HVAC Design in Animal Facilities

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The HVAC system in an animal research facility provides an important role in the overall function of experimental or breeding facilities. HVAC engineers often think of design objectives in terms of parameters such as temperature, humidity, and air-change rates. Published design guidelines provide a framework for overall system design but should not be applied without a full understanding of animal room risks, types of animal rooms, and types of caging systems.

The environmental criterion established for animal rooms is intended to provide for protection in three areas:

1. Comfort and wellness of the laboratory animals;
2. Metabolic stability in animals for clinical consistency of experimentation; and
3. Safety of the animal caregivers and other workers.

Many environmental factors could affect animals (comfort or metabolic stability) and workers. The most significant environmental factors that must be controlled and are the basis of HVAC system design criteria are: temperature, relative humidity, air movement velocity, carbon dioxide (CO_2) level, ammonia (NH_3) level, andparticulate matter

Types of Animal Rooms

HVAC design for animal rooms will vary based on the type of animal room involved. The final criteria for the animal room will be based on the following considerations: type of animals housed, function (breeding or experimentation), biological safety level (BSL), and caging system used.

This article's discussions are based primarily on rodents (mice and rats), but within reason, most can be extrapolated and applied to larger animals as well. The distinction between breeding and experimentation is not generally addressed in published guidelines, but this can have an impact on the desired directional pressurization of the space.

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	Basic BSL Requirements				Additional Animal Requirements		
	BSL-4	BSL-3	BSL-2	BSL-1	ABSL-4	ABSL-3	ABSL-2
Separation	Separate Building	Restricted Access	Lockable Doors	Doors			
Windows	Sealed, Breakproof	Sealed	Operable With Screens OK	Operable With Screens OK			
Ventilation	Dedicated, 100% OA	Ducted Exhaust, 100% OA	100% OA			10–15 AC/hr per GCULA	10–15 AC/hr per GCULA
Exhaust Filtration	HEPA Required	HEPA if Near S/A Intake					
Supply Filtration	HEPA Required	No Direction Indicated	No Specific Requirements				
HEPA Handling	Decon or BIBO Required						
Room Differential Pressure	Monitor and Control	Monitor and Control					
BSC Types	Class III Ducted	Class II Recirc. Allowed	Class II				
Vacuum System	Dedicated System Reqt.	Dedicated or Protected OK		No Specific Requirements			
Vacuum Filtration	HEPA Within Place Decon.	HEPA or Disinfect Trap					
Waste Treatment	Pretreat Dirty Side Waste	No Direction Indicated	No Specific Requirements			Disinfectant in Trap	Disinfectant in Trap
Sewer Vent Protect	HEPA Required						
Handwash Sink	Reqt. With Hand-Free Operation	Reqt. With Hand-Free Operation	Regular Sink Allowed				
Lab Liquid/Gas Supply	BFP Required	No Direction Indicated	No Specific Requirements				
Commission/ Qual.	Required	Required					

Table 1: Summary of animal room requirements.

For example, breeding rooms often are maintained at a positive directional pressure to ensure a clean environment for the animals. Experimental holding areas, on the other hand, generally will be maintained at a negative directional pressure. The desired directional pressure for both breeding and experimental holding areas will vary depending on requirements of the specific research.

The BSL is determined based on the agents and the types of manipulations involved (see sidebar "Discussion of Biosafety Level"). Guidance on BSL (referred to as ABSL for animal facilities) is provided in Reference 1. Biological safety criteria should be determined by the principal investigator, a safety officer or industrial hygienist, not by an HVAC professional. The safety level classification of the space is a significant parameter in determining HVAC system criteria. This is discussed in more detail in the section on design criteria.

In dealing with animal facilities as opposed to conventional laboratories, remember that biological safety relates both to the protection of people (caregivers and the environment outside the animal facility) and to the protection of other research animals. For example, if an agent is inadvertently introduced into the breeding population, a significant investment of time and money can be lost as these "contaminated" animals may not be valid for the intended research.

Caging Systems

The HVAC system can control the environment in the animal room but it is the environment in the animal cage that affects the animals. Caging systems for rodents generally involve a small polycarbonate cage installed on a cage rack. Cages generally hold up to eight mice, and the racks vary but generally hold between 42 and 140 cages. Cage racks can be either fixed or portable. The most common type of cage rack is portable (based on the authors' experience). Portable racks can be rolled around, which facilitates cage changing and cleaning.

The three common cage system types are: open cages, microisolator cages, and individually ventilated cages.

Open cages include a polycarbonate, rectangular container with a wire lid. With this cage type, significant natural convection occurs from the cage interior to the room.[5] Levels of CO_2, NH_3, and moisture (relative humidity) remain close to the levels in the general room. Cross contamination from cage to cage and caregiver exposure to allergens originating from the cage is significant with this cage type.

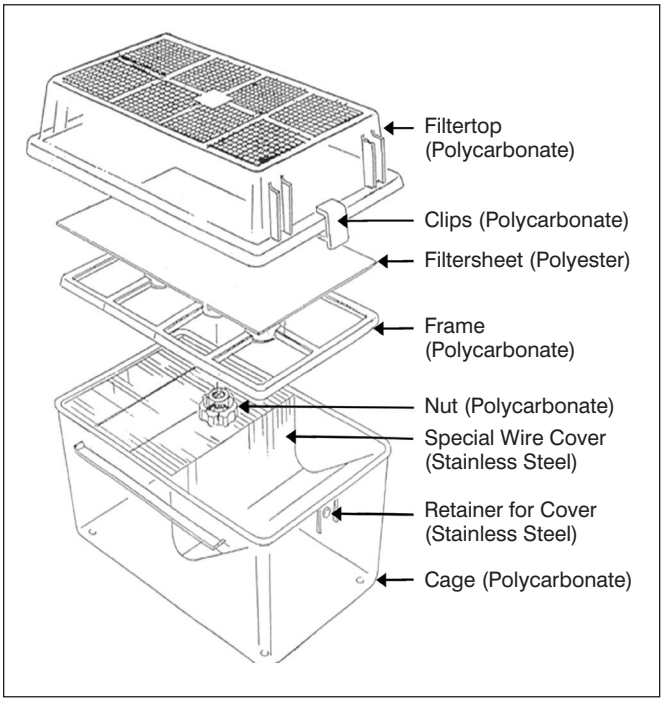


Figure 1: Microisolator cage with filter top.

Microisolator cages include a filter media at the top of the cage that limits cross contamination and introduction of allergens originating from within the cage (see *Figure 1*). In addition, though, this filter restricts natural convection and the ventilation rate of the cage is reduced. This leads to higher concentrations of CO_2 and NH_3 and higher humidity levels in the cages.[6]

Individually ventilated cage (IVC) systems include fans and filters on the racks that can individually ventilate each cage (see Page 38). These systems can be supply-only or supply and exhaust. Supply-only (positive pressure) systems have been shown to maintain proper CO_2 and NH_3 concentrations and humidity levels but do not appreciably reduce the introduction of allergens from the cages to the space. Systems with integral exhaust can be set to neutral, positive, or negative pressure in the cages. If the pressure is set to neutral or negative, the introduction of allergens is reduced significantly.[6]

IVC systems generally include integral fans and, therefore, require power connections (typically 120 volts). It is best to locate these power connections at or near the ceiling, so that they are not damaged as racks are moved in and out of rooms. Supply intake and exhaust discharge can be directly to the room or can be connected to the building systems. Connection to building systems is generally achieved with a snorkel-type flexible connection that can be easily removed as racks are moved.

Design Criteria

The following are the most commonly referenced U.S. guidelines used to establish design criteria in animal facilities:

• *Biosafety in Microbiological and Biomedical Laboratories*;[1]

Discussion of Biosafety Level

The biosafety level of a space sets the safety standard for the physical barrier and for the procedures and practices that must be used. The primary source for direction in determining this is the BMBL.[1] The BMBL includes specific requirements for a large number of specific agents. The types of agents addressed are bacterial, fungal, parasitic, prionic, rickettsial, and viral.

The type of agent is only one factor that determines the BSL. Other specific factors are:

- Virulence, pathogenicity, and communicability;
- Function of the laboratory;
- Procedures and manipulations involving the agent
- The endemicity of the agent; and
- Availability of vaccines or other therapies.

Recommendations in the BMBL "presuppose a population of immuno-competent individuals." The BMBL further assumes "activities typically associated with the growth and manipulation of the quantities and concentrations of infectious agents required to accomplish identification or typing." Activities involving larger volumes/concentrations or manipulations which produce aerosols may result in higher BSL classifications.

The BMBL further recommends that laboratory directors select a higher BSL than indicated in the BMBL when the situation warrants it. Factors that may lead to this are uniqueness of proposed activities or proximity of laboratory to sensitive areas (such as patient care or animal breeding areas). The laboratory director also has the discretion to allow BSL-3 activities (for example) in a BSL-2 laboratory, but with enhanced safety practices and procedures.

• *Guide for the Care and Use of Laboratory Animals;*[2] and
• *NIH Design Policies and Guidelines.*[3]

Canada also has a widely referenced guideline that has similar criteria to the U.S. guidelines:

• *Guide to the Care and Use of Experimental Animals.*[4]

These documents cover far more than HVAC system criteria, and, in some cases, cover both general laboratories and animal facilities. The fundamental HVAC parameters that must be determined based on these documents are the following:

• Temperature range;
• Humidity range;
• Minimum ventilation rate (air-change rate);
• Filtration (exhaust and supply);
• System segregation; and
• System redundancy.

A summary that incorporates the U.S. guidelines is presented in *Table 1*. These standards only provide general guidelines and cannot simply be incorporated without additional considerations. For example, the BMBL guideline includes several statements similar to "Additional environmental protection

should be considered if recommended by the agent summary statement, as determined by risk assessment, the site conditions, or other applicable federal, state, or local regulation."

The *NIH Design Policies and Guidelines* is a document developed for work on the National Institute for Health campus. Many institutions apply for grants through the NIH and to qualify for grants, this document may be referenced. It includes some unique requirements relative to humidification and system redundancy, as is discussed next.

Temperature and Humidity

Temperature range is based on both the comfort and stability of the animals and comfort and safety of caregivers. Caregivers often are gowned and masked, so they may desire a temperature somewhat lower than may be ideal for the animals. Relative humidity (which can be affected by temperature) is important to both the animals and the caregivers. From the animals' perspective, a lower humidity is desirable because less NH_3 is produced from bedding at lower humidity levels.[7] On the other hand, the effect of allergens is dramatically reduced at higher relative humidity levels, and this results in a better environment for the caregivers.[7] Humidity effects are discussed in more detail later. In general, the temperature setpoint should be between 68°F to 75°F (20°C to 24°C) with humidity maintained at 40% to 60% RH. The *Guide for the Care and Use of Laboratory Animals*[2] does allow for relative humidity as low as 30%, and this should be considered over the 40% RH minimum for colder climates.

Individually ventilated cage system.

Ventilation

The optimal air-change rate for a given space varies based on the type of animal, the type of cage system, and the types of agents used. Internal heat gains are seldom the driving factor. The primary purpose of ventilation is to provide dilution to maintain acceptable levels of CO_2 and NH_3. Target levels of CO_2 are similar to those for human occupancies, and the threshold for health effects from CO_2 are very high. Control of NH_3 levels in cages is an important consideration. NH_3 levels above 200 ppm are pathological in animals and will interfere with experiments. Even at 25 ppm, some effects can be seen in animals, but this level is a generally accepted threshold for research animals.[5]

A ventilation rate of 10 to 15 ACH is indicated in *Guide for the Care and Use of Laboratory Animals*[2] for animal rooms and this is widely regarded as the standard. Recirculation is specifically prohibited by References 1 and 3 but allowed if sufficiently filtered by Reference 2. In practice, animal rooms are generally 100% outside air. Memarzadeh[7] concluded that ventilation rates above 10 ACH did not materially improve the environment within the cages for microisolator type cages and that 10 ACH provided more than enough dilution of CO_2 and NH_3 in the occupied space. This certainly would be the case as well for IVC type cages. Higher ventilation rates only should be required if open cages are used or if there is a BSL-3 or higher classification. Ventilation rates below 10 ACH have been considered with IVC cages since the exhaust from the cages is HEPA filtered. Dilution of CO_2 and NH_3 is still required for the occupied space and additional research may be required to determine the impact of lower overall ventilation rates.

Defining ventilation rates based on air changes is the most commonly referenced approach but ventilation can also be determined based on the total mass of mice in a room. ASHRAE[8] provides a recommendation of 0.85 cfm per 100 grams of body mass of mice. In the configuration referenced, a room with single-density racks had a ventilation rate equivalent to 5 ACH and a room with double-density racks had a ventilation rate equivalent to 10 ACH. In both cases, NH_3 levels in the rooms were reported to be acceptable after five days without changing cage bedding.

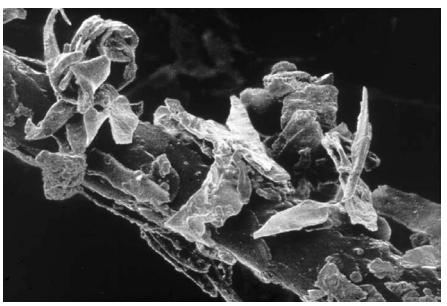
Filtration

Filtration needs to be considered for both supply and exhaust. The standard guidelines provide criteria for filtration but the designer must provide additional considerations beyond what is included in the guidelines. For example, breeding facilities are considered BSL-1 because no dangerous agents are involved but they generally require a high level of filtration on supply. This requirement is based on the need to preserve the cleanliness of the breeding environment, so that the animals produced there will not bias the experiments in which they are eventually used. Generally speaking, HEPA final filtration should always be provided in breeding facilities. For most experimental animal areas, 60% or 90% final filtration would be appropriate. The exception would be experimental areas where immunocompromised animals are used.

Filtration of exhaust air may be considered to maintain cleanliness in ductwork, to protect other HVAC equipment such as heat recovery coils, or to capture hazardous compounds from the exhaust. In general, at least a 30% filter would be provided in the exhaust if a heat recovery coil is present, whether the system involved animals or not.

Determining whether additional protection is needed, using higher efficiency filtration at heat recovery coils or additional filtration at the room exhaust ductwork, depends on the type of caging system used and the type of animals housed. Fur, dander, and fragments of bedding are present in animal rooms and can find their way into ductwork and onto coils. It is becoming more common to include exhaust filtration in animal facility HVAC systems even when no dangerous agents are used based on the desire to control the movement of animal-produced allergens.

Besides protecting HVAC equipment, the other reason to filter exhaust is to capture hazardous aerosolized materials. Two categories of compounds need to be considered. The first are the hazardous materials or pathogenic organisms that may be used in experiments that lead directly to the BSL rating of the area. The standard guidelines are clear on the minimum requirements for the various biological safety levels (see *Table 1*).



Animal dander.

Additional filtration should be considered if an agent used in the experimentation could pose a risk to people or other animals, especially if breeding is done in any part of the facility. As stated earlier, the HVAC engineer is not the most qualified party to determine the risk level associated with a specific agent. The risk assessment depends on the specific use of the agent in the lab, and usually is evaluated by a facility biosafety professional or committee.

The second area of concern relative to exhaust filtration is the control of allergens produced by the animals themselves. This includes fur, dander, saliva, urine, etc. These powerful allergens are reported to cause allergic symptoms in 33% of animal caregivers and to cause animal-induced asthma in 10% of caregivers.[9] Of these, dander is perhaps the most pervasive and potentially problematic (see photo). Dander consists primarily of particles of animal skin. The particles are very small, in the 5 to 20 micron range. They often attach to fur, dust, or other particles. To capture dander with a reasonable effectiveness, a minimum filter efficiency of 90% is required.

Segregation

System segregation refers to whether a system is dedicated to animal areas or serves other general areas as well. Independent systems for all animal areas is a requirement of NIH[3] but only required for ABSL-4 by BMBL.[1] There are two reasons why it is beneficial to segregate animal area systems from general systems.

The first is for cleanliness or safety purposes. The guidelines differ on this requirement but hazards exist in animal areas that must not be introduced to other areas.

The second reason is for cost considerations. Systems serving animal areas usually have higher requirements for filtration, humidification, emergency power, and redundancy than general systems. Dedicated systems for animal areas can allow inclusion of these features without causing a cost premium (both initial and operational) on general systems.

It is the author's observation that the general industry practice is to separate animal area systems from general systems. The architectural layout of research buildings is not always conducive to total segregation between animal and general areas. In these cases, 100% outside air animal area systems may need to serve some general office or lab areas. This does not necessarily create any cleanliness or safety issues but results in an increase in the size of the more expensive animal systems. For these reasons, every effort should be made to segregate the systems.

Redundancy

Redundancy is a very important consideration in animal room design. The animals often are involved in long-term experimentation that demands a stable environment. An interruption in the ventilation or air-conditioning system could lead to stress on the animals that may affect the research or breeding program. If a researcher is forced to start over, it can cause a significant financial loss to the institution. In addition to protection of the research program, redundancy is important for BSL-3 and higher facilities to ensure the containment of harmful agents. In these facilities, the HVAC system is an important part of the barrier between potentially harmful agents and the unprotected public as well as the general animal population.

The referenced documents are not consistent in their requirements for HVAC system redundancy. The *NIH Design Policies and Guidelines*, however, includes the following statement "HVAC systems must be both reliable and redundant and operate without interruption. There are no exceptions."[3] This statement is clear but to accomplish it can be very intensive. Neither the Biosafety in Microbiological and Biomedical Laboratories[1] nor the Guide for the Care and Use of Laboratory Animals[2] has an equivalent requirement regarding system redundancy.

In practice, it is not common to see completely redundant equipment on all systems serving animal areas in other than ABSL-4 facilities. Systems can be prioritized in terms of their impact on safety and animal stability. Exhaust systems can be backed up relatively easily and maintaining exhaust is the most important system from a safety standpoint. Redundant exhaust is almost always seen in ABSL-3 and higher spaces and is often seen in lower risk facilities as well. It is usually relatively easy to provide redundancy for heating systems as well. Boiler plants are often arranged with multiple boilers to allow an N+1 configuration. Heating pumps and other components can be backed up at a relatively moderate cost. Cooling system

redundancy is another priority and can be achieved in the same manner as described for boilers, although additional electrical impacts must be considered. Incorporation of thermal storage is another approach that can achieve cooling redundancy.

Failure of the heating system can result in temperatures that are life threatening to the animals. Failure of the cooling system can lead to high temperatures that may affect some research but would not generally be considered as dangerous to the animal population. The delivery of heat may be integral to the air supply system or could be independent. Cooling almost always will be delivered by the overall supply system. An independent heating delivery system such as radiant panels can allow for delivery of heat with a supply air failure. If a system with independent heating terminals is provided, the terminal units must be cleanable.

Providing redundancy for supply systems generally is more involved than providing redundancy for other systems. Failure of the supply system generally will cause an interruption of cooling and possibly heating as well. If a non-critical supply system is in the same building as the animal supply system, the two can be interconnected and the non-critical system used to back up the animal system. If this type of arrangement is not possible, a parallel air supply system must be provided to achieve full redundancy. Parallel systems are going to increase cost directly and indirectly due to the increase in the requirement for mechanical room space. Due to potential cost and space impact, all aspects of system redundancy should be considered carefully.

Emergency power is an important redundancy consideration in addition to system or equipment redundancy. In general, exhaust fans and heating system components in animal facilities are the first priority for emergency power. Cooling systems often are a priority as well but their large loads can have a big impact on the generator size. Supply fans can be placed on emergency power without serious impact on the generator but the benefit is reduced some if the cooling plant is not on emergency power as well. Some massive and prolonged power outages in recent years have led many toward 100% emergency power backup for animal facilities, but this is not a strict requirement of the referenced guidelines.

Conclusion

This article demonstrated the range of factors that must be considered in the HVAC system design for an animal facility. Ventilation rate (10 to 15 ACH), temperature range (68°F to 75°F [20°C to 24°C]), and humidity range (30% to 60% RH) generally can be established directly from the guidelines. Other design criteria, such as filtration, pressurization, segregation, and redundancy, will have varying requirements based on the specific activities in the animal facility. Factors that may contribute to establishing these criteria include research functions, biological safety level, and the caging system used. The culture of the institution may be important as well. Costs can escalate dramatically as redundancy and other system enhancement are used, but this must be balanced against the goal of providing a comfortable, safe, and stable environment for research animals and caregivers.

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