UNIVERSITY OF CALIFORNIA

High-Containment Facility Operations, Maintenance, & Validation Standard

April 2025

Introduction

The University of California (UC) is home to some of the world's most advanced and pioneering biomedical science and clinical research. Consistently ranked among the leaders in the field of Infectious Disease research, the UC is often called upon to provide critical expertise in response to worldwide public health crises. Infectious Disease research involving highly pathogenic and primarily aerosol transmissible agents (i.e., Risk Group 3 agents) has the potential to present significant risk to individuals, the community, and the environment. The ability to safely conduct these research activities is largely dependent upon highly engineered Biosafety Level 3 (BSL-3) facilities, the highest-level containment facilities currently operated by the UC. These facilities are designed and engineered to provide appropriate risk-based physical containment according to industry standards and UC best practices. Such highly engineered facilities require equally rigorous validation standards, coupled with careful monitoring and periodic maintenance to maintain operational integrity.

Several authorities have published guidance and methodologies for the validation, operations, and maintenance of high-containment facilities. The following sources were used in the development of this Standard:

- Biosafety in Microbiological and Biomedical Laboratories (BMBL), 6th Edition, 2020
- NIH Design Requirements Manual (DRM), 2024
- NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), 2024
- Industry Standards and Best Practices
- ANSI/ASSP Z9.14-2020 Testing and Performance-Verification Methodologies for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Ventilation Systems

The information presented in these documents outlines operation and maintenance minimum standards for UC high-containment facilities. Robust operations and maintenance (O&M) protocols help ensure continuity of research as well as protection of the individual, the community, and the environment.

Application

The High-Containment Facilities Operations, Maintenance, and Validation Standard represents the UC requirements for operations, maintenance, and validation of high-containment laboratories at UC locations. This Standard must be referenced and used by all UC stakeholders, including investigators, researchers, architects, engineers, and facilities management, as well as outside contractors. They provide the necessary tools and information for the integration of high-containment laboratories as robust, long-term, operational units at their respective locations beyond the initial scope of planning, construction, and commissioning of such facilities. While incorporating all applicable regulatory requirements, the standards identify UC requirements, and document best practices for consideration during the facility risk

assessment. This Standard is intended to allow locations to operate each laboratory to a minimum standard, while incorporating requirements commensurate with the facility risk assessment. This Standard pertains to all high-containment facilities, existing and planned within the UC system, and is intended to provide standards and guidance for operations, maintenance, and validation of such facilities to ensure consistency in practices and management. This Standard is intended to address operational, maintenance, and validation needs that may affect the safe operations of a high-containment facility. This Standard has been approved by the UC High-Containment Laboratory Oversight Committee (HCLOC) and must be incorporated or referenced in Campus Building Standards. All high-containment laboratory locations used by UC personnel must conform to all applicable UC requirements. This includes leased locations and affiliate institutions. Newly planned construction of leased facilities and affiliate institutions must conform to all UC high-containment policies and standards.

Note: Facilities required to comply with the Federal Select Agent Program and/or other federal or state regulations may have additional requirements beyond UC Standards. In addition to the UC Standards, locations must reference and comply with applicable federal regulations when operating, maintaining, and validating high-containment facilities.

Scope and Responsibility

This Standard applies to all high-containment facilities operated within the UC system. Such facilities include all Biosafety Level 3 (BSL-3), Animal Biosafety Level 3 (ABSL-3), Biosafety Level 3 Plant (BSL-3P), Arthropod Containment Level 3 (ACL-3), and Biosafety Level 3 Agricultural (ABSL-3 Ag) facilities. All high-containment facilities owned and/or operated by UC personnel must conform to the requirements laid out in this and other established Standards. This includes leased locations and affiliate institutions. Non-UC personnel who work in or visit UC operated facilities covered by this Standard must conform to these requirements.

This Standard outlines specific responsibilities for key stakeholders involved in the operation, maintenance, and validation of UC-operated high-containment facilities.

- **Facility/Lab Manager** (If applicable) is responsible for day-to-day operational oversight of the facility, coordinating maintenance and yearly decontaminations, and serving as the manager for facilities.

- **UC Facility Owners (PI/Animal Care Group/Department/School)** are responsible for maintenance of containment equipment not integrated into the facility, such as animal cage racks and non-ducted biosafety cabinets, as applicable.

- **High-Containment Laboratories Director (HCLD)** is responsible for the management, oversight, and implementation of an O&M program in collaboration with applicable personnel within the local management structure.

- **Local High-Containment Laboratory Oversight Group (HCLOG)** is responsible for ensuring that facilities are validated annually and maintained by the HCLD in accordance with this Standard. The HCLOG must review findings, make recommendations, and serve

as a resource for reviewing and consulting on policies, standards, and recommendations related to operations, maintenance, and validation of high-containment facilities. Committee composition is decided at the local level and should be consistent with the original directive issued by UCOP. The HCLOG is composed of stakeholder representatives and meets on a regular basis, depending on the high-containment program needs.

- **UC High-Containment Laboratory Oversight Committee (UC HCLOC)** is responsible for serving as the oversight body and acting as resource for supporting locations in adhering to this Standard. Requirements for membership are listed in the UC HCLOC Charter. The HCLOC develops guidance and standards for the management of all UC high-containment facilities. The HCLOC also oversees annual reviews of local HCLOG activities, including design deviation requests and annual performance verification reports.

- **Local Facilities Operations & Management Group** is responsible for maintenance of UC facilities and containment infrastructure. The local O&M group may choose to perform the work with trained internal staff or pay a qualified third-party vendor for services.

Financial Support/Funding

An important consideration in the operation of a high-containment facility is the institutional support and funding mechanism for management and oversight of such facilities. Each location must develop and implement a plan for ensuring to provide long-term funding support for annual validation, routine facility maintenance and repair, and emergency response to ensure long-term success and safe operation of their high-containment facilities.

In establishing the funding structure, each location should consider the scope and expectations of the research to be conducted in the high-containment facility. Locations may choose to operate their facilities in various ways, such as:

- A single investigator assigned/operated facility.

- A shared facility assigned to and operated by multiple investigators and research groups who may cycle in and out of the facility.

- An institutional core facility operated by a single facility management structure, but in which multiple projects and agents of varying risk profiles may exist in the facility.

Regardless of how locations choose to operate their facilities, every location is responsible for ensuring that a funding mechanism is in place for each facility for routine maintenance, repairs, and annual validation. The funding mechanism must include plans to address the ebb and flow of research funding and for the acquisition of monetary support in the event of emergency situations. If the institution declines to support it, the facility may require decommissioning, and this must be reported to the UC HCLOC within the calendar year.

Since individual location frameworks for oversight, research support, occupational health, and facility operations, maintenance, and repair differ, it is at the discretion of stakeholders to employ the funding mechanism(s) that meet the operational maintenance and oversight needs of their high-containment facilities. Examples of funding mechanisms include:

- Agreement and establishment of expected financial commitments and scope of responsibility through a Memorandum of Understanding (MOU) among various campus stakeholders.
- Establishment of a recharge structure in which recovered funds are pooled and utilized for outlined budget items, such as annual validation, equipment certification, repairs, and other necessities.
- Establishment of an annual budget by an investigator-headed research group, outlining funds earmarked for specific operational safety items, such as annual validation and equipment certification. Note that any such budget must include a framework for oversight of critical safety items in the absence of investigator funds or in the instance of investigator departure.

Management

A clear and effective management structure is a key oversight mechanism in the operation and maintenance of high-containment facilities. While the local HCLOG serves as the ultimate decision-making body, day-to-day operational oversight is necessary for the safe operation of facilities. While facility-specific management structures are left to the discretion of the location, a sound management structure may incorporate the following:

- Identify key management personnel for operation and oversight of the facility or facilities.
- Describe responsibilities of key management personnel for operation and oversight of the facility or facilities.
- Identify operational documentation necessary for operation and oversight of the facility or facilities.
- Identify groups responsible for the provision, management, and maintenance of safety-specific supplies, such as PPE.
- Identify chain of command processes and points of contact for key stakeholder groups for emergency response.

The section on location involvement provides an example of groups to consider for incorporation into the proposed management structure for a given facility or facilities.

Location Involvement

Operation of a high-containment facility requires the involvement of specific campus experts and stakeholders in management, support, and funding structures. Active communication is essential between the following groups:

- **Researcher group**
    - Principal Investigator to oversee lab operations
    - High-containment (BSL-3) Facility or Lab Manager(s)
    - Lab members
- **EH&S and local and systemwide leadership**
    - HCLD who develops and implements the high-containment safety program
    - Biosafety Officer
    - Institutional Biosafety Committee (IBC) and other oversight committees depending on facility use and research needs (e.g., Responsible Official for Select Agents)
- **Local Facilities and Construction group(s)**
    - Facilities, construction, and planning leadership liaison for high-containment major repairs
    - High-containment maintenance group to correct issues, provide preventative maintenance, and run annual performance verification tests
- **Fund administrators**
    - Funding program oversight, acquisition, and distribution depending on the funding structure laid out by each location
- **Occupational Health**
    - Occupational Health liaison to maintain a program for medical clearance, health surveillance, and protocols for exposure control
- **Special department groups**
    - Animal welfare and veterinary staff for ABSL-3 facilities
    - Greenhouse facility management for BSL-3P
    - Other departmental groups for specialized BSL-3 facilities
- **First responders**
    - Local police and fire department liaisons for emergency training and response in high-containment facilities

It is up to each location to identify different stakeholders and designate subject matter experts as representatives for each group.

Operations

Administrative - Documentation and Record Keeping

The following documentation should be kept, electronically or printed, according to the UC Records Retention Schedule:

1. **Training Records**

Training requirements for work in or entry into, as in the case of visitors and regulators, hgh-containment facilities are detailed in the UC Biosafety Level 3 (BSL-3) Training Standard. Training records must be maintained for the following groups, as applicable to the specific facility:

- Researchers
- Animal Care Personnel
- Safety Personnel
- Facility Services
- First responders
- Others: Vendors, Visitors, Regulators

Before starting on high-containment training, the users seeking independent access must complete all other biosafety, animal, or plant facility training in accordance with their local requirements, including but not limited to, Bloodborne Pathogens, Spill Control and Report, General Safety, Emergency Building response, Injury and Illness Prevention Plan, Aerosol Transmissible Disease Pathogens, etc. The training record will be reviewed/approved by the HCLD before access is granted.

2. **Annual Performance Verification Results**

- Failure test scenarios - Supply fan(s), exhaust fan(s), power outage (simulated or full)
- Systems and controllers' update
- Walkthrough checklist
- Biosafety cabinets annual certification
- HEPA filters annual certification (e.g., HVAC exhaust, animal caging ventilation system, etc.)
- Other annual certifications or checks (e.g., fire extinguishers, etc.)

3. **Inventory of Biological Agents**

All locations operating high-containment laboratories must maintain an accurate inventory of all RG3 pathogens contained and handled at high-containment facilities, including identifying the organism and locations.

- Facilities that utilize Select Agents must keep inventories in accordance with federal regulations for Inventory of Select Agents and Toxins.
- Facilities that do not utilize Select Agents should maintain a general inventory of biological agents in the facility.
- Locations will keep information on agent details, such as strain IDs and nucleic acid modifications, in accordance with their IBC policies.

4. **Facility-Specific Biosafety Manual**

- Approved by the HCLD and the BSO with input from the HCLOG members.
- Coordinated with the IBC.
- Must be reviewed and revised annually or when significant changes in protocol or procedures are made.

5. **Occupational Health Program and Personnel Risk Assessments**

- Coordinated by HCLD and Occupational Health Director with input from subject matter experts, as appropriate.
- Approved by the IBC.
- Must be reviewed annually, when new agents are added, or when personnel health status changes.

6. **Current Roster of Users with High-Containment Facility Access**

- Final approval conducted by the HCLD with input from the PI/supervisor and/or local HCLOG and/or IBC.

7. **Laboratory Inspection Records**

- Coordinated by the HCLD with input from lab managers.

8. **Must be updated annually.**

- Inspection findings/resolutions shared with the local HCLOG and/or IBC as applicable.

Maintenance

An effective high-containment program depends upon the continuous operation of a highly engineered facility providing physical containment for RG3 agents.

The UC BSL-3 Laboratory Design Standard is a guide for the construction and maintenance of high-containment facilities systemwide that follows CDC, NIH, and industry standards for high-containment facilities. The document can be found on the UC HCLOC website.

Successful implementation of this Standard requires identifying facility needs and generating a maintenance plan with short- and long-term maintenance cycles. Maintenance plans should follow guidance based on manufacturer recommendations, biosafety best practices, and applicable regulatory requirements.

An annual preventative maintenance program must be in place following the UC BSL-3 Preventative Maintenance Checklist (Appendix A). Annual performance verification (APV) tests following the ANSI Z9.14 Standard are performed for each facility are reported to the local HCLOG. Examples of maintenance checks included in an APV are facility integrity, plumbing, electrical, HVAC, and equipment tests. Fan failure and power failure tests provide insight as to whether a facility can maintain containment in the case of a blackout/brownout, equipment failure, or other incidents that compromise the differential pressure and directional airflow of the facility.

During annual preventative maintenance and validation, the facility is generally taken out of operation to allow facilities personnel and vendors to enter the facility in a low-risk environment. In these cases, infectious materials are secured, waste is autoclaved, and the facility is decontaminated via surface, gas, or vapor decontamination, as warranted by a proper risk assessment.

Annual performance verification reports are documented, and deficiencies are addressed in a timely manner. Corrective actions must be documented to maintain a thorough record of facility maintenance and repairs. Decisions to defer maintenance of the facility or essential equipment must be based on a risk assessment that is documented, including who was involved, the risk assessment for deferment, and any risk mitigation strategies until maintenance is resumed.

As part of the overall maintenance program, a plan must be in place for urgent maintenance or repairs in the event of an emergency, such as an earthquake, fire, equipment failure, etc. The plan should identify key personnel, procedures, and funding sources for timely action.

Validation

Annual validation is vital to confirm safe and continuing operations of high-containment facilities as equipment ages. HVAC equipment requires periodic and consistent maintenance to ensure optimum performance and function. A properly functioning HVAC system ensures safety for users, surrounding areas, and the outside environment.

- Facilities must be validated annually in accordance with the most current version of ANSI/ASSP Z9.14 Testing and Performance-Verification Methodologies for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Ventilation Systems and the current edition of Biosafety in Microbiological and Biomedical Laboratories (BMBL).

    - If a specific situation requires a temporary delay or deferral of validation beyond the annual deadline, such proposals must be coordinated by the HCLD and appropriate subject matter experts and reviewed by the local HCLOG.

- Facilities must be re-validated in accordance with the ANSI/ASSP Z9.14 standard following any significant change or renovation.
- It is the responsibility of the HCLD and the HCLOG to conduct a facility risk assessment to determine the applicable components of the ANSI standard to conduct the facility validation.
- Containment equipment must be validated in accordance with manufacturer recommendations or industry standards.
- HEPA filters must be tested annually.

Exceptions

Locations must comply with the UC Biosafety Level 3 Operations, Maintenance, and Validation Standard. When justified by a documented risk assessment and with an included corrective action plan, the local HCLOG may approve exceptions. Financial constraints cannot be identified as a primary reason for an exception. UC HCLOC input may be sought by the local HCLOG.

Revisions to the Standards

A full review of the UC Biosafety Level 3 Operations, Maintenance, and Validation Standard must be conducted at least every two years, and revisions will be made if necessary. Between full reviews, the Standard may be revised on an as needed basis via continual evaluation and application. Through the use of this Standard, any identified gaps, errors, or sections requiring further clarification will be noted and highlighted by the HCLDs for inclusion in the review and revision process. Corrections, clarifications and all identified issues will be presented to the UC HCLOC for review, confirmation and approval. Once approved by the UC HCLOC, updates will be completed and distributed to each location. Revised versions of the Standard must receive approval by the UC HCLOC prior to implementation.

List of Codes, Standards and Guidelines

- Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition, 2020. The BMBL is published jointly by the U.S. Department of Health and Human Services, the Centers for Disease Control and the National Institutes of Health. The guidance document describes Biological risk assessment, lab practices, safety equipment, and facilities requirements required for designing and operating laboratories at Biosafety Levels (BSL) 1 through 4.

- NIH Design Requirements Manual (DRM) Rev 2.0: 3/8/24 https://orf.od.nih.gov/TechnicalResources/Documents/DRM/DRM2.003122024.pdf

- ANSI/ASSP Z9.14-2020 Testing and Performance-Verification Methodologies for Ventilation Systems for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Facilities - Applied Biosafety Journal Article describing the ANSI standards can be found here. This document can be purchased and here is a PDF preview of the ANSI standards.

- NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), 2024

- University of California Environment, Health & Safety (EH&S) Laboratory Safety Design Guide,(UC Lab Design Guide) Second Edition, September 2007

- University of California Environment, Health & Safety (EH&S), High-Containment Laboratory Oversight Committee, (UC HCLOC)

- University of California Information Technology Services, UC Records Retention Schedule

- University of California BSL-3 Laboratory Design Standards, 2022

Appendix A. UC BSL-3 Preventative Maintenance Checklist

Event/Test	Responsible Party*	Frequency	Scheduled Date	Completion Date	Notes
Shutdown and/or Decontamination and Annual Verification					
Pre-Shutdown Preparation	EH&S/ Researcher	Annual			May include inventory audit, equipment preparation, locking and sealing of live material, clearing and decontamination of benchtop surfaces, floors, etc., autoclaving and removal of waste.
Decontamination of BSL-3 Suite	EH&S/ Contractor	Annual			For laboratories which do not conduct annual gas or vapor decontamination, surface decontamination may be conducted as part of the preparation for annual verification.
Annual Verification of Laboratory and HVAC in Accordance with ANSI Z 9.14		Annual			Verification should be conducted in accordance with the most recent version of the standard. Applicable components of the standard and acceptance criteria should be determined during the facility risk assessment.
Building Management					
Test Smoke Detectors/Fire System	FM	Annual			All alarms (fire, air flow, security, etc.) have been checked and are functioning according to established specifications. Smoke detectors, heat sensors, and fire sprinkler heads have been inspected and tested.
Test alarm notification system	FM	Annual			

Event/Test	Responsible Party*	Frequency	Scheduled Date	Completion Date	Notes
BAS system	FM	Annual			If a Building Automation System has the capacity to monitor and record performance measurements, e.g. differential pressures, the entity is encouraged to capture and store data from potential failure events, drills, etc. This information may provide verification of system performance. In addition, any programmed alarms should be verified for proper functioning.
HVAC					
Replace HEPA filters on vacuum system	Contractor	As Needed, Test Annually			
Replace HEPA filter in exhaust	Contractor	As Needed, Test Annually			Laboratory HVAC HEPA filters, if present, have been certified annually.
Test air flow alarm	FM	Annual			Inward directional air flow has been confirmed by observation for the laboratory.
Vacuum System (belt, motor)	Contractor	Annual			
Calibrate Air Flow Monitors	Contractor	Annual			The means of detecting air flow (telltale, magnehelic or digital gauge, Baulin-Tube, etc.) has been confirmed to accurately reflect observed air flow. It is recommended that digital or magnehelic gauges be calibrated annually.
Ductwork integrity	Contractor	Annual			
Replace fan belts	Contractor	Annual - As Needed			Exhaust fan motors have been checked and routine maintenance conducted.
Plumbing					
Replace sink foot activated faucet pedals (cartridge/piston)	FM	As Needed, Inspect Annually			

Event/Test	Responsible Party*	Frequency	Scheduled Date	Completion Date	Notes
Change water intrusion monitor batteries	FM	Annual			If present. Best practice, not required.
Inspect and test backflow preventors	FM	Annual			
Verify plumbing fixtures, shutoffs, and drains	FM	Annual			
Verify anesthetic and laboratory gas fixtures and shutoffs	FM	Annual			
Electrical					
Replace light bulbs/lamps	FM	As Needed			Inspection and re-lamping should be scheduled on a pre-determined basis to avoid equipment failure. An example would be a three year cycle minimum or as needed.
Verify all electrical outlets	FM	Annual			
Verify all Emergency electrical outlets during power failure	FM	Annual			
Replace batteries in equipment, if applicable	FM	Annual			
Facility Integrity/Finishes					
Close and latch, lubricate doors	FM	Annual			All doors are fully self-closing
Repaint chipped areas	FM	Annual			
Check all penetrations - recaulk if needed	FM	Annual			The laboratory has been checked for unsealed penetrations, cracks, breaks, etc. and these have been repaired if present.
Clean floors (clean and wax)	FM	Annual			

Event/Test	Responsible Party*	Frequency	Scheduled Date	Completion Date	Notes
Inspect and adjust hands-free sinks and faucets	FM	Annual			
Replace sink foot activated faucet pedals (cartridge/piston)	FM	As Needed, Inspect Annually			
Autoclave/Equipment					
Autoclave Calibration and Test	Contractor	Commissioning of Equipment			Decontamination systems (autoclave, room decontamination systems, digesters, liquid effluent systems, etc.) have been confirmed to be operating correctly. Best practice is to requalify annually.
Replace Fire Extinguisher	FM	Annual			
Test BSC alarms	FM/Contractor	Annual			
Eyewash/shower in good working order	EH&S	Monthly Test - Annual Evaluation for repairs			Drench showers, eye wash stations, and hands free sinks have been confirmed to be operating properly.
Replace sink foot activated faucet pedals (cartridge/piston)	FM	Every Odd Year			
Certify Exhaust HEPA Filters	Contractor	Annual			Certification should include in-line HEPA leak test.
Certify Biosafety Cabinets	Contractor	Annual			
Certify Containment Equipment (MGIT, Ultracentrifuge, etc.)	Contractor	Annual			Seals on centrifuges, Class III cabinets, gloves on Class III cabinets, etc. have been checked and replaced if required. Annual preventative maintenance should be conducted.
Review Spill Kit Contents	EH&S	Annually			
Replace Expired First Aid Kit Contents	EH&S	Annual - As Needed			

Event/Test	Responsible Party*	Frequency	Scheduled Date	Completion Date	Notes
Check UPS batteries	FM/Contractor	Annual			Institution may wish to implement a scheduled replacement.
AED Check	EH&S	Annual			
Test and replace reusable PPE (PAPR, etc.)	EH&S	Annual - As Needed			Follow manufacturer schedule for preventative maintenance.
Animal Infrastructure					
Certify Rodent Cage Rack	Contractor	Annual			
Certify Anesthesia Equipment	Contractor	Annual or per institutional requirement			
Check door sweeps	FM	Annual			
Confirm functionality of temperature and humidity controls	FM	Annual			
Review integrity of reusable caging	EH&S/Husbandry	Annual			
Security					
Test door alarms & interlock system	FM	Annual			
Test alarm notification system	FM	Annual			May include testing of panic buttons, duress codes, motion sensors, etc.
Verify security camera functionality	FM	Annual			
Adjust door sweeps	FS	Annual			
Change door lock batteries	FS	Annual			
Administrative					
Remove decontaminated equipment	FM	As Needed	Remove decontaminated equipment		
Biosafety Inspection	EH&S	Minimum Annual	Biosafety Inspection		

Event/Test	Responsible Party*	Frequency	Scheduled Date	Completion Date	Notes
Review Training Records	EH&S	Annual	Review Training Records		
Set up Emergency Drills	EH&S	Annual (Best Practice or FSAP)	Set up Emergency Drills		
Occupational Health Review	EH&S/OH	Annual	Occupational Health Review		

**the tasks and responsible party may vary depending on facility-specific protocols and design.*