BRITISH STANDARD

BS EN
1174-1 : 1996

Sterilization of medical devices —
Estimation of the population of micro-organisms on product

Part 1. Requirements

The European Standard EN 1174-1 : 1996 has the status of a British Standard

ICS 07.100.10;11.080

Committees responsible for this British Standard

The preparation of this British Standard was entrusted to Technical Committee CH/67, Sterilization of medical devices, upon which the following bodies were represented:

Association of British Health-Care Industries
Association of Contact Lens Manufacturers
Association of the British Pharmaceutical Industry
British Anaesthetic and Respiratory Equipment Manufacturers Association
British Surgical Trades Association
Central Sterilising Club
Department of Health
Department of Trade and Industry (National Physical Laboratory)
Hospital Infection Society
Institute of Sterile Services Management
Medical Sterile Products Association
Panel on Gamma and Electron Irradiation
Parenteral Society
Royal College of Pathologists
Royal Pharmaceutical Society of Great Britain
Sterilised Suture Manufacturers Association
Surgical Dressings Manufacturers Association

This British Standard, having been prepared under the direction of the Health and Environment Sector Board, was published under the authority of the Standards Board and comes into effect on
15 August 1996

Amendments issued since publication

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The following BSI references relate to the work on this standard:
Committee reference CH/67
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Contents

National foreword

This Part of BS EN 1174 has been prepared by Technical Committee CH/67 and is the English language version of EN 1174-1 *Sterilization of medical devices — Estimation of the population of micro-organisms on product — Part 1: Requirements*, published by the European Committee for Standardization (CEN).

Terms defined in clause **3** are italicized where they appear elsewhere in the text.

Cross-references

Publication referred to	Corresponding British Standard
EN ISO 9001 : 1994	BS EN ISO 9001 : 1994 *Quality systems. Model for quality assurance in design, development, production, installation and servicing*
EN 46001 : 1993	BS EN 46001 : 1994 *Specification for application of EN 29001 (BS 5750 : Part 1) to the manufacture of medical devices*

Note that the latest edition (1994) of EN 29004, mentioned in annex A, is numbered EN ISO 9004-1, the English language version of which is BS EN ISO 9004-1 : 1994.

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

EUROPEAN STANDARD
NORME EUROPÉENNE
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EN 1174-1

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Descriptors: Medical equipment, sterilization, quality, estimation, contamination, designation, micro-organisms, microbiological analysis, inspection

English version

Sterilization of medical devices — Estimation of the population of micro-organisms on product — Part 1: Requirements

Stérilisation des dispositifs médicaux — Estimation de la population de micro-organismes sur au produit —
Partie 1: Exigences

Sterilisation von Medizinprodukten — Schätzung der Population von Mikroorganismen auf Produkt —
Teil 1: Anforderungen

This European Standard was approved by CEN on 1996-01-18. 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.

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

Central Secretariat: rue de Stassart 36, B-1050 Brussels

Foreword

This European Standard has been prepared by Technical Committee CEN/TC 204, Sterilization of medical devices, the secretariat of which is held by BSI.

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 1996, and conflicting national standards shall be withdrawn at the latest by August 1996.

This European Standard has been prepared under a mandate given to CEN/CENELEC by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directives.

For relationship with EU Directive(s), see informative annex ZA, which is an integral part of this standard.

This European Standard consists of a series of standards. It includes the following parts:

EN 1174 *Sterilization of medical devices — Estimation of the population of micro-organisms on product*

Part 1: *Requirements*

Part 2: *Guidance*

Part 3: *Guide to the methods for validation of microbiological techniques*

This standard has been considered by CEN/TC 204 as one of a sequence of European Standards concerned with three common sterilization processes and their control. These standards are:

EN 550 *Sterilization of medical devices — Validation and routine control of ethylene oxide sterilization*

EN 552 *Sterilization of medical devices — Validation and routine control of sterilization by irradiation*

EN 554 *Sterilization of medical devices — Validation and routine control of sterilization by moist heat*

EN 556 *Sterilization of medical devices — Requirements for medical devices to be labelled 'STERILE'*

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.

Contents

Introduction

A sterile product item is one which is free of viable micro-organisms. The European Standards for *medical devices* require, when it is necessary to supply a sterile product item, that adventitious microbiological contamination of a *medical device* from all sources is minimized by all practical means. Even so, product items produced under standard manufacturing conditions in accordance with the requirements for quality systems for medical devices (see EN 46001 or EN 46002) may, prior to sterilization, have micro-organisms on them, albeit in low numbers. Such product items are non-sterile. The purpose of sterilization processing is to inactivate the microbiological contaminants and thereby transform the non-sterile items into sterile ones.

The inactivation of a pure culture of micro-organisms by physical and/or chemical agents used to sterilize *medical devices* often approximates to an exponential relationship; inevitably this means that there is always a finite probability that a micro-organism may survive regardless of the extent of treatment applied. For a given treatment, the probability of survival is determined by the number and resistance of micro-organisms and by the environment in which the organisms exist during treatment. It follows that the sterility of any one item in a population of items subjected to sterilization processing cannot be guaranteed and the sterility of the processed population of items is defined in terms of the probability of the existence of a non-sterile item in that population.

Requirements for the quality system for the design/development, production, installation and servicing of *medical devices* are given in EN 46001 and EN 46002 which supplement the EN ISO 9000 series of European Standards. The EN ISO 9000 series of standards designates certain processes used in manufacture as special if the results cannot be fully verified by subsequent inspection and testing of the product. Sterilization is an example of a special process because process efficacy cannot be verified by inspection and testing of the product. For this reason, sterilization processes need to be validated before use, the performance of each process monitored routinely and the equipment properly maintained.

European Standards specifying procedures for the validation and routine control of the processes used for the sterilization of *medical devices* have been prepared (see EN 550, EN 552 and EN 554). However, it is important to be aware that exposure to a properly validated and accurately controlled sterilization process is not the only factor associated with the provision of assurance that the product is sterile and, in this respect, suitable for its intended use. Indeed for the effective *validation* and routine control of a sterilization process, it is also important to be aware of the microbiological challenge which is presented to that process, both in terms of number, identities and properties of micro-organisms.

The pre-sterilization microbiological contamination is the sum of contributions from a number of sources: therefore it is important also to give attention to factors including the microbiological status of incoming raw materials and/or components, their subsequent storage and the control of the environment in which the product is manufactured, assembled and packaged.

The term *bioburden* is commonly used to describe the population of viable micro-organisms present on a material or *product*. It is not possible to determine the exact *bioburden* and therefore, in practice, a *viable count* is determined using a defined technique. Validation exercises are performed to relate this *viable count* to a *bioburden estimate* on a material or product by application of a *correction factor*.

The knowledge of the *bioburden* results from the investigation of microbiological contamination levels. *Bioburden* estimations are performed in a number of separate situations as part of the:

a) *validation* and *revalidation* of a sterilization process for which the extent of exposure to sterilizing conditions is to be directly related to the *bioburden estimate*;

b) *validation* and *revalidation* of a sterilization process for which the extent of exposure to sterilizing conditions is not to be directly related to the *bioburden estimate*, but for which a general knowledge of *bioburden* is required;

c) routine control of the manufacturing process for a sterile product for which sterilization *validation* was as stated in a) above;

d) routine control of the manufacturing process for a sterile product for which sterilization *validation* was as stated in b) above.

Bioburden estimations may also be employed as part of the quality system for the manufacture of *medical devices* as an element of:

e) an overall environmental monitoring programme;

f) the assessment of the efficacy of a cleaning process in removing micro-organisms;

g) the process monitoring for products which are supplied non-sterile but for which the microbiological cleanliness is specified;

h) the monitoring of raw materials, components or packaging.

The estimation of the *bioburden* of a *medical device* generally consists of four distinct stages:

– removal of micro-organisms from the *medical device*;

– transfer of these isolated micro-organisms to *culture conditions*;

– enumeration of the micro-organisms with subsequent characteristics;

– application of the *correction factor(s)* determined during *bioburden* recovery studies in order to calculate the *bioburden estimate* from the *pre-sterilization count*.

It is not possible to define a single technique to be used for the removal of micro-organisms in all situations because of the wide variety of materials for construction and design of *medical devices*. Furthermore, the selection of conditions for enumeration will be influenced by the types of contaminant which may be anticipated.

This part of the standard therefore specifies the general criteria to be applied to the estimation of *bioburden*. Parts 2 and 3 of this European Standard provide guidance on techniques which may be suitable in particular applications and methods which can be used for validating the techniques.

1 Scope

1.1 This Part of EN 1174 specifies general criteria to be applied in the estimation of the population of viable micro-organisms on a *medical device* or on a component, raw material or package. This estimation consists of both enumeration and characterization of the population.

NOTE 1. Prior to routine use, a technique for estimating the population of micro-organisms on *product* is validated. The level to which, during characterization, identification is necessary is dependent on the use to be made of the data generated.

NOTE 2. Parts 2 and 3 of this European Standard will provide guidance on selection of a technique and outline method(s) which may be used to validate the technique selected.

NOTE 3. A bibliography of useful standards is given in annex A.

1.2 This Part of EN 1174 is not applicable to the enumeration or identification of viral contamination.

1.3 This Part of EN 1174 is not applicable to the microbiological monitoring of the environment in which *medical devices* are manufactured (see note 1).

NOTE 1. Standards on environmental monitoring are being prepared by CEN/TC 243.

NOTE 2. Attention is drawn to the standards for quality systems (see EN 46001 or EN 46002) which control all stages of manufacture including the sterilization process. It is not a requirement of this standard to have a complete quality system during manufacture but certain elements of such a system are required and these are normatively referenced at appropriate places in the text.

2 Normative references

This Part of the European Standard incorporates by dated or undated reference, provisions from other publications. These normative references are cited in appropriate places in the text and the publications are listed hereafter. For dated references, subsequent amendments to or revision of any of these publications apply to this Part of this European Standard only when incorporated in it by amendment or revision. For undated references, the latest edition of the publication referred to applies.

EN ISO 9001 : 1994	*Quality systems — Model for quality assurance in design, development, production, installation and servicing* (ISO 9001 : 1994)
EN 46001 : 1993	*Quality systems — Medical devices — Particular requirements for the application of EN 29001*

3 Definitions

For the purposes of this Part of EN 1174, the following definitions apply.

3.1 bioburden

Population of viable micro-organisms on a *product* and/or a package.

3.2 bioburden estimate

Value established for the number of micro-organisms comprising the *bioburden*, by applying to a *viable count* or *pre-sterilization count* a factor compensating for the *recovery efficiency*.

3.3 correction factor

Numerical value applied to a viable count or *pre-sterilization count* to compensate for incomplete removal of micro-organisms from *product* and thus produce a *bioburden estimate*.

3.4 culture conditions

Stated combination of conditions, including the growth medium with the period and temperature of incubation, used to promote germination, outgrowth and/or multiplication of micro-organisms.

3.5 medical device

Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of

– diagnosis, prevention, monitoring, treatment or alleviation of disease;

– diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;

– investigation, replacement or modification of the anatomy or of a physiological process;

– control of conception;

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means [EN 46001 : 1993].

3.6 pre-sterilization count

Viable count obtained prior to sterilization.

3.7 product

Finished *medical device* or constituent(s) thereof, such as raw material, sub-assembly or intermediate device.

3.8 recovery efficiency

Measure of the ability of a specified technique to remove micro-organisms from *product*.

3.9 revalidation

Set of documented procedures to confirm an established *validation*.

3.10 validation

Documented procedure for obtaining, recording and interpreting the data required to show that a process will consistently comply with predetermined specifications.

NOTE. In the context of estimating the *bioburden*, the 'process' is the test methodology and the 'product' is the test result. The *validation* of a technique for *bioburden* estimation consists of a series of investigations to determine the effectiveness and reproducibility of the test method.

3.11 viable count

Number of micro-organisms estimated by growth of discrete colonies under the stated *culture conditions*.

NOTE. A discrete colony may not necessarily originate from a single viable micro-organism.

4 General

4.1 Documentation

4.1.1 Documented procedures and instructions on the testing techniques to be employed and on the use and operation of all relevant equipment shall be available. These procedures and instructions shall be approved on issue and shall be controlled as specified in **4.5** of EN ISO 9001 : 1994.

4.1.2 The procedures and instructions required by this Part of EN 1174 shall be implemented effectively.

4.1.3 Calculations and data transfers shall be subject to appropriate checks.

NOTE. If calculations are performed by electronic data processing techniques, the software should be validated prior to use and records of this *validation* should be retained.

4.1.4 Records of all original observations, calculations, derived data and final reports shall be retained as specified in **4.16** of EN ISO 9001 : 1994. The records shall include the identity of all personnel involved in sampling, preparation and testing.

4.2 Personnel

4.2.1 Responsibility for *bioburden* estimation shall be assigned to specific personnel as specified in **4.1.2.2** and **4.18** of EN ISO 9001 : 1994.

4.2.2 Training shall be performed in accordance with documented procedures. Records of the relevant qualifications, training and experience of technical personnel shall be maintained.

4.3 Equipment

4.3.1 All items of equipment required for correct performance of the specified tests and measurements shall be available.

4.3.2 All equipment requiring planned maintenance shall be maintained in accordance with documented procedures. Records of maintenance shall be retained.

4.3.3 An effective system shall be established, documented and maintained for the calibration of all equipment with measurement or control functions. This system shall comply with **4.11** of EN ISO 9001 : 1994.

4.4 Media and materials

Methods shall be established and documented for the preparation and sterilization of materials used in *bioburden* estimation, including appropriate quality tests.

NOTE. Appropriate quality tests should include growth promotion tests on batches of media or each batch of medium.

5 Selection of product

5.1 The procedures for selection and procurement of *product* for testing shall be established to ensure that the *product* is representative of routine production.

5.2 If a specified portion of *product* is to be used, it shall be selected to possess micro-organisms representative of the whole product. If it has been demonstrated that the micro-organisms are evenly distributed on *product*, the portion shall be selected from a random location. In the absence of such a demonstration, the portion shall be made up of pieces of *product* from a number of random locations.

6 Selection of technique

6.1 For an identified *product*, factors relevant to the efficiency of removal of viable micro-organisms from *product* shall be considered and recorded if such removal is part of the technique. Such factors shall include:

a) ability to remove microbiological contamination;

b) possible type(s) of contaminating micro-organism and their locations on *product*;

c) effect(s) of the removal method on the viability of microbiological contamination;

d) the physical or chemical nature of *product* to be tested.

6.2 If the physical or chemical nature of *product* to be tested (see d) of **6.1**) is such that substances can be released which would adversely affect either the number or the types of micro-organism detected, then a system to neutralize, remove or, if this is not possible, minimize the effect of any such released substance shall be used. The effectiveness of each system shall be demonstrated.

NOTE. Subsequent Parts of this European Standard will describe methods which can be used to assess the release of microbicidal or microbiostatic substances.

6.3 *Culture conditions* shall be selected after consideration of the types of micro-organism expected to be present. The results of this consideration and the rationale for the decisions reached shall be documented.

6.4 The selected technique shall be validated as specified in clause **7**.

7 Validation of technique

7.1 Each procedure for the *validation* of *bioburden* estimations shall be documented.

7.2 The *validation* procedures shall consist of the following steps:

a) assessment of the adequacy of the technique used to remove micro-organisms from the product, if such removal is part of the technique;

b) assessment of the adequacy of the technique used to enumerate removed micro-organisms, including microbiological counting techniques and *culture conditions*; and

c) establishment of the *recovery efficiency* of the method used in order that the *correction factor* can be calculated.

NOTE. Subsequent Parts of this European Standard will describe methods which can be used in the *validation* of techniques for *bioburden* estimation.

7.3 Any change in a routine method shall be assessed. This assessment shall include:

a) evaluation of the change;

b) establishment of the *recovery efficiency* of the revised method.

8 Revalidation

8.1 The *validation* data and any subsequent *revalidation* data shall be reviewed periodically and the extent of *revalidation* determined and documented. Procedures for the review of *validation* and *revalidation* shall be documented and records of the *revalidation* shall be retained.

8.2 A *revalidation* report shall be documented. The report shall be signed by the persons designated by the same functions/organizations that prepared, reviewed and accepted the original *validation* report.

9 Use of technique

9.1 *Pre-sterilization counts* shall be performed in accordance with documented sampling plan(s) with defined sampling frequency and sample size.

9.2 If contaminants that are not normally encountered are isolated during *pre-sterilization counts*, they shall be characterized. The potential effect of such contaminants on the manufacturing process, including the sterilization process, shall be considered and documented.

9.3 Acceptable limits for either *pre-sterilization counts* or *bioburden estimates* shall be established on the basis of previous data and documented. If these limits are exceeded, corrective action shall be undertaken as specified in **4.14** of EN ISO 9001 : 1994. Established limits shall be reviewed formally at defined intervals and revised if necessary.

9.4 The use of statistical methods to define sample size, sampling frequency and acceptable limits shall conform to **4.20** of EN ISO 9001 : 1994.

9.5 If *pre-sterilization counts* are to be used to determine the extent of treatment of a sterilization process (unless a requirement in a standard for the validation of the particular sterilization process specifies otherwise), then:

a) a *correction factor*, based on *recovery efficiency* as determined during *validation* (see **7.2**), shall be applied to the *pre-sterilization count* to calculate the *bioburden estimate* before the extent of treatment is determined; and

b) the resistance of the micro-organisms comprising the population present on *product* shall be considered in determining the extent of treatment.

NOTE. In applying microbiological data to establishing a sterilizing dose for sterilization by irradiation (see annex A of EN 552 : 1994), a *pre-sterilization count* can be used to select the verification and sterilizing doses.

9.6 If *bioburden estimates* have been used to determine the extent of treatment of the sterilization process:

a) consideration shall be given to the effect on the assurance of sterility if the acceptable limits are exceeded; and

b) the characterization of contaminants that are not normally encountered shall include an estimation of the resistance of those contaminants to the sterilization process.

The consequences in b) of the presence on *product* of contaminants with high resistance to the sterilization process on the assurance of sterility shall be considered.

All these considerations shall be documented and included in the determination of corrective action. This corrective action shall be in accordance with **4.14** of EN ISO 9001 : 1994.

9.7 Changes to *product* and/or processes shall be reviewed formally to determine whether they are likely to result in a change in the *bioburden* (see also **9.3**). The results of the review shall be documented. If a potential change in the *bioburden* is determined, specific *bioburden* estimations shall be performed to evaluate the effects of the change.

Annex A (informative)
Bibliography

EN 550 *Sterilization of medical devices — Validation and routine control of ethylene oxide sterilization*

EN 552 : 1994 *Sterilization of medical devices — Validation and routine control of sterilization by irradiation*

EN 554 *Sterilization of medical devices — Validation and routine control of sterilization by moist heat*

EN 556 *Sterilization of medical devices — Requirements for medical devices to be labelled 'STERILE'*

EN 724 *Guidance on the application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for non-active medical devices*

prEN 866-1 *Biological systems for testing sterilizers — Part 1: General requirements*

prEN 1174-2 *Medical devices — Estimation of the population of micro-organisms on product — Part 2: Guidance*

prEN 1174-3 *Medical devices — Estimation of the population of micro-organisms on product — Part 3: Guide to the methods for validation of microbiological techniques*

prEN 1632 *Cleanroom technology — Biocontamination control*

EN ISO 9002 *Quality systems — Model for quality assurance in production, installation and servicing (ISO 9002 : 1994)*

EN 29004 *Quality management and quality system elements — Guidelines*

EN 45001 *General criteria for the operation of testing laboratories*

EN 46002 *Quality systems — Medical devices — Particular requirements for the application of EN 29002*

Annex ZA (informative)

Clauses of this European Standard addressing essential requirements or other provisions of EU Directives

This European Standard has been prepared under a mandate given to CEN/CENELEC by the European Commission and the European Free Trade Association and supports essential requirements of EU Directives 90/385/EEC and 93/42/EEC.

WARNING. Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

The following clauses of this standard as detailed in table ZA.1 are likely to support requirements of the Directives 90/385/EEC and 93/42/EEC.

Compliance with the clauses of this standard provides one means of conforming with the specific essential requirements of the Directives concerned and associated EFTA regulations.

Table ZA.1 Correspondence between this European Standard and EU Directives

Clauses/subclauses of this European Standard	Corresponding essential requirements of Directive 90/385/EEC	Corresponding essential requirements of Directive 93/42/EEC
Clauses 4, 5, 6, 7, 8 and 9	I.1	I.1

List of references

See national foreword.

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389 Chiswick High Road
London
W4 4AL