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Standard Guide for Biopharmaceutical Facilities Architectural Design Considerations[1]

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1. Scope

1.1 This guide covers architectural design considerations for buildings and facilities used in the biological processing industry to make drugs, chemicals, and other products.

1.2 These designs are intended to meet current good manufacturing practices (cGMP) criteria and guidelines published by the U.S. Food and Drug Administration (FDA) for processes and products manufactured under CFR Title 21.

1.3 While the guidelines described are general in nature, they are not expected to apply to all of the possible biotechnical processes used in the industry today. Accordingly, the user of this guide must exercise good engineering judgment in specific design applications to select the proper guidelines that apply.

1.4 In addition to the cGMP guidelines provided herein, other regulations and guides should be considered that are promulgated by other federal agencies such as the Occupational Safety and Health Administration (OSHA), the U.S. Environmental Protection Agency (EPA), the U.S. Drug Administration (USDA), the National Institute of Health (NIH), and so forth.

1.5 While the buildings will be designed to meet specific functional requirements and comply with local zoning ordinances, building codes, handicapped employee standards, and so forth, these considerations are not included in this guide.

1.6 The values stated in SI units are to be regarded as the standard.

1.7 *This standard does not purport to address all of the safety problems, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *Code of Federal Regulations:*
CFR Title 21, Parts 58, 210, 211, 212, 606, 809, 820[2]

2.2 *Other Document:*
NIH Guidelines, Containment Area Designations[3]

3. Terminology

3.1 *Definition:*

3.1.1 *cGMP*—abbreviation for current good manufacturing practices as defined in CFR Title 21, Parts 210 and 211.

4. Significance and Use

4.1 This guide is intended for use in designing laboratory, pilot plant, commercial production buildings that will use processes involving living organisms to produce products. These products are also manufactured under the FDA and other federal agency regulations.

4.2 These guidelines include the layout of facilities, design of containment areas, ventilation and air quality, personnel areas, special processing hazards, controlled environment areas, and other items.

4.3 This guide is for use by engineers, architects, and owners of biopharmatechnical manufacturing facilities to consider the special factors in laying out the facilities to meet cGMP requirements and other good engineering principles.

4.4 By using these guidelines along with other design criteria required by a variety of regulatory agencies, a validation effort can be achieved more easily to meet agency requirements and obtain operating permits.

4.5 This guide is intended to provide general guidelines for consideration and application in a variety of plant operations and processes in which the designers can make specific decisions concerning the exact architectural design features to use.

5. Summary of Guide

5.1 This guide provides architectural design principles to consider when applying federal regulations to biopharmatechnical plant facilities construction and functions. Check lists for specific plant operation activity areas presented with criteria for their design and layout considerations. Environmental considerations are also included for aseptic and special laminar

[1] This guide is under the jurisdiction of ASTM Committee E-48 on Biotechnology and is the direct responsibility of Subcommittee E48.01 on Materials for Biotechnology.

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[2] Available from Standardization Documents Order Desk, Bldg. 4, Section D, 700 Robbins Ave., Philadelphia, PA 19111-5094, Attn: NPODS.

[3] Available from National Institutes of Health, (NIH), 9000 Rockville Pike, Bethesda, MD 20892.

flow zones of operation. Fermenter area layout and space considerations are presented. When containment and closed area operations are necessary, the general criteria to be considered by the designer is presented based on NIH Guidelines and good engineering practices.

5.2 Plant layout considerations are included for all normal sections of a biotechnical operating plant.

6. Guidelines

6.1 First, establish which regulations apply to the specific project design. Review 21 CFR, Parts 210, 211, 212, and so forth; NIH Guidelines; and other specific information from federal agencies that applies to the functions intended in these facilities. For example, 21 CFR, Part 606, relates to cGMP for blood and blood components; Part 809 to in-vitro diagnostic products for human use; Part 820 to medical devices; Part 58 to nonclinical laboratories; NIH guidelines to containment requirements, and so forth.

6.2 Adequate laboratory facilities must be provided for the testing of process intermediates and products (see section 21 CFR, Part 211.22). The quality control function of the site requires adequate laboratory space and facilities.

6.3 Manufacturing employees must have education and frequent training (see section 21 CFR, Part 211.25), which requires training space or dedicated rooms for the cGMP training. This space can sometimes be combined with an eating area or conference room.

6.4 Personnel must wear appropriate clothing and protective items (see 21 CFR, part 211.28), which implies storage area lockers for clean and dirty work clothes and change lockers for street clothes. Change rooms, laundry rooms, clothing staging areas, and storage rooms may also apply.

6.5 Personnel sanitation and health activities require adequate wash rooms, showers, toilets, and storage areas for supplies, according to Part 211.28.

6.6 Building design and construction features in Part 211.42 require adequate space for the manufacturing, processing, packing, or holding of a drug product. These areas include the following:

6.6.1 Receipt and identification of raw materials,

6.6.2 Storage offtest and ontest raw materials,

6.6.3 Sample preparation and testing,

6.6.4 *In-process Materials*—Ontest and offtest,

6.6.5 Manufacturing equipment,

6.6.6 Equipment holding, cleaning, and staging,

6.6.7 Packaging and labeling,

6.6.8 Quarantine storage of finished products,

6.6.9 *Utilities*—Inert gases, steam generators, water for injection (WFI), treated water, air (utility, clean, instrument, and sterile), and so forth,

6.6.10 *Sterilization Systems*—Clean-in-place and sterilize-in-place,

6.6.11 Waste treatment,

6.6.12 Offices, personnel change rooms, and containment access areas, and

6.6.13 Control room, quality assurance and quality control areas, and so forth.

6.7 The controlled environment area must be environmentally controlled, with special air quality, lighting, and construction (see 21 CFR, part 212.3) to minimize contamination from air-borne particulates, including microorganisms. Personnel entering the controlled environment area must use appropriate non-linting garments inside it that are not to be used outside it, including in the changing area. This means that the design of facilities will include a gowning area and garment storage areas adjacent to the controlled environment area.

6.7.1 *Gowning Area Design Considerations*:

6.7.1.1 Sole means of personnel entry and exit, except for emergency exit.

6.7.1.2 Located immediately adjacent to work areas.

6.7.1.3 Equipped with containers for the disposal of used clothing and protective equipment.

6.7.1.4 Clean air supplied to the gowning area will have a negative air pressure relative to the contained work area and positive air pressure relative to the adjacent non-controlled areas. Differential pressures may be 1.3 to 3.8 mm water gage.

6.7.1.5 Provide hand washing facilities and warm-air drying equipment within the gowning area similar to surgical room washing facilities operated by foot or knee.

6.7.1.6 The gowning room should have a higher pressure than the wash room and have loading changers to insert personnel clothing items into the room. Air showers and air locks should be considered.

6.7.1.7 Finishes within the gowning room should be of the same quality as those in the controlled environment work area.

6.7.1.8 The use of HEPA filters and ultraviolet lights should be considered for garment lockers.

6.7.1.9 Doors should remain closed when not in use; consider using automatic door closure and interlocks.

6.7.2 The air quality for controlled environment areas is described in 21 CFR, Parts 212.221 to 222. Consider the following:

6.7.2.1 *Temperature Range*—22 ± 3°C.

6.7.2.2 *Humidity Range*—30 to 50 % relative humidity.

6.7.2.3 *Pressure Differential*—0.05 in. (1.27 mm) of water, minimum, with all doors closed relative to the adjacent less clean area.

6.7.2.4 *Sterility, HEPA Filtration*—Not to exceed a particle count (0.5 µm size) of 100 000/ft^3 when measured with automatic counters, or 700 particles of 5.0 µm size using a manual microscopic method. For sterile air over filling lines, a 100 count is maximum for 0.5 µm particles at the point of use.

6.7.2.5 *Air Change Rate*—20/h, minimum.

6.7.3 Construction considerations must be designed to prevent the physical facilities from becoming a source of particulate contamination:

6.7.3.1 Coating on all surfaces must resist deterioration and flaking.

6.7.3.2 Surfaces should be able to be cleaned effectively and easily.

6.7.3.3 Smooth, hard surfaces clean best; use coatings such as epoxy, cove bases flush with wall, covered corners, sealed joints, flush fitting doors and windows, wall protection, and corner guards.

6.7.3.4 Conceal all ducts, conduits, piping, etc. above ceilings and behind walls. Exposed pipe and conduits for equipment connections should be installed vertically.