INTERNATIONAL STANDARD

ISO 19001

First edition
2002-11-15

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

Reference number
ISO 19001:2002(E)

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Printed in Switzerland

Contents

Page

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 3.

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 International Standard 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*.

Annex A of this International Standard is for information only.

Introduction

This International Standard relates to EN 375 and EN 376 and should be used in conjunction with these.

The use of reagents required for staining in biology as well as the specific examples of information supplied by the manufacturer for four 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 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 biology. 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 normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 31-8, *Quantities and units — Part 8: Physical chemistry and molecular physics*

ISO 1000, *SI units and recommendations for the use of their multiples and of certain other units*

EN 375, *Information supplied by the manufacturer with in vitro diagnostic reagents for professional use*

EN 376, *Information supplied by the manufacturer with in vitro diagnostic reagents for self-testing*

3 Terms and definitions

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

3.1
information supplied by the manufacturer
all printed, written, graphic or other information annexed to, or accompanying an in vitro diagnostic reagent

3.2
label
any printed, written or graphic information placed on a container

[EN 375]

3.3
in vitro diagnostic reagent
reagent that, used alone or in combination with other in vitro diagnostic medical devices, is intended by the manufacturer to be used in vitro for examination of substances derived from human, animal or plant sources, for providing information relevant to the detection, diagnosis, monitoring or treatment of physiological states, states of health or disease, or congenital abnormality

3.4
staining
impartment of colour to a material by means of reaction with a stain or chromogenic reagent

3.5
dye
coloured organic compound that, when dissolved in a suitable solvent, can impart colour to a material

NOTE The physical origin of colour is the selective absorbance (and/or emission) in the visible region of the electromagnetic spectrum between 400 nm and 800 nm. Dyes are molecules with large systems of delocalized electrons (conjugated π-electronic system). The light absorbance characteristics of dyes are displayed by absorbance spectra, resulting from plotting absorbance of light against wavelength. The shape of the spectra and the wavelength at maximum absorbance depend on the chemical structure of the dye, the solvent and on the conditions of the spectral measurements.

3.6
stain
solution of one or more dyes at defined concentrations in a defined solvent used for staining

NOTE The stain can be prepared by directly dissolving the dye in the solvent or by dilution of a stock solution with suitable agents.

3.6.1
stock solution of stain
stable defined solution of one or more dyes at a higher concentration than that used for staining

NOTE Stability refers to constant properties of the dye even in the presence of other dyes.

3.7
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 A typical chromogenic reagent is:

a) diazonium salt;

b) Schiff's reagent.

3.8
fluorochrome
reagent that emits visible light when irradiated with excitation light of a shorter wavelength

3.9
antibody
specific immunoglobulin formed by B-lymphocytes in response to exposure to an immunogenic substance and able to bind to this

NOTE The molecule of an immunogenic substance contains one or more parts with a characteristic chemical composition, an epitope.

3.9.1
polyclonal antibody
mixture of antibodies capable of reacting specifically with a certain immunogenic substance

3.9.2
monoclonal antibody
antibody capable of reacting specifically with a single epitope of a certain immunogenic substance

3.10
nucleic acid probe
single stranded oligonucleotide or polynucleotide of defined length complementary to specific sequences of nucleotides in nucleic acids

3.11
lectin
protein of non-immunogenic origin with two or more binding sites that recognize and bind to specific saccharide residues

4 Requirements for information supplied by the manufacturer

4.1 General requirements

4.1.1 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 31-8, ISO 1000, EN 375 and EN 376. Special attention shall be given to cautionary statements as given in EN 375. 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.

4.1.2 Product name

The product name shall include CAS-registry number and Colour Index name and number, where applicable.

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.

4.1.3 Description of reagent

The description of the reagent shall include appropriate physico-chemical data accompanied by relevant data sheets for each batch. The data shall contain at least 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 limits of interfering substances.

For coloured organic compounds, the data shall also contain:

d) the molar absorbance (this can be substituted by content of the pure dye molecule but not by content of total dye);

e) the wavelength or wave number at maximum absorbance;

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

4.1.4 Intended use

A description shall be provided giving guidelines for staining in biology and for qualitative and quantitative procedures (if applicable). This shall include information on:

a) type(s) of biological material and handling and treatment before staining, e.g.:

   1) whether cell or tissue samples or both can be used;

   2) whether frozen or chemically-fixed material or both can be used;

   3) protocol for tissue processing;

   4) which embedding media can be used;

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 outlined by the manufacturer;

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 ratio of fluorochrome/protein (F/P).

4.2.2 Metal salts

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:

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, as appropriate, 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, clone, method of production (tissue culture supernatant or ascitic fluid), immunoglobulin subclass and light chain identity;

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

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

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

f) a declaration of purity, purification techniques and detection methods for impurity (e.g. Western blotting, immunohistochemistry);

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

4.2.4 Nucleic acid probes

Nucleic acid probes offered for staining in biology shall be accompanied by the following information:

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;

e) a description of form (lyophilized powder or solution) and amount (pg or pmol) or concentration (pg/ml or pmol/ml) as appropriate and if in solution, the nature and concentration of diluent or medium;

f) a declaration of purity, purification techniques and detection methods for impurity, e.g. HPLC (high performance liquid chromatography);

g) appropriate references to publications dealing with the source description of DNA sequence, existence of any known patents and information on application of the nucleic acid probe.