SLOVENSKI STANDARD
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Čiste sobe in podobna nadzorovana okolja - Kontrola biokontaminacije

Cleanrooms and associated controlled environments - Biocontamination control

Reinräume und zugehörige Reinraumbereiche - Biokontaminationskontrolle

Salles propres et environnements maîtrisés apparentés - Maîtrise de la biocontamination

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13.040.35	Brezprašni prostori in povezana nadzorovana okolja	Cleanrooms and associated controlled environments

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Cleanrooms and associated controlled environments -- Biocontamination control

Salles propres et environnements maîtrisés apparentés - Maîtrise de la biocontamination

Reinräume und zugehörige Reinraumbereiche - Biokontaminationskontrolle

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If this draft becomes a European Standard, 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.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
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European foreword

This document (prEN 17141:2017) has been prepared by Technical Committee CEN/TC 243 “Cleanroom technology”, the secretariat of which is held by BSI.

This document is currently submitted to the CEN Enquiry.

Introduction

This European Standard establishes the principles and basic methodology of a formal guidance on the establishment of microbiological contamination control requirements for controlled zones. It describes the principles of microbiological control and gives guidance on microbiological qualification/verification of the controlled zone as built, at rest and in operation in order to establish a process for maintenance and demonstration of control.

In keeping with the principles of the CEN standardization process this standard will not prescribe any specific rules for any or every particular industry, but rather provide applications guidance and a toolbox and things to consider in a number of key industries. Industries where this standard is expected to have particular application are Life Science Pharma/Biopharma, Life Science Medical Devices, Healthcare/Hospitals and Food. These industries use cleanrooms or clean controlled environments and there is no common European guidance giving best practice and guidance for establishing control and then demonstrating control of viable microbiological contamination in air and on surfaces.

This standard is limited to viable microbiological contamination but will specifically exclude any treatment of Endotoxins, Prions and viruses. These exclusions are dealt with adequately in other standards and industry guidance.

Guidance in Life Science Pharma/BioPharma is important because:

In the Life Science industry there are many different standards, guidelines and references in use. These include the EMA and PIC/s Annex 1 GMP guidance on Sterile Medicines as well as the FDA guidance under the 2004 Aseptic Processing guidance document. There is also WHO GMP guidance. The European Pharmacopeia and USP as well as guidance documents from industry associations including PDA, ISPE and PHSS.

While there is already enough regulation in the Life Science Pharma and Biopharma industry there is a need to offer clear guidance and resolve conflicts and confusion in specific areas of biocontamination control such as choice of environmental monitoring (EM) sampling methods, how to use the data collected for trending and the role of Rapid Microbiological Measurement (RMM) or Instantaneous Microbiological Detection (IMD).

Therefore it is the intention of this standard is to serve as a supplement to the body of existing guidance documents. This standard is intended to offer good science in biocontamination control and encourage regulators to refer to the new standard for viable microorganisms and bicontamination control.

Guidance in life science medical devices is important because:

While EN ISO 14971 covers Medical device and gives the risk assessment requirements for biocontamination control in a clean controlled environment there is no specific guidance on GMP. Existing regulatory guidance in FDA aseptic processing does not cover medical devices and EU GMP regulations in Annex 1 is for sterile medicines.

Biocontamination on medical devices can cause serious harm to patients. Medical devices come in a variety of forms and materials; assembly includes both manual and automatic operations. Biocontamination of medical devices should be prevented by aseptic processing and/or removed by sterilization. Medical Devices consist of various materials, shapes, sizes and functions.

Guidance in healthcare in hospitals is important because:

While there are national recommendations for operating theatres in hospitals there is no European standard for biocontamination control in these types of clean controlled environments. And GMP guidelines in Biocontamination control are limited to hospital pharmacies and tissue establishments under EU directives.

A European standard on biocontamination control can provide an important contribution to improving patient safety and can be applied in healthcare/hospitals in many areas, including operating rooms for infection-prone surgery, immuno-compromised wards, microbiology laboratories, isolation rooms etc.

Biocontamination control can provide an important guidance on best practice in microbiological measuring methods to be used including trouble shooting, trending and tracking of anti-microbial resistant microorganisms.

The intention of this standard is to give guidance on best practice in the field of biocontamination control, monitoring and methods in clean controlled environments for Healthcare in Hospitals.

Guidance on food is important because:

In food industries there aren't, at present specific standards regarding biocontamination control in cleanrooms or clean controlled environments. Ultra clean filling, high care area and middle care are very important elements of biocontamination control in clean controlled environments. The existing EN ISO 14698-1:2003, and EN ISO 14698-2:2003 are general requirements and are not seen as sufficiently detailed for the food industry. This standard will give specific guidance for the food industry.

Cleanrooms and clean controlled environments are used in the food industry to avoid dangerous microorganisms acting as biological contamination or biocontaminants, improve shelf life by reducing the use of artificial preservatives and improve the organoleptic quality of products. Environmental monitoring is a method to identify potentially harbouring and difficult to remove microorganisms.

Examples include:

— cutting and packaging (meat, ham, salami, fish, etc.);

— production and packaging (baby food, pet food, dairy products, cheese, etc.);

— only packaging (fresh fruit, fresh juice, vegetables, etc.);

— ready to use/eat products.

It is useful to have specific surface and air cleanliness levels of microbiological contamination in selected areas or clean zones in cleanrooms and clean controlled environments. This standard will give guidance on appropriate methods for establishing control, selecting appropriate alert and action levels and setting up an environmental monitoring plan as part of demonstrating control.

1 Scope

This European Standard establishes the principles and basic methodology of a formal system of biocontamination control in Cleanrooms and associated controlled environments. These principles are based on establishing control and then on demonstrating control.

This standard specifies the methods required for assessing risk monitoring risk zones in a consistent way and for applying control measures appropriate to the degree of risk involved.

It will also give guidance on the assessment and verification of microbiological sampling devices, with the aim of helping users standardize their monitoring so that results from one facility to another can be compared.

Within this standard, only microbiological hazards are addressed.

There is specific guidance given on common applications, including Food, Hospitals and Life Sciences (Pharma/Biopharma and Medical Devices).

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
viable
<of microflora> capable of being cultured with microbiological methods

3.2
viable particle
particle that contains one or more living microorganisms

3.3
biocontaminant
contaminant with viable microorganisms (or from biological origin)

3.4
clean controlled environment
designated space in which the concentration of biocontaminants in air and/or on surfaces is controlled and specified, and which is constructed and used in a manner to minimize the introduction and impact of contamination

Note 1 to entry: Levels of cleanliness attributes such as particle concentrations in air are specified by class(es).

3.5
microflora
bacteria, microscopic algae and fungi

3.6
microflora control
actions/formal system in a production area that controls the microflora that can cause infection, disease or spoilage, or otherwise affect product quality (e.g. measurements, cleaning & disinfection program, cleanroom technics.)

3.7
microbiological control
control of microbiological number and types, present in the clean zone, that can cause infection, disease or spoilage, or otherwise affect product quality

3.8
culturable
having the ability to grow and form colony forming units, using microbiological culturing techniques

3.9
non-culturable
having no ability to grow and form colony forming units, using microbiological culturing techniques

3.10
colony forming unit
CFU
unit that has the ability to produce a colony of microflora discernible by an observer

Note 1 to entry: The number of viable micro-organisms that form visible counting units on the culture media. The unit consists of one or a group of microbiological cells

3.11
objectionable species
species of microflora that has been identified as harmful, whether to the product or to the intended recipient

3.12
aseptic
technique that prevents the contamination of microorganisms that cause diseases or are harmful to the product

3.13
sterile
free from living or viable microorganisms

3.14
sterilisation
process that eliminates all forms of life from an item/product

Note 1 to entry: Technically a 6 logarithmic reduction in colony forming units.

3.15
impact assessment
assessment determining the likelihood of contamination that can give an adverse effect on a product or living being

3.16
critical area
space around object that can cause unwanted contamination of this object

3.17
control point
location in the clean zone/cleanroom/critical area, which a control measure is applied

3.18
critical control point
location in the critical area where control is essential to eliminate or reduce biocontamination risk

3.19
environmental monitoring
EM
measurement of defined parameters at periodic intervals

4 Establishment of control requirements

4.1 Formal system of microbiological control

A formal system of microbiological control shall be established, implemented and maintained. The formal system will assess and control factors that can affect the impact of microbiological on the quality of the process and product. There are a number of accepted methods for establishing a formal system by risk assessment [4], [5]. The hazard analysis critical control point (HACCP) system [6], [7], [8], [9] is commonly used. The fault tree analysis (FTA) [10], or the failure mode and effect analysis (FMEA) [11], or any other validated equivalent system can be used.

4.2 Formal system quality attributes

To assess and control the microbiological hazards, any selected system shall address the following principles:

a) identification of potential hazard(s) to the critical product quality attributes, assessment of the likelihood of occurrence of these hazard(s), and identification of measures for their prevention or control;

b) designation of critical areas and determination of critical control points, procedures, operational steps and environmental conditions that can be controlled to eliminate the hazard(s) or minimize the likelihood of their occurrence;

c) establishment of levels to ensure biocontamination control;

d) establishment of an environmental monitoring and observation schedule;

e) establishment of corrective actions to be taken when monitoring results indicate that a particular point, procedure, operational step or environmental condition is not under biocontamination control;

f) establishment of procedures, which may include supplementary tests and procedures, to verify that the chosen formal system is working effectively;

g) establishment of training procedures;

h) establishment and maintenance of appropriate documentation.

4.3 Impact assessment

The impact shall be assessed of operations, personnel and equipment in a cleanroom, clean zone or clean controlled environment which contribute to microbiological contamination, such as:

a) compressed gases;

b) room air;

c) manufacturing equipment;

d) monitoring/measuring devices;

e) storage containers;

f) number of persons present in zone;

g) unprotected surfaces of personnel;

h) personal attire;

i) protective clothing;

j) walls/ceilings;

k) floors;

l) doors;

m) benches;

n) chairs;

o) air admitted from other sources;

p) objectionable species (or species of interest) should be carefully considered. As part of the process design and risk species of interest for the process and product should be identified Refer to Appendices for examples in different applications, including food spoilage microorganisms in the food industry and pathogenic microorganisms in the Hospitals/Healthcare industry.

A decision shall be made as to whether microbiological levels are to be set numerically regardless of the species isolated or by the numbers of objectionable organisms – or both. This decision again will come out of the process design and impact assessment.

Factors that need to be taken into consideration during the impact assessment for determining objectionable species should include:

a) potential for spoilage of product prior to end of shelf life;

b) potential for health issues for product user;

c) microbiological species, (e.g. survival possibility, or possible toxins);

d) numbers of organisms at time of test;

e) product form (e.g. does the product contain preservatives, or any potential growth substrates);

f) intended product use (e.g. food, pharmaceutical, cosmetic);

g) product target population (e.g. patient, child, immuno-compromised recipient);

h) product/user contact areas – administration or application route.