Commissioning to Support the Shutdown, Decontamination and Restart of an ABSL3 Facility

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Synopsis

Many conventional commissioning practices focus on ensuring that facilities meet design requirements. More progressive commissioning practices are forward looking to ensure that the facility can achieve the longer term, ongoing goals of maintainability, performance reliability, research and production capability, safety, environmental protection, and security. This is particularly applicable to and important for biocontainment facilities. Ultimately, during the full life cycle of a biocontainment facility there will likely be a need to have a complete facility shutdown, complete decontamination, and facility re-start. This may be necessary to perform preventative maintenance, calibration, repairs, facility modifications, new equipment installations, and facility re-commissioning that cannot be accomplished during normal operations. In many cases the biocontainment facility serves a crucial role in the business objective of the organization. Therefore, the need to have the facility back in operation quickly, while ensuring the safety of personnel, is of paramount importance.

This paper will first address the process, personnel requirements, commissioning tests, and lessons learned during the initial, pre-operational, commissioning process to support the shutdown, decontamination, and restart of a 10,000 sq ft, animal biosafety level 3, (ABSL3) enhanced biocontainment facility completed in 2005. The paper will then discuss the effectiveness of the initial commissioning process, the challenges encountered, and the lessons learned as a result of the 2006 actual shutdown, decontamination, and restart of the ABSL3 facility.

About the Author

Mr. Lopez's experience includes the management of major capital projects, facilities operations and maintenance, research engineering, procurement, property, quality, environmental restoration, and environment, health, and safety. This includes 30 years of design, construction, and operating experience with a wide variety of research animal facilities and facilities designed to work with hazardous chemical, radioactive, and biological aerosols. Since 1994, Mr. Lopez has been responsible for ten BSL2 and BSL3 projects totaling 16,000 square feet. A significant portion of Mr. Lopez's experience and effort since 2004 has been focused on the successful design, construction, commissioning, validation, operation, and maintenance of a 10,000 square foot ABSL3 bio-containment facility. This facility is designed and operated for GLP compliant research using multiple research animal species and bio-agents including CDC select agents. Mr. Lopez also conducts training in the area of facility design and engineering controls for bio-containment facilities. Mr. Lopez has participated in national bio-containment conferences as a speaker in the areas of bio-containment facility design, commissioning, and operation.

Facility Description and Function

A 9,500-square foot animal biosafety level 3 (ABSL-3) research facility (see Figure 1) was completed in 2005 at the Lovelace Respiratory Research Institute (LRRI). This facility was designed and constructed for in-vivo infectious disease research using multiple animal species and a variety of infectious materials, including materials on the Centers for Disease Control and Prevention (CDC) select agent list.

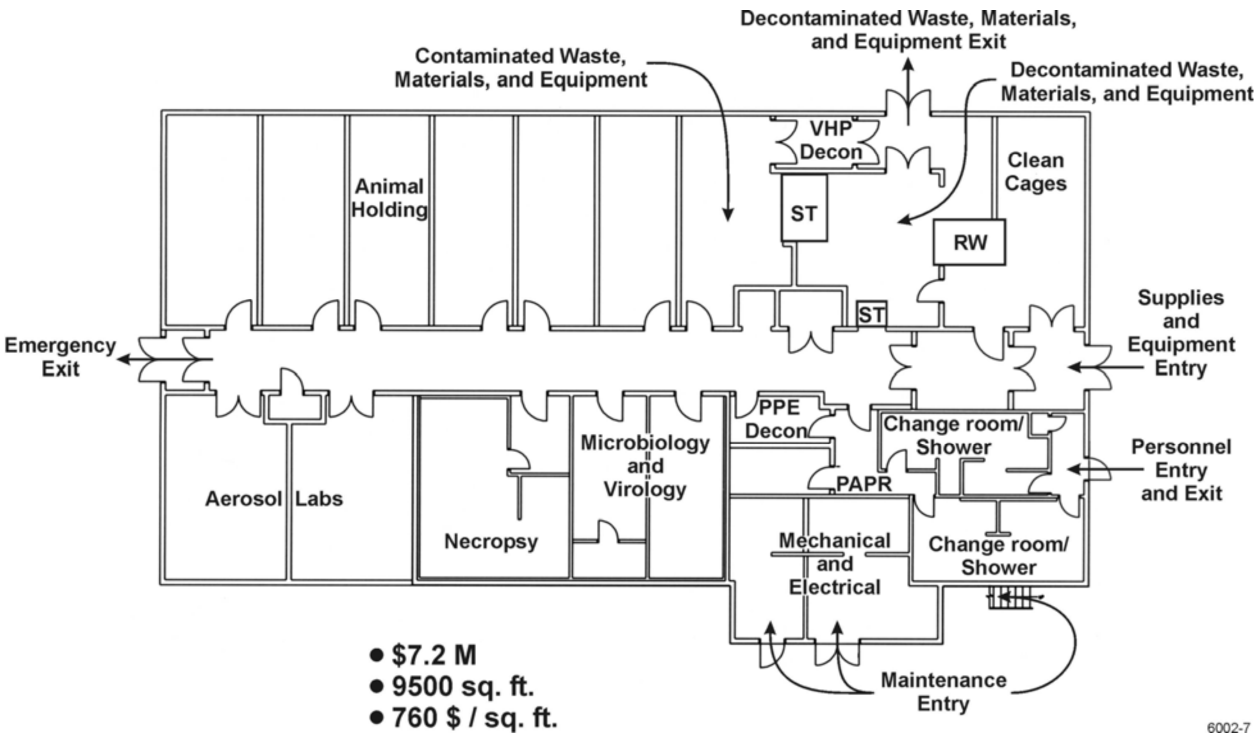

Figure 1. Floor Plan of the ABSL-3 Facility

A unique feature of the LRRI ABSL-3 facility is its equipment and design elements that allow work with aerosolized materials. Furthermore, the facility is designed to support U.S. Food and Drug Administration (FDA) related research.

The Commissioning and Validation Approach

The function and regulatory requirements for the ABSL3 Facility dictate that the performance of many elements of the facility must be thoroughly inspected, performance tested, and the results documented. The process to accomplish these objectives is referred to as “Commissioning and Validation” (CxVx).

Many of the CxVx requirements are prescribed by regulations, standards, and guidelines. However, a complete CxVx plan also requires the professional judgment of project team members composed of subject matter experts. The application of risk assessment principles is also a key element of any effective CxVx plan. A poorly planned CxVx endeavor can consume extraordinary levels of effort, resources, and costs. The principle of diminishing returns definitely applies throughout the CxVx process.

A comprehensive and effective CxVx program should include the following fundamental elements.

- Establishing the CxVx team with authorities, roles, and responsibilities.
- Determine what components, subsystems, and systems are to be included in the CxVx Program.
- Identifying what CxVx actions are required for each project element including components, subsystems and systems.
- Develop a written CxVx Plan complete with objectives and inspection and test procedures.
- Implementation of the CxVx including training for personnel performing CxVx to communicate procedures to be followed and documentation requirements.
- Development and maintenance of clear documentation.
- A method for tracking execution of the CxVx Plan A method for tracking test failures, deficiencies and resolution.
- A method for review, approval and acceptance of tests and ultimately acceptance of the facility

There are many models for identifying the actions required for each project element. Figure 2 presents the model used for the ABSL3 project.

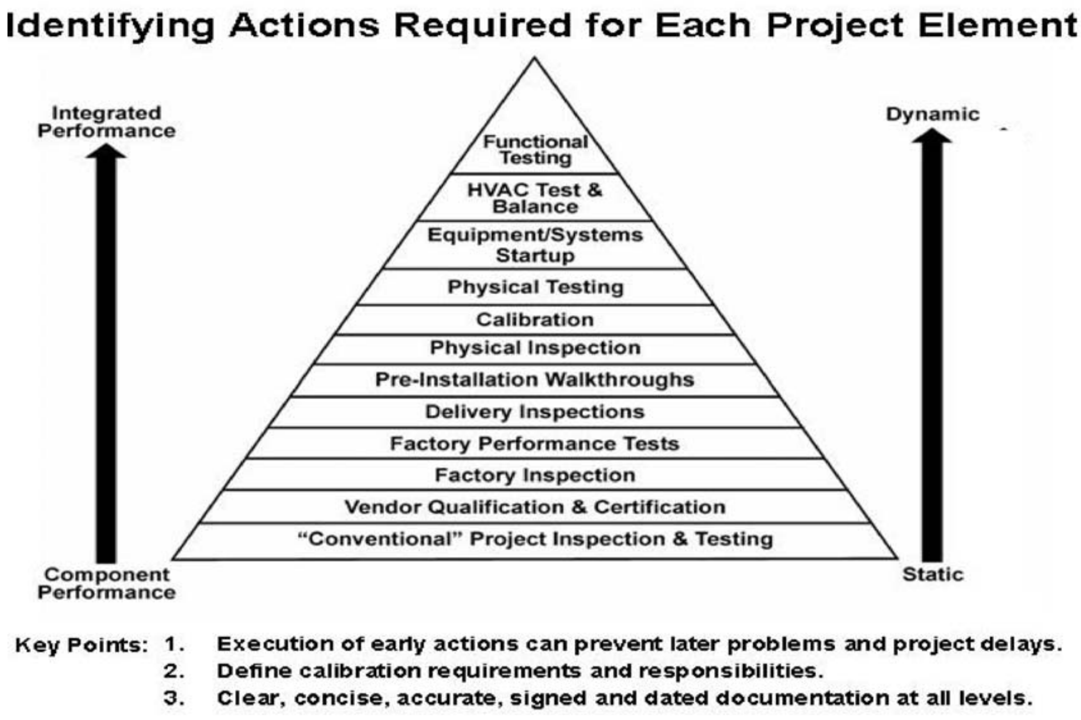

Figure 2. Actions Considered and Evaluated for Each Project Element

Ultimately it is functional testing which demonstrates that the facility will operate as intended. Further, it is through functional testing that the integrated performance of the facility is measured. The performance of functional testing can have many objectives. These can include:

- Testing to achieve design and specification requirements.
- Testing performance and response to abnormal operating conditions, such as the loss of normal electrical power and the transfer to emergency power.
- Test performance beyond design conditions, (i.e. stress test) such as evaluating performance of air handling systems beyond normal operating range.
- Testing to support ongoing operations and maintenance.

Testing to support operations and maintenance is the primary focus of this paper. Complex facilities such as BSL3 and BSL4 biocontainment facilities are subjected to very high demands relative to performance and reliability. Further, it is very difficult to curtail research operations or production operations in such facilities. Accordingly, when the opportunity presents itself for a shutdown, all work must be done in a very efficient, productive, and safe manner. The greatest productivity during a shutdown can be achieved if the facility can be released from the normal, full containment procedures including the use of full personal protective equipment, entry and exit monitoring, and decontamination associated with individual work packages. Achieving this goal requires that all the shutdown, decontamination, and startup processes be commissioned before biohazardous materials are used in the facility, i.e. during the initial CxVx conducted as part of the facility construction, and occupancy phases.

Functional Testing to Support Facility Shutdown, Decontamination and Startup

There are many elements and actions required to ensure the performance of the facility as illustrated in the previous Figure 2. A total of 250 inspections and functional tests were included in the CxVx for the ABSL3 facility. However, with respect to the shutdown, decontamination, and restart of the ABSL3 there were three critical elements that required special consideration for functional testing during the commissioning stage of the project. These included 1) exhaust fan switchover 2) pressure gradient/directional airflow control and 3) vaporized hydrogen peroxide (VHP) decontamination. The commissioning actions for each of these are detailed in the sections that follow.

Commissioning of Exhaust Fan Switchover

The ABSL3 facility heating, ventilating, and air conditioning system (HVAC) is separated into four zones for areas within containment based on function, risk, and hazard. Each zone is equipped with two exhaust fans. One fan operates (lead) while the second remains in standby (lag). The standby fan is designed to automatically start should the primary fan fail for any reason. Further, manual switchover of the fans would be necessary to perform fan maintenance. Conventional functional testing might have as its objective a successful switchover from lead to lag fans. This does not provide sufficient performance verification for a BSL3 or BSL4 facility. Not only do the fans need to switch but containment must be maintained during the switchover. Containment is defined by the maintenance of required pressure gradients throughout the facility. The functional test performed to demonstrate maintenance of containment required that 25 differential pressure monitoring points be trended during fan switchover testing. During initial functional testing some pressure gradients reversed. Progressive changes to the fan switchover control sequence and retesting were required to ultimately achieve containment during switchover. Control sequence changes focused on the timing sequence for lag fan startup, ramp-up speed, and isolation damper opening and closing.

Commissioning of Pressure Gradient/Directional Airflow Control System

The pressure gradient control system is an individual room based, constant air volume system with an air offset control that uses air volume measuring stations and air control valves. The offset between the supply and exhaust air for each individual room is controlled to a specified quantity to achieve the required negative or positive pressure. Functional tests conducted demonstrated the performance of the control system to meet the following objectives.

- Ability to maintain rooms at a negative pressure. Typically this is the normal mode of operation for rooms within containment.
- Ability to maintain rooms at a positive pressure. This would be necessary when an individual room is decontaminated while the rest of facility is potentially still contaminated. This minimizes the potential for recontamination.
- Ability to maintain pressure gradients during the closing and opening of individual room bioseal isolation valves.
- Ability to maintain pressure gradients when ceiling access doors or ceiling tiles are removed to access equipment for maintenance.
- Ability to maintain pressure gradients when HEPA filter exhaust plenums are being isolated for filter testing and replacement.

The functional testing demonstrated the ability of the pressure gradient control system to maintain pressure gradients. However, this functional testing also identified the need to follow a very prescribed sequence of steps for all manual operations such as bioseal valve operation along with control system operation to maintain containment. Improper sequence of operation could result in pressure gradient reversals. Accordingly, the preparation of specific, written operating procedures for individual rooms were developed for such activities as room isolation for VHP decontamination or opening of ceiling access doors.

Commissioning of Vaporized Hydrogen Peroxide (VHP) Decontamination

The decontamination method used for decontamination of rooms, Class III biological safety cabinets, ductwork, HEPA filter exhaust plenums, and equipment leaving containment is VHP. This method requires the proper performance of the VHP equipment, preparation of room, isolation of room, ventilating of room, and restoration of room to normal operation. Each of these processes required commissioning to clearly demonstrate performance. The commissioning of the VHP process included the following.

VHP Decontamination Equipment

The performance of the VHP unit was subjected to several stages of commissioning and validation:

- The VHP unit manufacturer performed installation qualification verifying that the unit and any supporting infrastructure such as electrical power met manufacturer specifications.
- Manufacturer then performed an operational qualification to verify that unit performed in accordance with manufacturer specifications.
- Owner then conducted performance qualification that evaluated decontamination performance under actual operating conditions. All rooms within containment were decontaminated individually. This included preparation of room, placement of bioindicators inside room, isolation of room, decontamination, exhausting of room, incubation of bioindicators, and restoration of room to normal operation.

The most significant lessons learned from the VHP commissioning included the need for specific procedures for the isolation of rooms as described above for the pressure gradient control system, the need for careful preparation of room to allow VHP contact, the need for good room air circulation during the VHP decontamination phase, and the need to decontaminate double HEPA filter exhaust plenums both in a forward and reverse direction to achieve decontamination of all the housing and filters.

The Shutdown, Decontamination and Startup of the ABSL3 Facility

The shutdown, decontamination, and startup of the ABSL3 Facility occurred during a twenty day period in July 2006. The facility shutdown provided an opportunity to perform activities that could not be performed or were very difficult to perform during normal operations. These activities included work in the following categories 1) preventative maintenance 2) calibration 3) inspections 4) re-certification and revalidation 5) facility and equipment repairs 6) facility and equipment modifications and 7) new equipment installations.

The principle phases for the shutdown, decontamination, and startup of the ABSL3 facility included the following.

- Planning
- Decontamination
- Work Performance
- Restoration of Operations, i.e. startup

Each of these is discussed in the sections that follow.

Planning

It is very important to have all stakeholders involved in both planning and execution. This is required to ensure that planned work is completed but even more importantly to ensure that there is 1) no environmental release of bioagents into the environment, 2) no recontamination of space that has been decontaminated and 3) no personnel exposure to bioagents. Activities must occur in a precise planned fashion that is understood by all participants to ensure that all activities are coordinated. Accordingly, pre-shutdown planning and daily coordination meetings were held to address the following:

- What are requirements and methods for securing biohazard materials left in facility?
- Who must be escorted into facility and who can be an escort?
- What operations/rooms would continue in operation while other rooms were being decontaminated?
- What would be the sequence for decontamination of rooms and equipment such as Class III biological safety cabinets?
- What would be procedure for preparing a room for decontamination?
- What equipment and surfaces would not be subject to decontamination?
- What would be the procedure for preventing recontamination after decontamination?
- What work activities would be conducted during the shutdown and who would be responsible?
- What would be the sequence of work activities?
- What supplies, equipment, parts would be required?
- What would be the procedure for entry of service personnel?
- What would be reentry procedure, including personal protective equipment requirements after decontamination was complete?
- What biohazards still existed after decontamination and how were these to be identified?
- What would be safety and biosafety practices during the shutdown?
- What would be status of HVAC containment control system during shutdown?
- What would be sequence of facility restart activities?
- What would be the process work safety review during shutdown?
- What were the critical operations and what were contingency plans?
- What would be method of communicating and coordinating daily work?
- What would be method for release of equipment, rooms, and facility for reuse after shutdown?

All of these issues were addressed by the team members during the pre-shutdown planning meeting and at daily status and coordination meetings. Team members included representatives from facilities maintenance, animal care, biosafety, regulatory compliance, lab research, procurement, information systems, and quality assurance. All meeting attendance was documented for verification of attendance.

Decontamination

The VHP decontamination process proved to be the most demanding in terms of planning and execution. It also constituted the critical path for shutdown and restart process. The underlying objective was to complete the VHP decontamination of 1) 20 rooms (5,000 square feet, 52,000 cubic feet), 2) two Class III biological safety cabinets, 3) Four HEPA filter exhaust plenums, and 4) all equipment to be removed from the facility. This was to be done within a ten day period using one VHP unit located within containment. The decontamination was to be done in a sequential manner recognizing that some research and animal rooms would be in use while others were being decontaminated. A typical VHP decontamination cycle requires approximately 6-8 hours, from room preparation through venting of room. However, the room cannot be released until the result of the bioindicator incubation test is complete. This requires 48 hours after completion of decontamination. These objectives and performance criteria ultimately resulted in a plan that required a 24 hour/day continuous decontamination process for the ten day period. The typical decontamination process consisted of the following steps:

- Room preparation including removal of all possible materials and equipment, opening of all cabinets, drawers and equipment requiring internal decontamination, hazard labeling of equipment that would not be internally decontaminated, placement of chemical indicators and bioindicators within the room, placement of VHP circulating fans within the room, hazard postings at entry to room and setup and connection of VHP unit.
- Room isolation including shutoff of supply and exhaust air following prescribed procedure to maintain room containment. Isolation also included sealing of doors, access panels and any other room openings.
- VHP decontamination cycle including the dehumidification, conditioning, and decontamination phases.
- Removal of VHP in room by opening of room supply and exhaust air supplies following prescribed procedure to maintain room at a negative pressure and to prevent release of VHP to remainder of facility.
- Room VHP concentration sampling.
- Reversal of room pressure gradient from negative to positive to prevent recontamination of room.
- Inspection of chemical indicators. Although chemical indicators do not provide proof of decontamination, they do provide an indication of adequate VHP surface contact. Failure of the chemical indicator is a good indication of VHP decontamination failure. Since decontamination verification by bioindicator takes a minimum of 48 hours, delays in re-decontaminating a room, should a bioindicator indicate decontamination failure, can be avoided by the used of the chemical indicators.
- Room entry to remove bioindicators using entry decontamination procedures to prevent recontamination of room.
- Locking of room and posting of signage indicating room has been decontaminated.
- Bioindicator incubation
- Release of room for entry after decontamination of remainder of facility
- Reversal of room pressure gradient from positive to negative after decontamination of remainder of facility to maintain containment in room should there be an unplanned release of any bioagent from equipment which was not decontaminated.
- Performance of work activities in room

A very important decontamination preparation step is the full servicing, inspection, and testing of the VHP unit including availability of critical spare parts and supplies before the decontamination process begins.

VHP decontamination of each room was carefully documented to include 1) checklists, 2) drawings indicating placement of chemical indicators, bioindicators, and circulating fans, 3) chemical indicator strips results and 4) bioindicator results and VHP unit cycle and concentration printouts.

Work Performance

Prior to the initiation of work in the shutdown facility, training was provided to all staff regarding procedures and precautions required for working in the laboratory. These included requirements for individual work task safety reviews, personal protective equipment requirements, and precautions regarding any equipment or area that was not decontaminated. Precautions were also provided regarding work that might involve disruption of the physical facility that might pose an exposure risk, such as removal of wall material or drilling of holes into a wall. Localized chemical disinfectant was used in most cases to deal with any areas of concern. All work activities were included on a shutdown master schedule indicating when activities were to be done and an individual assigned to each task. All work was assigned a priority level with the highest priority given to items impacting containment and regulatory compliance. The following is a summary of work performed during the shutdown.

Preventative Maintenance

Preventative maintenance included such work as the following:

- Autoclave and sterilizer servicing
- Research equipment servicing
- Air handling unit and exhaust fan servicing
- Hands-free sink control servicing
- Supply and exhaust system prefilter change out
- Laboratory vacuum pump servicing
- Refrigerator and freezer servicing
- Variable frequency drive servicing
- Effluent decontamination system servicing
- General housekeeping
- Patching and painting of walls, doors
- Relamping of light fixtures

Calibration

Calibration activities included such work as the following:

- Calibration of all environmental control temperature and humidity sensors
- Calibration of room supply and exhaust air valves

- Calibration of room differential pressure magnehelic gauges and electronic sensors.
- Research equipment calibration such as incubator CO_2 sensors.

Inspections

Inspection activities included such work as the following:

- Inspection of all walls, floors, and ceilings for cracks, opening and failure of seals around piping, conduit, and ductwork
- Ceiling light fixtures
- Emergency and exit light inspection
- Door hardware inspection
- Sterilizer and autoclave bioseal inspection
- PPE inspection

Many of the inspections focused on the physical barrier required for containment.

Recertification and Revalidation

Recertification and revalidation activities included such work as the following:

- In-place testing of supply and exhaust air system HEPA filters
- Class II biological safety cabinets certification
- Class III biological safety cabinets (gloveboxes) certification
- Backflow prevention certification
- Exhaust fan switchover sequence revalidation
- Facility access control system revalidation

Other Activities

Other work activities included standard work order system backlog that included facilities and equipment repair, facility and equipment modifications, and new equipment installation and testing.

Restoration of Operation

Restoring the facility to its normal containment operating mode focused on the verification that normal operating parameters and processes were in place. These included the following measures:

- The VHP decontamination process described above results in the pressure gradient control system being restored to its normal operating mode. However, verification of

pressure gradient conditions and control set points were still required. This was done by trending all 25 pressure gradient monitoring and control points for a 24 hour period
- Review and clearance of all building systems alarms
- Removal of all equipment, tools, instruments, and supplies from containment
- Return of equipment to containment that had been removed for decontamination
- Removal of all special hazard and work procedure signage
- Verification of all access control and surveillance systems
- Release of facility for use as a full containment facility. This required the status review of all work activities and any issues and concerns. Upon acceptance of facility readiness status, facility was approved for reuse by the biosafety officer/responsible official.
- Posting of signage at entry doors and notification of personnel that that facility was now operating as a full containment facility.

Summary and Lessons Learned

The overall shutdown, decontamination and restart process was judged to be very successful based upon maintenance of schedule, completion of work activities, no incidents of release of bioagents to the environment and no personnel exposure incidents. This success was due primarily to 1) the preoperational commissioning and validation conducted 2) a solid team with effective means of communication, 3) documented operating and maintenance procedures and 4) effective general biocontainment and shutdown training. However, there were clearly some areas for improvement and lessons learned as follows.

VHP Decontamination

- One individual was initially assigned as the primary person for conducting the VHP decontamination. It quickly became evident that due to the full time, continuous nature of the decontamination process, additional trained personnel were needed.
- The reliability of the VHP unit is critical. There were some VHP equipment malfunctions. Although spare parts and trained repair personnel were available, the schedule was impacted. Having a second VHP unit is advisable for complete facility decontamination.
- The VHP decontamination of the central hallway within containment had not been validated during the pre-operational validation phase of project. Full VHP decontamination of the hallway could not be achieved. Additional chemical disinfecting was employed to achieve full decontamination. Large rooms and particularly long and narrow rooms such as hallways pose special challenges for VHP decontamination. Options for improving VHP decontamination of such rooms are currently being evaluated.

Pressure Gradient Control

Extensive commissioning of the pressure gradient control system had been conducted during the pre-operational project phase. However, the VHP decontamination step involving reversing the room differential pressure from negative to positive to prevent recontamination had been tested on a room-by room basis. This demonstrated ability of the pressure gradient control system to maintain room positive without impacting containment for other rooms. However, it was discovered that as the number of rooms being reversed increased, the pressure gradients between containment and non-containment areas began decreasing. The underlying cause was that the reversal of room pressure gradients introduced more air into the central hallway approaching the capacity of hallway HVAC system to remove this additional air. Temporary measures were taken to increase the air removal capacity and permanent changes to the hallway exhaust system are being planned. Commissioning of a complete facility decontamination should be considered as part of a risk based commissioning plan development process.

Facility Entry During Shutdown

Initial instructions were provided verbally to staff regarding entry, personal protective equipment, and work precautions during the shutdown. Compliance with these requirements was not consistent. Subsequently, written instructions were provided to all individuals and training was conducted. Instructions were also posted at facility entries.