Research Vivarium Design Considerations Optimizing and Supporting Biosignal, Biodevice, and Biomedical Engineering

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Abstract. Contemporary biomedical research supporting biosignal, biodevice, and biomedical engineering will be conducted in either new or remodeled animal facilities. It is important for researchers, veterinarians, and architects to have a better understanding of each other’s needs when considering new or remodeled facilities; especially in light of new regulatory and voluntary compliance standards. Contemporary facilities are more than ‘animal warehouses,’ they play an integral part of the research program by offering procedure and research support facilities. By maintaining the animals in the controlled environment found in the vivarium, fewer research variables are introduced (e.g., transportation, disease). The presentation will offer insights on facility needs, design considerations, and potential pitfalls to the attendees. The cost of contemporary animal facilities is more expensive than most institutions anticipate, but can be properly managed; the importance of life cycle cost will also be discussed.

1 General Design

Vivarium design must be in close collaboration with a knowledgeable architect and credentialed laboratory animal veterinarian. In the absence of either, it will be worth the investment to bring in consultants in both these areas to ensure, among other matters, appropriate materials, design, equipment, and perhaps most importantly integrating investigator needs. Together the architect and veterinarian will work to meet the current and future needs of researchers based on institutional data and an institutional master plan. New construction is optimal as it permits the best ‘fit’ for researcher needs and expectations. Remodeling, even extensive remodeling, may give the illusion of cost savings, but may fail to meet research needs, construction schedules, or poorly utilize space. New construction is frequently better at optimizing savings from building orientation, construction materials, and most importantly research integration.

Facilities must be designed and constructed to meet local regulatory requirements and should meet the Association for the Assessment and Accreditation of Laboratory Animal Care—International (AAALAC) accreditation standards; however, there are instances where there is conflict between building codes and expected vivarium design and construction practices. Here, the knowledgeable architect and credentialed laboratory animal veterinarian can meet and work with the local authorities to understand the need for the deviation(s). The vivarium must address the concerns for

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animal health and well being in addition to human health and safety.

The species used deserves strong consideration; however, building design must ensure a high degree of flexibility. Species such as mice, rats, and rabbits must be kept in a Specific Pathogen Free (SPF) environment, in a low traffic/vibration area (best on higher floors), and away from noisier animals. Whatever species is used a clear understanding of their entry into the vivarium, maintenance, and use must be conveyed to the selected architect and veterinarian.

Small animal holding rooms frequently do not require drains and are flexible enough to house many species. Large animal holding will require drains, and the drains should be appropriately sized and supplemented with a rim flush or garbage disposal.

Specialized equipment must be thoroughly understood and properly planned. Equipment frequently includes imaging (e.g., MRI, radiography), behavior/ physiology core facilities, and an irradiator. The imaging and irradiator equipment will drive construction practices including shielding, structural loading capacity, security, and outside user access and availability.

Specialized services are an important component of contemporary vivaria. These services frequently include the barrier and barrier practices for the SPF containment, surgical facilities for both large and small animals, a transgenic core facility, and a containment facility.

The facility must be close to the research or research hubs for the institution. Centralized facilities are more cost effective and easier to keep in regulatory compliance than decentralized facilities. Storage is a key component and usually the first removed when ‘value engineering’ occurs; facilities will need at least 20% storage space; storage needs are more recognized as the vivarium’s occupancy increases. Closely evaluate storage needs and appropriately determining the HVAC needs for these areas.

Facility design must include disaster and emergency preparedness. Although a disaster’s likelihood is small, it must be incorporated into a facility disaster plan. Clearly this is another advantage of having additional storage capacity for food, bedding, water, and other essential supplies.

Doors, walls, and floors transcend all vivarium areas. Long lasting polymer doors offer cost saving advantages over the alternatives and must incorporate door protection (e.g., door guards, kickplates), sanitation, and equipment floor. Walls must be sanitizable, free of cracks/pinholes, and protected. Flooring must be durable, sanitizable, and low maintenance.

2 Housing

This section will focus on barrier housing as it has a greater impact on cost than most other types of housing. Barrier housing will meet the requirements of an ABSL 2 facility as established by the US Health and Human Services [6]. Housing needs must be established early as they impact a host of other areas including the doors, elevators, cage wash, and autoclaves. It is important to remember that the barrier starts at the cage level. Keeping the animals disease-free is important to ensuring research results are reliable.

There is a general misconception that animal holding facilities must be dual corridor (e.g., clean and dirty corridor). Corridor space can account for 30-50% of a facility employing a dual corridor paradigm; while a single corridor facility can account for as little as 17% [1]. Holding areas generally consist of a single-room or suite off a main corridor.

Holding rooms employ various strategies to ensure disease prevention including stocking with disease-free animals, testing various cell lines/tumors, sanitizing items entering the cage (e.g., food, bedding, enrichment), employing IVCs/microisolator tops, using cage change stations, and developing an effective sentinel and quarantine program.

Other considerations include sterilization access for barrier and containment housing, janitor's closets, nearby research support space (e.g., surgery, imaging, irradiator). It is ideal to provide sufficient facilities and procedure space to permit most research activities to occur within the vivarium. Animals used in containment-based research frequently cannot leave the facility. Barrier animals leaving the facility cannot return to their original room, unless it has been determined they are disease-free. Most facilities provide a 'return room' for those animals leaving the barrier facility. This room must be of sufficient size to house sufficient animals, frequently over a long period of time; alternatively animals can be quarantined to evaluate their health status.

Housing, especially for small animals, will have the greatest cost impact on a facility. This includes heating, ventilation, and air conditioning (HVAC), high efficiency particulate arrestance (HEPA) filtered air, and caging. The caging must be carefully considered and greatly impacts life cycle costs. For instance, in two cost equivalent systems, one system 10 parts per cage, while the competitors have 5; furthermore, one caging system (the same system with the higher parts) requires at least annual HEPA filter replacement. Over a few years the additional cage equipment storage requirement and HEPA filtration replacement costs for the 'equal cost' caging system will greatly increase animal maintenance costs.

Room layouts are frequently driven by projects, money, or multiple users; frequently a blend of layouts is required. Project layouts are frequently smaller utilizing more single-sided cage rack. Money driven layouts want to maximize animal population in a given floor area; this layout frequently employs ventilated racks and smaller aisle widths. Money driven layouts while increasing animal density, may come at the cost of decreased cage changing and worker productivity. The multiple user rooms are quite common, especially in academic institutions. These consist of larger holding rooms, ventilated racks, and wider aisle widths.

It is important for the facility to be properly wired and 'future-proofed' to ensure a research benefit for many years. The building should be equipped with cell phone repeaters, wired and wireless internet access, generous electrical outlets, and other services needed for research and vivarium support equipment. A thorough understanding of the various needs initially and a periodic review is essential to ensuring the vivarium remains relevant.

3 Procedure Space

Generally a 1:1 ratio of housing to procedure rooms is ideal. It is advantageous to incorporate a modicum of housing capabilities in the procedure space; in addition incorporate a biosafety cabinet (e.g., Type II A2, Type II B2) and various piped gasses (e.g., oxygen, vacuum, air, carbon dioxide). Additional services/equipment, or augmentation of the existing, may be needed based on research paradigms employed. It is important to understand which procedures an institution permits in a housing room.

Research equipment brought into research space must be appropriately disinfected; and since some research may occur outside of a HEPA filtered cage change station, the room containing this equipment should be periodically sanitized. The chemicals used on surfaces must be equipment friendly. Many institutions fumigate large pieces of research equipment (e.g., microscopes, computers) before entering animal facilities; this usually consists of exposure to vaporized hydrogen peroxide (VHP) or chlorine dioxide (CD). VHP is corrosive to some surfaces, requires longer exposure and a post-exposure wipe down, and is not a sterilant. Overall CD is more advantageous than VHP.

Surgery is perhaps the most commonly required procedure space. The surgery requirement will vary according to the species used. Regardless, it is important to provide the following areas when surgery is performed: animal, surgeon, and instrument preparation; operating area; and animal recovery. Specialized equipment is frequently needed in the operation area and every effort should be made to periodically clean and/or fumigate this area, especially in areas with unavoidable clutter. Personnel exposure to anesthetic gases or carcinogenic anesthetics (e.g., urethane) must be minimized and appropriate control measures taken (e.g., downdraft surgery tables, flexible snorkel, fume hood).

4 Vivarium Support Equipment

Sanitation is essential in contemporary vivarium and proper equipment is critical to ensure minimal service disruption and safeguarding the institution’s investment in their biomedical research models. Overall it is best to purchase equipment using non-proprietary parts and to employ an suitably-trained engineer for repairs ad preventative maintenance. The equipment below may require some degree of isolation to ensure noise and vibration originating from it does not result in research interference; in addition the HVAC and all equipment should undergo testing and commissioning prior to occupancy and periodically thereafter.

4.1 Autoclave

Autoclaves must be of sufficient size to sterilize a wide variety of equipment (e.g., cages, water bottles, racks, IVCs). The autoclave is the most frequent bottleneck therefore a accurate assessment of autoclave needs is essential along with an evaluation of other strategies. Other strategies include purchasing irradiated diet over autoclaveable and utilizing automatic watering over bottled, autoclaved water; the latter is an important consideration as the liquid autoclave cycle can be twice as long as that for dry goods. Alternatives exist to some autoclave uses; however, these may be subject to regulatory approval.

4.2 Cage Wash

There are many ways to wash cages, with contemporary facilities using either a rack or tunnel washer. Throughput must be evaluated as well as the cage wash dimensions. Some cage wash vendors have smaller height rack washers that restrict their use to a few cage manufacturers. In the process they may not meet the future needs of the facility or may be unable to clean larger pieces of equipment. It is best to purchase a full-height rack washer.

4.3 Automatic Watering

Automatic watering offers many cost saving advantages over providing bottled water and it acts to increase the throughput of autoclaves and cage washers. It permits faster cage changes and reduces work-related repetitive stress injuries. Data suggests [3-5] that water bottle failures are greater than those of automatic watering systems.

5 Research Interference

- Partial build-out/shell space: This option is frequently considered; however, when considering the potential losses associated with future research interference, equipment cost increases, and research program stability, this option must be carefully weighed. The outcome frequently depends on the meaning ‘partial.’
- Radio Frequency Identification (RFID) is gaining popularity to determine animal census. Consideration must be given to determine if this technology will interfere with telemetry and other studies. Likewise, what are the impacts of neighboring telemetry devices/studies.
- Floors and walls are strong considerations as imaging modalities require various forms of shielding (e.g., walls, ceiling) and concrete pad (e.g., MRI) to minimize interference. It is important to have a broad understanding of the research plans and needs to minimize the likelihood of a costly renovation.
- Punch-outs permit relatively easy building access via large removable walls or ceilings. Punch-out placement may enhance the building’s flexibility while ensuring it can be appropriately serviced and updated.
- Nearby construction can impact delicate research equipment. Likewise it can negatively impact animals, especially those on behavioral and physiology experiments. It is important to understand the construction occurring ‘in the neighborhood’ as well as in a given building/facility. Vibration and noise can and will negatively impact animal-based research.

6 Costs

There are many ‘costs’ impacting a vivarium. These include the building cost, construction cost, equipment cost, and life cycle cost. Each must be closely evaluated and options considered before ‘value engineering’ forces building alterations resulting in a less than optimal research facility. Likewise, administrators and scientists must develop realistic expectations of facility costs and their benefits.

7 Conclusions

There are many factors impacting the cost of contemporary vivarium design and construction in addition to those presented. It is important to start with a knowledgeable architect and credentialed laboratory animal veterinarian to provide the researchers and institutional administration with options that best meet the needs of the biomedical research team while reducing building, construction, and life cycle costs. These additional costs will most frequently negatively impact the researchers most by reducing a vivarium’s potential as a powerful research support tool.

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