SLOVENSKI STANDARD
SIST EN 12297:1999

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Biotehnologija – Oprema - Navodilo o preskusnih postopkih za ugotavljanje sterilnosti

Biotechnology - Equipment - Guidance on testing procedures for sterilizability

Biotechnik - Geräte und Ausrüstungen - Leitfaden für Verfahren zur Prüfung der Sterilisierbarkeit

Biotechnologie - Equipement - Guide des procédures d'essai pour le contrôle de la capacité a la stérilisation

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ICS

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English version

Biotechnology - Equipment - Guidance on testing procedures for sterilizability

Biotechnologie - Equipement - Guide des procédures d'essai pour le contrôle de la capacité à la stérilisation

Biotechnik - Geräte und Ausrüstungen - Leitfaden für Verfahren zur Prüfung der Sterilisierbarkeit

This European Standard was approved by CEN on 2 March 1998.

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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of an identical text or by endorsement, at the latest by September 1998, and conflicting national standards shall be withdrawn at the latest by September 1998.

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 European Standard gives guidance on general testing procedures to assess the sterilizability for microorganisms of equipment (components and units of equipment) used in biotechnological processes.

This European Standard gives guidance on the assessment of the sterilizability of biotechnological equipment with respect to a release of process microorganisms that can affect the safety of the worker (occupational health) and/or that can have adverse effects to the environment.

This European Standard is applicable to plants or components, such as valves and fittings, tanks, pumps, piping, separating and filling devices as well as instrumentation in contact with process fluids.

This European Standard applies if the intended use of the equipment includes hazardous or potentially hazardous microorganisms.

This European Standard is not applicable to testing for sterility of media and equipment prior to processing or operation, respectively.

NOTE 1 : For disinfection of external surfaces such as walls, working benches and floors, attention is drawn to national and European Standards.

NOTE 2 : For sterilization of equipment and media in autoclaves attention is drawn to national and European standards such as EN 285 and EN 554 (see annex C [21], [22]).

2 Definitions

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

2.1 component of equipment

Technical entity which forms part of a unit of equipment.

NOTE : Examples of components of equipment are vessels, valves and sensors.

2.2 direct test method (in biotechnology)

Test method which employs microorganisms for quantification.

2.3 indirect test method (in biotechnology)

Test method which employs physical and/or chemical means for quantification.

2.4 microorganism

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

NOTE : For the purposes of this standard, 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.

2.5 process microorganism

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

2.6 sterile

State of being free from viable microorganisms.

NOTE 1 : In practice no such absolute statement regarding the absence of viable microorganisms can be proven. However, sterile conditions can be regarded as established by using an accepted or recognized method of sterilization.

NOTE 2 : The process of inactivation of viable microorganisms during a sterilization procedure is usually described by an empirical mathematical function, commonly an exponential function. By their mathematical nature, such functions can be reduced to very low numbers, but not to zero. However, these empirical functions can be applied to control or assess the process parameters of a sterilization procedure to realize a desired degree of inactivation of viable microorganisms.

2.7 sterilizability

Ability of components of equipment, units of equipment or plants to be made sterile.

2.8 sterilization

Process used to reach a sterile state.

2.9 Sterilizing In Place (SIP)

Sterilization without opening or dismantling of components of equipment and/or unit of equipment.

2.10 target microorganism

Process microorganism and/or other microorganisms relevant for the specific process.

NOTE : For safety testing procedures, non-pathogenic microorganisms should be used where possible.

2.11 unit of equipment

Assembly of components used to perform one or more unit operations.

3 Testing

3.1 General

Testing procedures for sterilizability are required to verify whether equipment can be sterilized, so that potential risks to occupational health and/or the environment are eliminated. In particular it should be established that, for example, for maintenance work the utilized microorganisms are inactivated to such a degree that no harm results to maintenance staff or to the environment from residual process microorganisms. Testing procedures should be designed to ensure that relevant information on sterilizability can be obtained.

3.2 Methodology

To determine the sterilizability of plant and equipment choose and specify an appropriate test method or combination of test of methods (see annexes A and B) :

a) specify an appropriate indicator related to the proposed use of the equipment ;

b) select the analytical procedure to be used to determine the quantity of this indicator which is present in the equipment or plant. The appropriate biological indicator is preferably not harmful for the worker and/or the environment ;

c) specify a sterilization protocol including, as a minimum, the specification of the sterilizing agent and the mode of application ;

NOTE 1 : Potential hazard to the operator during sterilization should be assessed.

NOTE 2 : Factors such as duration, temperature and dose should be included into the protocol.

3.3 Testing procedure

Carry out the testing procedures as follows :

a) load the equipment or plant with the indicator under conditions representative of conditions during processing ;

b) using the analytical procedure defined in 3.2, determine the quantity of indicator substance present at the time at which sterilization procedures would be applied ;

c) apply the sterilization protocol specified in 3.2 to the plant or equipment being tested for sterilizability ;

d) using the analytical procedure selected in 3.2, determine the quantity of indicator present in the equipment or plant after application of the sterilization protocol ;

e) using the data obtained, express the sterilizability of the equipment or plant ;

f) determine the appropriate sterilizability class to the equipment under test as described in the equipment standards with respect to the chosen indicator and sterilization protocol.

3.4 Choice of test methods

If the results of the test method should be quickly available and with a limited amount of work involved in sterilizability demonstration runs, indirect test methods should be used. Indirect test methods may however only be applied if a validated correlation between the measured effect and the desired performance has been shown.

When direct test methods are used, they should be carried out using appropriate controls in order to eliminate false positive results as a consequence of incorrect handling of the samples. This means that parallel to the test sample preparation another culture tube is handled in the same way as the original sample but without inoculation as well as the inclusion of media samples which are sterilized by a validated sterilization.

3.5 Direct test methods

The validation of a sterilization cycle can be done by analysis of an undiluted sample of the sterilized process medium and by performing microbiological challenge tests. Microbiological challenge tests are usually carried out by filling the equipment or component to be investigated to a representative volume with a suitable medium and adding indicator microorganisms. This type of testing procedure is required if the indicator or process microorganism(s) which is to be detected is present around or even below the detection limit of the test method of choice. A reliable reduction rate of indicator microorganism can be determined whenever the number of colony forming units which can be detected is high enough to allow the determination of statistically reliable inactivation kinetics, for example depending on the evaluation method 100 to 1000 colony forming units/ml are required.

NOTE : Preferably an immobilized indicator microorganism should be used.

The efficacy of a heat sterilization is proved by the absence of process or indicator microorganisms. Examples of appropriate indicator microorganisms are given in the references listed in annex C [1] to [4], [9] to [12], [14]. The type of microorganism to be selected as indicator microorganism depends on the characteristics of the process microorganism and should be representative for a worst case situation.

The choice of a specific indicator microorganism should ensure that the degree of sterilization is measurable within a certain period of time during the sterilization procedure. In order to comply with these boundary conditions for gas sterilization procedures, e.g. ethylene oxide or formaldehyde, representative indicator microorganism(s) should be selected (see annex C [3], [4], [14]).

Test sets with immobilized indicator microorganisms, which can be prepared in laboratories or purchased, should be placed at relevant places inside the equipment. The appropriate places for indicator microorganisms should be identified either by suitable test methods or by risk assessment, Hazard Analysis Critical Control Points (HACCP) or Hazard and Operability studies (HAZOP). An example of a microbial challenge test method is given in annex C [7].

3.6 Indirect test methods

Indirect test methods can be applied when direct test methods are not available or inappropriate. They can be validated by a direct test methods with respect to two dominating physical and/or chemical parameters which are time of treatment and the required temperature or dose. These two parameters should be monitored inside a defined unit(s) of equipment at the places which are identified to show the worst sterilization conditions either by direct test methods or risk analysis.

4 Documentation

The equipment manufacturer/supplier and/or the user should establish and document the testing procedure(s) used for the assessment of the sterilizability of the component or unit of equipment. This documentation should include the applied test conditions (test method, indicator and analytical procedure) and the results of the test.