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Technical specifications of cleanroom design for cell culture

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1 Scope

This document specifies the general requirements for cleanroom design for cell culture, ventilation and purification, enclosure structure, electrical and information technology, water supply and drainage, gas pipelines, and safety requirements.

This document applies to cleanroom design for cell culture for human use. Other cell culture cleanrooms refer to this document.

2 Normative references

The following referenced documents are indispensable for the application 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.

GB 5749, *Sanitary standard for drinking water*

GB 17945, *Fire Emergency Luminaries*

GB/T 29469, *Cleanrooms and associated controlled environments - Evaluation of performance and rationality*

GB/T 36372, *Cleanrooms and associated controlled environments - General technical requirements of combined envelope structure*

GB 50016, *Code of Design on Building Fire Protection and Prevention*

GB 50457, *Code for design of pharmaceutical industry cleanroom*

GB 50472, *Code for design of electronic industry cleanroom*

GB 50591, *Code for Construction and Acceptance of Cleanroom*

3 Terms and definitions

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

3.1 cell culture

A process of growing, expanding, and maintaining the biological properties of extracted cells.

4 Requirements

4.1 General requirements

4.1.1 The design of site selection, ventilation and purification, envelope structure, electrical and information technology, water supply and drainage, gas pipelines, safety and other aspects shall be carried out in combination with the cell culture process and environmental requirements.

4.1.2 An area with less vibration, electromagnetic radiation, and noise shall be selected. When the area of a new cleanroom is greater than or equal to 3000 m^2, while meeting the above requirements, the building where it is located shall be selected in an area with good natural environment and low gas pollution.

4.1.3 When the area of a newly built, renovated or expanded cleanroom is greater than or equal to 3000 m^2, the design of the cleanroom shall be closely connected with the overall design of the building where it is located. After negotiating with the user to determine the process requirements and cleanroom location, the design will be prioritized based on consultation with the overall design. Propose requirements for building structure, power, HVAC, water supply and drainage, electrical and other aspects to the overall design.

4.1.4 Full consideration shall be given to preparation process flow, equipment configuration, safety and reliability of equipment and facilities, various interfaces, flow of people, logistics, storage of items (necessary) in-situ inactivation and disinfection of hazardous waste products, construction and installation, equipment installation, inspection and maintenance and other related requirements.

4.1.5 The cleanliness and other relevant requirements of each area shall comply with 4.2.

4.1.6 The purpose shall be to protect personal safety. Consider a plan to evacuate cleanroom staff as soon as possible in an emergency and minimize damage to the cleanroom and support areas.

4.1.7 On the basis of meeting the process requirements and operating cycle, it shall focus on saving energy, protecting the environment, and being economically reasonable.

4.1.8 When the cleanroom area is greater than or equal to 2000 m^2, the design evaluation shall be carried out in accordance with the requirements of GB/T 29469. If the area is less than 2000 m^2, it can choose whether to conduct design evaluation.

4.1.9 For cleanrooms containing cell cultures carrying infectious agents, a biosafety plan shall be developed based on risk assessment. Ensure that its production and operation process does not cause pollution or harm to personnel and the environment. Avoid cross contamination.

humidity loads of various equipment within the system need to be considered at the same time).

NOTE: Pay attention to extreme climates, especially the demand for cold and heat sources with sustained extreme temperatures and humidity.

4.3.1.3 The division of purification air-conditioning systems shall be determined after technical and economic comparison based on process requirements, floor plan, biological safety, etc. Take effective measures to avoid contamination and cross-contamination. Meet the following requirements:

a) The air conditioning system shall be set up separately from areas without cleanliness requirements.

b) Production units with different process requirements shall be equipped with separate purification and air-conditioning systems.

c) Functional areas with different operating shifts or usage times shall be equipped with separate purification and air-conditioning systems.

d) In areas with large differences in indoor heat and moisture load characteristics, separate purification air conditioning systems shall be installed.

4.3.1.4 When there are ventilation equipment such as biological safety cabinets and local exhaust devices in the cleanroom, measures shall be taken to maintain indoor pressure stability during the opening, closing and operation of the equipment.

4.3.1.5 It must be conducive to cleanroom disinfection, sterilization, automatic control and energy-saving operation. Comply with the following regulations:

a) Positive pressure cleanrooms shall use circulating air conditioning systems.

b) When toxic, harmful, or combustible gases are involved (excluding cell culture areas carrying infectious agents), a partial or overall full exhaust system shall be adopted based on risk assessment.

c) Measures shall be taken to dilute and replace room gas after disinfection and sterilization.

4.3.1.6 The design of the cleanroom exhaust system meets the following requirements:

a) The exhaust systems of different purification air-conditioning systems shall be set up independently.

b) When harmful substances, odors, large amounts of heat, moisture or volatile gases are produced, a separate exhaust system shall be set up.

c) Measures shall be taken to prevent the infiltration of outdoor gas.

d) For exhaust systems containing water vapor and condensable substances, a slope shall be set. Set up a discharge port at the local lowest point of the pipeline.

4.3.1.7 For air conditioning systems that use circulating air, a primary (medium) efficiency air filter shall be installed at the return air outlet of the cleanroom as appropriate.

4.3.1.8 The opening and closing of the supply air, return air and exhaust air of the purification air conditioning system shall be interlocked and comply with the following regulations:

a) The chain procedure of the positive pressure cleanroom is to start the air supply fan first, then start the return air fan (if any) and exhaust fan. The chain procedure shall be reversed when closing.

b) The chain procedure of the negative pressure cleanroom is to start the return air fan and exhaust fan (if any) first, and then start the air supply fan. The chain procedure shall be reversed when closing.

4.3.2 Airflow organization

4.3.2.1 Airflow complies with the following regulations:

a) The clean area shall adopt a one-way flow pattern.

b) Areas outside the clean area may use non-unidirectional flow patterns. Non-unidirectional flow patterns need to reduce the vortex area.

c) Airflow distribution shall be even. The air flow rate shall meet the requirements of production technology and human hygiene.

4.3.2.2 When setting up a unidirectional flow workbench in a non-unidirectional flow cleanroom, its location shall avoid being close to the air supply and return vents.

4.3.2.3 If there is a local exhaust device, it shall be arranged on the downwind side of the cleanroom (area).

4.3.3 Parts and materials

They shall comply with the relevant requirements of GB 50457 and GB 50591.

4.3.4 Special requirements for cell culture areas carrying infectious agents

4.3.4.1 Biosafety plans for various working conditions in the area (operating or not, entry and exit of equipment and facilities, maintenance, troubleshooting, etc.) shall be jointly developed with relevant process personnel.

4.3.4.2 The cell culture area carrying the virus and the adjacent room or area shall maintain a negative pressure. The pressure difference shall not be less than 10 Pa.

GB 50016.

4.5.2 Illumination

4.5.2.1 Lighting fixtures shall be dedicated to cleanrooms. The maintenance and replacement of lamps shall avoid adverse effects on the cleanroom environment.

4.5.2.2 The illumination and illumination uniformity of each area meet the requirements of Table 3.

4.5.2.3 Emergency lighting and evacuation lighting shall be set up. It shall comply with the regulations of GB 17945.

4.5.3 Intelligent information system

4.5.3.1 Fire safety emergency broadcasts shall be set up.

4.5.3.2 The following terms apply to cell culture cleanrooms with intelligent information requirements.

4.5.3.3 The architecture and system configuration shall meet the requirements of business systems and management systems for network segmentation. Information security requirements for network physical isolation and logical isolation shall be met. It shall meet energy-related functional requirements. Improve operational efficiency, reliability and safety.

4.5.3.4 Communication interfaces and protocols that are open and comply with international and current national standards shall be provided.

4.5.3.5 The user operation interface shall be able to be set according to usage requirements.

4.5.3.6 A monitoring system for controlled environmental parameters shall be set up.

4.5.3.7 A closed-circuit television surveillance system can be set up according to the requirements of production management and production technology, which can watch and record the entire process in real time from multiple angles and without blind spots.

NOTE: The automatic monitoring device is installed on the ceiling.

4.5.3.8 The access control management system shall be set up according to functional partitions. The access control management system shall realize linkage control with the emergency escape and automatic fire alarm systems. The access control system shall be automatically deactivated in the event of an emergency or fire. Ensure that emergency escape routes are clear during evacuation.

4.5.3.9 There shall be a communication system to facilitate contact with relevant departments.

4.5.3.10 When using flammable, explosive and other dangerous media, corresponding monitoring and alarm devices shall be set up indoors and in the monitoring room.

NOTE: Subclauses 4.5.1 and 4.5.3 are applicable to pharmaceutical and cell culture cleanrooms used for cell therapy.

4.6 Drainage

4.6.1 General provisions

4.6.1.1 It shall comply with the relevant requirements of GB 50472 and GB 50457.

4.6.1.2 Casings shall be installed where the water supply and drainage branch pipes pass through the ceiling, walls and floors of the cleanroom. There shall be reliable sealing measures between pipes and sleeves.

4.6.1.3 Measures shall be taken to prevent condensation and burns on the outer surface of the pipe.

NOTE: This article applies to pharmaceutical and cell culture cleanrooms used for cell therapy.

4.6.2 Water supply

4.6.2.1 Water quality shall comply with the requirements of GB 5749.

4.6.2.2 Water supply pipes and accessories shall be corrosion-resistant and easy to install and connect.

4.6.3 Drainage

4.6.3.1 The drainage system shall be determined based on the characteristics, concentration and volume of discharged wastewater.

4.6.3.2 The drainage equipment in the cleanroom and the equipment connected to the gravity return pipe shall be equipped with a water sealing device below the discharge outlet. The water seal height shall not be less than 50 mm. Drainage outlets of process equipment shall be equipped with air blocking devices. The drainage system shall have a complete ventilation system.

4.6.3.3 The drainage riser shall not pass through a cleanroom with a cleanliness level higher than or equal to ISO 6 and its corresponding level. There shall be no inspection opening when the drainage riser passes through other cleanrooms.

4.6.3.4 Floor drains shall not be installed in ISO levels 5, 6 and corresponding cleanrooms. If a cleanroom lower than the above-mentioned requirements must be installed, the floor drain must be made of material that is not prone to corrosion, has a smooth inner surface, is not prone to scaling, has a sealing cover, is easy to open, must be resistant to sterilization, and can prevent the backflow of waste water and gas.

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