SLOVENSKI STANDARD
SIST EN 12296:1999

01-december-1999

Biotehnologija – Oprema - Navodilo o preskusnih postopkih za ugotavljanje čistosti

Biotechnology - Equipment - Guidance on testing procedures for cleanability

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

Biotechnologie - Equipement - Guide des procédures d'essai pour le contrôle de la capacité au nettoyage

Ta slovenski standard je istoveten z: **EN 12296:1998**

ICS:

07.080 Biologija. Botanika. Zoologija Biology. Botany. Zoology

SIST EN 12296:1999 **en**

EUROPEAN STANDARD
NORME EUROPÉENNE
EUROPÄISCHE NORM

EN 12296

March 1998

ICS

Descriptors: biotechnology, medical equipment, cleaning, disinfection, contamination, micro-organisms, noxious micro-organisms, tests, safety, hygiene conditions, inspection, accident prevention, environmental protection, work safety

English version

Biotechnology - Equipment - Guidance on testing procedures for cleanability

Biotechnologie - Equipement - Guide des procédures d'essai pour le contrôle de la capacité au nettoyage

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

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

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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.

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of an identical text or by endorsement, at the latest by September 1998, and conflicting national standards shall be withdrawn at the latest by September 1998.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

Introduction

The cleaning of plant and equipment is an essential element of biotechnology processes in order to protect the safety of people and the environment and to avoid harmful operational effects through the accumulation of soil.

Testing procedures should be developed and documented to ensure that relevant information on cleanability is available. Standards (e.g. EN ISO 9000 series, see annex C [9]), guidelines (e.g. Good Manufacturing Practice (GMP) see annex C [10]) state general procedures of good practice which facilitate high quality manufacturing if followed. This European Standard refers to assessing the cleanability of equipment used in biotechnology, where additional specific requirements related to safety and to special features of biotechnological processes are required. It should be read in association with the more general standards and guidelines as mentioned above. In particular this European Standard states the principles on which test methodology is based. Informative guidance on selection of test methods is provided in annex A.

The extent to which it is necessary to remove soil from equipment and plant varies substantially with the process. In some cases abundant residues after cleaning do not harm people or the environment or do not cause difficulties in the process. In others very low residues are essential. The complete removal of soil on surfaces cannot be achieved, because for example all surfaces are adsorptive to some degree.

1 Scope

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

This European Standard applies primarily if the intended use of equipment includes the use of potentially hazardous microorganisms. This European Standard also applies to non-hazardous microorganisms and/or to residual soil which can adversely affect sterilization processes or which can cause cross-contamination of products or processes.

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

2 Definitions

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

2.1 clean

Condition of (a) product, surface, device, gases and/or liquids with residual soil below a defined threshold level.

2.2 cleanability

Ability to be made clean.

2.3 cleaning

Removal of soil.

2.4 Cleaning-In Place (CIP)

Cleaning without dismantling of components of equipment and/or unit of equipment.

2.5 components of equipment

Technical entity which forms part of a unit of equipment.

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

2.6 contamination

Presence of soil.

2.7 residual soil

Soil left after cleaning.

2.8 soil

Material, including microorganisms, metabolites and components of process media present on a surface.

2.9 unit of equipment

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

3 Testing

3.1 General

The requirements for cleanability vary with process, especially in relation to its assessed risk. Therefore cleanability classes for biosafety are defined in individual equipment standards. This will allow the manufacturers of plant and equipment to state the performance of their equipment using test methods, including visual inspection, developed according to the principles described in 3.2. It will also allow users of equipment to define their requirements in simple terms. These classes define performance only in relation to a defined indicator substance(s) and one or more defined cleaning protocol(s) and are relevant to the proposed use in the equipment. The cleanability class assigned to the equipment is likely to vary with the indicator and cleaning protocol chosen.

The soil adhering to surfaces at the end of a biotechnology process will contain many constituents. The indicator substance chosen to demonstrate the cleanability should be representative of those constituents that have an impact on safety aspects in relation to the need to protect people, the environment or features of the process. A brief description of indicators and test methods is given in annex B.

3.2 Methodology

To determine the cleanability 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 sampling procedure and the analytical procedure to be used to determine the quantity of this indicator which is present on relevant equipment surfaces or on surfaces in the plant ;

c) specify a cleaning protocol including, as a minimum, the specification of the constituents of the cleaning material and the mode of application.

NOTE 1 : Potential hazards to the operator during cleaning should be assessed.

NOTE 2 : Factors such as the duration, temperature and fluid flow rates of cleaning should be included in the protocol.

NOTE 3 : The cleaning protocol can consist of a number of successive operations.

3.3 Testing procedure

Carry out the testing procedures as follows :

a) load the equipment or plant with the indicator under normal operating conditions or in a way which simulates these ;

b) run the equipment and/or plant under normal or simulated-normal conditions until the load containing the indicator has been discharged from the equipment and the equipment and/or plant is ready to be cleaned ;

c) using the analytical procedure selected in 3.2, determine the quantity of indicator substance present after discharge of the load but before cleaning ;

d) apply the cleaning protocol specified in 3.2 to the plant or equipment being tested for cleanability ;

e) using the analytical procedure selected in 3.2, determine the quantity of indicator substance present on the relevant surface(s) of the equipment and/or plant after application of the cleaning protocol ;

f) using the data obtained, express the cleanability of the equipment or plant ;

g) determine the appropriate cleanability class to the equipment under test as described in the equipment standards with respect to the chosen indicator substance and cleaning protocol.

NOTE : The procedure described by European Hygienic Design criteria Group (EHEDG) (see annex C [2]) can be quoted as an example of the application of 3.2 above, in which the indicator substance is the spores of a specific bacterium, the analytical procedure is a culturing method which detects the number of this bacterium present before and after cleaning and in which the cleaning protocol is described (see annex C [3]).

Clearly other approaches can be used for the indicator substances could be another microorganism, a specific member of a chemical group such as a defined protein, carbohydrate or lipid, a specific compound known to be harmful to people or to the environment, or to future processing (see annex B). Potential cleaning protocols can be simple, for example a wash with water applied through a hosepipe or complex, as with sophisticated in-place cleaning involving the use of hazardous chemicals at high temperature.

Many test methods are possible, ranging from the use of a biological indicator to the use of chemical assays, immunological techniques, fluorescence assays and physical test methods, including microscopy (see annex B).

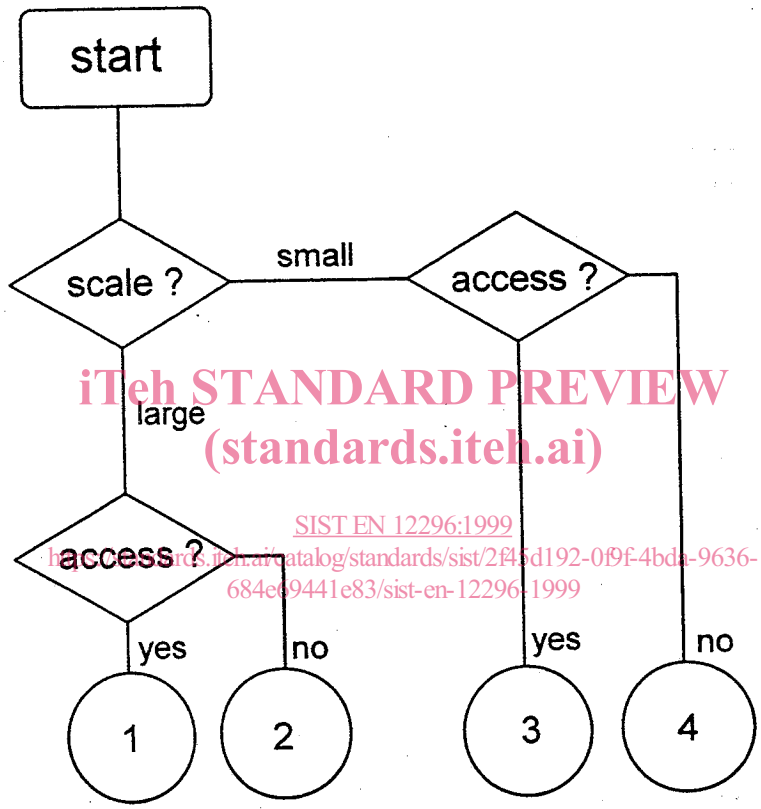
4 Documentation

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

Annex A (informative)

Selection guide on test methods for cleanliness

Figure A.1 gives guidance on the selection of test methods for cleanability. It represents a decision tree for selection of a cleanability test method based on scale, and access of the equipment.



1 rinse (see B.4), visual inspection (see B.2), swab (see B.3), optional
2 rinse, test following batch for contamination (see B.5)
3 rinse *, visual inspection, swab *
4 rinse, test following batch for contamination optional
* compare results, if they are consistent sample rinse-fluid only

Figure A.1 : Decision tree for selection of a cleanability test method.