BRITISH STANDARD

BS EN
375:2001

Information supplied by the manufacturer with in vitro diagnostic reagents for professional use

The European Standard EN 375:2001 has the status of a British Standard

ICS 11.100

National foreword

This British Standard is the official English language version of EN 375:2001. It supersedes BS EN 375:1992 which is withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/69, In vitro diagnostic systems, which has the responsibility to:

— aid enquirers to understand the text;

— present to the responsible European committee any enquiries on the interpretation, or proposals for change, and keep the UK interests informed;

— monitor related international and European developments and promulgate them in the UK.

A list of organizations represented on this committee can be obtained on request to its secretary.

Cross-references

The British Standards which implement international or European publications referred to in this document may be found in the BSI Standards Catalogue under the section entitled "International Standards Correspondence Index", or by using the "Find" facility of the BSI Standards Electronic Catalogue.

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This British Standard, having been prepared under the direction of the Health and Environment Sector Committee, was published under the authority of the Standards Committee and comes into effect on 15 March 2001

Summary of pages

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EUROPEAN STANDARD

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EUROPÄISCHE NORM

EN 375

January 2001

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Supersedes EN 375:1992

English version

Information supplied by the manufacturer with in vitro diagnostic reagents for professional use

Informations fournies par le fabricant avec les réactifs de diagnostic in vitro pour usage professionnel

Bereitstellung von Informationen durch den Hersteller von Reagenzien für in-vitro-diagnostische Untersuchungen zum Gebrauch durch Fachpersonal

This European Standard was approved by CEN on 6 December 2000.

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

Management Centre: rue de Stassart, 36 B-1050 Brussels

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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.

The European Diagnostic Manufacturers Association (EDMA) has contributed to its preparation.

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 2001, and conflicting national standards shall be withdrawn at the latest by July 2001.

This European Standard supersedes EN 375:1992.

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For relationship with EU Directive(s), see informative Annex ZA, which is an integral part of this standard.

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.

1 Scope

This standard specifies the requirements for the information supplied by the manufacturer of in vitro diagnostic reagents including reagent products, calibrators, control materials and kits for professional use, which hereafter are called IVD reagents.

NOTE This standard can also be applied to accessories.

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 (including amendments).

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 standard, the following terms and definitions apply.

3.1
active ingredient
constituent that participates in the reaction used to measure or detect the analyte

3.2
batch
lot
defined amount of material, either starting material, intermediate or finished product which is uniform in its properties and has been produced in one process or series of processes

3.3
batch code
lot number
code that is a distinctive combination of numbers and/or letters which specifically identifies a batch and permits its manufacturing history to be traced

3.4
calibrator
substance, material or article intended by its manufacturer to be used to establish the measurement relationships of an in vitro diagnostic medical device

3.5
control material
substance, material or article intended by its manufacturer to be used to verify the performance characteristics of an in vitro diagnostic medical device

3.6
expiry date
date up to which product performance is assured by the manufacturer based on the stability of the IVD reagent

3.7
immediate container
primary container
packaging which protects the contents from contamination and/or other effects of the external environment

NOTE Examples are a sealed vial, ampoule or bottle, a foiled pouch, or a sealed plastics bag containing e. g. culture media, microtitration plates or coated tubes.

3.8
internal quality control
operational techniques and activities at the point of use that are used to fulfil requirements for quality of services

NOTE Internal quality control comprises all steps of activity for production of results from collection of sample and measurement of a measurable quantity to reporting of result of measurement.

3.9
in vitro diagnostic reagent
IVD reagent
in vitro diagnostic medical device which is a reagent, reagent product, calibrator, control material or kit

NOTE 1 For the definition of an in vitro diagnostic medical device see [13].

NOTE 2 In some cases a particular IVD reagent, as defined for use in human medicine, may serve also in veterinary medicine.

3.10
kit
set of components (reagents and/or other materials) packaged together

3.11
kit component
in vitro diagnostic medical device intended to be part of a kit

NOTE Typical kit components are e. g. antibody solutions, buffer solutions, calibrators or control materials.

3.12
label
printed, written or graphic information placed on a container

3.13
outer container
sales packaging
material used in the packaging of the immediate container(s) of (an) IVD reagent(s) consisting of a single entity or an assembly of different or identical components

3.14
professional use
use by personnel who have received special education and training with regard to procedures utilizing in vitro diagnostic medical devices

3.15
reagent product
reagent carrier
product in which the reagents are fixed to or included in a carrier

EXAMPLES
Reagent strips, slides, discs and sticks.

3.16
shelf life
period until expiry date

3.17
specimen
biological material which is obtained in order to detect or to measure one or more quantities

3.18
stability
ability of an IVD reagent when kept under specified conditions, to retain throughout the shelf life its properties and/or performance within limits specified by the manufacturer

3.19
trueness
closeness of agreement between the average value obtained from a large series of test results and an accepted reference value [ISO 3534-1]

NOTE Directive 98/79/EC uses ‘‘accuracy’’ synonymously with ‘‘trueness’’, whereas the term ‘‘accuracy’’ includes both ‘‘trueness’’ and ‘‘precision’’, according to ISO 3534-1 and ISO 5725-1.

4 Requirements for labels

4.1 Outer container

4.1.1 General

The label for an outer container shall give the information specified in 4.1.2 to 4.1.10.

Requirements concerning the language(s) of the country in which the IVD reagent is distributed shall be met. Information which is a proper name, address or symbol does not require to be expressed in multiple languages.

4.1.2 Manufacturer

The name and address of the manufacturer shall be given.

NOTE The manufacturer is the entity which has taken legal responsibility for the IVD reagent.

The name and address of the authorized representative shall also be given when this is a legal requirement.

4.1.3 Product name

The product name shall be given.

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

4.1.4 Microbiological state

If necessary for proper performance of the IVD reagent, the microbiological state or state of cleanliness, e. g. “microbiologically controlled” or “sterile”, shall be given.

4.1.5 Batch code

A batch code shall be given.

If a kit contains different components bearing different batch codes, the batch code given on the outer container shall enable the individual product histories to be traced from the manufacturer's production file.

NOTE The graphical symbol as given in EN 980 should be used.

4.1.6 Expiry date

An expiry date based upon the stated storage instructions shall be given. This shall be expressed as the year, the month, and, where relevant, the day in that order. In the case of year and month this means that the expiry date is the last day of the month indicated. The label of the outer container shall give the expiry date of the component having the earliest expiry date or an earlier date if appropriate.

NOTE 1 The graphical symbol as given in EN 980 should be used.

NOTE 2 The format for the expiry date should be either “CCYY-MM-DD” or “CCYY-MM”.

4.1.7 Contents

The content in terms of e. g. mass, volume, volume after reconstitution and/or the number of measurements shall be given.

In the case of a kit the components shall be designated in the same way as on the immediate containers as specified in 4.2.3.

Information on additional materials, e. g. accessories, may be given on the label and/or in the instructions for use where practicable and appropriate.

4.1.8 Intended purpose

Where appropriate, the intended purpose shall be given.

EXAMPLES
— Measurement of glucose concentration in serum,
— measurement of thromboplastin time.

Additionally the in vitro use of the reagent shall be indicated.

NOTE A graphical symbol for in vitro diagnostic medical device should be used. [1)]

[1)] Graphical symbol as given in ISO 15223/DAM 1: 1999 and as proposed for a future revision of EN 980.

4.1.9 Storage and handling information

The storage conditions necessary to assure the stability of the product in the unopened state shall be indicated. Recommended storage temperature intervals shall be given.

EXAMPLES

2 °C to 8 °C	or	2 ... 8 °C	or	graphical symbol according to ISO 7000-0632
-18 °C or below	or	≤ -18 °C	or	graphical symbol according to ISO 7000-0533

Other conditions that affect stability, e. g. light or humidity, shall be mentioned.

Any other particular measures to be taken in the handling of the product shall be given (e. g "treat as fragile").

4.1.10 Warnings and precautions

If an IVD reagent is considered dangerous (e. g. chemical, radioactive or biological risk), the outer container shall be labelled with the appropriate danger symbol(s). If in the case of chemical hazards the IVD reagent is not accompanied with instructions for use giving appropriate risk and safety phrases, these phrases shall be given on the label of the outer container.

NOTE For chemical hazards labelling see [11].

4.2 Immediate container

4.2.1 General

The label for an immediate container shall give the information specified in 4.2.2 to 4.2.10 in legible characters and/or symbols. If the available space is too small for this purpose, the information may be reduced to 4.2.2, 4.2.3, 4.2.5, 4.2.6 and 4.2.10.

Information consisting of proper names and symbols does not require expression in multiple languages.

If the immediate container is also the outer container, the requirements for the label as specified in 4.1 apply.

4.2.2 Manufacturer

The name of the manufacturer shall be given. Alternatively, an unequivocal trade name or logo is sufficient.

4.2.3 Product name

The name shall ensure proper identification to the user of the product. Additionally, in a kit each component shall be identified by name, letter, number, symbol, colour or graphics in the same manner as described in the instructions for use or on the outer container.

4.2.4 Microbiological state

If necessary for proper performance of the IVD reagent, the microbiological state or state of cleanliness, e. g "microbiologically controlled" or "sterile", shall be given.

4.2.5 Batch code

A batch code shall be given.

NOTE The graphical symbol as given in EN 980 should be used.

4.2.6 Expiry date

An expiry date based upon the stated storage instructions shall be given. This shall be expressed as the year, the month, and, where relevant, the day in that order. In the case of year and month this means that the expiry date is the last day of the month indicated.

NOTE 1 The graphical symbol as given in EN 980 should be used.

NOTE 2 The format for the expiry date should be either "CCYY-MM-DD" or "CCYY-MM".

4.2.7 Contents

The content in terms of e. g. mass, volume, volume after reconstitution and/or the number of measurements shall be given.

4.2.8 Intended purpose

The in vitro use of the reagent shall be indicated.

NOTE A graphical symbol for in vitro diagnostic medical device should be used[1)].

4.2.9 Storage and handling information

The storage conditions necessary to assure the stability of the product in the unopened state shall be indicated. Recommended storage temperature intervals shall be given.

EXAMPLES

2 °C to 8 °C	or	2 ... 8 °C	or	graphical symbol according to ISO 7000-0632
- 18 °C or below	or	≤ - 18 °C	or	graphical symbol according to ISO 7000-0533

Any other particular measures to be taken in the handling of the product shall be given (e. g "treat as fragile").

4.2.10 Warnings and precautions

If an IVD reagent is considered dangerous (e. g. chemical, radioactive or biological risk) the immediate container shall be labelled with the appropriate danger symbol(s).

NOTE For chemical hazards labelling see [11].

[1)] See page 6.

5 Requirements for instructions for use

5.1 General

IVD reagents shall be accompanied by instructions for use. These instructions may alternatively be given on the outer container or in an operational manual which, together with the instructions for use of an instrument or of other parts of the analytical system, allow the user to safely and properly carry out the procedure.

If an IVD reagent is not accompanied by detailed instructions, the information given shall make reference to the correct version of instructions provided in another manner. However, the minimum information provided together with the IVD reagent shall cover all aspects of safe handling and storage prior to its use.

Complete instructions for use may be supplied as part of the built-in software of a dedicated analytical system or by electronic means. Parts of the instructions for use can be given in a coded format, e. g. barcode or chip, and be explained in the manual of the analytical system.

NOTE Immediate access of the user to the complete instructions for use can be ensured by means of an electronic databank (Internet) or a free of charge return telefax system (polling).

If symbols and identification colours used on labels do not conform to European or International Standards, such symbols and identification colours shall be explained in the instructions for use.

Languages shall be used in accordance with the requirements of the countries in which the IVD reagent is distributed.

5.2 Manufacturer

The name and address of the manufacturer shall be given.

NOTE The manufacturer is the entity which has taken legal responsibility for the IVD reagent.

The name and address of the authorized representative shall also be given when this is a legal requirement.

5.3 Product name

The product name as specified in 4.2.3 shall be given.

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

5.4 Microbiological state

If necessary for the proper performance of the IVD reagent, the microbiological state or state of cleanliness, e. g. microbiologically controlled or sterile, shall be given.

5.5 Intended purpose

The intended purpose shall be given.

EXAMPLES
— Measurement of glucose concentration in serum,
— measurement of thromboplastin time.

5.6 Warnings and precautions

If a danger or hazard (e. g chemical, radioactive or biological) is associated with an IVD reagent or with its use, any special warnings and precautions shall be stated.

> NOTE For chemical hazards provisions see [9] to [11]. The information to be reported on the safety data sheet according to EU Directive 91/155/EEC can be included in this section of the instructions for use.

Where an IVD reagent includes substances of human or animal origin, a warning shall be given concerning their potentially infectious nature taking into account the risk posed by the nature or amount of the substances.

Possible risks resulting from misuse which may be reasonably anticipated shall also be indicated. If appropriate, information on the safe handling and disposal of materials used shall be given.

5.7 Composition

The nature and amount or concentration of the active ingredients in the IVD reagents shall be given as well as information on other ingredients that may influence the measurement (e. g. stabilizers, type of organism, host system).

In the case of a kit, the components shall be designated in the same way as on the immediate containers as specified in 4.2.3.

When possible, quantities shall be expressed in units according to ISO 1000.

5.8 Storage and shelf life after first opening

The storage conditions and shelf life following the first opening of the immediate container, together with the storage conditions and stability of working reagents shall be given, if different from those stated in 4.1.6, 4.1.9, 4.2.6 and 4.2.9.

5.9 Additional special equipment

Any special equipment required for proper performance and/or safe use but not necessarily provided shall be listed; information necessary to enable that special equipment to be identified for proper use shall be given.

5.10 Specimen

The type of specimen to be used and any special conditions of collection, pretreatment and, if necessary, storage conditions as well as instructions for the preparation of the patient shall be given.

5.11 Procedure

A detailed description of the procedure to be followed, which can be clearly understood by the operator, shall be provided.

5.12 Methodology

5.12.1 Principle of the method

Information on the principle of the method indicating the type of reaction (e. g. chemical, microbiological or immunochemical) and a description of the indicator or detection system shall be given.

5.12.2 Performance characteristics and limitations of the method

The specific analytical performance characteristics (e. g. analytical sensitivity, analytical specificity, trueness, repeatability, reproducibility, limits of detection and measurement interval, including information needed for the detection of known relevant interferents) and the limitations of the method shall be described. Where appropriate, information on the diagnostic sensitivity and specificity shall be given taking account of the intended use of the results in the diagnostic procedure.

5.12.3 Reagent preparation

All required aspects of reagent preparation including reconstitution, incubation and dilution shall be described.

5.13 Calculation of analytical results

The mathematical approach and if appropriate the name and version number of the computer programme upon which calculation of the analytical results is made shall be given.

When possible, results shall be expressed in units according to ISO 1000.

5.14 Changes in the procedure and in the performance

It shall be ensured that the user is informed of any substantial changes in the procedure and/or analytical performance of the IVD reagent and of measures to be taken in this event.

5.15 Internal quality control

Suitable procedures for internal quality control shall be given including a means for the user to establish criteria for assessing the validity of the measurement procedure.

5.16 Traceability of calibrators and control materials

Information shall be given on the metrological traceability of the values assigned to calibrators and control materials, referring to available reference materials of higher order (e. g. WHO[1)]), or International or European reference materials), or literature or other available documents or source of reference material.

5.17 Reference intervals

If known, the reference intervals and, where significant, a description of the reference population or a pertinent literature reference shall be given.

When possible, reference intervals shall be expressed in units according to ISO 1000.

5.18 Literature references

Literature references shall be given if applicable, e. g. for reference intervals.

5.19 Date of issue or revision

The date of issue or latest revision of the instructions for use shall be given.

[1)] World Health Organization

Annex ZA (informative)

Relationship of this document with EC Directives

This European Standard has been prepared under a mandate given to CEN/CENELEC by the European Commission and the European Free Trade Association, and supports essential requirements of the EC Directive 98/79/EC.

> **WARNING**: Other requirements and other EU Directives **may** be applicable to the product(s) falling within the scope of this standard.

The following clauses of this standard, as detailed in Table ZA.1, are likely to support requirements of the Directive 98/79/EC.

Compliance with these clauses of this standard provides one means of conforming with the specific essential requirements of the Directive concerned and associated EFTA regulations.

Table ZA.1 — Correspondence between this European Standard and Directive 98/79/EC

Clauses/sub-clauses of this European Standard	Essential requirements of Directive 98/79/EC	Qualifying remarks/Notes
3.2	B.8.6	
3.3	B.8.6	
4.1.1	B.8.1, B.8.2	
4.1.2	B.8.4 (a)	
4.1.3	B.8.4 (b)	
4.1.4	B.8.4 (c)	
4.1.5	B.8.4 (d), B.8.6	
4.1.6	B.8.4 (e)	
4.1.7	B.8.4 (b)	
4.1.8	B.8.4 (g), B.8.5	
4.1.9	B.8.4 (h)	
4.1.10	B.8.3, B.8.4 (j)	
4.2.1	B.8.1, B.8.2	
4.2.2	B.8.4 (a)	
4.2.3	B.8.4 (b)	
4.2.4	B.8.4 (c)	
4.2.5	B.8.4 (d), B.8.6	
4.2.6	B.8.4 (e)	
4.2.7	B.8.4 (b)	
4.2.8	B.8.4 (g), B.8.5	

(continued)

Table ZA.1 — Correspondence between this European Standard and Directive 98/79/EC

(concluded)

Clauses/sub-clauses of this European Standard	Essential requirements of Directive 98/79/EC	Qualifying remarks/Notes
4.2.9	B.8.4 (h)	
4.2.10	B.8.3, B.8.4 (j)	
5.1	B.8.1, B.8.2	
5.2	B.8.7 (a)	
5.3	B.8.7 (a)	
5.4	B.8.7 (a)	
5.5	B.8.5, B.8.7 (a)	
5.6	B.8.3, B.8.7 (a), B.8.7 (n), B.8.7 (s)	
5.7	B.8.7 (b)	
5.8	B.8.7 (c)	
5.9	B.3.1, B.8.7 (e)	
5.10	B.8.7 (f)	
5.11	B.8.7 (g)	
5.12.1	B.8.7 (h)	
5.12.2	B.8.7 (d), B.8.7 (h)	
5.12.3	B.8.7 (h), B.8.7 (o)	
5.13	B.8.7 (i)	
5.14	B.8.7 (j),	
5.15	B.8.7 (k)	
5.16	B.8.7 (k)	
5.17	B.8.7 (l)	
5.19	B.8.7 (u)	

Bibliography

[1] EN 591, *Instructions for use for in vitro diagnostic instruments for professional use*

[2] EN 980, *Graphical symbols for use in the labelling of medical devices*

[3] EN 28601, *Data elements and interchange formats — Information interchange; representation of dates and times (*ISO 8601:1988 and technical corrigendum 1:1991*)*

[4] ISO 3534-1, *Statistics — Vocabulary and symbols — Part 1: Probability and general terms*

[5] ISO 3864, *Safety colours and safety signs.*

[6] ISO 5725-1, *Accuracy (trueness and precision) of measurement methods and results — Part 1: General principles and definitions*

[7] ISO 7000, *Graphical symbols for use on equipment – Index and synopsis*

[8] ISO 15223/DAM 1, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Amendment 1*

[9] Council Directive of 27 June 1967 (67/548/EEC) on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, OJ, 1967, No L 196.

[10] Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations, (99/45/EC), OJ, 1999, No L 200.

[11] Directive 1993/72/EC of 1 September 1993, modified, adapting to technical progress for the nineteenth time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (93/72/EC), OJ, 1993, L 258.

[12] Commission Directive of 5 March 1991 defining and laying down the detailed arrangements for the system of specific information relating to dangerous preparations in implementation of Article 10 of Directive 88/379/EEC (91/155/EEC), OJ, 1991, No L 76

[13] Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices, OJ, 1998, No L 331

[14] International Vocabulary of Basic and General Terms in Metrology, 2nd edition, Geneva, ISO, 1993

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