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Cleanrooms and associated controlled environments —

Part 4: Design, construction and start-up

Salles propres et environnements maîtrisés apparentés —

Partie 4: Conception, construction et mise en service

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 209, *Cleanrooms and associated controlled environments*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 243, *Cleanroom technology*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO 14644-4:2001), which has been technically revised.

The main changes are as follows:

— normative content has been extended;

— the process of gathering and defining requirements has been added;

— the scope has been extended from classified cleanrooms to include additional cleanliness attributes;

— the entire text has been revised or clarified to aid its application.

A list of all parts in the ISO 14644 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user’s national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Cleanrooms and associated controlled environments provide for the control of airborne particulate contamination and, if relevant, other forms of contamination, to levels appropriate for accomplishing contamination-sensitive activities. Products and processes that benefit from the control of airborne contamination include those in such industries as aerospace, microelectronics, pharmaceuticals, medical devices, food and research and development laboratories and some applications in healthcare.

Cleanrooms and associated controlled environments are classified for air cleanliness by particle concentration (ISO 14644-1). Cleanliness attributes relating to chemicals, nanoscale particles and viable particles (microorganisms), as well as cleanliness of surfaces, can also be considered.

This document is one of the series of International Standards concerned with cleanrooms and associated controlled environments prepared by ISO/TC 209.

This document provides guidance for the design, construction and start-up of cleanrooms, both new and those undergoing modification or refurbishment. In this edition, a more structured approach is provided with separate normative sections on requirements, design, construction and start-up, supported by four corresponding informative annexes.

For this edition, key recommendations and considerations include:

a) A structured approach with a logical sequential flow through the design, construction and start-up stages. There will normally be reviews and iterations of the requirements, contamination control concepts, layouts and other considerations. The final design should be reviewed against the requirements before construction commences and when construction is complete. The operation and performance are verified against the requirements during start-up.

b) Inclusion of other cleanliness attributes. The ISO 14644 series has parts that deal with other cleanliness attributes, namely chemicals, nanoscale particles, macro-particles and, in ISO 14698, viable particles (microorganisms), as well as cleanliness of surfaces. These other attributes should be considered if relevant, bearing in mind that the primary requirement for a cleanroom or clean zone is that it meets a classification by airborne particle concentration according to ISO 14644-1.

c) Importance of a contamination risk assessment. Assessments should be carried out to better understand the contamination risk and its impact on the process and product and to identify the critical control points (locations) in the cleanroom or clean zone.

d) A clear statement of requirements, namely everything needed for input into the design, including the purpose of the cleanroom and the acceptance criteria for performance parameters. This is critical and should be documented prior to the start of the design process.

e) Ventilation effectiveness. This revision focuses on the importance of ventilation effectiveness through control of air-flow patterns and clean-up recovery rates. Two measures are identified: air change effectiveness (ACE) and contaminant removal effectiveness (CRE).

f) Using air supply rate for calculations of contaminant dilution and removal. This will make it possible to achieve energy-efficient cleanrooms while achieving the required level of air cleanliness.

g) Energy efficiency and life cycle considerations. Energy efficiency in cleanrooms is very important and is covered by ISO 14644-16.

h) A clean build protocol. This is included to minimize contamination during construction of the cleanroom.

Information directly relevant to cleanrooms and associated controlled environments is included in the informative annexes. Supporting information is given in the Bibliography.

Cleanrooms and associated controlled environments —

Part 4:
Design, construction and start-up

1 Scope

This document specifies the process for creating a cleanroom from requirements through to its design, construction and start-up. It applies to new, refurbished and modified cleanroom installations. It does not prescribe specific technological or contractual means of achieving these requirements. It is intended for use by users, specifiers, designers, purchasers, suppliers, builders and performance verifiers of cleanroom installations. The primary cleanliness consideration is airborne particle concentration. Detailed checklists are provided for the requirements, design, construction and start-up, which include important performance parameters to be considered. Energy management design approaches are identified to support an energy-efficient cleanroom design. Construction guidance is provided, including requirements for start-up and verification. A basic element of this document is consideration of aspects, including maintenance, that will help to ensure continued satisfactory operation for the entire life cycle of the cleanroom.

NOTE Further guidance is given in Annexes A to D. ISO 14644-1, ISO 14644-2, ISO 14644-8, ISO 14644-9, ISO 14644-10, ISO 14644-12 and ISO 14644-17 provide complementary information. ISO 14644-7 offers guidance on design, construction and requirements for separative devices (clean air hoods, glove boxes, isolators and mini-environments).

The following subjects are mentioned but not addressed in this document:

— specific operational activities, processes to be accommodated and process equipment in the cleanroom installation;

— fire and safety regulations;

— ongoing operation, cleaning and maintenance activities, which are covered by ISO 14644-5.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 14644-1, *Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration*

ISO 14644-16, *Cleanrooms and associated controlled environments — Part 16: Energy efficiency in cleanrooms and separative devices*

3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1 General

3.1.1
air change effectiveness
ACE
ratio between the recovery rate at a location or locations in a *cleanroom* (3.1.4) and the overall recovery rate of the cleanroom after a contamination event

Note 1 to entry: The recovery rate is defined and measured in accordance with ISO 14644-3.

[SOURCE: ISO 14644-16:2019, 3.2.7]

3.1.2
classification
method of assessing level of cleanliness against a specification for a cleanroom or clean zone

Note 1 to entry: Levels should be expressed in terms of an ISO Class, which represents maximum allowable concentrations of particles in a unit volume of air.

[SOURCE: ISO 14644-1:2015, 3.1.4]

3.1.3
cleanliness
condition not exceeding a specified level of contamination

[SOURCE: ISO 14644-15:2017, 3.5]

3.1.4
cleanroom
room within which the number concentration of airborne particles is controlled and classified, and which is designed, constructed and operated in a manner to control the introduction, generation and retention of particles inside the room

Note 1 to entry: The class of airborne particle concentration is specified.

Note 2 to entry: Levels of other cleanliness attributes, such as chemical, viable or nanoscale concentrations in the air, and also surface cleanliness in terms of particle, nanoscale, chemical and viable concentrations, might also be specified and controlled.

Note 3 to entry: Other relevant physical parameters might also be controlled as required, e.g. temperature, humidity, pressure, vibration and electrostatic.

[SOURCE: ISO 14644-1:2015, 3.1.1]

3.1.5
clean zone
defined space within which the number concentration of airborne particles is controlled and classified, and which is constructed and operated in a manner to control the introduction, generation and retention of contaminants inside the space

Note 1 to entry: The class of airborne particle concentration is specified.

Note 2 to entry: Levels of other cleanliness attributes, such as chemical, viable or nanoscale concentrations in the air, and also surface cleanliness in terms of particle, nanoscale, chemical and viable concentrations, might also be specified and controlled.

Note 3 to entry: Other relevant physical parameters might also be controlled as required, e.g. temperature, humidity, pressure, vibration and electrostatic.

Note 4 to entry: A clean zone(s) can be a defined space within a cleanroom or might be achieved by a separative device. Such a device can be located inside or outside a cleanroom.

[SOURCE: ISO 14644-1:2015, 3.1.2]

3.1.6
commissioning
planned and documented series of inspections, adjustments, measurements, tests and verifications carried out systematically to set the installation into correct technical operation as specified

Note 1 to entry: The objective evidence needed for a verification can be the result of an inspection or of testing other forms of determination, such as performing alternative calculations or reviewing documents

3.1.7
contaminant
particle, chemical or microorganism that adversely affects the product or process

3.1.8
contaminant removal effectiveness
CRE
ratio of particle concentration in the air leaving the cleanroom to the average of particle concentration in the working plane of the cleanroom, when particles entering from filtered supply air are ignored

Note 1 to entry: If the air leaves the cleanroom at more than one point then the weighted average of the particle concentrations based on the relative flowrates can be used.

Note 2 to entry: The number and positioning of the sampling locations for determining the average particle concentration in the working plane of the cleanroom can be based on the method given in 14644–1.

Note 3 to entry: The local particle concentration is dependent on the airflow pattern in the cleanroom and may vary significantly in the cleanroom. CRE in a sub-area of interest in the cleanroom may be calculated by selecting a single sampling location considered to be representative of the characteristics of the sub-area of interest.

Note 4 to entry: Particles may be replaced by another airborne contaminant.

[SOURCE: ISO 14644-16:2019, 3.2.5, modified — Definition revised and notes to entry added].

3.1.9
customer
person or organisation that could or does receive a product or a service that is intended for or required by this person or organisation

EXAMPLE Consumer, client, end-user, retailer, receiver of product or service from an internal process beneficiary and purchaser.

Note 1 to entry: A customer can be internal or external to the organization.

[SOURCE: ISO 9000:2015, 3.2.4]

3.1.10
non-unidirectional airflow
non-UDAF
air distribution where the supply air entering the cleanroom or clean zone mixes with the internal air

[SOURCE: ISO 14644-1:2015, 3.2.8 modified — Definition revised.]

3.1.11
particle
minute piece of matter with defined physical boundaries

[SOURCE: ISO 14644-1:2015, 3.2.1]

3.1.12
setting to work
activities to bring a system from a static state into correct operation

3.1.13
source strength
number of airborne particles or other airborne contaminants considered emitted per time unit expressed as a rate

Note 1 to entry: A source can be a person, equipment or an object.

Note 2 to entry: Each rate should be indicated with a specific particle size. Particles are often emitted in multiple sizes and each size may have a different rate.

3.1.14
start-up
period following the construction of an installation when the systems and installation are brought into active service, including all commissioning activities, training and handover to the customer

3.1.15
supplier
organisation that provides a product or a service

EXAMPLE Producer, distributor, retailer or vendor of a product or service.

Note 1 to entry: A supplier can be internal or external to the organization.

Note 2 to entry: In a contractual situation, a supplier is sometimes called a "contractor".

[SOURCE: ISO 9000:2015, 3.2.5]

3.1.16
unidirectional airflow
UDAF
controlled airflow through the entire cross-section of a cleanroom or a clean zone with a steady velocity and airstreams that are considered to be parallel

Note 1 to entry: This type of airflow results in a directed transport of particles and other contaminants from the clean zone.

[SOURCE: ISO 14644-1:2015, 3.2.7, modified — Note 1 to entry added.]

3.1.17
ventilation effectiveness
dimensionless index that relates to both the dilution and removal of indoor airborne contaminants as it determines how effectively the filtered supply air is distributed to the critical areas in the occupied space and the contamination removed by the air leaving the room

Note 1 to entry: Ventilation effectiveness can be expressed in terms of air change effectiveness (ACE) or contaminant removal effectiveness (CRE). In cleanrooms, mostly ACE is used.

3.1.18
verification
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

Note 1 to entry: The objective evidence needed for a verification can be the result of an inspection, testing or other forms of determination, such as performing alternative calculations or reviewing documents.

Note 2 to entry: The activities carried out for verification are sometimes called a qualification process.

Note 3 to entry: The word "verified" is used to designate the corresponding status.

[SOURCE: ISO 9000:2015, 3.8.12]

3.2 Installation

3.2.1
air-handling unit
AHU
unit or plant comprising fan, filtration, heating, cooling, humidification or dehumidification and mixing of fresh air and recirculated air, that provides conditioned air to a room or facility

3.2.2
air diffuser
device placed at the outlet of a room air supply terminal to improve distribution and mixing of supply air with room air

Note 1 to entry: A mesh grille or a perforated screen is not considered to be a diffuser.

3.2.3
installation
cleanroom or one or more clean zones, together with all associated structures, air-treatment systems, services and utilities

[SOURCE: ISO 14644-1:2015, 3.1.3]

3.2.4
filter system
assembly composed of filter, frame and other support mechanism or other housing

[SOURCE: ISO 14644-3:2019, 3.3.4]

3.2.5
final filter
last high-efficiency air filter in the system before the air enters the cleanroom or clean zone

Note 1 to entry: Terminal filter is a final filter located at the point where the air enters the cleanroom

[SOURCE: ISO 14644-3:2019, 3.3.5, modified — Definition revised and Note 1 to entry added.]

3.2.6
turn-down
controlled reduction of airflow velocity in unidirectional airflow cleanrooms and clean air devices or airflow rates in non-UDAF cleanrooms in order to save energy during periods when the cleanroom is not in operation

[SOURCE: ISO 14644-16:2019, 3.2.8]

4 Abbreviated terms

ACE	air change effectiveness
AHU	air-handling unit
CRE	contaminant removal effectiveness
ESD	electrostatic discharge
HEPA	high-efficiency particulate air (filter)
HVAC	heating, ventilation and air conditioning
MCP	microbe-carrying particle

non-UDAF	non-unidirectional airflow
UDAF	unidirectional airflow
ULPA	ultra-low penetration air (filter)
URS	user requirement specification

5 General

A cleanroom or clean zone can be used to protect products and processes that are sensitive to airborne particles and other types of contaminants. A cleanroom installation can be new or the expansion or modification of an existing installation.

The life cycle of the cleanroom shall be considered from the outset. This includes its design, construction, start-up, occupation, operation, renovation, expansion, repair and demolition and consequent recycling or disposal.

An analysis of the need for a cleanroom and its justification shall be performed. This analysis shall address, but is not limited to:

a) contamination risk to product, processes, people and environment (6.1);

b) statutory requirements;

c) relevant regulations;

d) business-related aspects (financial viability and resource capability);

e) future needs.

The flowchart in Figure 1 is intended to guide the user through this document with a logical sequence of the work. The annexes are aligned with the clauses in the main text (requirements, design, construction and start-up).

There shall be a review after each step based on the requirements and previous steps. In a small project these steps may be simplified.

This document can also be used for non-classified clean controlled environment and controlled zones.

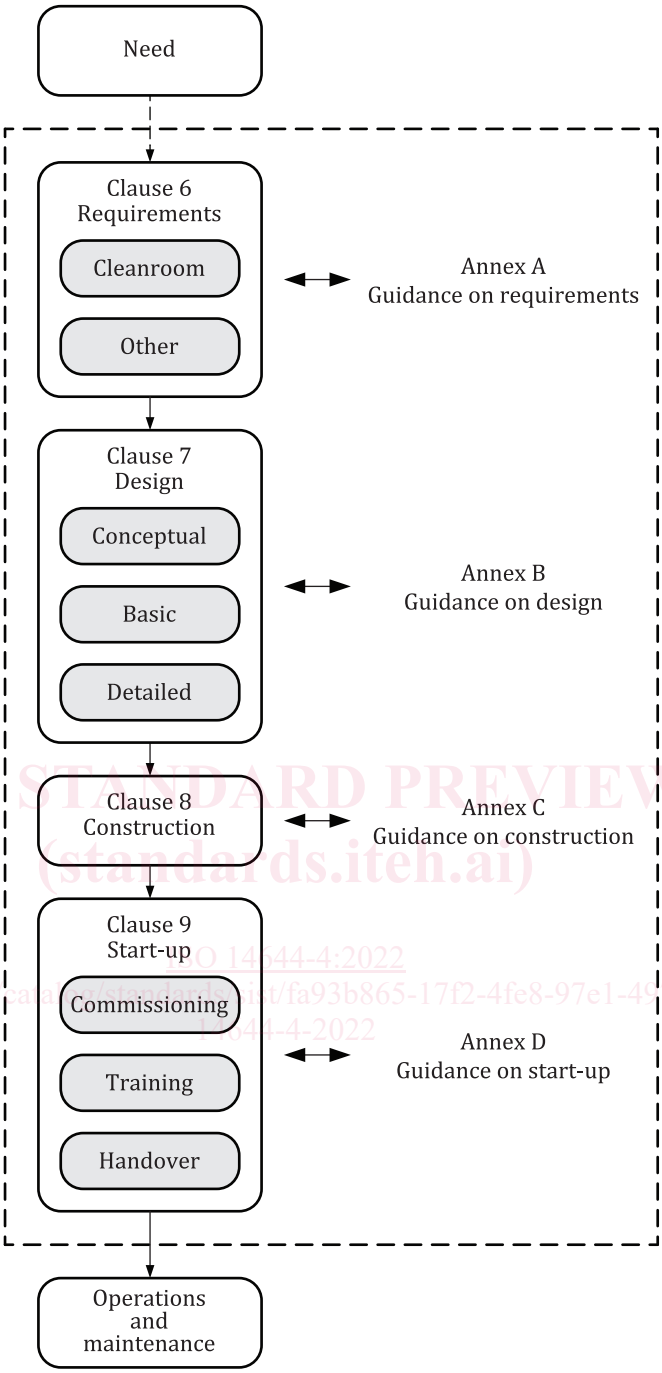

Figure 1 — Flowchart: from requirements to design, construction and start-up

6 Requirements

6.1 Cleanroom requirements

Cleanroom features and contamination control requirements are established as necessary to reliably and repeatably create environments of desired quality to protect patients, products, processes, personnel or the environment. An assessment can be carried out in order to identify potential risks of the facility to be designed.

The following items shall be considered and defined as appropriate by the customer and designer:

a) the intended use of the installation and the operations to be carried out therein;

b) regulatory requirements;

c) the relevant parts of ISO 14644 that will be used, including number, edition and year of publication;

d) the air cleanliness class at the designated particle size(s) and the defined occupancy states in accordance with ISO 14644-1;

e) any other requirements with respect to particles or other contaminants in air or on surfaces (e.g. particle number concentration and particle deposition rate) (see Clause A.4);

f) considerations of any other performance requirements such as ESD or vibration;

g) temperature, humidity, processes and operator comfort considerations;

h) performance parameters and their acceptance criteria, with any specific requirements for alert and action limits and their management;

i) entry and exit of personnel, equipment and materials, in terms of quantity, movement and controls applied, such as decontamination and gowning;

j) sources of contamination and their source strength data;

k) methods of testing, measurement and monitoring to meet the acceptance criteria;

l) cleanroom environmental control by stand-alone systems or integrated into building management system (BMS);

m) requirements for monitoring of environmental conditions and other parameters;

NOTE Guidance for monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration can be found in ISO 14644-2.

n) intended life cycle of the installation;

o) intended operational cycles and turn-down periods;

p) changes of the installation anticipated over time to be provided for in the design;

q) the intended location of the installation and any site constraints;

r) the identification of external environmental influences;

s) critical dimensions and weight restrictions, including those related to available space;

t) process and product requirements that affect the installation, including cleaning and disinfection;

u) the process equipment list with utility requirements;

v) the preferred contamination control concepts and overall strategy for contamination control;

w) environmental and energy efficiency targets;

x) process hazards;

y) internal cleanroom surface and finish requirements (including the need for smooth, impervious finishes which are cleanable and resistant to cleaning and decontamination agents and free of gaps or pathways to uncontrolled areas);

z) required availability in terms of acceptable downtime and back-up strategy in the event of failure;

aa) strategy of maintenance operations, space and time needed to maintain the installations during the process cycle;

ab) any other factors or constraints, not listed above, imposed by the operating requirements over the life cycle of the cleanroom;

ac) specific industry guidance.

Additional information on mechanisms of contamination and cleanliness attributes is given in Annex A, together with a comprehensive checklist regarding requirements.

6.2 Other requirements

The following items shall be considered and defined as appropriate:

a) roles and responsibilities of all involved parties during execution of the project;

b) project budget;

c) a time schedule, including milestones for provision of necessary information and documentation;

d) procedure for managing changes;

e) verifications to be carried out at each stage of the project and related documentation;

f) acceptance criteria for the various project stages, if applicable;

g) scope of documentation at designated project stages, its data format and approval procedures (see 9.5);

h) training for cleanroom personnel and technical staff who will manage, use, clean, test and maintain the installation;

i) any other approvals (e.g. management, financial, quality, process, regulatory, statutory);

j) competence and experience of designers, installers, constructors, commissioners and testers or verifiers, specifically in relation to cleanrooms and cleanroom technology;

k) required experience, roles and responsibilities for approvals.

6.3 Documentation

The requirements shall be agreed and documented to form a basis for subsequent anticipated design and allow changes to be managed in a traceable manner.

NOTE In some industries this is documented in a URS.

7 Design

7.1 General

The output of the requirements (Clause 6) is the input for the design. The design of the cleanroom shall take into account an effective contamination control strategy for all aspects of its construction, testing, operation, maintenance and life cycle. There are typically three stages in the overall design process: conceptual design, basic design and detailed design.

Depending on the nature and scale of the project, these stages can be executed in one or more steps with appropriate design iterations and reviews.

The design process shall progress in an agreed manner, shall take into account all the agreed requirements and shall be documented.