INTERNATIONAL STANDARD

ISO 19001

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In vitro diagnostic medical devices — Information supplied by the manufacturer with in vitro diagnostic reagents for staining in biology

Dispositifs médicaux de diagnostic in vitro — Informations fournies par le fabricant avec les réactifs de coloration de diagnostic in vitro utilisés en biologie

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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 19001 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 19001:2002), which has been technically revised.

Introduction

This International Standard relates to ISO 18113-1 and ISO 18113-2, which can be used in conjunction with it.

The use of reagents required for staining in biology as well as the specific examples of information supplied by the manufacturer for two staining procedures as provided in Annex A are based on a European consensus; they constitute the scientific justification for the requirements listed in Clause 4. This information is intended to assist manufacturers, suppliers and vendors of dyes, stains, chromogenic reagents and other reagents used for staining in biology in complying with the required specific product data.

In vitro diagnostic medical devices — Information supplied by the manufacturer with in vitro diagnostic reagents for staining in biology

1 Scope

This International Standard specifies requirements for information supplied by the manufacturer with reagents used in staining in biology. It applies to producers, suppliers and vendors of dyes, stains, chromogenic reagents and other reagents used for staining in histology and cytology including bacteriology, haematology, histochemistry, as performed in medical laboratories, both routine and research bacteriology. The requirements for information supplied by the manufacturer specified in this International Standard are a prerequisite for achieving comparable and reproducible results in all fields of staining in biology.

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 80000-1, *Quantities and units — Part 1: General*

ISO 80000-9, *Quantities and units — Part 9: Physical chemistry and molecular physics*

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

ISO 18113-2, *In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 2: In vitro diagnostic reagents for professional use*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
antibody
specific immunoglobulin formed by B-lymphocytes in response to exposure to an immunogenic substance and able to bind to this

Note 1 to entry: The molecule of an immunogenic substance contains one or more parts with a characteristic chemical configuration, an epitope.

3.2
blocking reagent
reagent that is used to reduce the inherent background of a sample before staining

3.3
chromogenic reagent
reagent that reacts with certain chemical groups present or induced in cells and tissues with the formation of a coloured compound in situ

EXAMPLE Diazonium salt, Schiff's reagent.

3.4
dye
coloured organic compound that, when dissolved in a suitable solvent, can impart colour to a material

3.5
fluorochrome
reagent that emits visible light when irradiated with excitation light of a shorter wavelength

Note 1 to entry: Any of various fluorescent substances used in biological staining to produce fluorescence in a sample.

3.6
in vitro diagnostic reagent
IVD reagent
chemical, biological or immunological component, solution or preparation intended by the manufacturer to be used as an IVD medical device

[ISO 18113-1]

3.7
information supplied by the manufacturer
labelling
written, printed or graphic matter

— affixed to an IVD medical device or any of its containers or wrappers or

— provided for use with an IVD medical device,

related to identification, technical description, and use of the IVD medical device, but excluding shipping documents

EXAMPLE Labels, instructions for use.

Note 1 to entry: Catalogues are not considered labelling of IVD medical devices.

[ISO 18113-1]

3.8
label
printed, written or graphic information placed on a medical device or its container

Note 1 to entry: A label permanently affixed to an IVD instrument is considered marking.

[ISO 18113-1]

3.9
lectin
protein of non-immunogenic origin with two or more binding sites that recognize and bind to specific saccharide residues

3.10
monoclonal antibody
antibody capable of reacting specifically with a single epitope of a certain immunogenic substance

3.11
polyclonal antibody
mixture of immunoglobulin molecules, secreted against a specific immunogenic substance, each recognizing a different epitope

3.12
staining
impartment of colour to a material by means of reaction with a stain or chromogenic reagent

3.13
stain
solution of one or more dyes at defined concentrations in a defined solvent used for staining

Note 1 to entry: The stain can be prepared by directly dissolving the dye in the solvent or by dilution of a stock solution with suitable agents.

3.14
stock solution of stain
stable defined solution of one or more dyes at a higher concentration than that used for staining

Note 1 to entry: Stability refers to constant properties of the dye even in the presence of other dyes.

3.15
nucleic acid probe
single- or double-stranded oligonucleotide or polynucleotide of defined length complementary to specific sequences of nucleotides in nucleic acids

4 Requirements for information supplied by the manufacturer

4.1 General requirements

4.1.1 Chain of suppliers

When a manufacturer uses materials supplied by a producer, the manufacturer has an obligation of assuring that the producer meets the quality systems described in ISO 9001 and ISO 13485.

4.1.2 Warning and precautions

The manufacturer of reagents used for staining in biology shall provide information regarding warning and precautions in accordance with ISO 18113-1 and ISO 18113-2.

4.1.3 Format of Information supplied by the manufacturer

The format of the information supplied by the manufacturer with reagents used for staining in biology shall be in accordance with ISO 80000-1 and ISO 80000-9. Furthermore, where relevant, the requirements as specified in 4.1.4, 4.1.5 and 4.1.6 shall be met for the various reagents used for staining in biology.

4.1.4 Information supplied by the manufacturer with reagents used for staining in biology

Information supplied by the manufacturer with reagents used for staining in biology shall be in accordance with ISO 80000-1 and ISO 80000-9. Information shall be provided regarding warning and precautions. ISO 18113-1 and ISO 18113-2 regarding warnings and precautions apply. Furthermore, where relevant, the requirements as specified in 4.1.2, 4.1.3 and 4.1.4 shall be met for the various reagents used for staining in biology.

4.1.5 Product name

The product name shall, where relevant, include CAS-registry number [7] and Colour Index name and number.[23]

NOTE 1 CAS-registry numbers are the Chemical Abstracts Service registry numbers. These are unique numerical code numbers assigned to chemical substances indexed by Chemical Abstracts.

NOTE 2 The Colour Index gives a 5-digit number, the C.I. number and a specially constructed name to most dyes.

4.1.6 Product identity

The description of the reagent shall include appropriate physico-chemical data accompanied by relevant data sheets for each batch. The data shall contain the following information:

a) the molecular formula including counter-ion;

b) the molar mass (g/mol) clearly stating whether this is with or without counter-ion;

c) the permissible [or allowable] limits of interfering substances;

d) handling and storage.

For coloured organic compounds, the data shall also contain:

e) the molar absorbance (this can be substituted by content of the pure dye);

f) the wavelength or wave number at maximum absorbance;

g) thin layer chromatographic, high performance liquid chromatographic, or high performance thin layer chromatographic data.

4.1.7 Suggested use

Suggested use(s) shall be provided giving guidelines for staining in biology

This shall include information on:

a) type(s) of biological material and handling and treatment before staining;

NOTE 1 Information on type of biological material and its handling and treatment can be found in Reference.[15]

EXAMPLE Whether cell or tissue samples or both can be used; whether frozen or chemically-fixed material or both can be used; protocol for tissue processing; which embedding media can be used.

NOTE 2 Reference[15] gives procedures for use in the testing of dye, stain, chromogenic reagent, fluorochrome, antibody and nucleic acid probe used for staining in biology.

b) details of a suitable reaction procedure used by the manufacturer for testing the reactivity of the dye, stain, chromogenic reagent, fluorochrome, antibody, nucleic acid probe or lectin used for staining in biology;

c) result(s) expected when using the reaction procedure on the suggested type(s) of material in the way detailed by the manufacturer;

EXAMPLES See A.2 and A.3.

d) notes on suitable positive and negative control tissue and on interpretation of the result(s);

e) references to published results obtained using the product in the way suggested by the manufacturer.

4.2 Additional requirements for specific kinds of reagent

4.2.1 Fluorochromes

Independent of the type of application, fluorochromes offered for staining in biology shall be accompanied by the following information:

a) selectivity, i.e. a description of the target(s) which may be demonstrated using the conditions specified;

b) excitation and emission wavelengths;

c) for fluorochromes conjugated to antibodies, the amount-of-substance ratio of fluorochrome conjugated to protein (F/P amount-of-substance ratio) is essential for quantitative purposes. The F/P ratio is calculated by separately determining the protein and fluorochrome amount-of-substance concentrations of the conjugate based on absorbance measurements and then expressing these concentrations as a ratio.

4.2.2 Metal salt compounds

When offering metal compounds for use in metal uptake procedures in staining in biology, the following additional information shall be included:

a) the systematic name;

b) purity.

4.2.3 Antibodies

Antibodies offered for staining in biology shall be accompanied by the following information unless superseded by national governing regulations:

a) a description of the antigen (immunogenic substance) against which the antibody was raised, and if the antigen is defined by the cluster of differentiation systems, a CD number. This description shall contain the type of (macro)molecule detected, which part of the molecule has been detected, its cellular localization, and in which cells and/or tissues it is found, and any cross reactivity with other epitopes;

b) for monoclonal antibodies, animal host species, clone, method of production (tissue culture supernatant or ascitic fluid), immunoglobulin subclass and light chain identity;

NOTE Reference[8] gives an update on modern immunohistochemical procedures.

c) for polyclonal antibodies, animal host and whether whole serum or the gammaglobulin fraction is used;

d) a description of form (solution or lyophilized powder), amounts of total protein and specific antibody, and, if in solution, the nature and concentration of diluent or medium;

e) a description of any molecular linkers or extenders added to the antibody;

f) a declaration of purity, purification techniques and detection methods for impurity;

EXAMPLE Western blotting, immunohistochemistry.

g) appropriate references to publications dealing with application of the antibody.

NOTE Examples of procedures that may be used by the manufacturer or end user may be found in CLSI guideline I/LA28.[8]

4.2.4 Nucleic acid probes

Nucleic acid probes offered for staining in biology shall be accompanied by the following information unless superseded by national governing regulations:

a) the base sequence and whether the probe is double- or single-stranded;

b) the molar mass of the probe or the number of bases and, if applicable, the number fraction (in percent) of guanine-cytosine base pairs;

c) marker used (radioactive isotope or non-radioactive molecule); for non-radioactive markers, point(s) of attachment to the probe (3' and/or 5') and substance fraction in percent of probe marked;

d) the target gene (DNA or RNA sequence) detected;