INTERNATIONAL STANDARD

**ISO 18113-2**

Second edition
2022-10

# 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

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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).

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).

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.

This document was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 140, *In vitro diagnostic medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO 18113-2:2009), which has been technically revised.

The main changes are as follows:

— Added Information pertaining to (unique device identifier-device identifier) UDI;

— Updated with examples to reference European Union and other regulations;

— Added additional detail for clarification;

— Updated the Bibliography.

A list of all parts in the ISO 18113 series can be found on the ISO website.

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.

# Introduction

Manufacturers of in vitro diagnostic (IVD) reagents for professional use, supply users with information to enable the 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 International Medical Devices Regulators Forum (IMDRF) encourages convergence of the evolution of regulatory systems for medical devices at the global level. Eliminating differences among regulatory jurisdictions can allow patients earlier access to new technologies and treatments. This document provides a basis for harmonization of labelling requirements for IVD reagents for professional use.

This document 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 document is intended to support the essential labelling requirements of all the IMDRF[8] 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 document is also intended to be used together with ISO 18113-1 and ISO 18113-3.

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

Part 2:
# In vitro diagnostic reagents for professional use

## 1 Scope

This document specifies requirements for information supplied by the manufacturer of in vitro diagnostic (IVD) reagents, calibrators and controls intended for professional use.

This document can also be applicable to accessories.

This document is applicable to the labels for outer and immediate containers and to the instructions for use.

This document does not apply to:

a) IVD instruments or equipment;

b) IVD reagents for self-testing.

## 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 8601-1, *Date and time — Representations for information interchange — Part 1: Basic rules*

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

ISO 15223-1, *Medical devices — Symbols to be used with information to be supplied by the manufacturer — 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*

## 3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

## 4 General

### 4.1 Essential requirements

The requirements of ISO 18113-1 apply.

For the use of symbols, the requirements of ISO 15223-1 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.

NOTE A UDI is not required on the immediate label of kit components unless the component is a device in its own right.

## 5 Content of the outer container label

### 5.1 Manufacturer

The name and address of the manufacturer shall be given. The address indicates a single point at which the manufacturer can be contacted, e.g. street, number, city, postal code, country. If a full address is not practical, an abbreviated version may be sufficient provided the full address is included in the instructions for use.

If an Authorized Representative is acting on behalf of the manufacturer in the country/jurisdiction, whether the regulatory authority having jurisdiction requires that the label shall also contain the address of the Authorized Representative, should be taken into consideration.

### 5.2 Identification of the in vitro diagnostic (IVD) reagent

#### 5.2.1 IVD reagent name

The name or trade name of the IVD reagent shall be given. This brand or trade name should allow its differentiation from other products of the same or similar type. 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/lot number

A batch code/lot number, 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.

#### 5.2.3 Unique device identifier (UDI)

It should be taken into consideration that if an IVD reagent is subject to unique identification rules by the regulatory authority, the outer label should provide the UDI including the UDI carrier (Automatic Identification Data Carrier 'AIDC' format), and Human Readable Interpretation (HRI).

When AIDC carriers other than the UDI carrier are part of the product labelling, the UDI carrier shall be readily identifiable.

The UDI shall include both the UDI device identifier (UDI-DI) and the UDI production identifier (UDI-PI); specific exemptions which are provided by regulations should be taken into consideration.

For the IVD reagent, the UDI-PI shall include at least the batch code and the expiry date.

If there also is a manufacturing date on the label for reasons other than batch control purposes, it does not need to be included in the UDI-PI; specific requirements provided by regulations should be taken into consideration.

If there are significant constraints limiting the use of both AIDC and HRI on the label, the AIDC format shall be generally preferred except for environments where HRI is more appropriate to the user.

The UDI carrier should be readable during normal use, storage conditions, and throughout intended life of the IVD reagent. ISO/IEC 15415 should be referred to for bar code specifications and symbol quality criteria.

Local, national or regional regulations can apply.

NOTE 1 The content, format, and size of the UDI is specified by the accredited UDI issuing agency selected.

NOTE 2 HRI text is not the same as the text that is already placed on the label and is a legible interpretation of the data characters encoded in the UDI Carrier.

## 5.3 Contents

The net quantity of contents expressed in terms of mass, volume, volume after reconstitution, numerical or a combination of these or other terms that accurately reflect the contents shall be indicated.

## 5.4 Intended use/Intended purpose

If the intended use is not indicated by the name of the IVD reagent or an appropriate symbol, then an abbreviated intended use that contains enough detail for the user to identify the device and its use shall be given. A full intended use statement shall be given in the instructions for use.

NOTE In some countries, authorities having jurisdiction can set local requirements for the content of the intended use statement. For example, in the European Union, an indication is given that the device is intended for near-patient testing.

## 5.5 In vitro diagnostic use

The IVD use of the reagent shall be indicated.

EXAMPLES “For in vitro diagnostic use” or the graphical symbol for “in vitro diagnostic medical device”.

## 5.6 Storage, transport, 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. Use of non-specific temperature or humidity indications that are open to interpretation shall be avoided.

EXAMPLE 1 2 °C to 8 °C or 2…8 °C or graphical symbol; −18 °C or below or ≤ −18 °C or graphical symbol.

Other conditions that affect stability shall be indicated.

EXAMPLE 2 Light, humidity.

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

EXAMPLE 3 Fragile.

EXAMPLE 4 Keep vials protected from light.

Other protective measures which users should take to mitigate conditions that can affect stability shall be stated.

## 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 8601-1 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 hazard pictogram(s). The appropriate signal word, product identifiers, hazard statements and precautionary statements should be included. However, where there is insufficient space, the hazard pictogram shall be given on the outer container label and the other information shall be given in the instructions for use.

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 can 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 the information listed below, the information about contents (6.4), IVD use (6.5), and storage and handling conditions (6.6) and manufacturer address (6.2) may be abbreviated or eliminated.

Local, national or regional regulations can apply.

## 6.2 Manufacturer

The manufacturer shall be identified. The name of the manufacturer or an unequivocal trade name or logo is sufficient. For inclusion of the manufacturer address, see 5.1.

## 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/lot number

A batch code and where appropriate, a lot number, shall be given.

### 6.3.3 Unique device identifier (UDI)

Whether a UDI is required by the regulatory authority should be taken into consideration. If so, the UDI should be included as specified in 5.2.3.

It is possible that the UDI on the immediate container label will not be the same as the UDI on the outer container. Applicable regulations can apply.

## 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 IVD use of the reagent shall be stated.

EXAMPLES "For in vitro diagnostic use" or the graphical symbol for "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 hazard pictogram(s). The appropriate signal words, product identifiers, hazard statements and precautionary statements should be included. However, where there is insufficient space, the hazard pictograms shall be given on the immediate container label and the other information shall be given in the instructions for use.

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 hazard and precautionary statements, these statements shall be given on the label of the immediate container.

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

# 7 Content of the instructions for use

## 7.1 Manufacturer

The name, registered trade name, or registered trade mark and address of the manufacturer shall be given. The manufacturer address shall contain information related to the physical location such as street/road, number/house/floor, city, state/region, postal code, country, if available. A telephone

number and/or fax number and/or website address or email address to obtain technical assistance shall be provided.

## 7.2 Identification of the IVD reagent

The name or trade 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/intended purpose

The intended use shall be described in appropriate detail, including:

— the measurand;

— target population;

— primary sample type(s);

— its function (e.g. screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic);

— whether the device is used for qualitative or quantitative examinations;

— the specific disorder, condition or risk factor of interest that it is intended to detect, specify, or differentiate;

— the intended user (e.g. laboratory professional use, healthcare professional use at the point of care/near-patient);

— where appropriate, if the device is automated or intended to be used with a specific instrument.

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

NOTE 1 In some countries, authorities having jurisdiction can set local requirements for devices intended for use as a companion diagnostic. For example, in the European Union, the International Non-proprietary Name (INN) can be given.

NOTE 2 Medical use can 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 principles shall be described in enough detail to allow the user to understand how the IVD medical device is able to carry out its function.

## 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.

Information shall be provided regarding maximum (self-allowed) batch to batch variation due to the manufacturer's calibration value assignment methodology of the end user control and calibrator material. This may be understood as providing a value which links the primary reference material set to the end user calibrator and control materials.

The value, the uncertainty value derived for the user calibrator and or user control and the level of bias due to the process which can be expected, may be stated.

The manufacturer may provide uncertainty as a range of values within which the true value lies with a specified level of confidence; this can be expressed as, e.g.: 9,8 XX/YY to 10,2 XX/YY, or as 10,0 XX/YY ± 0,2 XX/YY, or as 10,0 XX/YY ± 2 %, with AA% Confidence.

In addition to the information specified in the instructions for use, the manufacturer can choose to make additional information available through other documents or upon request.

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

NOTE 2 'control material' is only included if it is used to verify the trueness of measurements, while precision control materials and control materials to which intervals of values per method/manufacturer have been assigned are outside the scope and then ISO 17511 does not apply.

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 can apply.

## 7.6 Components

A list of all components/materials provided including the nature, number, amount, concentration or content of the reactive ingredients, shall be given.

EXAMPLE 1 Antibody.

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

EXAMPLE 2 Phosphate buffer 10 mM.

## 7.7 Additional required equipment and/or materials

Any special equipment and/or materials required for proper performance and safe use of the IVD medical device 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 and/or measures to be taken and limitations of use regarding the device

Information shall be given in the form of warnings, precautions and/or measures to be taken:

— in the event of malfunction of the device or its degradation as suggested by changes in its appearance that can affect performance;

— as regards the exposure of the reagent(s) to reasonably foreseeable external influences or environmental conditions, e.g. magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature.

If an IVD reagent is considered hazardous, the instructions for use shall include the appropriate signal words, product identifiers, hazard pictograms, hazard statements and precautionary statements. 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 can apply.

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

NOTE 1 Information that enables users to reduce a risk is called “information for safety”. See ISO 14971.

If an IVD reagent includes substances of human, microbial 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. See [intended use on label].

NOTE 2 In some countries, authorities having jurisdiction can set local requirements for the contents of warnings and precautions and/or measures to be taken and limitations of use regarding the device. For example, in the European Union, the instructions for use give precautions related to materials incorporated into the device that contain or consist of substances which are carcinogenic, mutagenic or toxic for reproduction, or endocrine disrupting substances or that can result in sensitization or an allergic reaction by the patient or user. They also give notice to the user that any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

## 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.

Should the sample need to be shipped, and need special packing such as freezing, then those instructions shall also 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. Process for validation of quality control procedures maybe found in ISO 15198.

NOTE Users are responsible for determining the appropriate quality control procedures for their laboratory and for being aware of 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, and any additional software or database required for the interpretation of the 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 specified, 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 ISO 18113-1:2022 3.2 for terms and definitions.)

EXAMPLES Quantitation limit, analytical specificity (including interfering substances), trueness and precision (repeatability, intermediate precision and reproducibility), cut-off value. 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 Clinical performance characteristics

The diagnostic performance characteristics relevant to the intended use shall be described (see ISO 18113-1:2022 3.2 for terms and definitions.)

EXAMPLES Diagnostic sensitivity, diagnostic specificity. This list is not intended to be exhaustive.

### 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. For qualitative procedures, the measuring interval may be given where appropriate.

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 [9] to [16].

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.

## 7.20 Document control

The date of issue or the latest revision of the instructions for use and an identifier shall be given or if they have been revised, the date of issue, revision number and/or identification number of the latest revision of the instructions for use, with a clear indication of the introduced modifications.

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