

Biotechnology — Equipment — Guidance on testing procedures for leaktightness

The European Standard EN 12298:1998 has the status of a
British Standard

ICS 07.080 07.100.01

NO COPYING WITHOUT BSI PERMISSION EXCEPT AS PERMITTED BY COPYRIGHT LAW

BSI
Documents



Document Sharing Hub

National foreword

This British Standard is the English language version of EN 12298:1998.
The UK participation in its preparation was entrusted to Technical Committee CII/58, Biotechnology, 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.

A British Standard does not purport to include all the necessary provisions of a contract. Users of British Standards are responsible for their correct application.

Compliance with a British Standard does not of itself confer immunity from legal obligations.

Summary of pages

This document comprises a front cover, an inside front cover, the EN title page, pages 2 to 15 and a back cover.

This British Standard, having been prepared under the direction of the Sector Board for Materials and Chemicals, was published under the authority of the Standards Board and comes into effect on 15 October 1998

© BSI 1998

ISBN 0 580 30069 2

Amendments issued since publication

Amd. No.	Date	Text affected

ICS

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

English version

Biotechnology — Equipment — Guidance on testing procedures for leaktightness

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

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

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

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.

This European Standard exists 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, Czech Republic, 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

© 1998 CEN All rights of exploitation in any form and by any means reserved worldwide for CEN national Members.

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.

Contents

	Page
Foreword	2
1 Scope	3
2 Definitions	3
3 Testing	3
4 Documentation	5
Annex A (informative) Guidance on selection of test methods	6
Annex B (informative) Testing procedures for leak rate	11
Annex C (informative) Bibliography	15

1 Scope

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.

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

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]

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.

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

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.

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;
- 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.

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 aerosolized microorganism;
- 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.

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

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 estimates of the volume of carrier fluid are also made.