SLOVENSKI STANDARD
SIST EN 12075:1999

01-december-1999

Biotehnologija - Procesi in proizvodnja v industrijskem obsegu - Fermentacijski in zaključni procesi

Biotechnology - Large-scale process and production - Procedures for fermentation and downstream processes

Biotechnik - Verfahren im Großmaßstab und Produktion - Vorgehensweise für die Bereiche Fermentation und Aufarbeitung

Biotechnologie - Procédé a grande échelle et production - Procédures pour les procédés de fermentation et de traitement aval

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English version

Biotechnology - Large-scale process and production - Procedures for fermentation and downstream processes

Biotechnologie - Procédé à grande échelle et production - Procédures pour les procédés de fermentation et de traitement aval

Biotechnik - Verfahren im Großmaßstab und Produktion - Vorgehensweise für die Bereiche Fermentation und Aufarbeitung

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CEN

European Committee for Standardization
Comité Européen de Normalisation
Europäisches Komitee für Normung

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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of an identical text or by endorsement, at the latest by August 1997, and conflicting national standards shall be withdrawn at the latest by August 1997.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 supports industrial activities in the area of biotechnology covering operations with both non-genetically modified microorganisms and genetically modified microorganisms (GMMs), with both non-pathogenic and pathogenic microorganisms (see annex A [1], [2]).

Fermentation processes vary widely in their nature and design. Generally prokaryotic or eukaryotic microorganisms, plant cells, mammalian cells or insect cells are cultivated and processed in such a way as to produce a desired end-product such as biomass, pharmaceuticals, additives, metabolites and foodstuffs.

1 Scope

This European Standard specifies the principles for the assessment and selection of fermentation and downstream operations so that they are carried out in a manner which ensures the safety of personnel, the environment and product and contributes to product quality.

This European Standard is intended for use by those designing and/or operating processes and by other interested parties.

Unit operations are not described in detail and individual production processes can require specific equipment or unit operations which are not described here.

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 12460 Biotechnology - Large-scale process and production - Equipment implementation according to the degree of hazard

prEN 12461 Biotechnology - Large scale process and production - Guidance for the handling, inactivating and testing of waste

3 Definitions

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

3.1 bioaerosol

Colloid dispersed solid or liquid particles in a gaseous environment presenting negligible gravitational settling, containing microorganisms.

3.2 biocontamination

Presence of undesired microorganisms.

3.3 closed system

System where a barrier separates microorganisms/organisms from the environment. [EN 1620]

3.4 controlled area

Area constructed and/or operated in such a manner as to limit contamination of the other areas by microorganisms/organisms from within the controlled area [EN 1620].

3.5 downstream process

Sequence of operations following the fermentation.

3.6 fermentation

Biotechnical process where the target product is formed while cultivating the process microorganism(s) [EN 1620].

3.7 fermenter

Closed or open vessel where a culture of microorganisms is grown under controlled conditions.

3.8 hazard

Intrinsic potential property or ability of something (e.g. any agent, equipment, material or process) to cause harm [EN 1620].

NOTE : Harm is an injury or damage to health of people and/or to the environment.

3.9 inactivation

Destruction of microorganisms.

3.10 master cell bank (MCB)

Stock of cells from which all subsequent cell banks are derived [EN 1619].

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 3.11.

3.11 microorganism

Microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material [EN 1619].

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.

3.12 pathogen

Microorganism causing disease [EN 1620].

3.13 physical containment

System for confining a microorganism/organism or other entity within a defined space [EN 1620].

3.14 process microorganism

Microorganism used for production purposes in a biotechnological process or constituting (part of) the product itself.

3.15 risk

Probability of occurrence of a hazard causing harm and the degree of severity of the harm.

3.16 sterilization

Validated process used to reach a state free from viable microorganisms.

NOTE : In a sterilization process, the nature of microbiological death or reduction is described by an exponential function. Therefore, the number of microorganisms that survive a sterilization process can be expressed in terms of probability. While the probability can be reduced to a very low number, it can never be reduced to zero.

3.17 unit operation

Operation to perform a single chemical, physical or mechanical activity.

NOTE 1 : Examples of unit operations are heat transfer, mixing, separating including filtration and centrifugation, and sterilization.

NOTE 2 : Combinations of unit operations constitute a process step. For example, downstream process step could consist of separation, extraction, concentration and drying.

3.18 waste

By-product arising from a process or unwanted substance or article derived from any activity.

NOTE : Examples of waste are scrap material, effluent, unwanted residue or surplus arising from any process or activity or any substance or article which is discarded or to be disposed of as being broken, contaminated, spoiled, or worn out.

3.19 working cell bank (WCB)

Stocks of cells derived from the master cell bank (MCB), which are used for inoculation [EN 1619]

NOTE : The term working cell bank covers all type of cells i.e. microorganisms as defined in 3.11.

4 Process description

4.1 General

Fermentation and downstream processes consist of a number of unit operations linked together to produce a product. There is a wide range of unit operations and a general schematic diagram is shown in figure 1. The unit operations can be categorized into process steps which are described in 4.2 to 4.5.

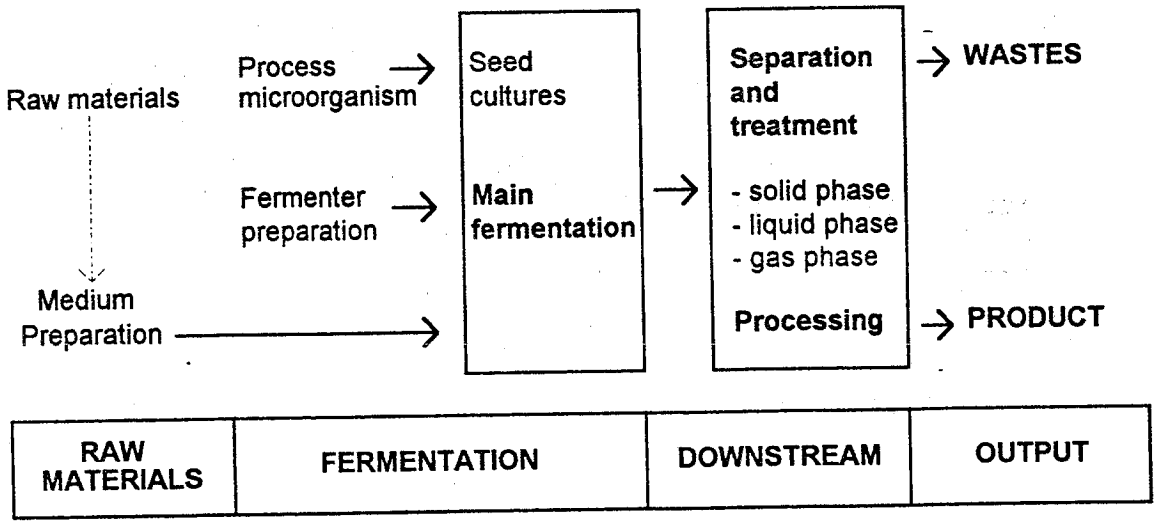

Figure 1 : Schematic diagram of a biotechnological manufacturing process