Designing the SPF Barrier

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Scientific discovery is dependent on the ability to formulate a process, reproduce tests, and compare results. The critical 'reproducibility' requirement is met by breeding animal stock that provides a consistent, quantifiable baseline for experimentation.

Animal barrier facilities are designed and operated to provide pathogen free environments for the animals bred within. These facilities, sometimes referred to as specific pathogen-free (SPF) facilities, may be designed as stand-alone buildings used for production facilities or as components of larger animal research programs.

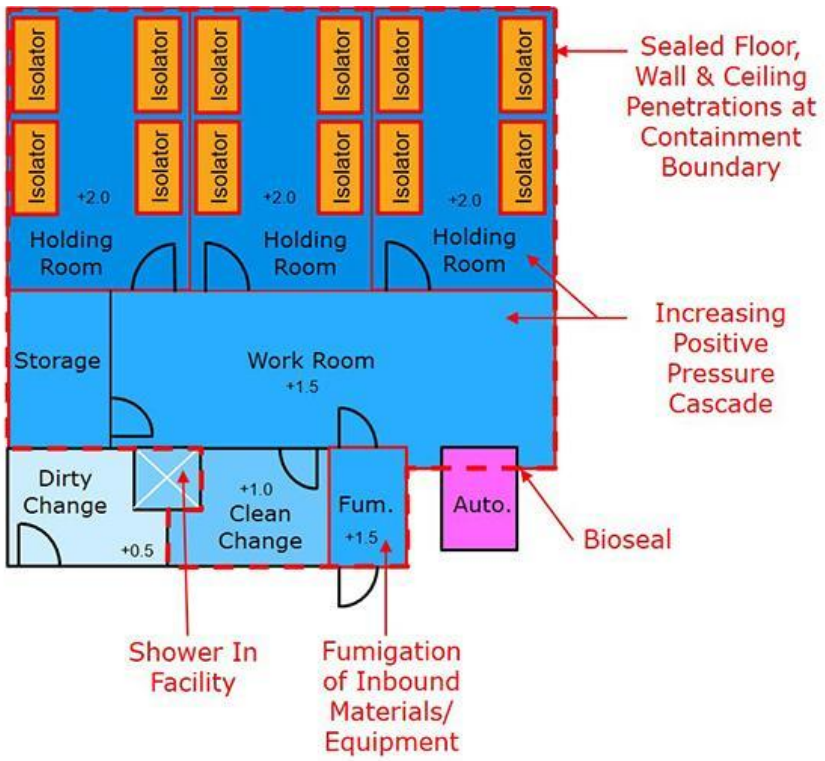
Scientific need defines both the barrier requirements as well as the pathogen exclusion of any given colony, but the use of barrier facilities in breeding is generally based on the need to precisely control the health status of the research animals, provide genetically equivalent sample stock, optimize breeding and life span, and increase the repeatability and reproducibility for animal experiments. Animals are either born within or received into the barrier facility only after meeting rigorous

testing to confirm they are free of the defined list of pathogens that are considered undesirable within the breeding colony.

Germfree, Gnotobiotic, or SPF?

Depending on the breeding requirements, the barrier may be defined as the microisolator environment in which an animal is housed or as the entire suite. Animals born via c-section and housed in closely monitored aseptic microisolator environments do not develop complex microflora and can be classified 'germfree' or 'gnotobiotic,' allowing the researcher to control exposure to relevant microorganisms relevant to their research.

Conversely, animals bred within open or exposed caging systems within a barrier facility do develop microflora and are not classified gnotobiotic due to their exposure to microorganisms within the room. These animals "may be referred to as specific pathogen-free (SPF) to indicate that the colony from which they originated tested negative for certain pathogens and perhaps other adventitious agents that may interfere with research without causing disease. For mice and rats, SPF refers to animals that are free of most exogenous viruses and other pathogenic microorganisms."[1]



Designing for Containment

To support the rigorous breeding and health testing protocols of these animal colonies, barrier and SPF facilities are designed

as containment facilities, making both isolation and sealability important factors in the design.

Traditional containment design prevents pathogens from leaving the containment envelope by using negative pressure cascades and sealed boundaries. SPF facilities use similar boundary strategies, with a positive pressure cascade to prevent entry of outside air and pathogens to maintain laboratory breeding colonies free of diseases that would conflict with or inhibit research results.

Similarly, the entry and exit sequences into a barrier facility are designed to prevent contaminants entering from corridors. Sequences are arranged to provide sterilization of both personnel and materials inbound to the area. These perimeter spaces—change areas, showers, autoclaves and fumigation chambers—are designed as slightly positive to the corridor, with spaces becoming increasingly differentially pressure positive the further inbound into the barrier suite they are located. The animal holding rooms, where colonies are born and reared, are the most positive to the surrounding support spaces which maximizes isolation of the animals and ensures the desired health status.

High containment design capitalizes on the physical isolation provided by a box-in-a-box design by providing a physical separation of the containment block inside a zone that is not bound by exterior wind and temperature conditions. Not only does this type of separation lessen the strain on the mechanical system, but it also lessens the transmission probability between one side of the wall and the other via improperly sealed penetrations that permit possibly contaminated air, water or vermin from adjacent spaces to infiltrate the barrier facility.

Enhanced mechanical isolation of the positive pressure environment is critical when a barrier facility is incorporated into a greater research facility, particularly in areas where a physical isolation via buffer is not planned. This may include HEPA filtration of the supply air, but also should include directional airflow to support positive pressure cascade from clean to potentially contaminated spaces.[2]

In order to maintain pressure differentials, Air Pressure Resistant (APR) or gasketed doors may be used at the barrier

boundaries to contain decontamination gases and meet room volume testing criteria.

Consider Physical and Operational Requirements

The design should consider both the physical requirements of the barrier space as well as the operational needs of this specialized function. Barrier suites should be located within a clearly demarcated, access-controlled area inside the building. Travel paths of materials, animals and personnel should be carefully planned to eliminate unnecessary exposure to contaminants and minimize travel distance to support functions such as loading docks.

Ideally, the barrier facility would have dedicated loading areas. Because barrier facilities are designed to rear young animals that will ultimately be transported elsewhere for use, the final destination of the animals should be understood clearly at the conceptual level. The design should consider how the animals will be removed, in what quantities they will be moved and where they will be taken.

Change sequences should be incorporated at the suite entry to permit personnel to change into complete SPF-dedicated personal protective equipment (PPE) including sterilized footwear, scrubs or gowning, eyewear, and any additional safety covering necessary for working with animals. Change sequences should also provide either an air, or preferably, a water shower to ensure that personnel are thoroughly clean prior to donning sterilized PPE and entering the suite. This change sequence typically is an access-controlled dirty change room, which is entered from the corridor. Outer clothing and footwear is removed and stored, personnel then use the pass-through body shower before entering a clean change room where the sterilized PPE is donned before entering the barrier core.

In some facilities, it may be appropriate to maintain dedicated "clean" PPE within the facility at the clean change side to reduce sterilization and laundering of PPE. Similarly, all incoming materials including food and bedding must be sterilized at the barrier boundary. Wrapped food and bedding may be fumigated within a sealed chamber upon entry, while other non-perishable items may be autoclaved at the boundary. In the case of poultry-breeding facilities that receive eggs to be hatched, a UV chamber may be needed for

sterilizing the packaging of incoming eggs without harming the egg itself. At all perimeter entries for both personnel and materials, interlocked, access-controlled doors should be provided.

Special Considerations for Animal Rooms

Interior spaces within a breeding suite may include multiple holding rooms for animal rearing, separate procedure space, sterile material storage areas and work rooms for staging, logging and support equipment. Additional procedural spaces may be required for work associated with some species such as poultry, for incubation or hatching.

Unless the facility has dedicated processes involving a single species, animal holding rooms should be designed to accommodate a range of species to permit future changes in operations. As such, animal holding rooms, as well as fumigation entry points to the suite, shall be designed for worst-case scenario caging or isolator size requirements and should include turn-radii and doors sized to accommodate larger caging. If a range of species will be housed, design requirements regarding noise, vibration, temperature, humidity and lighting for all species under consideration must be met. In barrier suites where multiple holding rooms are included, zone isolation of the separate holding rooms to permit individual decontamination of the spaces is advisable.

The walls and ceilings within a barrier facility must withstand the pressure differentials within the suite, as well as prevent vermin transmission. Penetrations must be tightly sealed to meet room volume testing and facilitate decontamination of the suite. Integral epoxy floor, wall, and ceiling coatings are recommended though monolithic, slip resistant surfaces. Special consideration should be given to flooring and wall finishes, particularly in rooms that have open pens or where free-roaming poultry will be housed. Some species are prone to eating, pecking or clawing room finishes and could contribute to the rapid deterioration of the containment boundary, making it difficult to maintain appropriate pressure cascades.

All finishes must be resistant to chemical disinfectants and designed to withstand hot water hose-down procedures. Capped floor drains should include deep seal traps filled with chemical disinfectant. Drinking water must be treated as a

consumable and be sterilized. If an animal watering system is provided, it should include reverse osmosis treatment to remove potentially infectious agents. Sterilization of incoming materials requires direct access to a double door autoclave or similar chemical disinfection device. Where containment boundary equipment such as an autoclave or pass box are provided, bioseals shall also be included.

As scientific rigor continues to evolve, it has become increasingly important to document any external factors that might have an impact on the final research data. This includes, and truly begins, with proving that animal models forming the basis of research are as homogenous as feasible from the outset, and this has driven demand for rigorous design of SPF barrier facilities. Ensuring optimal design and operations strategies, in conjunction with strong biosafety practices, are keys to a successful breeding program and enable scientific discovery.

References

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Rainey Hufstetler *is a registered architect with 15 years of high containment design expertise in highly technical laboratory and animal facilities. Her experience is focused primarily on large academic and government bio-containment research facilities with an emphasis on specialty cores: whole animal imaging, cellular imaging, insectary, aerobiology, etc. She has written and presented to a variety of audiences including I2SL, CDC and ABSA on sustainable approaches in containment facility design.*

Image: The Joseph E. Walther Hall (Research III Building) at Indiana University School of Medicine. Photo courtesy of HERA laboratory planners