SLOVENSKI STANDARD
SIST EN 12298:1999

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Biotehnologija – Oprema - Navodilo o preskusnih postopkih za ugotavljanje prepustnosti

Biotechnology - Equipment - Guidance on testing procedures for leaktightness

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

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Biotechnologie - Equipement - Guide des procédures d'essai pour le contrôle de l'étanchéité

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ICS

Descriptors: biotechnology, medical equipment, leaktightness, leak tests, contamination, micro-organisms, noxious micro-organisms, tests, safety, inspection, accident prevention, environmental protection, work safety

English version

Biotechnology - Equipment - Guidance on testing procedures for leaktightness

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

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Foreword

This European Standard has been prepared by the 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of an identical text or by endorsement, at the latest by september 1998, and conflicting national standards shall be withdrawn at the latest by september 1998.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

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

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This European Standard gives guidance on the assessment of the leaktightness 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.

2 Definitions

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

2.1 components 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.

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2.3 indirect test method (in biotechnology)

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

2.4 leakage

Egress from equipment

2.5 leak rate

Egress from equipment per unit of time.

2.6 leaktightness

Ability of component of equipment or unit of equipment to limit egress.

2.7 microorganism

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

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

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2.8 process microorganism

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

2.9 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.

2.10 unit of equipment

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

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3 Testing

3.1 General

The selection of a test method depends on a number of factors, including equipment size, pressurization ability and constraints on intrusion by test fluid. Guidance on selection of test methods is provided in annex A.

To achieve relevant information on leaktightness, the design of the test method should be based on an appropriate risk analysis.

NOTE 1 : It can be necessary for the test method to comprise one full cycle of the normal operation of the equipment. More operating cycles and/or extreme conditions such as highest pressure, highest rotational speed, range of temperature on repeated cycle basis can be required.

NOTE 2 : In case of overpressure, the equipment can be regarded as a pressure vessel. Appropriate European and national regulations should be followed.

The recommended test method for characterizing and comparing emissions of microorganisms from bioprocess equipment consists of measuring the leak rate. This enables equipment emissions to be compared independently of the microorganism concentration inside the equipment.

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As leakage can consist of aerosol and/or liquid, the leak rate comprises both liquid leak rates and aerosol leak rates.

If practicable from a technical and practical viewpoint direct test methods of determining leak rates are used since they are representative of the actual operating conditions. Indirect test methods are often more convenient in terms of speed, lack of contamination, economy, and ability for prolonged testing.

NOTE 3 : Data obtained from indirect methods should be correlated with the release of microorganisms. Currently, validated correlations are lacking. Until such validated correlations have been established, results from indirect test methods should be used in accordance with common practice.

NOTE 4 : Appropriate testing conditions for components of equipment are given in the relevant standards.

NOTE 5 : Additional information on test methods for leak testing can be obtained from annex C [12], [13], [14] and [15].

3.2 Methodology

To determine the leaktightness of plant and equipment, choose and specify an appropriate test method or combination of test 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 ;

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c) specify a pressurization protocol including time and pressure.

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

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 selected in 3.2, determine the quantity of indicator substance present at the time at which pressurization protocol would be applied ;

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

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

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

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

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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 leaktightness 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. The required correlations are prepared for each unit of equipment or component.

3.5 Direct test methods

3.5.1 Aerosol

An example of a direct test method of measuring the aerosol emission is quantitative bioaerosol monitoring. This can be carried out as described in 3.5.1.1 and 3.5.1.2.

3.5.1.1 *Preparation*

Quantitative bioaerosol monitoring is based on using the following :

a) characterized test microorganism preferably non-pathogenic ;

b) characterized capture method for aerosolised microorganism ;

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c) characterized detection method ;

d) controlled environment where a representative amount of air should be sampled over the test period ;

e) standardized microorganism concentration in a defined medium.

3.5.1.2 *Procedure*

Determine the leak rates for biotechnological equipment as follows :

a) ensure that the equipment under test is located in a controlled environment where emissions can be captured in a bioaerosol monitor ;

b) collect and assay a measurable quantity of microorganisms over a known sampling time in the bioaerosol monitor ;

c) calculate the airborne microorganism concentration within the controlled environment with the known volumetric sampling rate ;

d) calculate the emission rate from the airborne microorganism concentration multiplied by the total rate of removal of air from the controlled environment ;

e) calculate the leak rate by dividing the emission rate by the known microorganism concentration inside the equipment under test.

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NOTE : Details of methods and attributes are described by Behizad *et al.* (see annex C [3]) and Griffiths and DeCosemo (see annex C [4]).

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3.5.2 Liquid

Direct measurement of small flows of liquid leakage can be achieved semi-quantitatively by surface contact test methods such as swabbing and contact plates. In this case, estimates of the volume of carrier fluid are made. For larger leakage, liquid can be collected and the microorganism concentration determined. In this case also estimates of the volume of carrier fluid are made.

3.6 Indirect test methods

Indirect test methods can be used to determine the leak rate in aerosol or liquid form. If there are validated correlations to the release of microorganisms, these should be used and reported. In the absence of such correlations, the result of the indirect test method should be reported as a leak rate based on the test fluid or tracer used.

The following indirect test methods (see annex B) can be used for quantitative leaktightness measurement :

a) pressure stability test method with gas such as air, helium, sulphur hexafluoride (SF_6) tracer gas ;

b) pressure stability test method with liquid ;

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c) transmembrane gas diffusion and bubble point test method (filters only) ;

d) particle counting ;

e) tracer fluids ;

f) vacuum test method.

4 Documentation

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

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Annex A (informative)

Guidance on selection of test methods

A.1 General

Figures A.1 to A.4 give guidance for the selection of an appropriate test method for the equipment under test. At the bottom of each chart are numbers referring to the suggested test method(s). The test methods and their number are given in table A.1. The following clauses give information on the selection criteria. If several testing methods are available, one should be chosen with the help of BATNEEC (Best Available Technique Not Entailing Excessive Costs) *.

A.2 Performance classification (PC) or Operational Pre-Check (OPC)

PC refers to a situation ensuring that the equipment meets a specified performance standard. PC can be carried out by an equipment manufacturer or equipment customer (e.g. for commissioning of equipment).

OPC can be carried out by the user often after sterilization, cleaning, equipment maintenance or incident resulting in unplanned release to the workplace or the environment.

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A.3 Rapid results

Some test methods require time before the test results are available. This should not be a great problem for equipment testing generally, but can be a problem if a large number of components need to be tested in a reasonably short time.

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If rapid results are required, figure A.1 (PC), or figure A.2 (OPC) should be used. Otherwise figure A.3 (PC) or figure A.4 (OPC) should be used.

A.4 Equipment volume

The question of volume, in relation to equipment, is relatively arbitrary but it is an important consideration for certain test methods. For example, when pressure stability testing considerably more accurate results are obtained for small volumes. Also when testing with a gas such as helium, pressurising a large volume can be expensive.

A.5 Pressurization of equipment beyond its working pressure

Pressure is also an important consideration ; several of the test methods require the equipment to be pressurized above its normal working pressure with test pressures which are adjusted to the equation methods and the coefficients. The maximum permissible working pressure should not be exceeded.

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* Use of BATNEEC does not mean that financial issues moderate the degree of safety. Where several methods are available, the user can choose the most convenient, provided that it gives results of the necessary quality.