SLOVENSKI STANDARD
SIST EN 1619:1999

01-december-1999

Biotehnologija - Procesi in proizvodnja v industrijskem obsegu - Splošne zahteve za vodenje in organizacijo v postopkih shranjevanja sevov

Biotechnology - Large-scale process and production - General requirements for management and organization for strain conservation procedures

Biotechnik - Verfahren im Großmaßstab und Produktion - Allgemeine Anforderungen für Verwaltung und Organisation bei Verfahren zur Stammkonservierung

Biotechnologie - Procédé a grande échelle et production - Exigences générales de gestion et d'organisation pour les procédures de conservation des souches

Ta slovenski standard je istoveten z: **EN 1619:1996**

ICS:

07.080 Biologija. Botanika. Zoologija Biology. Botany. Zoology

SIST EN 1619:1999 **en**

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN 1619

July 1996

ICS 07.100.00

Descriptors: biotechnology, reproduction (biology), culture (biology), micro-organisms, designation, preservation, hazards, management, organization, storage

English version

Biotechnology - Large-scale process and production - General requirements for management and organization for strain conservation procedures

Biotechnologie - Procédé à grande échelle et production - Exigences générales de gestion et d'organisation pour les procédures de conservation des souches

Biotechik - Verfahren im Großmaßstab und Produktion - Allgemeine Anforderungen für Verwaltung und Organisation bei Verfahren zur Stammkonservierung

This European Standard was approved by CEN on 1996-05-02. CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration.

Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the Central Secretariat or to any CEN member.

The European Standards exist in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the Central Secretariat has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and United Kingdom.

CEN

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 233 "Biotechnology", the secretariat of which is held by AFNOR.

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 January 1997, and conflicting national standards shall be withdrawn at the latest by January 1997.

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

Introduction

This European Standard covers a wide area of applications of biotechnology. This European Standard supports industrial activities in the area of biotechnology covering both natural microorganisms and genetically modified microorganisms (GMMs) including both non-pathogenic and pathogenic microorganisms (see annex B [1], [2]).

NOTE : Non-genetically modified microorganisms include natural microorganisms and microorganisms improved by traditional techniques.

In order to obtain reproducible results, cell banks (master cell bank and working cell bank) of microorganisms chosen for production of a particular product are established.

1 Scope

This European Standard specifies general requirements for management and organization of procedures for conservation of microorganisms used for large-scale process and production. It is intended to secure safe handling and also to ensure that reproducible results are obtained in biotechnology processes.

This European Standard specifies methods of handling and preservation of microbial strains or cell lines obtained from animals, plants and viruses in order to get reproducible and safe cultivation processes for the industrial production of substances.

NOTE : Attention is drawn to the existing national regulations concerned with the handling of microorganisms.

This European Standard is applicable to microorganisms.

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.

prEN 12128 Biotechnology - Laboratories for research, development and analysis - Containment levels of microbiology laboratories, areas of risk, localities and physical safety requirements

3 Definitions

For the purposes of this standard, the following definitions apply :

3.1 characterization

Description of a number of properties of microorganisms according to EN 1619.

3.2 lyophilization

Preservation by freezing and dehydration under vacuum.

3.3 master cell bank (MCB)

Stock of cells from which all subsequent cell banks are derived.

NOTE 1 : MCB stock is not normally intended for use directly in production.

NOTE 2 : The term MCB covers all type of cells, i.e. microorganisms as defined in EN 1619.

3.4 microorganism

Any microbiological entity, cellular or non cellular, capable of replication or of transferring genetic material.

NOTE : The term microorganism covers the term of biological agent, according to the Directive 90/679/EEC : microorganisms, including those which have been genetically modified, cell cultures and human endoparasites which may be able to provoke any infection, allergy or toxicity.

3.5 pathogenicity

Ability to cause disease.

3.6 probe ; gene probe

Specific nucleic acid sequence used to identify certain DNA or RNA fragments by means of hybridization.

NOTE : The gene probe is labelled in a way that permits detection, e.g. by radioactivity.

3.7 stability

Ability of microorganisms to survive during storage while retaining initial characteristics such as expression of a marker or synthesis of a desired product.

3.8 working cell bank (WCB)

Stocks of cells derived from the master cell bank (MCB), which are used for inoculation.

NOTE : The term WCB covers all type of cells, i.e. microorganisms as defined in EN 1619.

4 Development of master and working cell banks

When a production strain has been developed by natural selection, any type of mutation, or by genetic engineering, a master cell bank (MCB) shall be established and shall be preserved by a defined or validated procedure (see clause 6).

When the MCB has been established a working cell bank (WCB) shall be established. Before this is used in industrial production, it should be characterized with the appropriate degree of scrutiny.

The stability of a microorganism used in large-scale processes requires that the properties of this microorganism with regard to safety and its production value are stable when preserved as MCB or WCB as well as when used under fermentation conditions. In the latter case it should be shown not to change characteristics under prolonged normal fermentation conditions unless it is the normal life cycle of the microorganism under the culture conditions used.

NOTE : General quality standards such as EN ISO 9000 series (see annex B [4]) may be used to ensure control of MCB and WCB quality. This should also ensure through adequate documentation that the control procedures are applied.

5 Classification of microorganisms

The microorganism shall be classified according to its degree of hazard to people, animals, plants and/or the environment. This classification shall be used in the risk assessment which determines the containment level required.

NOTE 1 : Annex A gives a common basis for classification.

NOTE 2 : European (see annex B [3]) and/or national lists of classification should be a primary source of information.

NOTE 3 : Genetically modified microorganisms are assessed according to the criteria listed in the Directive 90/219/EEC, Annex III (see annex B [1]).

6 Preservation

A defined or validated method of preservation shall be adopted.

NOTE 1 : Depending on survival and stability, the cell bank can be preserved lyophilized or kept frozen at - 70 °C or lower temperature (e.g. liquid nitrogen) in an appropriate medium.

NOTE 2 : A range of other procedures which may be also appropriate exist.

7 Characterization

In order to identify the microorganism, a wide range of procedures may be used to characterize it. The ones selected will depend on the microorganism's identity.

NOTE 1 : The following parameters should be determined where appropriate :

a) history of the strain or cell-line, e.g. origin, source, when and where first characterized and taxonomic description, and whether modified ;

b) physical description, e.g. microscopic and colonial morphology, Gram reaction, motility, spore formation (present or not) ;

c) physiological parameters, e.g. temperature (optimum), pH (optimum), aerobic, anaerobic and other gas atmosphere requirements ;

d) biochemical and molecular markers and/or properties tested by relevant available tests ;

e) nutritional requirements : nitrogen, carbon, and other energy sources, growth factors, vitamins, minerals (if known) ;

f) gene probes for specific factors ;

g) freedom from adventitious agents : cell lines should not contain unwanted viruses or mycoplasma ; bacteria should not contain unwanted phages.

NOTE 2 : Genetically modified microorganisms should be further characterized with reference to gene elements inserted on plasmids or on the chromosome, according to relevant national, European or international regulations.

8 Handling and storage

8.1 Preparation of cell banks (MCB and WCB)

a) microorganisms shall be stored in appropriate vials (tube, ampoule or flask) ;

b) each vial shall be clearly identified and this shall enable the user as appropriate to determine the content, production date, expiration date and reference number and category ;

NOTE : In order to avoid accidental loss, all cell banks should be stored in at least two different storage (freezing, etc.) units. These should, if possible, be located in separate rooms or buildings. The vials should be stored in containers inside the locked storage unit, which is accessible only to authorized individuals.

c) microorganisms shall be stored in containers or controlled areas appropriately designed for the containment level as indicated by risk assessment. If a secondary storage unit is used outside the required containers, this shall be in accordance with national and European regulations ;