SLOVENSKI STANDARD
SIST EN 12376:2000

01-januar-2000

Diagnostiļ ni medicinski pripomoļ ki in vitro ï Informacije, ki jih priskrbi proizvajalec diagnostiļ nih reagentov za barvanje in vitro v biologiji

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

In-vitro-Diagnostika - Bereitstellung von Informationen durch den Hersteller von in-vitro-diagnostischen Reagenzien für biologische Färbungen

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

Ta slovenski standard je istoveten z: **EN 12376:1999**

ICS:

11.100.10	Diagnostiļ ni preskusni sistemi in vitro	In vitro diagnostic test systems

SIST EN 12376:2000 **en**

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN 12376

January 1999

ICS 11.100

Descriptors: medicine, biology, in-vitro diagnostic, chemical reagents, coloration, definitions, information, labelling

English version

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

Central Secretariat: rue de Stassart, 36 B-1050 Brussels

Contents

Foreword

This European Standard has been prepared by Technical Committee CEN/TC 140 "In vitro diagnostic medical devices", the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by July 1999, and conflicting national standards shall be withdrawn at the latest by July 1999.

Annexes A and B are given for information.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Introduction

This European Standard relates to EN 375, *In vitro diagnostic systems - Requirements for labelling of in vitro diagnostic reagents for professional use* and EN 376, *In vitro diagnostic systems - Requirements for labelling of in vitro diagnostic reagents for self testing* 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.

1 Scope

This European 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 European standard are a prerequisite for achieving comparable and reproducible results in all fields of staining in biology.

2 Normative references

This European Standard incorporates, by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text and the publications are listed hereafter. For dated references, subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references the latest edition of the publication referred to applies.

EN 375	In vitro diagnostic systems - Requirements for labelling of in vitro diagnostic reagents for professional use
EN 376	In vitro diagnostic systems - Requirements for labelling of in vitro diagnostic reagents for self testing
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

3 Terms and definitions

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

3.1
information supplied by the manufacturer
All printed, written, graphic or other information affixed 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 employed 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: Typical chromogenic reagents are:

a) diazonium salts;
b) Schiff's reagent.

3.8
fluorochrome
Reagent which 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 conform with EN 375, EN 376, ISO 31-8, and ISO 1000. 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 as a minimum :

a) the molecular formula including counter-ion;

b) the molar mass (g mol $^{-1}$) clearly stating whether this is with or without counter-ion;

c) the allowable 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 wavenumber 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, for 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;

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 using the product in the way suggested by the manufacturer.

4.2 Additional requirements for specific kinds of reagents

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 system, a CD number. This description shall contain, as appropriate, the type of (macro)molecule detected, which part of the molecule is 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 per cent) 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 per cent 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.