Laboratory Design for Microbiological Safety

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Of the large amount of funds spent each year in this country on construction and remodeling of biomedical research facilities, a significant portion is directed to laboratories handling infectious microorganisms. This paper is intended for the scientific administrators, architects, and engineers concerned with the design of new microbiological facilities. It develops and explains the concept of primary and secondary barriers for the containment of microorganisms. The basic objectives of a microbiological research laboratory, (i) protection of the experimenter and staff, (ii) protection of the surrounding community, and (iii) maintenance of experimental validity, are defined. In the design of a new infectious-disease research laboratory, early identification should be made of the five functional zones of the facility and their relation to each other. The following five zones and design criteria applicable to each are discussed: clean and transition, research area, animal holding and research area, laboratory support, engineering support. The magnitude of equipment and design criteria which are necessary to integrate these five zones into an efficient and safe facility are delineated.

The magnitude of the annual national investment in new biomedical laboratory facilities, coupled with the problems arising out of unsafe designs in these facilities, justifies increased attention to engineering design criteria to maximize microbiological safety. A number of recent papers, conferences, and seminars have dealt with one or more aspects of microbiological laboratory planning and design (3, 15, 16, 20, 21).

Incorporation of microbiological safety measures in the design of biomedical laboratory facilities is needed for one or more of the following reasons: (i) to prevent the uncontrolled escape of infectious materials from the building to safeguard the health of the surrounding community; (ii) to assist in the prevention of accidentally acquired infections among building personnel; (iii) to prevent the unintentional spread of diseases among animals by animal-to-animal or man-to-animal transfer; and (iv) to prevent false laboratory results due to cross-contamination of microbiological cultures.

The purpose of this article is to describe and illustrate some of the principal building features and devices used to provide effective microbial containment for accomplishing the above aims. The article is a corollary to a movie with the same title that has been made by the Public Health Service Audiovisual Facility and sponsored by the National Cancer Institute. The film may be borrowed free of charge from the Public Health Service, Communicable Disease Center, 1600 Clifton Road, Atlanta, Ga. (Laboratory Design for Microbiological Safety—M-1091, 16 mm, sound and color, approximately 35 min).

The initial step that should be taken in the design process for a microbiological research laboratory is an analysis of the research activities to be undertaken, the hazards associated with the research and with each operation, and a functional evaluation of the relationships that will exist between each activity. This analysis should enable the laboratory director and the architect or engineer to estimate the extent of the hazardous operations and to concentrate and minimize the amount of containment equipment required, thereby realizing economic savings.

Determining what safety measures to incorporate in the design of infectious-disease laboratories has required much research and study. For instance, it was necessary to understand how laboratory workers become infected, how microorganisms might escape and spread within a building or escape to the surrounding community, how animal cross-infection and culture cross-contamination occurs, and other similar problems (6, 10, 12). From the results of a number of laboratory hazards studies (1, 9, 17, 18), two concepts emerged that have proved successful in designing biologically safe laboratories. The first is the concept of primary and secondary barriers for the laboratory containment of infec-
tious materials, and the second concept provides the designer a logical division of major functional zones within a typical laboratory building.

**Primary-secondary barrier concept.** Enclosures, barriers, or other containment devices that immediately surround the infectious or potentially infectious material are designated as primary barriers. These are the first line of defense (other than the test tubes, flasks, etc.) for preventing escape and possible spread of infectious microorganisms. Examples of primary barriers are ventilated microbiological cabinets, closed ventilated animal cages, closed centrifuge cups, and safety blender bowls (Fig. 1).

The secondary barriers in a laboratory are the features of the building that surround the primary barriers. These provide a separation between infectious areas in the building and the outside community and between individual infectious areas within the same building. Examples of secondary barriers are (i) floors, walls, and ceilings, (ii) ultraviolet (UV) air locks and door barriers, (iii) personnel change rooms and showers, (iv) differential pressures between areas within the building, (v) provisions for filtering or decontaminating potentially contaminated exhaust air, and (vi) provisions for treatment of potentially contaminated liquid wastes. These and other sec-
FIG. 2. Primary- and secondary-barrier concept.

FIG. 3. Five functional zones of hypothetical laboratory.
secondary barriers provide supplementary micro-
biological containment, serving mainly to prevent
the escape of infectious agents if and when a fail-
ure occurs in the primary barriers. Figure 2 is a
graphic representation of the functions of primary
and secondary barriers.

Actually, the more effective the primary bar-
riers are, the less need there is for emphasis on
secondary barriers. Therefore, during the design
phase of any infectious-disease laboratory, it is
both important and economically necessary first
to determine and select the primary containment
devices to be used, thereby reducing the
complexity and cost of the secondary barriers.

Functional zones of a laboratory building. Figure
3 illustrates five functional zones of a hypothetical
laboratory building for research with infectious-
disease agents. Obviously, there can be numerous
physical arrangements of these zones, but the
typical arrangement shown will illustrate their
relationship to each other and provide a basis for
a discussion of the design requirements for micro-
biological safety.

Clean zone. The clean zone of a laboratory
building (Fig. 4) contains the entrance area, the
office area, conference room and library, and
those functional rooms where administrative
operations, conferences, reading, writing, and
other tasks not involving infectious materials are
carried out. Also, within this zone are the transi-
tional rooms through which personnel and ma-
terials enter and leave the potentially infectious
parts of the building. These transitional rooms
preserve the integrity of the secondary barrier
when people and materials enter and leave the
infectious areas. In addition, the necessary ship-
ping, receiving, and clean storage areas are in
the clean zone. The mechanical equipment space, al-
though a clean area, will be discussed below.

Personnel should enter and leave the infectious
areas through clean and contaminated change
rooms, illustrated in the lower right hand portion
of Fig. 4. The clean change room should provide
lockers to store street clothing, storage shelves for
laboratory clothing, and appropriate toilet and
wash facilities. An air lock with a UV door
barrier and ceiling-mounted UV lamps separates
the clean from the contaminated change room.
Adjacent to this or between the two change rooms
should be located a shower room for use when
leaving the infectious areas. The contaminated
change room should contain a storage rack for
laboratory shoes, a bag for discarding laboratory
clothing upon exit, and suitable toilet facilities.
The use of UV lamps in the shoe storage rack
and clothing discard bag can be an effective
secondary barrier (11, 19).

Transitional arrangements for materials and
supplies generally are needed at two locations. At
the front of the building, provisions are usually
required for transferring books, data sheets, and
similar items between clean offices and offices in

![Fig. 4. Clean zone, clean and contaminated change rooms.](http://aem.asm.org/Downloaded from May 23, 2021 by guest)
the infectious area. Typically, this may include a small through-the-wall ethylene oxide gas chamber for the cold sterilization of heat-sensitive materials (8) and a UV apparatus for decontaminating sheets of paper passed out of the infectious area (13), as illustrated in Fig. 5. Transitional rooms at the rear of the laboratory are needed for receiving laboratory and animal room equipment and supplies and for removing equipment, trash, and other items from the infectious areas. A typical arrangement (Fig. 6) at the rear of the building will consist of a UV air lock for the inward passage of supplies, and clean and contaminated receiving rooms separated by large through-the-wall autoclaves that are also operable with mixtures of ethylene oxide gas. The use of small viewing windows and speaking diaphrams facilitates communication and operation in the front and rear transitional rooms.

Laboratory research zone. The laboratory research zone (Fig. 7) contains laboratories for infectious microbiological operations, exclusive of animal work. This zone is separated at least by a corridor from the zone where infected animals are used. In addition to laboratory rooms, this zone may contain potentially contaminated offices adjacent to offices in the clean zone, necessary toilets and change rooms, constant-temperature rooms for incubation and refrigeration, and instrument rooms for centrifuges and other research apparatus.

One of the most important tasks in planning the laboratory research zone is the selection of the primary barrier ventilated cabinets. Although cabinets are available in many shapes and sizes and constructed of a variety of materials, there are only two basic types: partial-barrier cabinets and absolute-barrier cabinets. Figure 8 shows a partial-barrier cabinet that provides an inward sweep of air through the open panel and away from the operator. This unit may also be used with a panel and gloves attached as shown in Fig. 9. Absolute-barrier cabinets are similar in appearance (Fig. 10), but are gas-tight and are operated at a constant negative air pressure. The selection of partial- or absolute-barrier cabinets will have a significant effect upon sizing of the air-handling equipment because the former require 300 ft³/min supply and exhaust, whereas the latter require only 3 to 10 ft³/min per 6-ft unit. Obviously, the selection of the types of cabinets for use with the infectious cultures will vary according to an assessment of the risk of the types of laboratory operations together with the particular microorganisms to be used. In reference to the hypothetical laboratory research zone (Fig. 7), it is assumed that 75% of the research area will be for low to medium risk work requiring partial-barrier cabinets, and 25% will need to be equipped with

**Fig. 5.** Transitional arrangements between clean and contaminated offices.

**Fig. 6.** Transitional arrangements between clean receiving area and contaminated research area.

**Fig. 7.** Laboratory research zone.
absolute cabinet systems for performing high-hazard operations. The absolute cabinet system terminates with a double-doored autoclave, and a germicidal liquid bath is also available for passing materials in and out of the system. At least some of the other laboratory rooms should have free-standing, single-door autoclaves. This reduces the need to transport potentially infectious materials in the corridors. In determining spatial arrangements for safety cabinets and the most effective and efficient room sizes, the bench concept developed by Norman (7) is appropriate, except that the cabinets replace the open bench in many of the activities.

Within the laboratory research zone, there are a number of design considerations that will directly influence the containment by the secondary barriers. The most important of these are as follows.

(i) Microbial filtration of non-recirculated air exhausted from the laboratory rooms. High-efficiency microbial filters (2) with 99% retention of 1.0-μm diameter particles usually are appropriate.

(ii) Microbial filtration of exhaust air from absolute-barrier safety cabinets and other apparatus where aerosols of infectious microorganisms are intentionally generated. Ultrahigh-efficiency filters (2) with 99.95% retention of 0.3-μm diameter particles are acceptable in these applications. In some instances, it also may be desirable to utilize an electric or gas-fired air incinerator in addition to the ultrahigh-efficiency filter for ultimate protection.

(iii) Air pressure balance within the zone should maintain the laboratory rooms negative to adjoining halls, and the cabinets negative to the laboratories. Differential air pressures are established by controlling the direction of air movement. A typical laboratory may be maintained at a pressure negative to surrounding areas by exhausting larger quantities of air than are supplied. Obviously, the balance of such a system can be significantly affected by the pumping action of doors, traffic, and other factors. The entire laboratory research zone should be maintained at a negative pressure compared to the noncontaminated zones.

(iv) Paints and coatings used on walls, wall curbs, ceilings, floors, and other surfaces must
be resistant to flowing steam and to the disinfectants used in the decontamination process and frequent washings. Walls, wall curbings, and ceilings should be free of cracks, and the coatings flexible enough to span minor shifts in the structural system. A monolithic covering is often used on the floors.

(v) Casework and other installed equipment, when possible, should be sealed to floors and walls to limit possible spread of contamination. Equipment not sealed to walls or floors should be movable or mounted on wheels to facilitate decontamination and cleaning.

(vi) Lighting fixtures, pipes, conduit, and other services that penetrate the secondary barrier wall must be designed and installed to preserve the biological separation between the contaminated and clean zones. Electrical conduit should be internally sealed. Fixtures should be sealed to the wall or ceiling or mounted away from the surface for ease of cleaning.

(vii) To limit personnel traffic, liberal use should be made of viewing windows and speaking diaphragms in doors or walls to laboratories, particularly doors to walk-in refrigerator and incubator rooms.

(viii) In some rooms it may be desirable to install ceiling-mounted UV fixtures operated from the corridor when the room is unoccupied. These fixtures aid in reducing nonspecific microbial contamination and are useful in case of an accidental spill of infectious material.

*Animal research zone.* When the animal research zone is used for relatively small laboratory animals, the rooms are usually located in the same building as the laboratory research zone. This zone typically includes rooms for animal inoculation and autopsy, and infected-animal holding rooms equipped with primary-barrier isolation equipment such as ventilated cages and UV cage racks (Fig. 11). In some instances it may be desirable to locate aerosol exposure equipment, such as the Henderson apparatus, in a room adjoining the animal room.

If not available elsewhere, the animal area should have an incinerator for disposing of animal carcasses, and a large autoclave for sterilizing cages and passing them into a cage-washing room.

In designing this zone, the type and degree of animal isolation should receive early consideration. It should always provide for safe working conditions for personnel and prevent undesired animal cross-infection. The caging system selected will affect the cost of the facility, and ventilated cages will have an impact upon the size of the air-handling equipment.

Dust filters should be installed at the air exhaust ducts of the animal rooms to prevent excessive loading of the downstream microbial filters with animal hair and dander. It is desirable to have these filters decontaminated in situ and changed by laboratory personnel. The recommended minimal ventilation rate (Guide for Laboratory Animal Facilities and Care, rev. ed., Public Health Service Publication 1024, Washington, D.C., 1965) for the rooms is 15 changes per hour of filtered, nonrecirculated, draft-free air of the relative humidity and temperature appropriate to the animal species. Since the walls and floors of animal areas will be decontaminated and washed frequently and exposed to urine and other wastes, careful selection should be made of wall paints and finishes.

Other design considerations of importance in the animal zone are: waterproof lighting fixtures in wash areas, floor drains, adequate storage areas, cage- and rack-washing equipment, automated animal care activities, etc. Although the nature of some disease agents in small animals is such that no special provisions are needed to pre-
vent cross-infection or to protect animal handlers, many infectious agents require animal isolation equipment for protecting personnel. In situations where a high degree of isolation is required and where animal-to-animal separation is needed, infected animals are held in small, individually ventilated cages (Fig. 12). In some instances, instead of closed ventilated cages, animals may be housed in cages under a UV barrier (14) as illustrated in Fig. 13. Nonportable ventilated animal compartments have been found to be effective in some infectious-disease laboratories. Each of the

![Fig. 12. Ventilated animal cage rack (with UV screen).](image1)

![Fig. 13. Nonventilated animal cage rack (with UV screen).](image2)

Horsfall units (5) shown in Fig. 14 holds one or two animal cages and is equipped with a viewing window and inlet and outlet air filters.

If the animal research zone uses infected large animals, such as horses and cattle, it may be in a remote wing or suite, or may even be located in a completely separated facility. In any case, since it is very difficult to provide primary barriers around large animals, greater emphasis is ordinarily placed on the secondary barriers. A typical suite for housing infected large animals (Fig. 15) would contain holding rooms with movable stanchions and partitions, and rooms or areas for animal inoculation, surgery, autopsy, and incineration of carcasses. In case the epizootic diseases being studied are transmissible to man, protection for operating personnel must be provided by protective garments and respirators or ventilated suits if needed. The large-animal zone should have change rooms and transitional rooms for movement of food and equipment as previously described.

**Laboratory support zone.** In many infectious-disease laboratories, the zone for laboratory support is best located outside the contaminated research zones. From an economic and functional standpoint, this location reduces the amount of secondary-barrier area required and provides an opportunity for grouping similar support functions in one area. An admitted disadvantage of locating the laboratory support zone outside the contaminated research zone is that washroom and animal-room personnel cannot move between the contaminated and clean zones without changing clothing and showering, and therefore additional personnel may be required.

A typical laboratory support zone (Fig. 16)
may include rooms for washing and sterilizing glassware and animal cages, preparing culture media, storing equipment, glassware, and animal cages, and repairing various laboratory items. In some instances, the support zone may contain animal rooms for the quarantine and acclimatization of animals before they are passed into the infectious area for use. Careful attention must be given to the design of the ventilation system for this zone because of the many heat-generating and odor-producing procedures which are carried out in the washing area. Also, because of the large

**Fig. 15.** Large-animal research zone.

**Fig. 16.** Laboratory support zone.
amount of water involved in washing operations, floors, walls, and other surfaces should be resistant to moisture. The room for culture media preparation should have a controlled movement of filtered supply air. To limit the ingress of microorganisms, air in the room and cabinetry always should be maintained at a positive pressure compared to the other laboratory support rooms.

**Engineering support zone.** The fifth functional zone provides engineering support for the entire facility. Included here are the necessary pipes, ducts, pumps, blowers and filters, the liquid waste treatment system, and most of the air-handling systems. Special engineering arrangements should maintain the integrity of the secondary barrier when penetration of the wall is made by pipes, wires, and ducts. As much of the engineering support equipment as possible should be located outside contaminated zones, to reduce the necessity of entrance of maintenance personnel. The zone can be comprised of space located on the grounds adjacent to the building, or in the attic, basement, or other building space. Because of the large amount of engineering equipment needed, as much as half of the total building area is sometimes required for this zone.

The equipment required to heat, cool, filter, and distribute the supply and exhaust air for the various building zones will occupy a large part of the engineering support zone. This equipment may represent an investment amounting to nearly one-half the cost of the facility.

Whenever a device or item of equipment is essential to the maintenance of a microbiological barrier and is subject to failure, "fail-safe" design features are required. This aspect should be accomplished through the use of redundant fans and motors, interlocked supply and exhaust fans to prevent pressurization of infectious areas, emergency electrical generators, filters in series with air incinerators, automatic cycling of autoclaves after the door on the infectious laboratory side is opened, etc. The inclusion of such items in a laboratory should be determined only after an assessment of the risks associated with the research activity has been made.

One vital consideration is the need to locate the air-intake grille upwind of the exhaust stack. In addition, there should be adequate physical separation between both to prevent cross-contamination. In the engineering support zone, air ducts going to each room in the infectious zone should deliver non-recirculating, filtered, and conditioned air.

The supply ducts need not be of air-tight construction, but exhaust air ducts coming from the infectious zone must be air-tight to assure no leakage of infectious microorganisms before the air reaches the exhaust filter plenum. Galvanized ducts with taped, epoxy-coated joints have been found satisfactory.

Exhaust air plenums are often sized to serve several laboratory rooms of about the same hazard level. They may be equiped either with high-efficiency spun-glass mats, or with ultrahigh-efficiency units for filtering air discharged from the rooms. Because the filters in a plenum must be changed periodically, provisions should be made for decontaminating both the filters and the plenum itself before entry by maintenance personnel. A mixture of steam and formaldehyde is frequently used as the decontaminant (4).

In virus laboratories, inlet air is often passed through ultrahigh-efficiency filters. This high-quality air is required to prevent accidental contamination of experimental cultures by endogenous organisms or by other organisms utilized in the research program. In tissue culture cubicles or other areas requiring this high-quality air supply, the use of a high-volume recirculated air system with ultrahigh-efficiency filtration should be considered if no hazards to operating personnel are created. This system will result in significant economies by reusing conditioned air, and will be acceptable if proper separation by zones of similar usage is employed.

An important part of the engineering support zone is the central control board (Fig. 17). Here, read-outs of all systems in the area can be monitored by engineering personnel. Such boards should have visual and audible alarms that will automatically signal the failure of any part of the system when preset limits of environmental factors such as temperature are exceeded. Another important item is a standby electrical generator that is used in the event commercial power supply

![Fig. 17. Central engineering control board.](http://aem.asm.org/)
is interrupted. Although it may not be possible to provide a generator large enough to supply full electrical requirements, the standby current should at least be sufficient for ventilated animal cages, ventilated cabinets, deep freezes, refrigerators, incubators, and emergency lighting. The standby units may be mounted in trailers to provide easy portability, or incorporated in the engineering support zone.

In some laboratories, facilities must be provided for treating contaminated liquid wastes. Two basic systems are usually employed: batch and continuous flow. However, if the hazards associated with the program are minimal and adequate space is available, a sanitary drain field can be utilized. Regardless of the system, in the laboratory no infectious culture fluids should be knowingly poured into drains without prior sterilization.

The batch system (Fig. 18) is used to collect potentially infectious effluents from infected animal areas by gravity flow. When a tank is about one-half full of liquid, the drain lines are closed and the liquid is sterilized by adding steam and holding for a period time. Usually, a second tank is automatically put into service at this time. All piping to the tank should have welded joints to assure no possibility of leakage. A concrete curb should be provided to contain the liquid in the event of a rupture in the system. The necessity for microbiological monitoring of the effluent from the system should be considered in the design process, to ensure that adequate valves, sampling ports, etc., are incorporated in the design for removing samples.

For larger volumes of effluent, a continuous-flow arrangement (Fig. 19) that utilizes injected steam to raise the liquid to a proper temperature may be used. In this case, the effluent-steam mixture flows through a series of retention tubes and is cooled through a heat-exchanger before being discarded.

Liquid waste treatment systems can be monitored and controlled from a central panel where flow arrangements, effluent volumes, treatment times, and temperatures are visually indicated.

**Literature Cited**


