SoBran BioScience

Effective Strategies to Safeguard Research Facilities and Personnel

MEETING REQUIREMENTS FOR ANIMAL BIOSAFETY LEVEL 3

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INTRODUCTION

Multiple aspects of critical research involve select agents, defined as pathogens or biological toxins, which have the “potential to pose a severe threat to public health and safety,” according to the U.S. Department of Health and Human Services and the U.S. Department of Agriculture.

For such research programs to be successful and safe they must be supported by specially trained staff, specialized equipment, and well-developed standard operating procedures.

This paper provides a blueprint for designing and operating research facilities where the potential for harmful exposure is high, in order to meet requirements for Animal BioSafety Level (ABSL) 3.

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PUTTING THE RIGHT STAFF IN PLACE

An ABSL3 facility requires extensive oversight and leaves little room for error. So how do you staff accordingly, especially when you are opening up a newly constructed facility?

It is important not to cut corners on your staffing plan. Keep in mind the detailed procedures that will need to be followed, the working conditions, and the need for an error-free work environment, and build those into your job descriptions and selection process.

When you determine the number of personnel and time required to handle the husbandry and technical workload, use less than the industry average performance standard quantifiers for a standard research facility. This will ensure there is time allotted for the additional personal protective equipment (PPE) requirements and ABSL3 daily environmental duties. Most important, it allows for the exacting attention to detail required to minimize workplace accidents and deviation from standard operating procedures.

It is essential to staff your team with some individuals that are experienced with the ABSL3 environment.

It is essential to staff your team with some individuals that are experienced with the ABSL3 environment. If your overall program has an existing ABSL3 suite, identify some of staff working there to transfer to your new facility, even if only for a fixed time period. Having a seasoned team will help your program get up and running quickly and will be extremely beneficial for training those staff with less experience.

Make sure you do all you can to retain and reward skilled care staff. Let them know they are valued and provide them a path for career advancement. You can accomplish this by structuring levels of animal caretakers, such as Animal Caretaker II (ACII) and Animal Caretaker III (ACIII). This type of structure provides

a mechanism to promote an individual who has the quality caretaking skills necessary to meet the performance standards of an ABSL3 suite.

When interviewing new candidates who do not have ABSL3 experience, it is important to determine if they have adequate skills to be trained. Conduct a reading comprehension exercise at the interview in order to determine that future staff members can comprehend signage and understand the context of standard operating procedures.

All employees will need to meet the occupational health requirements for an ABSL3 facility.

If your facility requires staff to have security clearances (usually Level 5 security clearance and/or Select Agent clearance), keep in mind that these clearances require investigation of an individual's criminal and financial history. To plan for obtaining appropriate clearances, prepare interview questions to address this as a job requirement and allot sufficient time for employees to go through the process.

TRAINING

Training is paramount in the implementation, operation, and management of any animal program. That is especially true in an ABSL environment.

Effective ABSL3 training should consist of didactic classroom instruction; mock training of procedures; and one-on-one, hands-on training that include working with the actual species and agents encountered in the facility.

Training typically involves several steps.

STEP 1. IDENTIFY QUALIFIED AND EXPERIENCED TRAINERS.

Potential trainers should not only have vast experience and knowledge of ABSL3 operations and procedures, but also be well versed in the safety and the handling of a multitude of species and agents.

STEP 2. DETERMINE TRAINING IMPLEMENTATION REQUIREMENTS.

Training implementation in an ABSL3 facility is driven by the program's Standard Operating Procedures (SOPs) as well as policies and procedures from other government agencies, such as the United States Department of Agriculture (USDA).

Specific surveillance requirements on 'Select Agents' (agents regulated by the USDA) is provided by the Institutional Occupational Health and Safety program in conjunction with program management. An occupational health specialist can assist with recommendations, in conjunction with the program's biosafety officer, to include in your training plan.

STEP 3. EFFECTIVE CLASSROOM TRAINING.

Classroom training consists of interactive presentations followed by evaluation, usually in the form of a short quiz. In addition, some hands-on training can be conducted in the classroom. This allows the students to practice procedures such as:

- Closing biohazard bags
- Medical instrument preparation
- Equipment disposal
- Decontamination of PPE
- Documentation requirements

STEP 4. MOCK SCENARIOS.

Upon completion of the classroom training, students move on to mock scenarios. Scenario training should include all aspects of working in the suite, such as sign-in procedures, aseptic cage change, technical manipulations, and exiting procedures.

This practice of training in a suite that is not posted as "biohazardous" is commonly referred to as working in a "cold suite." This allows personnel to experience the effects of working with additional PPE requirements, such as wearing Powered Air Purifying Respirators for extended periods; and become familiar with the added

procedures and precautions prior to entry into a “hot suite” (a suite that contains risk of biohazardous agents).

If training in a cold suite is not possible, training can move directly into a hot suite. Training within a hot suite should always be done in very small groups, typically one or two trainees with trainers assessing and monitoring them at all times. Personnel should never be allowed to work unsupervised until a trainer has assessed their abilities and deems them proficient. Actual training in a “hot” suite should be conducted with no more than two trainees.

STEP 5: INVESTIGATOR TRAINING.

Provide investigators with a facility/suite orientation, starting with an all-inclusive ABSL3 overview and a walkthrough of the suite. The majority of trainings for specific agents are conducted by the Principal Investigators or their designees.

STEP 6: DOCUMENTATION OF TRAINING.

Documentation of training is also paramount to the success of the mission. Training records are frequently reviewed during Animal Care and Use Committee (ACUC) and American Association for Accreditation of Laboratory Animal Care (AAALAC) inspections.

Simple check sheets help make sure training regimes are followed. Check sheets should list the necessary areas of training, such as dressing prior to entering the suite, animal husbandry, waste processing and disposal, and emergency egress procedures, just to name a few. Once the trainer is confident that the trainee is proficient in performing the procedure properly, both the trainer and trainee sign off that the training is complete. Tracking for all training can be captured in a series of spreadsheets or, ideally, a database. Individual employee training, completion of checklists, weekly training, and required trainings are some of the activities that should be tracked.

STANDARD OPERATING PROCEDURES

No two ABSL3 suites are alike. They vary in their entry and exit procedures, agent status, species housed, and PPE requirements.

Therefore, specific Standard Operating Procedures (SOPs) are a must. The process of completing and executing a new SOP or revision of an existing SOP requires the involvement of many key players. The original author, the user, the safety committee or safety representative, and program management staff should all be involved in the process.

The development of an SOP requires understanding of the task or procedure at hand, and the personnel, species, and risks involved. It may be necessary to bring in outside participants, such as vendors, safety representatives, and other experts in the field. Once an SOP is complete, it should be given a test run and any issues that are identified should be investigated and corrected.

TYPICAL STANDARD OPERATING PROCEDURES

- Entry Procedures
- Powered Air Purifying Respirators (PAPR)
- Daily Airflow
- Twice Daily Census Counts
- Handling of Agents, including Select Agents
- Species Specific Procedures
- Signage and Movement
- Equipment
- Exiting Procedures
- Emergency Egress Procedures

Entry procedures should include the proper steps to be taken when donning PPE, documenting entry, using PAPR, and entering the suite.

Procedures for using, documenting, and troubleshooting PAPRs are of great importance when training new personnel to work in the suite.

Daily airflow within animal rooms and ventilated caging needs to be documented daily and deficiencies must be reported to management immediately.

Exiting and emergency egress procedures must be outlined to ensure the safety of those outside of the suite.

Twice daily census counts are another area of great importance. Each individual animal must be counted twice daily and recorded on a census form and faxed to management. Deviations in the census counts must be addressed immediately.

The handling of agents is another area where procedures must be clearly defined, as well as their storage, usage, tracking, and disposal.

Signage and traffic patterns need to be accurate and easy to follow. Signs in an ABSL3 suite not only aid in entering and moving through the suite safely, but are also valuable when performing procedures such as donning a PAPR or loading and running an autoclave.

Equipment is another area for standard operating procedures, particularly for bio-containment caging systems, autoclaves, and specialized equipment such as inhalation chambers and anesthesia machines.

Exiting and emergency egress procedures must be outlined to ensure the safety of those outside of the suite. The safety department and program management staff need to agree on the procedures for exiting during an emergency. Does staff decontaminate and exit in full PPE or are other methods and safeguards in place? These are just a few examples of questions to address.

SPECIALIZED EQUIPMENT

The operation of an ABSL3 suite requires the use of specialized equipment.

Proper housing for laboratory animals is paramount in bio-containment environment. Bio-containment caging is a must, including negative air ventilated

rodent racks, primate, and ferret/rabbit racks. These racks consist of standard stainless steel rack construction with the addition of a glass door with a gasket that provides a seal. The rack is connected to a negative motor or to the facility exhaust system. There is often a pre-filter on the door or side of the unit. The downside to this system is the transportation of the animal to the hood or workstation. When chemical immobilization is not an option, the use of a jump boxes or transport cage to contain animals shedding virus is a must. The removal of the animal from the cage must be done quickly and safely to minimize the amount of time the animal is exposed to the room.

Autoclaves, of course, are a mainstay in ABSL3 suites. Bioseal autoclaves with interlocking doors are preferred. Depending on suite size, the number and size of autoclaves are important. The autoclave(s) must be large enough to handle the processing of dirty caging and equipment and the wastes that are produced. A sterilization time of at least one hour is recommended.

Autoclave monitoring is essential. Several types of monitoring devices should be employed, such as integrator strips and biological monitors.

The transportation of caging and equipment from the animal room to the autoclave is another concern. If caging will be staged prior to autoclaving, protective measures should be taken.

Caging and equipment need to be decontaminated prior to removal from the animal room. Following the initial decontamination, a cart or rack cover should be placed over the caging and a second decontamination performed prior to the move, usually chemically.

Biosafety cabinets are another staple piece of equipment in an ABSL3 suite. The preferred hood is a Class IIB hard ducted unit. Class IIB hoods exhaust 100 percent of the air to the outside, which allows work with chemicals and biohazardous agents to be performed in this hood. Class IIB hoods utilize dual High Efficiency Particulate Air (HEPA) filtration, filtering cabinet air and exhaust air down to 0.3 microns. Class IIA hoods are also utilized; they recirculate 70 percent of the air and exhaust 30 percent. Since these units do exhaust into the room, volatile or toxic chemicals may not be used in them.

Isolation rooms or cubicles can be very beneficial for suites that must maintain several agents in the same room. Cubicles turn a normal animal room into several small macro environments. The cubicles are negative to the room, which is negative to the corridor. The lighting, temperature, and humidity can be set individually. When utilized correctly, various species may be housed in the same room where normally there would be physiological issues. For example, a rack of ferrets in cubicle one (the hunters) and a rack of mice (the prey) can successfully be housed in the same room.

Transportation of ABSL3 agents is of major concern. Tissues and samples obtained from “hot” animals may have to be transported to an outside ABSL3 facility for processing. The best way to transport these is to use a rubber gas-keted biological carrier. These simple polypropylene, air-tight carrying cases can be easily decontaminated. Once the decontaminated carriers leave the ABSL3 suite, they are only to be opened in an ABSL3 suite or lab under the proper biosafety cabinet. Dry ice is never put in the container as it is airtight and will explode.

Communication with the outside is also essential. Processes for communicating accidents, injuries, and emergencies and regular day-to-day communication procedures must be available. Computers utilizing email and instant messaging are one way to communicate. Unfortunately, there may not be a person at the computer, so other methods such as two-way radios should be used by the suite supervisor and facility manager to communicate frequently. Written communication is accomplished by fax; for example, documents such as airflow and census counts can simply be faxed to facility management.

Reporting equipment such as computerized monitoring is extremely useful in tracking and monitoring airflow and temperature.

Security equipment such as electronic card readers is also vital when working with select agents.

SECURITY REQUIREMENTS

One facet of opening an ABSL3 suite is the determination of the security requirements for the personnel and the biological agents.

These requirements will be driven by the type of biological agents utilized within the suite. The biological agent requirements are determined by its agent category, such as USDA Agricultural Agent vs. Select Agent; keep in mind that some agents fall under both categories.

A quick resource to research an agent's category is the CDC website, specifically, http://www.cdc.gov/od/sap/docs/salist.pdf. Once you determine an agent's category, you can move forward in planning for the necessary security measures.

As noted above, your staffing plan should include resources with a level secret clearance. If you have hired certain individuals prior to their obtaining that clearance, you'll need to plan for that.

You must ensure that an unsecured employee is escorted by a cleared employee. You should also develop an organized approach to tracking all the stages of the clearance process to ensure an employee does not get "lost" in process, and have the appropriate contacts to follow up on clearance status. You must be prepared to terminate employment if an individual cannot obtain security clearance. Poor planning may cause staff shortages and a decline in operational outputs. If clearances are required, it is also important to plan for individuals who provide intermittent services, such as consultants and maintenance and repair workers.

There are additional security requirements at the room/cage level. At the room level, it may be necessary to track all personnel entering and exiting the room. This can be done through electronic keycard access or a second locking mechanism such as entry code locks and padlocks. If the latter is used, all personnel will be required to sign a log indicating room entry and exit times. At the cage level, it may be necessary to secure cage tops in a fashion that ensures the seal remains intact during an accidental drop, and that the cage is locked down when docked on the rack. When addressing large animal caging, a padlock on the door latch mechanism can be added to meet this requirement.

CONCLUSIONS

As ABSL3 labs come on line to meet the ongoing need for comprehensive research into the effects of harmful substances, the need for robust strategies to ensure the security of facilities and the safety of personnel also grows.

Program managers can create an integrated framework for ABSL3 lab management, based on careful consideration of the three most critical pieces of any operation: knowledgeable and well-trained staff, state-of-the-art equipment, and clearly defined and constantly evaluated procedures.

With this approach, lab management can successfully ramp up and maintain best-in-class environments for life-saving research.

ABOUT SOBRAN BIOSCIENCE

SoBran BioScience has nearly 20 years of experience supporting complex preclinical research and drug discovery. The team manages animal facilities and provides strategic and technical support for laboratory animal and contract research projects.

Compliance Expertise

With over 500 biomedical professionals, the team has experience in all aspects of *in vivo* research. Staff members are AALAS certified and support GLP research projects. SoBran management is ISO 9001:2008 certified and leads the industry in designing and managing ethical animal care programs that meet the most demanding regulatory standards. In addition to onsite support, SoBran offers AAALAC-accredited facilities with a guaranteed 5-day IACUC review and direct communication with laboratory personnel.

SoBran BioScience clients span government agencies, academic institutions, biotech and pharmaceutical companies, and include long-term engagements with the National Institutes of Health and Walter Reed Army Institute. The company has consistently been listed on the Inc. 500 and Black Enterprise Top 100.

Experienced Leadership

A former Air Force Officer, Amos Otis founded SoBran in 1987 on the Air Force values of integrity, service and excellence. Mr. Otis continues to lead SoBran guided by his commitment to education and training. He serves on the Board of Directors of the Federal Reserve Bank of Cleveland.

Dr. Gregory Kelly, Senior Vice President of Operations and head of the BioScience Division at SoBran, has conducted scientific research and directed large complex research programs in molecular biology and toxicology for over 30 years. Dr. Kelly serves as Chairman of the Greater Baltimore Council.

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