SoBran BioScience

Proactive Quality Assurance

ENSURING STANDARD OPERATING PROCEDURES IN AN ABSL3 ENVIRONMENT

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INTRODUCTION

As Animal Biosafety Level 3 (ABSL3) suites become more prevalent within the biomedical research community, laboratory animal care professionals are seeking ways to meet increasingly stringent policies and safety regulations.

Simply putting a set of standard operating procedures (SOPs) in place is not enough to ensure they are met by staff at all times. Implementing a proactive quality assurance (QA) program is central to achieving and sustaining ABSL3 requirements with consistency and confidence.

QA is not a “set it and forget it” approach. Effective QA demands continuous training and consistently challenges the process with rigorous inspections.

This paper outlines essential QA program elements, along with practical suggestions for effective QA activities applicable in all ABSL3 environments. It covers:

- Staff knowledge/proficiency
- Occupational health requirements
- SOP development, observations and challenges
- Effective documentation
- Environmental parameters
- Equipment operation
- Animal study proposal (ASP) review

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STAFF KNOWLEDGE/PROFICIENCY

Facility and position-specific training is a vital prerequisite for quality assurance. Individuals who perform QA must be knowledgeable of the ABSL3 environment and the biohazards it contains, and capable of asking the proper questions. This ensures potential issues are noted and corrected before they engender a crisis.

For all lab staff, understanding the "whys" behind each procedure increases ownership of job responsibilities and enhances quality and safety.

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.

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OCCUPATIONAL HEALTH REQUIREMENTS

Good data collection and tracking are critical to ensuring that occupational health requirements for each biohazardous agent are adhered to in an ABSL3 environment. This hinges on having complete and up-to-date information, consolidated from sources such as the biosafety office, occupational health specialist, and animal study proposals.

A database or spreadsheet must be developed and regularly reviewed/updated to capture the biohazardous agents and occupational health requirements for each animal study protocol. This helps ensure that managers and supervisors are aware of current safety and occupational health requirements for all animal care personnel and investigative staff.

Similarly, the program must track inoculation requirements and due dates for all staff, since required vaccines have various administration schedules.

Important information elements to collect and track include:

- Each employee's name
- All occupational health requirements
- Frequency of occupational health requirements (e.g., pre-employment, yearly, semi-annually)
- Dates requirements were met
- Procedural development
- Update
- Evaluation

SOP EFFECTIVENESS FOR FACILITY ACCESS

It's important to development, update, and evaluate comprehensive SOPs that cover signage and consider the realities of human behavior.

Every facility needs procedures and safeguards for access control to ensure that all personnel entering the suite are authorized users, receive proper safety training, and meet all occupational health requirements.

Exit procedures are equally important; the QA team should evaluate the exit plan, and inspect emergency equipment packets for contents, expiration dates, and emergency instructions that are current, clear, and easily followed by the users.

Effective signage reminds users of the required personnel protective equipment (PPE) to enter the suite, informs them of the biohazards within, and poses questions to force an automatic double-check of established procedures. Signs

should be easy to follow, including pictures and bulleted text that outlines pertinent information.

An ABSL3 suite includes more extensive signage than a general facility. For example, signage within the suite must ensure that all users entering each area are informed of additional PPE requirements and potential hazards for the animal or procedure room being entered.

Observations and challenges ensure that SOPs are consistently applied. When performing QA on the ante-rooms and donning area of the suite, the QA inspectors should challenge the posted processes. They should act as though they are new users and ensure it is possible to don the proper PPE and perform all necessary safety checks without prior knowledge, based solely on the posted instructions.

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EFFECTIVE DOCUMENTATION

It is fairly straightforward to evaluate formal process such as posted signage. It is more difficult – but also more important – to perform QA on actual behavior to ensure that users consistently follow procedures.

Documentation logs are an essential QA strategy to keep track of behavior. Examples include user sign-in/sign-out logs to track all occupants of the suite at a given time; logs that track each Powered Air Purifying Respirator (PAPR) unit, including who is using the PAPR and acknowledgement that safety checks were performed; and logs that record when the facility checks PPE for sound operation.

Documentation within an ABSL3 suite must be more frequent than in most laboratory environments, and rigorously accurate. For example, accurate airflow monitoring and records are essential, and should be completed daily. The airflow

log must be in a user-friendly format with no room for error or misinterpretation. It can be helpful to annotate the ABSL3 suite's floor plan with arrows indicating the airflow at each point.

General documentation QA of the ABSL3 suite should include inspection of biohazardous material labeling for animal caging, carcasses, tissues, and containment vessels. The labeling must be clear and concise to ensure there is no potential user misinterpretation. Documentation should include a daily animal census – including reporting of census fluctuations (e.g., animals received and euthanized) – and the QA team should review and evaluate them regularly as part of the overall inspection.

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QA of the ante-room supply inventory is important to ensure no one is tempted to cut corners due to lack of equipment.

Thorough QA inspections can be facilitated by developing a comprehensive series of check-off sheets for each area of the specific suite, including elements such as the following example for an ante-room:

- Ante-room check off sheet
- Door signs and PPE requirements
- Correct sign-in and sign-out log
- Properly utilized PAPR units plugged into battery charger when not in use
- HEPA filters in working order
- PAPR units signed out and tested for functional operation
- Biohazards listed on the door sign coincide with biohazards within the suite
- Supplies stocked
- All documentation reviewed

ENVIRONMENTAL PARAMETERS

ABSL3 suites require more frequent environmental parameter checks than a typical lab. The QA inspection needs to challenge and review the additional PPE requirements and the procedures listed at each animal and procedure room door with regard to the biohazards within the room.

If additional disinfectant or PPE procedures are required, ready availability of the disinfectants and additional PPE supplies ensures that the requirements can be easily met.

The QA team must also inspect all physical areas, including the presence and disposal of all sharp and glass items within the suite, ensuring these objects are limited and determining whether they could be replaced with plastic or dull implements. They should verify that the room is well organized, neat, and clutter free, allowing users to move freely within the suite without risk of PPE damage or user injury.

Another area of environmental concern is the removal of materials such as medical pathological waste, dirty caging, etc. The QA program must monitor these processes to ensure biohazard exposure will not occur, and the staff must inspect all areas in which materials could exit from inside the ABSL3 suite.

EQUIPMENT OPERATION

Autoclave procedures play a key role with QA. It is important to be able to easily confirm that items have been properly autoclaved before leaving the suite, which can be accomplished through environmental QA. The assessment should include steam, pressure, and sterilization processes, and can be accomplished through daily QA monitoring utilizing steam integrators with each load and performing periodic vacuum and microbiological testing.

The QA team should evaluate the documentation for these processes and monitor daily operation by ensuring that each autoclave load's steam integrator is attached to the autoclave print-out to indicate that sterilization occurred and autoclave time and temperature requirements were met.

It is also important to inspect the preparation of equipment before it goes into the autoclave, such as verifying that water is placed in autoclave bags to generate steam for the sterilization process, and proper placement of steam integrator strips throughout the load to monitor surface temperature as well as temperature inside the caging.

It is essential to question employees on autoclave procedures (including why each procedure is in place) and have them demonstrate the processes themselves.

ANIMAL STUDY PROPOSAL (ASP) REVIEW

The review process of any ASP is paramount to ensure the facility operation, husbandry, and technical needs of research are met.

Quality assurance actually starts during the pre-review process of an ASP. This is when suggestions for edits and SOP changes can be made to mirror ASP objectives to industry standards and requirements.

During the review, facility management considerations include:

- The species and number of animals to be housed per experiment
- Animal technical procedures
- Hazardous agents: handling, disposal and occupational health requirements
- Special husbandry requirements

Ongoing QA of ASPs must be continuous after ACUC approval is achieved and animals are housed in the vivarium. Examples of ongoing QA include:

- Ensuring every animal is assigned to the proper ASP number
- Animal technical procedures being performed are listed in the ASP
- Animals infected with any biohazardous agent are clearly marked and any special husbandry procedures are being followed

- Occupational health and PPE requirements are posted at the ABSL3 suite and animal room level entryways

CONCLUSION

This paper has provided a snapshot of general QA factors for a typical ABSL3 suite. A QA program must be customized for each suite to ensure procedures match specific infrastructure and biohazards.

To be most effective, QA should consistently challenge the processes, perform rigorous inspections, follow up promptly on any deficiencies or potential issues, and continuously train and educate suite users.

QA is designed to prevent problems by identifying a potential hazard or risk, and take appropriate action before it becomes the source of a crisis or exposure. A solid QA program will ensure the protection of individuals working within the ABSL3 suite, as well as the safety of the greater community surrounding the facilities.

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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.

ABOUT THE AUTHORS

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Melissa Marrah has over 20 years of experience in the biomedical field, and has been a member of the SoBran BioScience team since 2002.

As her primary role, Melissa is the Program Manager for SoBran's NIH/NIAID contract. In this role, she provides daily program and personnel management in support of ABSL1-3 animal facilities and program services. The level of effort includes facility management, husbandry, technical, research support, veterinary pathology and cryopreservation services, logistics, administrative, training and standard operating procedure development.

Bradley Fisher

Bradley Fisher is the Director of Government Operations for SoBran BioScience and has 20 years of experience in the animal laboratory field with an emphasis in management and training. Brad provides operational oversight, business development, and strategic planning for a multitude of DHHS and DoD biomedical research contracts. He is a Certified Manager of Animal Resources (CMAR), and a Laboratory Animal Technologist (LATG). In addition to membership in AALAS, ICPM and LAMA, he has served as NCAB AALAS Awards Chair and on the NCAB AALAS Seminar Committee.

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