# BSL3 Issues for Consideration Prior to Building a New Laboratory

Sandia National Laboratories

July 2008

A Biosafety Level 3 (BSL3) laboratory is significantly more complex than the more common Biosafety Level 2 (BSL2) laboratory. Biosafety levels are determined by a combination of procedures and practices, primary barriers (safety equipment), and secondary barriers (facility design and construction). The World Health Organization identifies BSL1 and BSL2 laboratories as basic laboratories, while BSL3 and BSL4 laboratories are referred to as containment laboratories. An institution planning to build a BSL3 facility should give careful consideration to all of the biosafety elements and biosecurity before deciding to proceed.

This document is not intended to be a comprehensive listing of all items that must be addressed when building and operating a BSL3 laboratory. Rather, it is designed to give institutions an overview of items that should be considered before starting on the process of designing, constructing, and operating a BSL3 laboratory. This outline does not address issues for animal BSL3 facilities; including a capability for animals adds many compounding factors to the process.

The process described here is divided into five phases: planning, design, construction, acceptance, and operation. An institution needs to think about all of these phases prior to committing to a new BSL3 facility. Although these phases are shown sequentially, many activities within different phases may take place concurrently. The timeline for each phase and the resources required can vary greatly depending on the size of the BSL3 project.

We recommend that a Technical Review Team (TRT) – consisting of external experts in biosafety, biosecurity, and biocontainment, and facility representatives from the scientific program, operations/maintenance, and management – take responsibility for the planning and operations phases. Ideally, the outside experts involved at this stage would not include the A&E firm, the Commissioning Agent, or the construction contractor. Ideally, the TRT would oversee the work of the A&E firm, the Commissioning Agent, and the construction contractor – those entities that are primarily responsible for the design, construction, and acceptance phases.

## *Planning Phase*

1. Conduct a high-level risk assessment to determine fundamental biosafety and biosecurity requirements – is a BSL3 necessary?
    a. Identify all of the biohazards, settings (labs, clinics, etc), and scale of activities and facility mission (research, diagnostic, routine manipulations, aerosolization, large volumes, etc).
    b. Work with multiple types of pathogens (bacteria, viruses, fungi) can be conducted in a facility, but should not be conducted in the same room

SAND No. 2008-XXXXX. Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-9AL85000.

simultaneously; stringent procedures must be used to minimize the chance of cross contamination.

c. Determine what work needs to be done at what biosafety level?
    i. How much work can be done in a BSL2?
    ii. Is a BSL3 needed for some activities or will a BSL2 with BSL3 work practices suffice?

2. Determine what guidelines and regulations will be followed.
    a. Biosafety and biosecurity guidance (latest editions): World Health Organization's *Laboratory Biosafety Manual* and *Laboratory Biosecurity Guidance*, US CDC & NIH's *Biosafety in Microbiology and Biomedical Laboratories*, etc. See references at the end of this document for additional information.
    b. Other regulations: local and national fire codes, International Building Code, local and national biosafety and biosecurity regulations, Good Laboratory Practices, Accreditation by the College of American Pathologists (CAP), etc.
3. Develop a staffing plan
    a. Does the facility need to hire any new staff for this lab?
    b. Does existing staff need to receive new training to work in or operate this lab?
4. Owner and planning team should strongly consider site visits to other operational BSL3 facilities to talk with those owners and users to understand:
    a. Scope, programming, time issues
    b. Lessons learned
5. Prepare the Basis of Design (BoD) (the owner's project requirements)
    a. It should include all planning assumptions and functional, operational, and performance requirements. This document
        i. Provides basis for evaluating proposed design options.
        ii. Establishes performance criteria for acceptance phase, commissioning, and over facility lifecycle.
        iii. Helps with early detection and diagnosis of O&M problems
        iv. Facilitates post-occupancy evaluations over facility lifecycle
    b. Relevant planning assumptions include biological agents to be used in the facility, planned scope of work activities, risk assessments, design assumptions, code and cost constraints, facility's functional use, definitions, acronyms, and glossaries.
    c. Relevant functional, operational, and performance requirements include occupancy requirements, listing types of areas with descriptions of how they will be used, flow diagrams for people, materials, and waste, descriptions of systems and options, quality of materials and constructions, utility and communication requirements, and information on equipment from manufacturers, including maintenance requirements.
    d. Conduct a specific biosafety and biosecurity risk assessment based on how the facility will be used, and analyze the results of this assessment.
        i. Based on the risk assessment and the possible Standard Operating Procedures, determine what must be engineered into the facility

versus what can be mitigated through work practices and administrative controls.

ii. Determine personnel, product and waste flow requirements.

iii. Results of risk assessment will drive many laboratory requirements. For example:

1. Are filters (HEPA, carbon, other) needed on the exhaust?
2. Is a personnel shower required?
3. How will liquid effluent be decontaminated?
4. How will solid waste be sterilized?
5. What types of primary containment will be used – re-circulating (Class II A2 Biosafety Cabinet), exhausted through a canopy (Class II A2 Biosafety Cabinet), or total exhaust (Class II B2 Biosafety Cabinet)?
6. Physical security requirements such as electronic access controls, alarms, guard station, fencing, etc.

e. Define the functional, operational, and performance requirements.

i. What are the anticipated equipment needs?

1. Freezers, autoclaves, incubators, centrifuges, etc.
2. Type of biosafety cabinets (impacts HVAC design)?
3. How much bench space is required? Consider benchtop versus fixed equipment.
4. What are the electrical requirements for the required equipment?
5. What equipment needs to be on emergency power?
6. Determine equipment sensitivities and need for vibration control in the structural design.

ii. Outline HVAC specifications

iii. What is the internal load (BTUs) in each room? Consider people, lights, equipment, growth of activities, air change rates, etc. This is a significant determining factor for the supply air requirements.

iv. Electrical outlets

1. Number and locations defined for normal power
2. Number and locations for emergency power

v. Determine methods for decontamination and waste handling

1. Surface decontamination – preferred method(s)?
2. Space decontamination – preferred method(s)?
3. Waste decontamination – preferred method(s)? Identify applicable regulations

vi. What utilities and communications are required? Where? Secured?

6. Outline the Commissioning Plan

a. Commissioning is a process to ensure that the building performs according to the design intent and the owner's needs.

b. Interview commissioning agents. Prepare to hire a third party commissioning agent to participate in the design, construction, and acceptance phases.

    c. Based on the budget, what level of commissioning assistance will be incorporated into the project?
7. Ensure adequate resources are available for the project, initial operations, and follow-on maintenance.
    a. Great variations between projects depending on size and complexity

***Design Phase***

1. Designing BSL3 laboratories is very different than designing clean rooms, other types of laboratories, or office buildings. Clean room design and construction principles are often opposite of what is needed for containment laboratories. There will likely be significant problems if the design team does not include individuals with prior relevant experience in the design of bioscience containment laboratories. Interview and select an experienced architect and engineering (A&E) firm to design the facility, including equipment specialists.
2. Interview and select an experienced biocontainment commissioning firm.
3. Decide whether to build a pre-fabricated facility or to pursue bricks-and-mortar construction (there are pros and cons to each); the Basis of Design document should guide this decision.
    a. Retrofitting an existing laboratory space is generally much more complicated than building a new facility.
4. Select a building location with consideration to
    a. Access, air intakes, exhaust intakes, environmental impacts, etc
5. Identify flows of personnel, materials, and waste.
    a. Think through procedural controls while making decisions about the engineering controls (primary and secondary barriers).
    b. Identify where doors are required to achieve a pressure differential between spaces; identify where doors are needed for programmatic reasons (security, to delineate research spaces, etc.).
    c. Determine amount of space needed (inside and outside of the BSL3) for storage of PPE, personal items, and other supplies; determine amount of space needed for donning and doffing of PPE.
    d. Determine where anterooms will be needed.
    e. Identify clean/dirty areas and corridors, and grey zones.
    f. Identify the BSL2 areas that support the BSL3 areas.
6. Prepare an architectural narrative
    a. Small-scale floor plan of entire facility
    b. Large-scale floor plan of each space
    c. Layout laboratory furniture and equipment using scaled replicas with lab personnel, integrating risk assessment requirements
    d. Identify building exterior elements
    e. Address laboratory casework considerations.
        i. Should be easy to clean and decontaminate, especially including counter top surfaces
        ii. Should have smooth edges with no gaps or void regions.

iii. Since most work in a BSL3 should be done inside a biosafety cabinet, a BSL3, in general, should require less casework than a BSL2.
iv. Casework material is an important consideration. Certain materials are not compatible with some of the surface decontaminants typically used (e.g. stainless steel and bleach).

f. Address autoclave considerations.
i. Pass-through autoclaves are generally ideal; stand-alone autoclaves need more intensive procedural controls.
ii. Need to consider throughput requirements, and maintenance requirements (service from outside BSL3, location of containment barrier compared to location of autoclave).
iii. Stainless steel capture hoods located over the autoclave doors provide a means by which steam deterioration of the ceiling can be minimized.

7. Prepare a mechanical narrative
a. Allocate mechanical space.
i. Mechanical space should be outside containment to the greatest extent possible.
ii. Equipment should be easily accessible for periodic maintenance, daily checks, and eventual replacement.
iii. Mechanical space requirements for BSL3 labs are far more extensive than for standard laboratories.
1. A net-to-gross ratio of approximately 3.8 or a building efficiency of 0.26 is a good planning number for BSL3 facilities.

b. Identify major pieces of equipment and include their specifications
i. Air handling units, exhaust fans, space air flow control devices, etc.

c. Preliminary mechanical calculations
i. Heating and cooling loads, supply and exhaust air quantities, etc

d. Preliminary HVAC controls flow diagram and sequence of operations
e. Determine specifications for building control systems
i. Choice of sensors, indicators, alarm points, including environmental monitors, etc.
ii. Choice of pressurization control, i.e. volumetric offset monitoring differential pressure or direct differential pressure control (much more difficult to maintain).
iii. Lab room or lab suite isolation capabilities for maintenance and decontamination.
iv. Security alarm control station
1. In emergencies, do doors fail-safe or fail-secure (e.g. with request to exit buttons)?

v. Variations
1. Occupied and unoccupied modes
2. Failure modes

a. Need to ensure room won't become positively pressurized if exhaust fails.
b. Need to ensure systems react appropriately when power is lost, when power is restored, and when equipment is taken off-line either by failure or planned maintenance.

8. Prepare an electrical narrative
    a. Identify major pieces of equipment and include their specifications
        i. Lights, emergency generators, transfer switches, fire alarm systems, etc
    b. Preliminary electrical calculations
        i. Normal power load, emergency power load, etc
    c. Preliminary HVAC electrical riser diagram
9. Prepare a plumbing narrative
    a. Identify major pieces of equipment and systems and include their specifications
        i. Plumbing fixtures, water heaters, fire suppression systems, etc.
        ii. Domestic water, deionized water, waste water, specialty gases, etc
10. Plan for schematic and design reviews. There are multiple steps in the design phase that should be subject to review by stakeholders team.
    a. Schematic planning (0-20%)
        i. Completed list of lab equipment for each space
        ii. Further develop floor plans
        iii. Develop personnel, material, and waste flow diagrams
        iv. Finalize the biosafety and biosecurity risk assessments
        v. Review budget including contingencies for design, bid, and construction
        vi. Coordinate between disciplines (structural, mechanical, electrical, plumbing, etc)
        vii. Calculate preliminary heating and cooling loads
    b. Design development (20% to 50%)
        i. Finalize floor plans
        ii. Finalize heating and cooling loads
        iii. Show duct and piping (but not sized yet)
        iv. Develop general specifications
        v. Review budget (design contingency should be reduced to half)
        vi. Coordinate between disciplines
    c. Construction documents (50% to 100)
        i. Complete floor plans and specifications
        ii. Review budget (design contingency should be zero)
        iii. Coordinate between disciplines
    d. Consider scientific peer review and value engineering study between 20 – 35% designs.
11. Complete the Commissioning Plan.
    a. Develop all of the commissioning specifications
    b. Seek peer review of the Commissioning Plan

***Construction Phase***

1. Interview and select a construction firm with relevant construction experience of containment laboratories.
    a. Hold pre-bid meeting for all interested bidders
    b. Ideally, firm selected will have experience constructing high containment laboratories
    c. Hold pre-construction meeting after contract has been awarded
        i. Coordinate site usage and establish schedule for construction coordination meetings
2. Engage design firm during construction phase
    a. To review submittals, clarify questions, and deal with any needed changes accordingly.
3. Conduct commissioning concurrent review.
    a. Review equipment submittals.
    b. Review shop drawings.
8. Have contractor use mock ups for critical building assemblies to help ensure success (provides quality control)
    a. BSL3 doors, walls, floors, ceilings, etc
1. Order and/or install necessary lab equipment. Some equipment needs to be installed during construction, such as
    a. Double door autoclaves, cage washers, liquid effluent decontamination systems
    b. Need to decide who installs any equipment – user/owner or contractor. This will require close coordination, especially if owner provides the equipment to the contractor.
2. Ensure appropriate construction techniques are used
    a. Wall construction
        i. Type of wall construction: concrete block, wall board, etc
        ii. Finish texture is important; must be smooth; can't decontaminate pinholes.
        iii. All penetrations into the containment envelope must be sealed or have the capability to be sealed.
    b. Floor construction
        i. Type of flooring construction: seamless vinyl flooring, epoxy sealed concrete
        ii. Tile is not usually appropriate. Monolithic with minimal seams is preferred.
        iii. Does wall/floor interface with cove edge?
    c. Ceiling construction
        i. Solid ceiling materials are preferred over tile.
        ii. All penetrations must be sealed. How are the lights mounted? Surface mounted lights are easier to seal. How are sprinkler heads mounted (if required)? Pendant mounted are easier to seal.
        iii. There should be as few horizontal surfaces as possible.

    d. Doors
        i. They should be self-closing and provide a controlled air gap for directional airflow; if the gap is not adequate, other provisions for controlled air flow must be made.
3. Address all relevant HVAC issues.
    a. Consider tradeoffs between occupant comfort, costs, and contamination control.
    b. Need to make careful choices on almost all components.
        i. Diffusers, valves, ducts, plenums
        ii. What redundancy requirements are necessary?
        iii. Dedicated versus manifold exhaust systems
        iv. Locate supply diffusers and exhaust grills away from primary containment devices.
        v. If HEPA is filtering the exhaust, where are the filters? Need to minimize length of contaminated duct (that needs to be leak tight), but need access to change, test, and decontaminate filters.
    c. Controlling air pressures versus air flows.
    d. Air change rates
        i. Affected by number of people in lab, how much equipment, type of biosafety cabinet (recirculating or not?).
        ii. Can't be too low or too high.
        iii. Can be misleading, since these rates are calculated by assuming complete mixing in the room, but there are many factors that impact this, e.g. how close is supply to exhaust?
4. Test, adjust, and balance (TAB) of air and water systems.
5. Conduct Commissioning Agent and A&E firm walk-throughs during construction.
    a. Verify correct components are installed properly.
    b. Verify integrity of finishes, seals, surfaces.
    c. Test components as installed (some will likely not be accessible once construction is complete). For example, it may be important to conduct pressure tests for ductwork and piping systems prior to those systems being insulated, and prior to the installation of the ceiling.
    d. Determine the schedule of equipment start-ups.

***Acceptance Phase***

1. Install remaining equipment.
    a. Fixed and bench-top laboratory equipment including biosafety cabinets, centrifuges, incubators, shakers, refrigerators, freezers, etc
    b. Communications and other equipment including network connections, telephones, computers, fax machines, etc
2. Conduct functional, operational, and integrated systems testing according to the Commissioning Plan
    a. Functional testing includes the physical performance tests of each major piece of equipment to ensure they are operating as designed

b. Operational testing includes the physical performance tests to make sure each major system operates as designed, including
    i. HVAC, Building control sequences, TAB verification of air and water, electrical systems, life safety systems, security systems, etc.
c. Integrated system testing is the physical performance tests to verify that the major systems interact as designed normal and failure conditions.
    i. Stability of airflow systems and directional airflow control under
        1. Normal operation modes
        2. Normal maintenance modes
    ii. Power failures and other integrated systems failure tests
    iii. Failure testing of equipment to assure safety, containment, and security is maintained
d. What are the trends under normal conditions (room pressure, temperature, humidity, lighting levels, etc.)?
e. Who performs the tests? Who pays if something needs to be retested?

3. Conduct any additional acceptance criteria testing as specified in the construction contract. What is the acceptance criteria for each test or for each item tested?
4. Conduct pre-operations training for lab personnel on specific operations/maintenance equipment and procedures.
    a. Normal operations and planted failure testing, e.g. systems failures created in a controlled manner to see how the building personnel respond
    b. Operations and maintenance staff
    c. Emergency responders
    d. Laboratory staff
    e. Facility manager, biosafety/biosecurity officer
5. Formally accept the lab. Complete any safety and security approval processes before moving into the lab.

***Operations Phase***

1. Write biosafety plan, biosecurity plan, incident response plan, personnel training plan, lab-specific and standard operating procedures.
2. Conduct operational training (biosafety, biosecurity, biocontainment) for personnel who will work in the lab, and who will maintain the lab.
    a. Lab scientists, technicians, and in-the-lab workers
    b. Lab support personnel (e.g. equipment maintenance, safety officer, security officer)
    c. Lab administrative personnel
    d. Lab management
3. Determine preventive maintenance, inspection, and performance testing schedules for all components of the BSL3 (i.e. procedures and practices, primary barriers, and secondary barriers). This includes, but is not limited to:
    a. Annual testing of HEPA filters in HVAC system
    b. Annual calibration of HVAC controls
    c. Monthly testing of emergency generator system
    d. Annual certification of biological safety cabinets

    e. Regular validation of autoclaves
    f. Review of biorisk program management systems
    g. Incident response exercises
4. Determine when manufacturers' equipment warranties start and how long they last?
    a. When equipment is purchased? When it is installed? When does owner take over the building?
5. Re-verify performance of major equipment before end of warranty phase using the original commissioning documentation as the basis.
    a. Check for seasonal variations of equipment and systems; conduct off-season commissioning.
6. Ensure resources for long-term operations and maintenance (rule of thumb: BSL3 labs cost three times as much to operate as a comparably-sized BSL2 lab). Operations and maintenance expenses can include, but are not limited to:
        a. Operational expenses, such as
            i. Personnel (researchers, technicians, administrative, maintenance, custodial, security personnel) labor costs, initial and refresher training costs, benefits
            ii. Utilities (electricity, water, heating fuel, laboratory gases)
            iii. Annual commissioning
            iv. Decontamination of lab
            v. Waste disposal
            vi. Pest and rodent control
            vii. Laboratory consumables
        b. Building maintenance expenses, such as
            i. Paint, ceiling, security systems and alarms, effluent treatment and disposal, fire protection systems and alarms
        c. Laboratory support equipment maintenance expenses, such as
            i. autoclaves – annual service and regular biological validation
        d. Electrical maintenance expenses, such as
            i. Lights, switch gears and generators, emergency generator fuel supply tanks, fuel leak detection systems
        e. HVAC maintenance expenses, such as
            i. Interlock exhaust/supply, alarms for HVAC filters, fan belt replacement, lubrication, replacement of pre-filters and final filters, annual certification and replacement as needed of HEPA filters, bubble tight dampers, controls calibration, cooling coil cleaning, fans and dampers, refrigerant charge
        f. Plumbing maintenance expenses, such as
            i. Sink/floor drain traps, vacuum filters and disinfectant traps, water heater, backflow preventers, eye wash and emergency showers
        g. Biosafety cabinet maintenance expenses, such as
            i. HEPA filter testing, HEPA filter replacement every 5 years or as needed; certification prior to putting biosafety cabinet into service, after repairs or moving, and annually

h. Lab equipment maintenance expenses, such as
    i. Centrifuges, incubators, freezers, specialty gas manifolds, pipettors cleaned and calibrated annually, vacuum pumps

***A Few Useful References to Help with BSL3 Decisions***


World Health Organization, *Laboratory Biosafety Manual*, 3rd edition, 2004, http://www.who.int/csr/delibepidemics/WHO_CDS_CSR_LYO_2004_11/en/.

World Health Organization, *Biorisk Management: Laboratory Biosecurity Guidance*, 2006, http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_EPR_2006_6.

CDC/NIH, *Biosafety in Microbiology and Biomedical Laboratories*, 5th edition, 2007, http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm.

US Department of Agriculture, 242-01M, *ARS Facilities Design Standards*, July 2002 edition, http://www.afm.ars.usda.gov/ppweb/242-01m.htm.

US National Institutes of Health, *Design Policy and Guidelines*, November 2003 edition, http://orf.od.nih.gov/PoliciesAndGuidelines/DesignPolicy/.

CEN Workshop Agreement, *International Laboratory Biorisk Management Standard*, CWA 15793:2008

J. Martin Farach, "Protocols drive laboratory upgrades to BSL-3 status," Laboratory Design, 2007. http://www.labdesignnews.com/LaboratoryDesign/LD0507FEAT_1.asp

T. Powers, "Strategies in Commissioning for Bio-safety," Conference Proceedings, National Conference on Building Commissioning, May 2-4, 2007. http://www.csemag.com/index.asp?layout=articlePrint&articleID=CA6442933

Stanley Stark, "Construction costs for new labs still escalating," Laboratory Design, 2006. http:// www.labdesignnews.com/LaboratoryDesign/LD0606FEAT_1.asp

"Lab Construction Costs up 6% for 2005," Building Design and Construction, 2005. http:// www.bdcnetwork.com/article/CA6256199.html