origin that present a risk of infection, a warning shall be given.

Information on the safe handling and disposal of hazardous materials shall be given.

If the IVD reagent is intended for single use, an appropriate warning shall be included.

7.11 Primary sample collection, handling and storage

The primary sample to be used and any special conditions of collection, pre-treatment and/or storage conditions including storage time limit, shall be specified.

Any special instructions for the preparation of the patient prior to primary sample collection shall be given.

7.12 Examination procedure

A complete, detailed description of the examination procedure to be followed shall be provided.

The procedure shall include all the steps necessary to prepare the sample, carry out the examination and obtain a result.

7.13 Control procedure

Adequate information about the performance of the IVD reagent and a means to verify that it is performing within specifications shall be provided.

NOTE Users are responsible for determining the appropriate quality control procedures for their laboratory and for complying with applicable laboratory regulations.

EXAMPLES Identification of acceptable control materials, frequency of examination of control materials.

7.14 Calculation of examination results

The mathematical approach used to calculate the examination result shall be explained, where applicable.

NOTE An example calculation can aid the user's understanding.

7.15 Interpretation of results

Where appropriate, criteria for acceptance or rejection of IVD examination results shall be specified, as well as whether additional examinations are required if a particular result is obtained.

EXAMPLE 1 Requirement to repeat an examination if the initial result is indeterminate.

If the examination procedure is intended to provide either positive or negative results, the criteria for positive and negative results shall be clearly defined, with cut-off values specified.

The diagnostic value of the examination results obtained shall be explained.

EXAMPLE 2 Information regarding the degree to which a negative result excludes or does not exclude the possibility of exposure to, or infection with, a particular organism.

If the IVD examination procedure requires the interpretation of visual observations, a clear description of the criteria shall be included, which may be a representation or reproduction of the possible results.

EXAMPLE 3 A colour chart for colorimetric reactions.

7.16 Performance characteristics

7.16.1 Analytical performance characteristics

The analytical performance characteristics relevant to the intended uses shall be described. (See Annex A of ISO 18113-1:— for terms and definitions.)

EXAMPLES For quantitative measurement procedures: quantitation limit, analytical specificity (including interfering substances), trueness and precision (repeatability, intermediate precision and reproducibility). This list is not intended to be exhaustive.

NOTE Performance can also be compared to that of an IVD reagent already on the market. A graphical representation with regression and correlation statistics can be helpful.

7.16.2 Diagnostic performance characteristics

For qualitative examination procedures, the diagnostic performance characteristics relevant to the intended use shall be described. (See Annex A of ISO 18113-1:— for terms and definitions.)

EXAMPLES Diagnostic sensitivity, diagnostic specificity, cut-off value.

7.16.3 Measuring interval

For quantitative examination procedures, the concentration interval over which the performance characteristics of the IVD reagent have been validated shall be given.

EXAMPLE 5 mmol/l to 500 mmol/l.

7.17 Biological reference intervals

For quantitative examination procedures, biological reference intervals shall be provided, along with a description of the reference populations including the number of subjects, and pertinent literature references.

Reference interval units shall be consistent with the units used for reporting examination results.

NOTE For information regarding the description of biological reference intervals, see References [6], [7] and [10] to [17].

Relevant medical decision values may also be given.

7.18 Limitations of the examination procedure

Any limitations of the examination procedure shall be described, including information regarding

a) known clinically relevant interfering substances,

b) the examination of inappropriate primary samples and potential consequences, if known,

c) factors and circumstances that can affect the result, together with precautions to avoid incorrect results,

d) potential for carryover.

The requirements of ISO 14971 pertaining to information for safety apply.

NOTE Information that enables users to reduce a risk is called “information for safety”. See ISO 14971.

7.19 Literature references

Pertinent literature references shall be given.

EXAMPLES Measurement method, biological reference intervals.

Bibliography

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[3] ISO 18153, In vitro *diagnostic medical devices — Measurement of quantities in biological samples — Metrological traceability of values for catalytic concentration of enzymes assigned calibrators and control materials*

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