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Preliminary Authorization Basis Document For the Proposed Biological Safety Level 3 (BSL-3) Facility (B368) at Lawrence Livermore National Laboratory Revision 2

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January 4, 2005

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Nonproliferation, Arms Control
and International Security

May 17, 2004

Ms. Camille Yuan-Soo Hoo, Manager
U.S. Department of Energy
National Nuclear Security Administration, Livermore Site Office
Building 311
Lawrence Livermore National Laboratory
7000 East Avenue
Livermore, CA 94551

Subject: Transmittal of Preliminary Authorization Basis Document Revision 2 for the Biological Safety Level (BSL-3) Facility

Dear Ms. Yuan-Soo Hoo:

Attached is a Revision 2 to the Preliminary Authorization Basis Document (PABD) dated 5/6/04 for the BSL-3 Facility. This document was revised at the request of NNSA/LSO staff, and reflects changes in the final design affecting the safety function of facility systems and equipment.

We have also updated the document to resolve the comments (except those deferred to the Final AB Document) provided by NNSA/LSO staff on the revised PABD dated 9/23/02 and incorporated the inputs of several Subject Matter Experts (SMEs) in the BSL-3 operations. Our responses to the comments are detailed in the Appendix to this Revision.

HC/AB-2004-140

If there are any questions, please contact Tom Altenbach at (925) 422-1285.

Sincerely,

Stephen Cochran

for Wayne J. Shotts
Associate Director
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Preliminary Authorization Basis Document

For the

Proposed Biological Safety Level 3 (BSL-3) Facility (B368)

at

Lawrence Livermore National Laboratory

Revision 2

April 2004

Prepared by

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Authorization Basis Section

Lawrence Livermore National Laboratory

Revised Preliminary Authorization Basis Document for the Proposed Biological Safety Level 3 (BSL-3) Facility (B-368) at Lawrence Livermore National Laboratory

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Acronyms and Abbreviations

AAALAC	Association for the Assessment and Accreditation of Laboratory Animal Care
ABSL	Animal biological safety level
AC	Administrative control
ANSI	American National Standards Institute
BA	Biological Assessment
BASIS	Biological Aerosol Sentry and Information System
BBRP	LLNL Biology and Biotechnology Research Program
BDRP	Biological Defense Research Program
BMBL	Biosafety in Microbiological and Biomedical Laboratories
BSC	Biosafety cabinet
BSL	Biosafety level
CAA	Clean Air Act
CDC	Centers for Disease Control and Prevention
CEQ	Council on Environmental Quality
CERCLA	Comprehensive Environmental Response, Compensation and Liability Act
CFR	Code of Federal Regulations
C&MS	Chemistry & Materials Science Directorate
DA	Department of the Army
DNA	Deoxyribonucleic acid
DOE	U.S. Department of Energy
DOT	U.S. Department of Transportation
EA	Environmental Assessment
EIR	Environmental Impact Report
EIS	Environmental Impact Statement
EPA	U.S. Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
ES&H	Environment, Safety, and Health
FHA	Fire Hazards Analysis
FSP	Facility Safety Plan
GC-MS	Gas Chromatography-Mass Spectrometry
HAP	Hazardous air pollutant
HCD	Hazards Control Department
HEPA	High efficiency particulate air (filter)
HHS	U.S. Department of Health and Human Services
HID	Human infective dose
HID_{50}	Human infective dose - 50 percent
HMIS	Hazardous Material Information System
H&S	Health and Safety
HV	High Voltage
HVAC	Heating, ventilation, and air conditioning
IACUC	Institutional Animal Care and Use Committee
IATA	International Air Transport Association
IBC	Institutional Biosafety Committee
ID_{50}	Infective dose - 50 percent

IH	Industrial Hygiene
IRB	Institutional Review Board
IS	Industrial Safety
ISM	Integrated Safety Management
ISMS	Integrated Safety Management System
IWS	Integration Worksheet
LBOC	Laboratory Biosafety Operations Committee
LD_{50}	Lethal dose at 50 percent mortality
LLNL	Lawrence Livermore National Laboratory
LR/SAT	Laboratory Registration/Select Agent Transfer
MCE	Maximum Credible Event
NAI	Nonproliferation, Arms Control, and International Security
NEC	National Electrical Code
NEPA	National Environmental Policy Act
NFPA	National Fire Protection Association
NIH	National Institutes of Health
NNSA	National Nuclear Security Administration
NPHs	Natural phenomena hazards
ORDA	Office of Recombinant DNA Activities
ORPS	Occurrence Report Processing System
OSHA	Occupational Safety and Health Administration
OSP	Operating Safety Plan
OSR	Operational safety requirement
PABD	Preliminary Authorization Basis Documentation
PC	Performance Category
PEIS	Programmatic Environmental Impact Statement
PFHA	Preliminary Fire Hazards Analysis
PPE	Personal protective equipment
RCRA	Resource Conservation and Recovery Act
RG	Risk Group
RL	Risk Level
RNA	Ribonucleic acid
RQ	Reportable Quantities
SMEs	Subject matter experts
SOP	Standard Operating Procedure
SR	Surveillance Requirement
SSCs	Structures, systems and components
STD	Standard
TLV	Threshold Limit Value
TPQ	Threshold Planning Quantity
TQ	Threshold Quantity
UC	University of California
U.S.	United States
USC	United States Code
VHP	Vaporous Hydrogen Peroxide

Executive Summary

Lawrence Livermore National Laboratory (LLNL) is proposing to construct a biosafety level 3 (BSL-3) facility at Site 200 in Livermore, California. Biosafety level 3 (BSL-3) is a designation assigned by the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) for handling infectious organisms based on the specific microorganisms and associated operations. Biosafety levels range from BSL-1 (lowest hazard) to BSL-4 (highest hazard). Details about the BSL-3 criteria are described in the Centers for Disease Control and Prevention (CDC)/ National Institutes of Health (NIH)'s publication "Biosafety in Microbiological and Biomedical Laboratories" (BMBL), 4th edition (CDC 1999). The BSL-3 facility will be designed, built, and operated in accordance with guidelines for BSL-3 laboratories established by the CDC and the NIH. This Preliminary Authorization Basis Documentation (PABD) for the proposed BSL-3 facility has been prepared in accordance with the current contractual requirements at LLNL. This includes the LLNL *Environment, Safety, and Health Manual* (*ES&H Manual*) and applicable Work Smart Standards, including the biosafety standards, such as the aforementioned BMBL and the NIH Guidelines for Research Involving Recombinant DNA Molecules.

The proposed BSL-3 facility is a 1,600 ft^2, one-story permanent prefabricated facility, which will have three individual BSL-3 laboratory rooms (one of which is an animal biosafety level-3 [ABSL-3] laboratory to handle rodents), a mechanical room, clothes-change and shower rooms, and small storage space (Figure 3.1).

No radiological, high explosives, fissile, or propellant material will be used or stored in the proposed BSL-3 facility.

The BSL-3 facility will be used to develop scientific tools to identify and understand the pathogens of medical, environmental, and forensic importance. Microorganisms that are to be used in this facility will be limited in quantity, type and form and handled in accordance with the BMBL requirements and the approval by the Institutional Biosafety Committee (IBC). The proposed facility will have the unique capability within DOE/NNSA to perform aerosol studies to include challenges to rodents (the rodents are infected with a microorganism and then observed for signs of illness) using infectious agents or biologically derived toxins (biotoxins). Rodents used in aerosol studies are housed in containment-caging systems, such as open cages placed in inward-flow ventilated enclosures.

1. Introduction

The Lawrence Livermore National Laboratory Integrated Safety Management (ISM) System Description (LLNL 2002) and the Task Plan for the Preparation of Authorization Basis Documentation for the proposed Biosafety Level 3 Laboratory at Lawrence Livermore National Laboratory (DOE 2002a) require a PABD be prepared for the proposed BSL-3 Facility. NNSA-OAK approval is required prior to its construction. This PABD formalizes and documents the hazard evaluation and its results for the BSL-3 facility. The PABD for the proposed BSL-3 facility provides the following information:

- BSL-3 facility's site description
- General description of the BSL-3 facility and its operations
- Identification of facility hazards
- Generic hazard analysis
- Identification of Controls Important to Safety
- Safety management programs

The PABD characterizes the level of intrinsic potential hazard associated with a facility and provides the basis for its hazard classification. The hazard classification determines the level of safety documentation required and the level of review and approval for the safety analysis.

The hazards of primary concern associated with the BSL-3 facility are biological. The hazard classification is determined by comparing facility inventories of biological materials and activities with the BSL-3 threshold established by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) for BSL-3 facilities.

2. Site Description

2.1 LLNL Livermore Site Description

The LLNL Livermore site (also known as Site 200) occupies a total area of about 1.3 square miles (821 acres). The City of Livermore's central business district is located about 3 miles west of the LLNL site. Sandia National Laboratories/California is located south of the LLNL site, across East Avenue, and extends for about three-quarters of a mile to the south. Greenville Road bounds the eastern side of the LLNL site, where mainly open fields and ranches extend to the east for many miles. Patterson Pass Road is located to the north of the LLNL site, where a water treatment facility and an industrial park are situated. Vasco Road is located along the western side of the LLNL site, where apartment buildings and residential housing tracts extend to the west.

Research operations at the LLNL Livermore site are conducted in approximately 600 facilities, including about 350 temporary structures or trailers. A thorough description of the LLNL site characteristics is available in the 1992 DOE Final Environmental Impact Statement for LLNL [DOE 1992].

2.2 Mission of the Proposed BSL-3 Facility

The mission of the proposed BSL-3 facility is to develop scientific tools to identify and understand the pathogens of medical, environmental, and forensic importance. This information is used to develop, demonstrate, and deliver technologies and systems to improve domestic defense and/or medical capabilities and, ultimately, to save lives in the event of a biological attack in support of our national security's nonproliferation mission.

The Biology and Biotechnology Research Program (BBRP) at LLNL will be the operator and primary user of the BSL-3 facility. Other potential users of the BSL-3 facility are the Nonproliferation, Arms Control, and International Security (NAI) Directorate, and the Chemistry and Materials Science (C&MS) Directorate.

2.3 BSL-3 Facility Location

The proposed location of the BSL-3 facility or B368 is located adjacent to the current parking area and access-drive directly adjacent to (east of) Building 365 and northeast of the intersection of Fifth Street and West Inner Loop (Figure 2-1).

The proposed BSL-3 facility is centrally located at LLNL. It is located approximately 810 meters (886 yards) from the north site boundary (Patterson Pass Road), 910 meters (995 yards) from the south site boundary (East Avenue), 915 meters (1000 yards) from the west site boundary (Vasco Road), and 930 meters (1017 yards) from the east site boundary (Greenville Road).

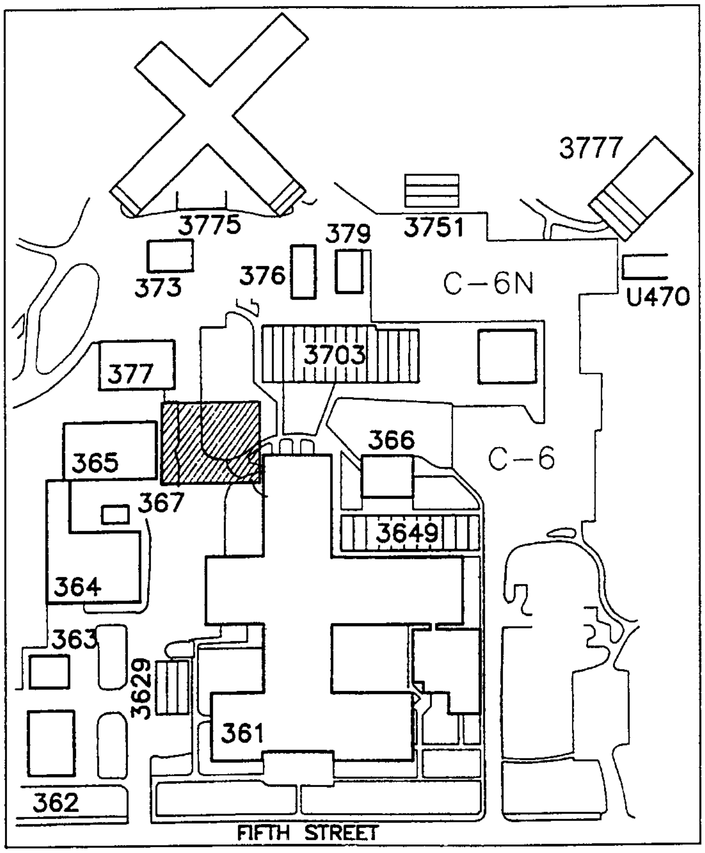

Figure 2-1. Map of the Building 360 Complex Area showing the location of the proposed BSL-3 facility (within cross-hatched area)

3. Facility Description

The proposed BSL-3 facility will be a one-story building with about 1600 ft^2 (149 m^2) of floor space (Figure 3-1) housing three BSL-3 laboratories (one with rodent handling and maintenance capability), showers, sinks, lavatories, and mechanical and electrical equipment areas. The BSL-3 facility will most likely be constructed using design-build modular construction methods using prefabricated modules. The modules will be constructed off-site, trucked to LLNL, and joined together by the modular laboratory vendor. Site utilities will be designed by LLNL and constructed via a purchase order construction contract. The new facility will be designed to the latest Performance Category 2 (PC-2) requirements of DOE STD-1020-2002[1]. Specifically the seismic design will conform to the 2000 International Building Code, Seismic Use Group III, Criteria 2/3, Maximum Credible Event (MCE) Ground Motion with an Importance Factor of 1.5. A peak wind gust of 91 mph will be used as the design wind load. Flooding is not a design consideration at the LLNL site. The interior surfaces of walls, floors, and ceilings of the BSL-3 laboratory areas will be constructed for easy cleaning and disinfection. The walls will be finished with an easily cleanable material with sealed seams, resistant to chemicals and disinfectants normally used in such laboratories. Floors will be monolithic and slip-resistant. All penetrations in floors, walls, and ceiling surfaces will be either sealed or capable of being sealed to facilitate disinfection, to aid in maintaining appropriate ventilation system air pressures, and to keep pests out. Laboratory furniture will be capable of supporting anticipated loading and use, and bench tops will be impervious to water and resistant to moderate heat, chemicals used, and disinfection solutions. Spaces between benches, cabinets, equipment and walls will be accessible for cleaning with disinfectants.

Each of the three BSL-3 laboratories will have at least one Class II, Type A-2 biological safety cabinet[2] (BSC) connected to the exhaust system by means of a thimble (Figure 3-2). Class II BSCs provide their own airflow, have high efficiency particulate air (HEPA)[3] filtration internally within the cabinet and will be designed to provide personal, environmental, and test material protection. The Class II, Type A-2 BSC is designed for sterile product preparation and biological experimentation involving agents of low and moderate risk. The thimble is an exhaust hood mounted over the BSC exhaust duct. The class II, Type A-2 BSC does not require a hard connection to the exhaust ductwork. BSC's with greater protection levels than class II, Type A-2 may be used if appropriate to provide additional ES&H protection.

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[1] STD-1020-2002 has been incorporated into the LLNL Work Smart Standards. It has stricter requirements than the previous STD-1020-1994.

[2] A BSC (biosafety cabinet) is a specialized type of hood and is the primary means of containment for working safely with infectious microorganisms (CDC 1999).

[3] A HEPA filter is a disposable, extended-medium, dry-type filter with a particle removal efficiency of no less than 99.97 percent for 0.3-micron particles.

The class II, Type A-2 BSC with the thimble connection has the advantage of being easier to control the airflows and maintain the system pressure gradients, thus safer to operate. The thimble connection reduces the magnitude of the variation of the airflow inside the BSC as exhaust airflows fluctuate. The variation of the exhaust flows can disturb the critical pressure relationships between airflows in the BSCs. Changes in air pressure may allow lab contaminants to enter the BSC creating "sample contamination" by pulling too much air into the BSC or allow the contaminants inside the BSC to escape causing a "containment impairment problem" by reducing air supply to the BSC. Therefore, a constant airflow is desired.

The class II, Type A-2 BSC re-circulates about 70% of the air volume within the BSC and the remainder 30% of the air is exhausted through a thimble connection to the building exhaust system. By setting the building exhaust system to pull more air than the BSC is putting out, room air coming through a thimble gap (the space between the BSC and the exhaust system) entrains the cabinet exhaust air and all of it is vented through the building's HEPA filter(s), then outside the building. The thimble connection provides a gap in the duct connection so that room air may also exit directly to the exhaust system without first going through the BSC. To minimize the possibility of infectious agents being released into the environment, a second HEPA will be installed in the facility exhaust system to compensate for the thimble connection to the Class II, Type A-2 BSC, which makes all room air at least doubly filtered.

HEPA filters in the building exhaust system will comply with LLNL *ES&H Manual,* Document 12.5, "High-Efficiency Particulate Air (HEPA) Filter System Design for LLNL Applications" and the Work Smart Standards referenced therein. All BSC air will be 100 percent exhausted to the outside through the building heating, ventilation, and air conditioning (HVAC) and HEPA filtration systems (air exhausted from BSCs is doubly-filtered). Class II Type A-2 BSCs are designed to operate at a minimum inward flow of 100 linear ft per min (30.5 linear m per min) at the front of the work zone (CDC 2000). BSCs will be located away from doors, room supply louvers, and heavily traveled laboratory areas. BSC interiors will be cleaned using appropriate methods, which could include ultraviolet light or chemical disinfection. BSCs will be tested and certified semiannually and after installation, repair, or relocation in accordance with CDC guidelines (CDC 2000). BSCs are connected to a standby circuit that supplies power from an emergency diesel generator to maintain airflow through the HEPA filters in the event of a power failure to the building.

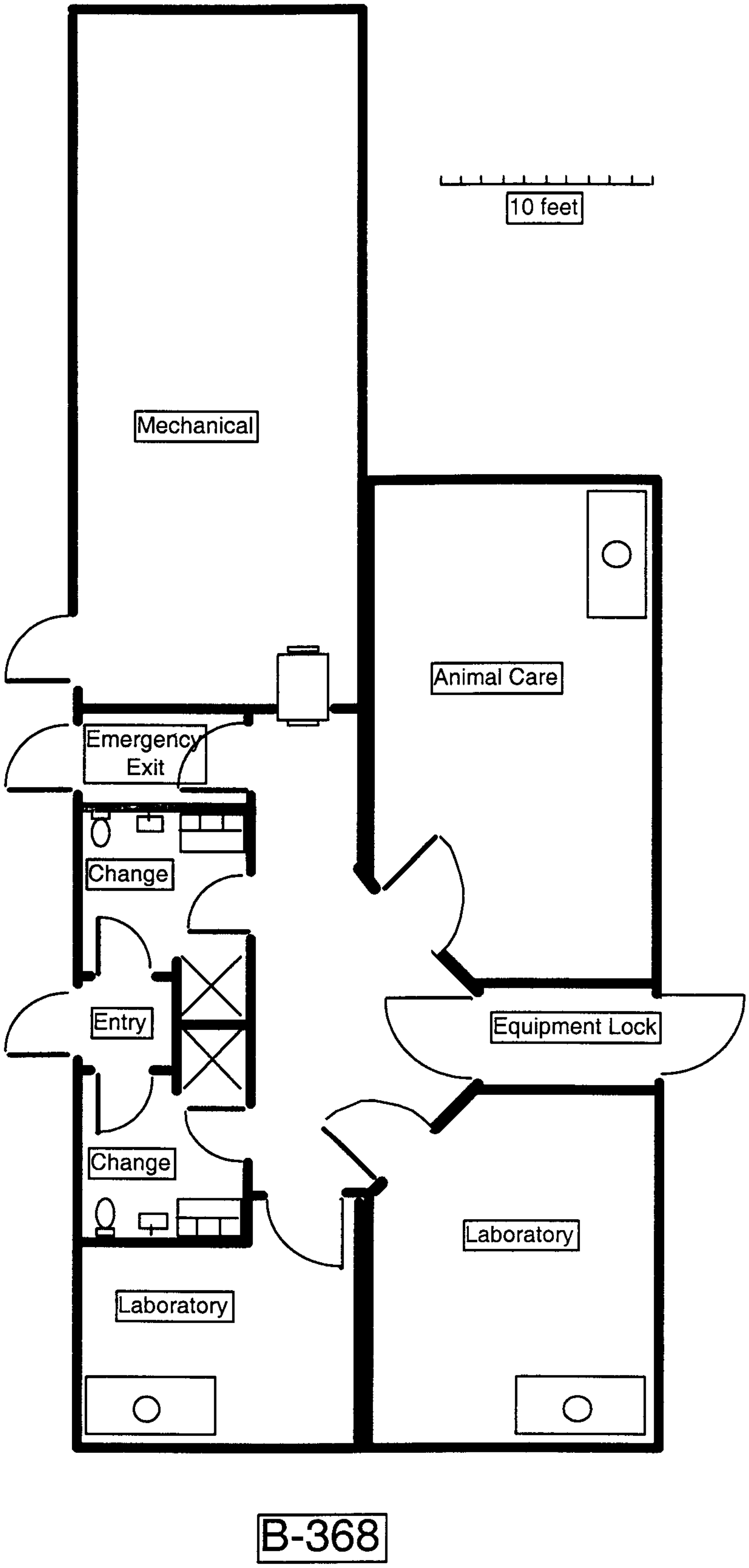


Figure 3-1. Conceptual floor plan for the proposed BSL-3 facility at LLNL.

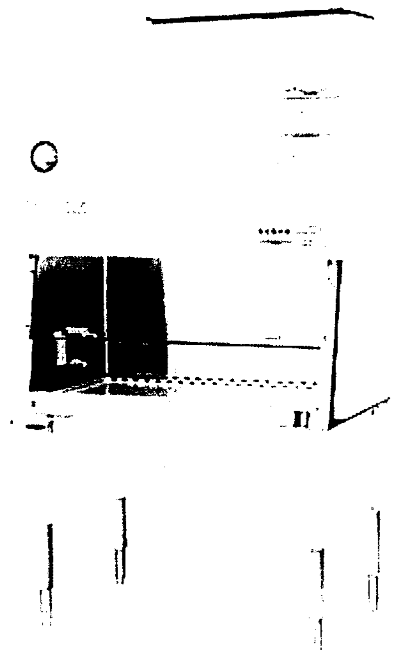


Figure 3-2. Photo of a Baker SterilGard III™ - Class II, Type A-2 BSC[4]

No windows will be installed in the BSL-3 laboratory's exterior walls. Non-opening observation windows will be placed in interior doors. Centrifuges or other equipment that have the potential to produce aerosols will be operated in BSCs or with appropriate combinations of personal protective equipment (PPE), physical containment, or control devices. Vacuum will be provided to critical work areas using portable vacuum pumps properly fitted with traps and HEPA filtration.

Each laboratory may also contain at least one refrigerator or freezer. Biological materials will be stored either in securable refrigerators for short-term use or in ultra-low temperature mechanical freezers operating between –50 and –85°C for long-term sample storage or archiving.

The ABSL-3 laboratory used for rodent handling will have a tissue digestor for the purpose of sterilizing all animal tissues at the conclusion of each study involving small rodents. Figure 3-3 shows an example of a tissue digestor unit that could be used. The digestor will use an alkaline hydrolysis process at an elevated temperature to convert all of the organic material (as well as infectious microorganisms) into a sterile aqueous solution of small peptides, amino acids, sugars, and soaps. The alkali will be used up in the process. Aside from the aqueous solution, the only byproducts will be mineral (ash) components of the bones and teeth.

[4] The use of a trade name does not constitute an endorsement nor does it indicate that the specific product would be purchased. This is only shown to be representative of the type of equipment that would be used.

The ABSL-3 laboratory used for rodent testing will also contain a rodent caging system similar to that shown in Figure 3-4. These ventilated cages will be provided with HEPA-filtered air; continuous forced airflow helps reduce both ammonia and carbon dioxide. The negative pressurization will provide continuous quarantine status, protecting personnel and preventing contact with the other rodents in the cage rack. The rodent caging system is connected to a standby power circuit to maintain airflow to the HEPA filters in the event of power failure to the building.

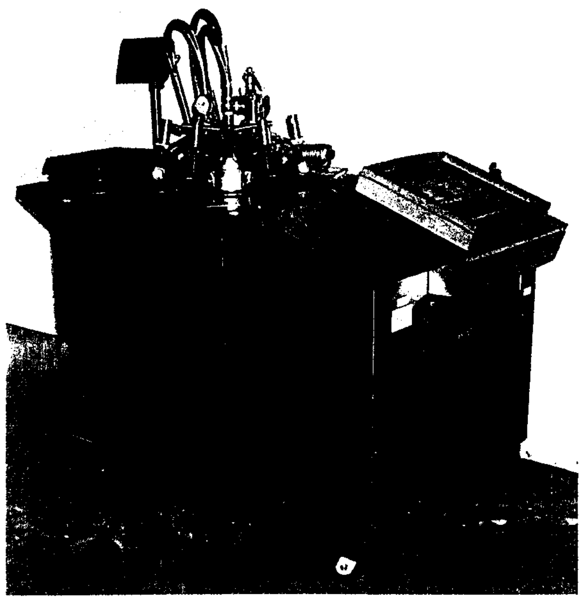
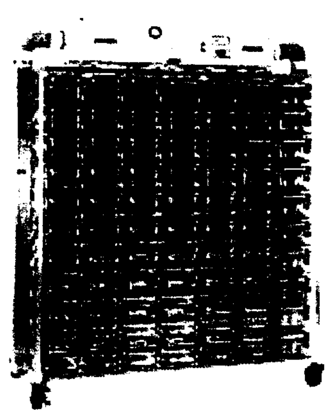


Figure 3-3. Photo of a Waste Reduction Inc. ™ small-capacity tissue digestor[5]



[5] The use of a trade name does not constitute an endorsement nor does it indicate that the specific product would be purchased. This is only shown to be representative of the type of equipment that would be used.

Figure 3-4. Photo of an Allentown Caging Equipment Co. BioContainment Unit for rodents.

A maximum of 100 rodents, mainly mice (some rats and possibly guinea pigs), will be present in the ABSL-3 laboratory at any one time. Once a rodent is being used in testing it will never leave the cage except for cage cleaning and inspection, which will occur only in the confines of the BSCs. Once removed from a cage, the rodents will only be placed back into a clean cage. The dirty cage and its contents will be autoclaved[6] prior to reuse. All rodents used will be supplied by the already-existing rodent quarantine facility located and operated in an adjacent building. The cage rack will be restrained from toppling over or losing cages in a seismic event.

Some rodents will be exposed to infectious agents in the BSC through inhalation via a device known as a collision nebulizer. This device creates aerosol particles of known size (depending upon the specific nozzle used) to which rodents will be exposed through a nosepiece. The nebulizer consists of a 32-ounce Pyrex™ glass liquid storage container with a T-shaped, stainless steel aerosol jetting-device operated by compressed air. The device will be used only in the BSC and will be chemically disinfected in place after use.

Access to the facility will be positively controlled using the LLNL security systems. There will be only one electrical room with access for maintenance from the exterior of the building. Entry of personnel into the BSL-3 laboratories will be through the change rooms that will serve as self-closing double-door access.

The BSL-3 facility will be equipped with an LLNL standard fire alarm and emergency paging system that is connected to the LLNL emergency operations center. Activation of pull stations, water-flow alarms, or mechanical room smoke detectors will be detected and responded to by the LLNL Fire Department.

Fire suppression for the BSL-3 facility will be provided by a standard wet-pipe fire sprinkler system. The sprinkler head temperature rating will be in the 155° to 165°F range. Water flow alarms will be connected to LLNL's fire alarm monitoring station. The electrical/exhaust system in B368 will function normally when the sprinklers activate. Water used for fire suppression that might become pooled on the building floor will be discharged from the floor drains to a retention tank system for containment, characterization, and disinfection as needed, prior to discharge to the sanitary sewer system. The retention tank can contain up to1,000 gallons. There are 2 water tanks that are interconnected. One tank is generally empty at all times. Total tank capacity is 2000 gallons. These tanks are enclosed on a concrete pad with a concrete dike. Total dike capacity is 1370 gallons. Thus the total usable capacity (with the tanks intact) is 3,370 gallons. Assuming a 20-minute discharge (again a very unlikely event as the fire department response time is in the 3 to 5 minute range and would confirm extinguishment and shutdown of the sprinkler system in the 5 to 10 minute range), the tanks and containment can handle this amount of discharge. HEPA filter banks in the building exhaust system will doubly filter all room air and provide tertiary filtration for exit air from the BSCs. Filter banks could be switched or alternated to permit disinfection and filter replacement. Staff technicians will conduct routine maintenance

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6 An autoclave is an apparatus using superheated steam under pressure to kill or sterilize microorganisms.

of the filter banks, including replacement of the filters. Replaced filters will be chemically sterilized prior to disposal.
The air-handling systems, including the heating, ventilation and air conditioning (HVAC) systems, will be designed in accordance with CDC guidelines to provide for individual temperature and ventilation control zones as required in the BSL-3 laboratories and support areas. A ducted exhaust HVAC system will draw air into the BSL-3 laboratories from the adjoining areas toward and through the BSL-3 laboratory areas with no recirculation from the BSL laboratories to other areas of the building. The supply fan will provide more than 2,500 cfm (ft^3/min) and will be interlocked with a duct-mounted smoke alarm to shut down if smoke is sensed. The BSL-3 laboratories will be under the most negative pressure with respect to all other areas of the building. Air discharged from the BSL-3 facility will be dispersed above the roofline and away from adjacent building air intake ducts. Exhaust stack outlets will be 10 ft (3 m) or greater above the roofline. Direction of airflow into the laboratories and the BSCs will be verifiable with appropriate gauges and an audible alarm system to notify personnel of HVAC problems or system failure. Operation of all equipment will be designed to avoid interference with the air balance of the BSCs or the designed airflow of the building.

The electrical power requirements for the BSL-3 facility will be about 145 kilowatts (kW). Of this total load, approximately 75 kilowatts (kW) of power is used for the building air handling, fire alarms, freezers, and lighting. A diesel generator in an adjacent building will supply the laboratories with electric power in the event of a power failure from the supply grid system for these systems. The diesel generator supplies B366 and part of B361. The existing loads were evaluated during preliminary design and there is adequate capacity for the BSL-3 load. In the event of a power outage, the generator will respond in 10 seconds to supply electricity to the laboratories so that workers could shut down the laboratories safely.

In the event of a power outage, all biological materials will immediately be placed in a "safe" configuration, such as confinement or chemical disinfection. As noted above, HVAC systems will be supplied with backup power from the diesel generator to minimize any interruption in service.

Should all power be lost to the building and the HVAC system, the air supply system will shut down and dampers will close automatically to prevent air migrating from the laboratory areas to other areas of the building.

All liquid biological-material waste from the BSL-3 laboratory work will undergo either autoclaving or chemical disinfection. This waste will then be discharged into the holding tanks through laboratory sinks, floor drains, or the tissue digestor. Wastewater from the holding tanks will be disinfected before being discharged into the sewage system. Tap water enters the BSL-3 laboratories through spigots in the sinks or showerheads. Backflow preventers are used at LLNL to protect the cross-contamination of the water distribution system.

4. Hazard Evaluation Study

This section presents the Hazard Evaluation Study of the PABD for the BSL-3 facility. The Hazard Evaluation provides a thorough identification of potential events, event initiators, preventive and mitigation features (design features, administrative controls). This Hazard Evaluation consists of three activities: hazard identification, hazard screening, and hazard analysis.

4.1 Hazard Identification

Hazards are primarily identified by listing the hazardous materials and the energy sources (including natural phenomena such as seismic events) that could be present in the proposed BSL-3 facility. Information for identifying hazards and determining their applicability to the BSL-3 facility is obtained from the BSL-3 project planning documentation (BSL-3 Laboratory Blue Book), the LLNL Environmental Assessment (EA) for the Proposed Construction and Operation of a Biosafety Level 3 Facility at Lawrence Livermore National Laboratory, Livermore, CA (DOE/EA-1442, December 2002) (DOE 2002b), discussion with BBRP facility personnel and other subject matter experts (SMEs), and process knowledge.

Table 1 summarizes the hazardous materials and energy sources that are identified for BSL-3 facility.

Table 4-1. Hazards Source List for the Proposed BSL-3 Facility

Sample Hazard Source Groups	Examples of Hazard Energy Sources
Electrical	Cable runs, electrical equipment, high voltage (up to 7500V from electrophoresis power supplies), motors, pumps, switchgear, wiring, charged capacitor (banks), high voltage (HV) transformers, static electricity.
Kinetic	Mass in motion, vehicle crash, objects falling onto building (e.g., trees toppled onto building by high winds or super-saturated ground), centrifuge.
Gravity-mass	Falling, falling objects, tripping, slipping, earthquakes.
Pressure	Compressed gases (nitrogen, air), ruptures, vacuum systems, noise.
Asphyxiants	Confined gases.
Chemical	Alcohols (methyl, ethyl, amyl, isopropyl), corrosive chemicals (sodium hydroxide), reactive chemical (hydrogen peroxide, flammable materials, asphyxiants (nitrogen, carbon dioxide, steam).
Heat and fire	Electrical equipment (autoclave), electrical wiring, combustible materials, flammable solvents, vacuum pump oils, lasers, reactions from chemical incompatibility.
Radiation, non-ionizing	Class 3B lasers in DNA sequencers, operated as class 1 lasers. Ultraviolet (UV) light from the BSC germicidal lamps.
Radiation, ionizing	X-ray producing equipment such as gas chromatograph-mass spectrometry (future operation).

Sample Hazard Source Groups	Examples of Hazard Energy Sources
Cold Sources	Liquid nitrogen, cryogenics.
Biohazards	Infectious RG2 or RG3 agents such as *Bacillus anthracis, Brucella abortus, Burkholderia pseudomallei, Francisella tularensis, Coccidioides immitis*, and biotoxins such as *Clostridium botulinum* toxin (botulism toxin), animal hazards (bites, scratches, allergic reactions), contaminated sharps (punctures and lacerations).
Explosives	None in the BSL-3 facility.
Fissile Material	None in the BSL-3 facility.
Radiological Material	None in the BSL-3 facility.

For work activities occurring in the BSL-3 facility, the most frequent hazards encountered will be:

- Human error
- Chemicals (fire, spill, chemical incompatibility)
- Construction/Maintenance
- Pressure
- Electrical
- Mass in motion (such as centrifuge)
- Radiation (ionizing and non-ionizing)
- Biohazards (e.g., pathogenic microbes, bites and scratches from infected rodents, contaminated sharps).

Table 4-2 summarizes the hazardous conditions that could arise during normal and abnormal operations in the BSL-3 facility. The causes were identified, along with appropriate preventive and mitigative safety features, and projected potential consequences.

Table 4-2. Hazards Characterization

Postulated Event Description	Causes	Unmitigated Consequences	Preventive Features Appropriate Review via IWS process is common to all		Mitigative Features	
			Design	Administrative	Design	Administrative
Electric shock	Poorly maintained or damaged equipment; electric short; wiring failure; human error.	Personnel injury or death (shock, burns); fire; equipment damage	Electrical wiring and equipment installed to National Electric Code (NEC) (ANSI/ NFPA 70); Requirements per *ES&H Manual*, Document 16.1.	Training; proper work procedures; analysis of lessons learned; inspection of equipment and personal protective equipment (PPE) for serviceability; grounding requirements; standards for use of extension cords, cables, boxes, plugs and receptacles per ES&H Manual, Document 16.1; Electrical Safety Advisory Board reviews.	Ground fault circuit interrupters; *ES&H Manual*, Part 16.	Onsite medical personnel; emergency services response; use of PPE per *ES&H Manual*, Part 16.
Falling, falling objects, mass in motion (vehicle crashes, tree topples), tripping, slipping	Falling; slipping; tripping; falling biosafety cabinets, rodent cage racks and freezers during seismic events; failure of centrifuge rotor; improper maintenance; inattention; human error, vehicle crashing into building, tree toppling onto building.	Personnel injury and contamination; equipment contamination and damage.	Seismic restraints for BSCs, rodent cage racks, freezers and large equipment; physical barriers like bumpers in the parking area and bollards between the edge of the road and the facility; trim trees so they cannot topple onto the facility.	Training; equipment maintenance; good housekeeping practices per *ES&H Manual*, Documents 15.3 & 15.4.	Rodent and pest controls; HEPA filters and ventilation system meet seismic criteria.	Safety shoes; training; emergency services response; LLNL Health Services Department.
Pressurized gases/liquids release	Container damage; supply line damage; worker error; earthquake; warming of trapped cryogen.	Asphyxiation; fire; equipment and/or facility damage; personnel injury; potential for contamination and release to environment due to breach of hazardous material container or line.	Protection of storage containers and lines; pressure relief devices; remote shutoff valves; earthquake resistant design and ventilation systems; robust container design; *ES&H Manual*, Part 18.	LLNL chemical safety plan; training; inspection; detailed engineering safety analysis; preventive maintenance and testing of pressure regulators and system boundaries; *ES&H Manual*, Part 18.	Limited mass; ventilation system.	Training; protective clothing; emergency response; protective clothing; IWS.

Postulated Event Description	Causes	Unmitigated Consequences	Preventive Features Appropriate Review via IWS process is common to all		Mitigative Features	
			Design	Administrative	Design	Administrative
Chemical spill	Equipment failure; human error; lack of procedure; inadequate use of procedure; seismic event.	Personnel exposure; illness; personnel injury; potential releases to environment.	Secondary containments for chemical storage; Containment in experiment systems; seismic restraints on equipment and shelving.	Use of appropriate containers; good laboratory practices; procedures, see *ES&H Manual*, Part 14.	BSCs.	Training; use of protective clothing and/or respirators, as needed; contingency planning; Industrial Hygienist response; Emergency Services response; physical separation of incompatible chemicals; H&S technicians response to spills.
Fire	Spill and ignition of flammable liquid due to operator errors; chemical reaction; electrical short or wiring failure; poor housekeeping (excess combustibles such as paper, wood, and chemicals); poor maintenance; laser malfunction; earthquake.	Personnel injury (e.g., smoke inhalation, burns); facility and equipment damage; potential chemical and biological material releases to environment.	Electrical equipment installed to NEC (ANSI/NFPA 70); thermostatic control unit; non-combustible construction; proper design; fume exhaust system; display on outside of lab door indicating equipment operational status.	Approved containers in approved storage cabinets; written procedures; good housekeeping; periodic equipment inspection and preventive maintenance; smoking prohibited; *ES&H Manual*, Document 22.5.	Fire detection and suppression equipment (i.e., sprinkler system, fire extinguishers).	Housekeeping (minimizes combustible loading in the facility); operator response to fire (shutdown process evacuate facility, notify fire department etc.); operator training; emergency services response; LLNL Health Services Department; *ES&H Manual*, Document 22.1.
Explosion	Incompatible chemicals mixed resulting in energetic reactions	Energetic release of energy dispersing chemicals and biological materials harmful to personnel and equipment; exposures to chemical fumes and possibly to biological materials.		LLNL Chemical Safety Plan; written procedures for chemical handling; Operational Safety Plans; storage separation of incompatible chemicals.		Emergency response training; PPE; equipment skid with overflow to drains; spill kits; emergency response to chemical spills; fire suppression equipment; LLNL Health Services Department.
Personnel exposure – non-ionizing radiation	Accidental exposure during maintenance; beam misalignment; operator error; interlock failure; beam scattering or specular reflection.	Exposure from non-ionizing radiation lasers; magnets; radio frequency; ultraviolet; personnel injury (eye damage and skin burns); fires; skin cancer.	Compliance with ANSI standard (ANSI Z136.1-2000) and *ES&H Manual*, Documents 20.7 & 20.8, display on outside of lab door indicating equipment operational status.	Installations, modifications, and operations conform to *ES&H Manual*; access control; laser safety glasses; written procedures; warning signs and warning light systems; preventive maintenance.	Neutral density filters; run-safe boxes.	Training; preventive maintenance; emergency response; IWS.

Postulated Event Description	Causes	Unmitigated Consequences	Preventive Features Appropriate Review via IWS process is common to all		Mitigative Features	
			Design	Administrative	Design	Administrative
Personnel exposure – ionizing radiation	Worker error; equipment failure; interlock failure; shielding failure; earthquake.	Exposure to radiation from radiation generating sealed sources (x-ray)	Interlocks and interlock monitors; shielding; ES&H Manual, Document 20.3.	*ES&H Manual*, Document 20.3; controls are commensurate with the level of hazard and may include warning signs and warning lights; controlled keys; radiation survey and interlock checks routinely and after modification or service of equipment; posted room; warning labels; worker training.		Medical treatment; *ES&H Manual*, Documents 20.3 & 20.4.
Exposure to LN/cryogen	Splashing or spilling of cryogenic material.	Serious injury; dermal contact with cryogenic material causes severe frostbite.	Container design.	PPE (i.e., face protection, cold-resistant gloves, cryogenic apron, arm sleeves); Chemical safety plan; *ES&H Manual*, Document 18.5.	Emergency eyewash and shower.	Emergency response to event (e.g., EMT response, etc.).
Seismic events	Falling biosafety cabinets, rodent cage racks, tall freezers, and equipment during seismic events.	Personnel injury and contamination; equipment contamination and damage.	Seismic restraints for BSCs, rodent cage racks, freezers and large equipment, piping, air handling systems.	Training; equipment maintenance; good housekeeping practices per *ES&H Manual*, Documents 15.3 & 15.4.	HEPA filters and ventilation system meet seismic criteria, PC-2 design.	Safety shoes; training; emergency services response; LLNL Health Services Department.
Biohazards	Equipment failure or defect; process failure; operator errors; failure of insect and rodent control program; transportation, seismic events.	Spreading of infectious agents, which may include bio-hazardous agents and bio-toxins; serious illness; permanent medical disabilities or deaths.	Standby power; retention tanks; BSCs; rodent caging system equipped with HEPA filter; containment centrifuge; negative ventilation flow; sequential facility HEPA filters.	Segregation of BSL-3 and ABSL-3 laboratories from office space; periodic equipment inspection and preventive maintenance; PPE (such as wraparound gowns and gloves); respirators; sharps controls; rodent pest control program; develop biosafety manual and procedures; trained operators; all infectious agent manipulations will be performed in the BSC or enclosed equipment; all biohazardous wastes to be sterilized by autoclaving or digesting method; access control, packaging and shipping in full conformance with DOT and IATA requirements, IBC.	Gauges and an audible alarm system to notify personnel of HVAC problems or system failure; safety centrifuge cup; self-closing double door access; locked storage freezer; tissue digestor.	Emergency response; evacuation; fire department response; LLNL Site Medical response; provisions of antibiotics and vaccines to the operators; Waste Management Plan & Emergency Action Plan; biohazardous wastes generated by a release collected in a holding tank and disinfected with sodium hypochlorite before disposal.

4.2. Hazards Screening

A comprehensive review of potential events associated with the proposed BSL-3 facility operations was performed. These potential events are discussed with respect to the hazards and associated consequences to potential accident scenarios.

The proposed BSL-3 facility has limited energy sources. It will not use dispersible radioactive materials, propellants, high explosive materials, or open flames. The quantities of hazardous chemicals stored in the facility at any one time is expected to be just a few liters each of typical liquid chemical, direct-contact disinfectant solutions (such as aqueous sodium hypochlorite) and biologic stabilizers (phenol). Chemicals needed to provide room fumigation such as paraformaldehyde or 35% hydrogen peroxide will be used in B368. While 35% hydrogen peroxide can be stored in small quantity in the facility (5- 10 liters), para-formaldehyde will not be stored in the facility but brought in only when required for fumigation. The hazardous chemicals used and stored will be tracked using ChemTrack (LLNL's computerized chemical inventory system) and handled according to the BBRP directives (LLNL 2000), the Building 360 Complex directives for Biohazardous Operations (LLNL 2001a), and the LLNL Chemical Hygiene Plan for Laboratories (LLNL 2001b). The quantities of chemicals used in the proposed BSL-3 facility will be well below their screening thresholds. For chemicals, a screening threshold based upon calculations of TEEL values for each chemical (LLNL *ES&H Manual*, Document 3.1). The chemical thresholds for B368 are the limits imposed on the Low hazard facility. The facility is not expected to generate any hazardous waste. Only small quantities of hazardous chemicals (sufficient for operations) will be present in the facility at any time. There will be no chemical storage in the facility except for the 35% hydrogen peroxide needed for operating the VHP system. These chemicals will either be used up in process (becoming non-hazardous) or will leave the facility as a stabilizing or sterilizing chemical for samples being sent to other laboratories for further tests. For example, phenol is used as a stabilizing chemical. It is added to a test tube containing cell culture and this sealed tube is secondary-contained and transferred to another laboratory outside of the B368 for DNA sequencing. About 30 lbs per month (14 kg per month) or 360 lbs per year (168 kg per year) of sodium hydroxide or potassium hydroxide will also be used for rodent tissue digestion/sterilization. These chemicals will be used up in the digestion process. Waste fluid generation from B368 may need pH adjustment (acid will be added to the waste stream at the Waste Retention Tank (WRT) located next to B-365) prior to discharge to the sanitary sewer system if it is too alkaline to meet discharge standards. The final waste products of hydrogen peroxide, when using as fumigant, are water and oxygen.

The potential events associated with the proposed BSL-3 facility are limited to biohazards and natural phenomena. The biohazardous materials used in BSL-3 facility consist of bacteria, fungi, rickettsia, viruses and other agents that require BSL-3 precautions. They will include, but not be limited to, *Bacillus anthracis, Brucella abortus, Burkholderia pseudomallei, Clostridium botulinum, Yersinia pestis, Coccidioides immitis, Coxiella burnetii,* and *Dengue* viruses. A tracking system will be established for all biohazardous materials used in the BSL-3 facility. While current plans will focus on these biohazards, future programs may require the use of other infectious agents in the BSL-3 category described in Section VII of the 4^{th} edition of the BMBL. Nevertheless, the controls identified in Section 5 will be adequate to handle all BSL-3 infectious agents. In addition, the change control process ensures that any new agents introduced into the facility will be approved by the IBC and handled according to appropriate BSL-3 protocols.

The pathogen library of the proposed BSL-3 facility will consist of up to 25,000 strains, securely stored at –80°C in sealed, 2-ml plastic capsules. Prudence dictates that there be at least two capsules of every sample, so the total will be about 100 liters of material. Concentrations of microbes in the solution are in order of 10^8 cells per cubic centimeter (10^8 cells/cm^3).

When a DNA sample is needed, a small volume of cell solution will be transferred to a 50-ml plastic container with growth media and incubated for several days. All open sample work will be performed in a BSC. The primary and secondary plastic containers are capped when they are outside of the BSCs to avoid spillage. Virus culture is somewhat more complex, but the small amounts of material that would be at risk at any given time are similar.

Protein expression experiments will require up to 1-liter batches of cultures of organisms. These will be prepared in individual 250-ml or smaller containers that will be doubly contained whenever they are handled outside of the BSCs. Concentrations will also be on the order of 10^8 cells/cm^3.

4.3 Hazards Analysis

Many of the hazards listed in Table 4-1 are Standard Industrial Hazards that are adequately covered by the OSHA regulations and therefore are not evaluated further in this Preliminary Authorization Basis Document. Standard Industrial Hazards are evaluated only to the extent that they could act as initiators or contributors to events that could result in biological or hazardous chemical releases. The primary hazards associated with the proposed BSL-3 facility will be biological hazards resulting from various failure modes such as manufacturing defects, equipment malfunctions, human error, fires, explosions caused by chemical incompatibilities or high pressures, transportation, and natural phenomena.

For the proposed BSL-3 facility, frequency-evaluation levels are qualitatively described in Table 4-3:

Table 4-3. Frequency-Evaluation Levels for the BSL-3 Facility

Frequency Level	Qualitative Description
Anticipated (A)	Events that might occur from operator error, equipment failure, violation of administrative controls or that have occurred in the operating history of other BSL-3 facilities
Unlikely (U)	Natural phenomena or events resulting from two independent failure modes (operator errors and/or equipment failures)
Extremely unlikely (EU)	Events resulting from more than two independent failure modes (multiple operator errors and/or equipment failures)

Table 4-4 defines the biological consequence levels for the workers and off-site public. For biological exposure, the consequence levels for workers and off-site public are categorized as High, Moderate, Low or Negligible.

Table 4-4. Biological Consequence Levels for Workers and Off-site Public

Consequence Level	Consequence to workers and off-site public
High (H)	Lethal
Moderate (M)	No immediate loss of life or permanent disabilities, and requires hospitalization
Low (L)	Treatable (e.g., vaccines, antibiotics) and does not require hospitalization
Negligible (N)	No treatment required except decontamination

The resulting risk matrices are presented in Tables 4-5 and 4-6 for workers and public, respectively. In these tables, the High, Moderate, Low, and Negligible risks are specified as Risk Level I, II, III and IV, respectively.

Table 4-5. Risk Binning Matrix for Workers

Consequence	Frequency		
	EU	**U**	**A**
H	Risk Level II	Risk Level I	Risk Level I
M	Risk Level III	Risk Level II	Risk Level I
L	Risk Level IV	Risk Level IV	Risk Level III
N	Risk Level IV	Risk Level IV	Risk Level IV

Table 4-6. Risk Binning Matrix for Off-site Public*

Consequence	Frequency		
	EU	**U**	**A**
H	Risk Level II	Risk Level I	Risk Level I
M	Risk Level III	Risk Level II	Risk Level I
L	Risk Level IV	Risk Level IV	Risk Level II*
N	Risk Level IV	Risk Level IV	Risk Level IV

*The risk matrix for off-site public is more conservative than for the exposed worker.

This PABD evaluates a spectrum of events, from high-frequency, negligible-consequence events to extremely-unlikely frequency, moderate-consequence events. Initiating events start a postulated scenario path leading to a release event of infectious agents. The following failure modes for consideration have been evaluated:

- Natural phenomena hazards (e.g., seismic event, high wind, floods)
- Manufacturing defects and equipment malfunctions, including human error (e.g., failure of the BSCs or HEPA filters or ventilation system, centrifuge accident, dropping/spilling container of culture, needle stick or cuts by sharp objects, leaking gas, spill and ignition of flammable liquid, wiring failure, transportation and transfer of biological samples)
- Vehicle crashes into the facility.
- Potential biological upset conditions in the BSL-3 facility.

The structures, systems, and components (SSCs) are assessed against a set of natural phenomena events that could affect the operations of the proposed BSL-3 facility as well as cause the release of infectious agents to the environment. The BSL-3 facility is constructed to Performance Category (PC)-2 criteria (see Section 3) and operated under the guidelines of LLNL *ES&H Manual*, Document 22.4. According to Document 22.4, all structures over 5 feet are seismically secured and incompatible materials shall be segregated to mitigate spills that may cause chemical and biological releases and fire or explosions due to chemical incompatibility.

The requirements of DOE STD-1020-2002 are to be applied to the design. Per the standard, the pre-fabricated structure will be designed and constructed using the International Building Code 2000 requirements. There will not be a separate seismic evaluation. While it is conservatively assumed that a large seismic event may cause some damage to the structure of the facility, it is Extremely Unlikely that biological materials will be released from this event.

High winds will cause similar but less damage to the facility than a seismic event. Per DOE-STD-1020-2002, Table 3-1, the wind-driven missile criterion is not required for PC-2 structures and no optional design criteria are listed for PC-2 structures. Therefore, the seismic event bounds events initiated by high winds. To the south of the site of the proposed BSL-3 facility, there are two large pine trees. Under high wind or super-saturated ground, these pine trees may be uprooted and topple onto the facility. The design feature of the facility will be to cut down the trees or keep them "topped" annually to prevent this scenario from occurring.

The LLNL Environmental Impact Statement (DOE 1992) supports the conclusion that flooding is not an issue at LLNL. However, accident scenarios involving a broken pipe or malfunction of the sprinklers causing flooding inside the BSL-3 facility have been evaluated. There will be floor drainage to prevent flooding, and the wastewater will be collected in the retention tank that will be sanitized with sodium hypochlorite prior to discharge. The floor drains will be sized to accommodate the flow from the discharging sprinklers in the room. The piping from the floor drains to the retention tank will be seamless, except at the connection points to the floor drains and to the pumps and tanks. This pipe will be buried underground and at an adequate depth so it cannot be damaged by heavy vehicle traffic.

For fire-related hazards, a Preliminary Fire Hazards Analysis (PFHA) was performed to identify the initiators of postulated fires and the controls to minimize the risk caused by the fires. Combustible loading in the BSL-3 facility will be kept low by good housekeeping practice; thus, a major fire will be unlikely. Open flames, sparks or other sources of ignition are not allowed in the BSL-3 facility. Flammable gases are not permitted and natural gas lines are not present (electricity is used for heating). The proposed BSL-3 facility will be equipped with smoke-detection and wet-pipe-sprinkler systems. Waterflow alarms will be connected to LLNL's fire alarm monitoring station so that designated responders will be notified.

Accident scenarios involving heat, fire, sunlight or wind would normally be seen to exacerbate or enhance a release or spread of the hazardous chemicals or radiological materials, but for the BSL-3 facility these conditions tend to render the infectious agents innocuous. Similarly, these organisms would likely be killed by direct exposure to heat, sunlight (UV radiation) or high wind (DA 1989). Catastrophic events such as fire, explosions, and airplane crashes, normally considered as initiating events in radiological or chemical accident analyses, were viewed as having the potential to actually reduce or eliminate the consequences of microbiological material releases. The endospores of the *Bacillus anthracis* are metabolically dormant and can survive extreme environmental conditions. After the spores enter an animal or human body, they germinate, changing from the resistant form into the growing and dividing vegetative form. The cell wall of the spore breaks down, the spore germinates, and the bacilli multiply rapidly. Sunlight (e.g., UV radiation) is detrimental to the survival of spores, even though the spores of *Bacillus anthracis* are more resistant to the effects of sunlight than its virulent vegetative cells [Setlow P. Environ Mol Mutagen. 2001;38(2-3):97-104. and Rice JK, Ewell M. Appl. Environ. Microbiol. 2001 Dec; 67(12):5830-2].

Wind has little effect on the survival of the *Bacillus anthracis* endospores. In fact, wind causes the dispersal of the aerosolized *Bacillus anthracis* as demonstrated in the Sverdlovsk Anthrax Outbreak of 1979 [Matthew Meselson et al., Science, 266 (5188):1202-8, November 14, 1994]. In the event of a spill of endospores in the BSL-3 facility, the infectious material will be sterilized by sodium hypochlorite solution or other sporicides.

The site of the proposed BSL-3 facility is located near a service road for the BBRP complex of buildings. The unmitigated frequency of a vehicle crashing into the BSL-3 facility is Anticipated. The vehicle impact may breach the protection envelope for the facility. The fuel leakage from the vehicle may initiate a fire. Design features of the facility will take credit for the installation of: a) bumpers in the parking area and b) bollards or physical barriers between the edge of the road and the BSL-3 facility. Based on the design feature of the facility, no release scenario is postulated.

By reviewing the *Final Programmatic Environmental Impact Statement; Biological Defense Research Program* (DA 1989) and discussing the potential accident scenarios with the BBRP personnel, the following scenarios are potentially anticipated and are evaluated: 1) dropping or spilling a culture container; 2) needle stick or cut with sharp instruments; 3) infectious aerosol inhalation; 4) rodent bite or scratch; 5) rodent escape from cage; 6) mosquitoes as infected vector; 7) manufacture defect or mechanical failure of the equipment; 8) on-site transportation and transfer scenario and 9) centrifuge accident.

4.3.1. Dropping or spilling of culture container (Scenarios SD-1 and SD-2)

The frequency of dropping or spilling a culture container in the BSL-3 facility is Anticipated. The consequences of the dropping or spilling of a culture container is very similar to those caused by an earthquake or high wind.

Two scenarios are evaluated: SD-1 occurs inside the BSC and SD-2 occurs outside the BSC (see Table 4-7).

4.3.1.1. Scenario SD-1:

A dropping or spilling of culture container inside the BSC is postulated. In this scenario, only BSL-3 workers are exposed to this type of risk. The unmitigated consequence to BSL-3 workers is Moderate for this scenario. The mitigated frequency or probability of this scenario is reduced to Unlikely because of preventive actions, such as using unbreakable plasticware instead of glassware, and seismic restraints to prevent tipping over of the BSCs and equipment. Mitigative controls for this scenario include: HEPA filters and the negative air system to confine microbes in the room; double air locks to prevent microbial migration; sealed surfaces on walls, floors and ceilings to make cleanup easy and to prevent microbial migration; providing respirators to workers; easy sterilization of any spills using sodium hypochlorite solution; the workers can shower and their clothes can be autoclaved; the whole room or whole suite of BSL-3 laboratories can be isolated and sterilized; and the exposed workers can be administered vaccines or antibiotics. The mitigated consequence for the SD-1 scenario to BSL-3 workers is Negligible. The mitigated consequence for the SD-1 scenario to the public is Negligible because all the exhaust air to the outside is triply filtered.

4.3.1.2. Scenario SD-2:

A dropping or spilling of culture container outside the BSC is postulated. The unmitigated consequence to BSL-3 workers and co-located workers or the public is Moderate for this scenario. The mitigated frequency or probability of this scenario is reduced to Unlikely because of preventive actions, such as using unbreakable plasticware instead of glassware, the sample being doubly-contained when it is outside the BSC and seismic restraints to prevent tipping over of the BSCs and equipment. Mitigative controls for this scenario include: HEPA filters and the negative air-pressure system to confine microbes in the room; double air locks to prevent microbial migration; sealed surfaces on walls, floors and ceilings to make cleanup easy and to prevent microbial migration; providing respirators to workers; easy sterilization of any spills using sodium hypochlorite solution; the workers can shower and their clothes can be autoclaved; the whole room or whole BSL-3 facility can be isolated and sterilized; and the exposed workers can be administered vaccines or antibiotics. The mitigated consequence for the SD-2 scenario to BSL-3 workers is considered Low rather than Negligible because no credit is taken for the BSC as one of the controls. The mitigated consequence for the SD-2 scenario to the public is Negligible because all the exhaust air to the outside is doubly filtered.

4.3.2. Needle stick or cut from sharp instrument (Scenario NS-1)

For a needle stick or cut from a sharp-instrument accident, a scenario NS-1 is postulated. In this scenario, a BSL-3 operator uses a Luer lock disposable syringe for dispensing animal blood after phlebotomy into tissue culture media. The Luer lock syringe is used in this test because the operator wants to remove the needle from the syringe before dispensing the drawn blood. This is to avoid damaging the blood cells. The operator uses the gripping forceps to remove the needle and during this process receives a needle stick on the forearm. Only a BSL-3 worker would be exposed to this type of risk.

The frequency of getting needle stick or cutting from sharps is Anticipated. The unmitigated consequence to BSL-3 workers is Low. The mitigated probability of this scenario is reduced to Unlikely because of the controls set up in the BSL-3 facility, e.g., implementing sharps disposal methods, and minimizing or eliminating the use of glassware. In addition, intrinsically safe needles (syringes that re-sheathe the needles or needle-less systems) are most often used in BSL-3 facilities. For mitigation, worker will promptly flush the affected area with water. Treatment will be administered as soon as possible. The mitigated consequence of this scenario to BSL-3 workers is Negligible because of the aforementioned controls.

Scenarios Involving Rodent Handling

The BSL-3 facility contains an ABSL-3 laboratory in which rodents are handled. The BSL-3 facility staff implements an aggressive rodent and pest control program that prevents rodents from escaping the ABSL-3 laboratory. The ABSL-3 laboratory is sealed with inward-opening doors. There is no record of a rodent escaping from an LLNL animal care facility in over 30 years.

4.3.3. Infectious aerosol inhalation (Scenario IAI-1)

Infected rodents and their bedding may generate infectious aerosols. BSL-3 workers who handle infected rodents or clean up their cages may inhale the infectious aerosol (scenario IAI-1 in Table 4-7). The frequency of a BSL-3 worker inhaling an infectious aerosol is Anticipated. The frequency of the public inhaling an infectious aerosol is Extremely Unlikely. The unmitigated consequences to BSL-3 workers and the public are Moderate. The mitigated probability of the BSL-3 workers is reduced to Extremely Unlikely because the ABSL-3 laboratory has the same physical characteristics and controls as any BSL-3 laboratory (rodents are housed in containment-caging systems, such as open cages placed in inward-flow ventilated enclosures [e.g., laminar flow cabinets], solid wall and bottom cages covered with filter bonnets) and the workers who enter the ABSL-3 laboratory must wear appropriate face/eye and respiratory protection (e.g., respirators and face shields). The mitigated consequences to BSL-3 workers are Low because of the availability of medical treatment for all of Risk group 3 agents. All maintenance and custodial personnel are also considered BSL-3 workers and receive appropriate training. Mitigated consequences to the public are Negligible due to the facility HEPA filtration and negative air pressure systems.

4.3.4. Rodent escapes from the cage (Scenario RE-1)

An infected rodent escaping from its cage is postulated in scenario RE-1 of Table 4-7. The consequence of this accident scenario is very similar to that caused by an earthquake that causes tipping of the rodent cage. The frequency that an infected rodent escapes from its cage is Unlikely because the cages that hold the rodents are mechanically locking. In the event that a worker handles a rodent out of its cage, the frequency of this rodent escaping from the handler becomes Anticipated. The mitigated frequency of rodent escape beyond the BSL-3 facility is Unlikely due to facility design. The ABSL-3 room is sealed with inward-opening doors and the room is designed to minimize hiding spaces. The unmitigated consequence to a BSL-3 worker is Low. The unmitigated consequence to the public is Negligible because the survivability of the laboratory-fed rodent in the natural environment is unlikely. The mitigated probability for this scenario remains Unlikely because a rodent can escape from its handler. The mitigated consequence of this scenario to BSL-3 workers remains Low for this reason. The mitigated probability and consequence to the public are Extremely Unlikely and Negligible, respectively, due to the implementation of the rodent and pest control program.

4.3.5 Rodent bite or scratch (Scenario RBS-1)

A person being bitten or scratched by an infected rodent is postulated in scenario RBS-1 of Table 4-7. The frequency of BSL-3 workers being bitten or scratched by the rodents is Anticipated. The frequency of public being bitten or scratched by the rodents escaping from ABSL-3 laboratory is Extremely Unlikely because the ABSL-3 laboratory implements an aggressive rodent and pest control program, and the ABSL-3 room is sealed with inward-opening doors to prevent rodents escaping. The unmitigated consequence to BSL-3 workers is Low. The unmitigated consequence to the public is Negligible because the survivability of the laboratory-fed rodent in the natural environment is unlikely. The mitigated probability and consequence to BSL-3 workers remain Anticipated and Low, respectively, even though only experienced handlers are allowed to work in the ABSL-3 laboratory and the exposed workers can be easily treated with vaccines or antibiotics. The mitigated probability and consequence to the public are Extremely Unlikely and Negligible, respectively.

4.3.6. Mosquitoes as infected vector (Scenario MIV-1)

A mosquito entering the BSL-3 facility and becoming an infected vector is postulated in scenario MIV-1 of Table 4-7. The frequency of a mosquito becoming an infected vector and transmitting the infectious agents to BSL-3 workers and public is Unlikely. The unmitigated consequences to BSL-3 workers and the public are Low. The mitigated probability for the BSL-3 workers is reduced to Extremely Unlikely because of the implementation of an aggressive pest control program in the facility. In addition, the use of HEPA filters and a negative pressure ventilation system in the facility will prevent a mosquito from escaping back into the local ecosystem. The use of PPE also reduces the probability of worker being bitten by the mosquito. The mitigated consequences to BSL-3 workers and the public are Negligible.

4.3.7. Manufacturing defects or mechanical failures of the equipment (Scenario MD-1)

A manufacturing defect or mechanical failure of the equipment in the BSL-3 facility is postulated (scenario MD-1 in Table 4-7). The frequency of a manufacturing defect or mechanical failure of the equipment, such as biosafety cabinets (BSCs), that would affect BSL-3 workers is Anticipated. The frequency of a manufacturing defect or mechanical failure of the equipment, such as BSCs that would affect the public is Unlikely. The unmitigated consequence to BSL-3 workers is Moderate and the unmitigated consequence to off-site public is Negligible. The mitigated probability of this scenario is reduced to Unlikely because the BSCs are leak-tested and certified semiannually, and the HVAC filter system is tested and certified annually. Under normal operating conditions, the front panel of the BSC is closed to the appropriate level to maintain a desired airflow rate. The BSCs are also equipped with alarms for low flow conditions. The mitigated consequences to BSL-3 workers and the public are Negligible because of these administrative controls and the availability of medical treatment.

4.3.8 On-site Transportation and Transfer Scenario (Scenario TT-1)

On-site transportation refers not only to the conveyance of the infectious agents by LLNL workers between the LLNL Receiving Department and B368, but also the packaging of the infectious materials. Transfer refers to the process of exchanging these materials between facilities. The federal government and state governments recognize infectious materials and vectors that may contain them as hazardous materials. Regulations on transportation are aimed at ensuring that the public and workers involved in the transportation are protected from exposure to the infectious agents that are contained in the packages and that the package prevents escape or leakage of the infectious agents. Protection is achieved by: a) the requirements for rigorous packaging that will withstand rough handling and contain all liquid material within the package without any leakage to the outside; b) appropriate labeling of the package with the biohazard symbol and other labels to alert the workers about the hazardous content of the package; c) documentation of the hazardous contents of the package should such information be necessary in an emergency situation and d) training of the workers so they can respond to emergency situations.

When infectious materials are sent to LLNL, they arrive via common carrier, such as Federal Express. They are delivered to LLNL Receiving Department staff (in B411) who is supposed to be advised in advance of any such shipments. When the package arrives at the LLNL Receiving Department, the Receiving personnel will inspect all inbound packages then contact the recipient, who has one hour to have it picked up. LLNL Receiving Department 's procedures specifically prohibit the Receiving Department personnel from unpackaging any such shipment. If a package containing infectious substances & etiologic agents is damaged or appears to have leaked, the LLNL Receiving Department staff will follow the Material Distribution Division (MDD)'s Operating Procedure by notifying the LLNL Fire Department (911) and Health and Safety (H&S) support staff for assistance. After bringing the package back to the BSL-3 facility, the recipient of the infectious materials will unpack the contents of the package in a BSC.

When a package containing infectious material is to be shipped off-site, the material will be packaged at the BSL-3 laboratory and delivered to the LLNL Shipping Department in full conformance with the U.S. Department of Transportation (DOT) and the International Air Transport Association (IATA) requirements.

In this scenario, a release of infectious material during on-site transportation is postulated (scenario TT-1 in Table 4.7). The unmitigated frequency of a release of infectious materials during on-site transportation that would affect the BSL-3 workers and public is Anticipated. The unmitigated consequence to BSL-3 workers and to off-site public is Moderate. The mitigated probability of this scenario is reduced to Unlikely because the infectious materials must be packaged according to IATA and DOT requirements. The mitigated consequence for the TT-1 scenario to BSL-3 workers is Low because the BSL-3 workers are trained in handling infectious materials, and spills can be easily sterilized using sodium hypochlorite solution; and the exposed workers can be administered vaccines or antibiotics. The mitigated consequence for the TT-1 scenario to off-site public is also Low because the treatment is available.

4.3.9 Centrifuge accident (Scenario CF-1)

A centrifuge rotor failure initiates an accident consisting of a *Coxiella burnetti* (Q-fever) release from the proposed BSL-3 facility is postulated (scenario CF-1 in Table 4-7). *Coxiella burnetti* probably represents the greatest risk of laboratory infection, according to the CDC. The organism is highly infectious and resistant to drying and the conditions of environmental exposure. The infectious dose of virulent Phase I organisms in laboratory animals has been calculated to be as small as a single organism. The estimated human infective dose ($HID_{25\text{-}50}$) (inhalation) for Q-fever is 10 organisms. Q-fever is the second-most commonly reported laboratory-associated infection (CDC 1999). The CDC identifies Q-fever as a disease commonly contracted occupationally by laboratory and animal care personnel (CDC 1999).

The unmitigated consequences of the postulated laboratory centrifuge accident scenario to the BSL-3 workers are Moderate and are considered to bound all the catastrophic release scenarios. However, engineering and procedural controls minimize opportunities for this hypothetical scenario, and mitigate the consequences. For example, men who were previously vaccinated and then exposed to aerosols of 150 or 150,000 infectious doses of virulent *Coxiella burnetii* did not consistently become ill (Benenson 1959). Therefore, since the centrifuge operator would have been vaccinated as a requirement of employment, it is questionable whether that worker would contract the illness. The frequency of this accident is considered Anticipated according to Table 4-3 because it is an event that has occurred in the operating history of another BSL-3 facility. Aerosolization of the product in a centrifuge can occur when a bottle or tube leaks or ruptures. However, by using a centrifuge that is equipped with a containment feature that protects the laboratory atmosphere from the release of potentially infectious aerosolized materials, the probability of worker contamination and the release of the infectious agent to the environment are significantly reduced. A containment device is a secondary gasket to seal the rotor or centrifuge lid, or safety cups and canisters that contain a ruptured tube and/or specimen.

The mitigated consequences to the public of the scenario are effectively reduced to Negligible because of preventive controls such as the HEPA filter and negative-pressure air system to confine microbes in the room; double air locks to prevent microbial migration; and sealed surfaces on walls, floors and ceilings to make disinfection and clean up easy and to prevent microbial migration. Mitigated consequences to the BSL-3 workers are Low because respirators are available to workers and other controls such as the spillage can be easily disinfected using sodium hypochlorite solution; the workers can shower and their clothes can be autoclaved to prevent cross-contamination; the whole room or whole suite of the BSL-3 laboratories can be isolated and sterilized; and treatment is available.

Table 4-7. Biohazards Evaluation Table

Hazard Summary					Controls		Event Rankings			
Event	**Process Activity**	**Hazard**	**Scenario**	**Cause**	**Preventive Features**	**Mitigative Features**	**Consequence**	**Frequency**	**Risk**	**Note**
SD-1	Operator handles BSL-3 infectious agents in the BSC	Potential release of infectious aerosols	Spilling/ dropping container in the BSC	Operator error or seismic event or high wind causing the spilling/dropping of the container	SSCs: BSC with seismic restraint	Use sealed, unbreakable plasticware, HEPA filter, negative air system, double air lock, sealed surface, PPE, respirators, room sterilization system, autoclaves, retention tank, Immunoprophylaxsis.	Minimal impact **Worker:** Unmitigated: Moderate Mitigated: Negligible **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Unmitigated: Anticipated Mitigated: Unlikely	**Worker:** Unmitigated: RL I Mitigated: RL IV **Public:** Unmitigated: RL IV Mitigated: RL IV	
SD-2	Operator handles BSL-3 infectious agents outside the BSC	Potential release of infectious aerosols	Spilling/ dropping container in the BSL-3 laboratory but outside the BSC	Operator error or seismic event or high wind causing the spilling/droping of the container	Double containment	Use sealed unbreakable plasticware, HEPA filter, negative air system, double air lock, sealed surface, PPE, respirators, room sterilization system, autoclaves, retention tank, Immunoprophylaxsis.	Possible impact to worker **Worker:** Unmitigated: Moderate Mitigated: Low **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Unmitigated: Anticipated Mitigated: Unlikely	**Worker:** Unmitigated: RL I Mitigated: RL III **Public:** Unmitigated: RL IV Mitigated: RL IV	

Hazard Summary					Controls		Event Rankings			
Event	**Process Activity**	**Hazard**	**Scenario**	**Cause**	**Preventive Features**	**Mitigative Features**	**Consequence**	**Frequency**	**Risk**	**Note**
NS-1	Operator handles infectious animals in the ABSL-3 laboratory	Infectious agents	Needle stick accident scenario: Operator accidentally self-injected infectious agent when handling animal	Operator error	Use intrinsic-cally safe needles	Immunoprophylaxsis, HEPA filter, negative air system, double air lock, sink for washing.	Possible impact to worker **Worker:** Unmitigated: Low Mitigated: Negligible **Public:** Not applicable	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Not applicable	**Worker:** Unmitigated: RL III Mitigated: RL IV **Public:** Not applicable	
IAI-1	Operator handles infectious rodents in the ABSL-3 laboratory	Infectious agents	Inhalation of infectious aerosols from rodents by the operator	Operator error	Animal containment cages.	PPE and respirators, well-trained operator; immunoprophylaxsis, HEPA filter, negative air system, double air lock.	Significant impact to worker **Worker:** Unmitigated: Moderate Mitigated: Low **Public:** Unmitigated: Moderate Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Extremely Unlikely **Public:** Unmitigated: Extremely Unlikely Mitigated: Extremely Unlikely	**Worker:** Unmitigated: RL I Mitigated: RL IV **Public:** Unmitigated: RL II Mitigated: RL IV	

Hazard Summary					Controls		Event Rankings			
Event	**Process Activity**	**Hazard**	**Scenario**	**Cause**	**Preventive Features**	**Mitigative Features**	**Consequence**	**Frequency**	**Risk**	**Note**
RBS-1	Operator handles infectious rodents in the ABSL-3 labora-tory	Infectious agents	Operator was bitten or scratched by infectious rodents	Operator error	None	PPE, respirator, immunoprophylaxsis, HEPA filter, negative air system, double air lock.	Potential impact to worker **Worker:** Unmitigated: Low Mitigated: Low **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Anticipated **Public:** Unmitigated: Extremely Unlikely Mitigated: Extremely Unlikely	**Worker:** Unmitigated: RL III Mitigated: RL III **Public:** Unmitigated: RL IV Mitigated: RL IV	
RE-1	Operator handles infectious rodents in the ABSL-3 laboratory	Infectious agents	Infectious rodents escaped from their cage	Seismic event or operator error	Seismic restraint on the animal containment cage, mechani-cally locking cage.	ABSL-3 laboratory is sealed with inward opening door to prevent animal escape; room is designed to minimize hiding places, pest & rodent control program in place, immunoprophylaxsis, PPE and respirators.	Potential impact to worker **Worker:** Unmitigated: Low Mitigated: Low **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Anticipated **Public:** Unmitigated: Unlikely Mitigated: Extremely Unlikely	**Worker:** Unmitigated: RL III Mitigated: RL III **Public:** Unmitigated: RL IV Mitigated: RL IV	

Hazard Summary					Controls		Event Rankings			
Event	Process Activity	Hazard	Scenario	Cause	Preventive Features	Mitigative Features	Consequence	Frequency	Risk	Note
MIV-1	Operator handles infectious rodents in the ABSL-3 labora-tory	Infectious agents	Mosquito entered into ABSL-3 lab, got infected and acted as vector	Operator error or the BSL-3 facility does not meet its design requirements; failure of HEPA filter	Animal containment cage	Room is designed to minimize hiding places, rodent and pest control program, negative pressure ventilation system, HEPA filter, PPE	Potential impact to worker **Worker:** Unmitigated: Low Mitigated: Negligible **Public:** Unmitigated: Low Mitigated: Negligible	**Worker:** Unmitigated: Unlikely Mitigated: Extremely Unlikely **Public:** Unmitigated: Unlikely Mitigated: Extremely Unlikely	**Worker:** Unmitigated: RL IV Mitigated: RL IV **Public:** Unmitigated: RL IV Mitigated: RL IV	
MD-1	Operator Handles liquid infectious agents	Inhalation of infecti-ous agents	Equipment malfunction	Manufacturer defect, operator error, system out of calibration	System tested and certified periodically	Negative pressure ventilation system, HEPA filter.	Potential impact to worker **Worker:** Unmitigated: Moderate Mitigated: Negligible **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Unmitigated: Unlikely Mitigated: Unlikely	**Worker:** Unmitigated: RL I Mitigated: RL IV **Public:** Unmitigated: RL IV Mitigated: RL IV	

Hazard Summary					Controls		Event Rankings			
Event	**Process Activity**	**Hazard**	**Scenario**	**Cause**	**Preventive Features**	**Mitigative Features**	**Consequence**	**Frequency**	**Risk**	**Note**
TT-1	Packaging or shipping or transport-ing of infectious agents	Infectious agents	Package was damaged or appeared to leak during shipping.	Operator error, vehicle crash	Use DOT and IATA requirements for transportation and transfer of infectious agents	Use sealed, unbreakable plasticware, immunoprophylaxsis.	Potential impact to worker **Worker:** Unmitigated: Moderate Mitigated: Low **Public:** Unmitigated: Moderate Mitigated: Low	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Unmitigated: Anticipated Mitigated: Unlikely	**Worker:** Unmitigated: RL I Mitigated: RL IV **Public:** Unmitigated: RL I Mitigated: RL IV	
CF-1	Operator Handles liquid infectious agents	Inhalation of infecti-ous agents	There is leakage from centrifuge tubes and some of the infectious agent is aero-solized	Operator error, defective centrifuge rotor	Use contain-ment centrifuge, safety cup.	HEPA filter, negative air system, double air lock, PPE and respirators, room sterilization system, immunoprophylaxsis.	Potential impact to worker **Worker:** Unmitigated: Moderate Mitigated: Low **Public:** Unmitigated: Moderate Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Unmitigated: Anticipated Mitigated: Unlikely	**Worker:** Unmitigated: RL I Mitigated: RL IV **Public:** Unmitigated: RL II Mitigated: RL IV	

5. Controls Selection

The combination of utilizing the guidelines, standards, practices and procedures established by the CDC, NIH, Health and Human Services Department, and public health services together with BSL-3 safety equipment and facility safety barriers significantly reduces the consequences for the release of the infectious agents.

To protect the public, workers and environment from adverse impacts of natural phenomena hazards (NPHs), the BSL-3 facility is built to Performance Category (PC)-2. The NPH mitigation requirements of Section 4.4 in DOE O420.1 utilize a graded approach in determining the structures, systems and components (SSCs) for the PC-2. The SSCs for the PC-2 are meant to ensure the operability of essential facilities (e.g., fire house, emergency response centers, hospitals) or to prevent physical injury to in-facility workers. SSCs designed to meet PC-2 requirements will sustain limited structural damage from design basis natural phenomena events, ensuring minimal interruption to the BSL-3 facility operation and minimal repair following the event. Table 5-1 lists all the SSCs that will be used in the proposed BSL-3 facility. The SSCs are classified into two categories: Important to Safety and Defense in Depth. The function of the Important to Safety SSCs is to protect workers by providing primary confinement of infectious agents. In some situations, those SSCs can reduce the risk rank from a higher Risk Level (RL) to a lower RL, such as RL-I to RL-II, or RL-II to RL-III or RL-IV. The Important to Safety SSCs are considered as primary barriers. From the data in the Biohazards Evaluation Table (Table 4-7), the following SSCs are classified as Important to Safety:

a) Biological safety cabinets (BSCs): BSCs are among the most effective and the most commonly used primary containment devices in laboratories working with infectious agents.
b) Double containment: When the infectious agents are handled outside the BSCs, the usage of double containment is required to reduce the risks of workers to be exposed to these infectious agents. Infectious agents are stored and transported in double containers in order to contain a spill if a container leaks or breaks.
c) Rodent caging system: In the ABSL-3 laboratory, the risk of infectious aerosols from infected rodents or their bedding is reduced by housing the rodents in containment caging systems, such as open cages placed in inward-flow-ventilated enclosures (e.g., laminar flow cabinets), solid wall and bottom cages covered with filter bonnets, or other equivalent primary containment systems.
d) Centrifuge: The containment centrifuge protects against the release of aerosolized infectious agents to the laboratory, reducing the risk of worker contamination.
e) HVAC: The negative-pressure ventilation system controls potential airborne contamination. It creates directional airflow that draws air into the BSL-3 laboratories from the adjoining areas toward and through the BSL-3 laboratories areas with no recirculation from the BSL-3 laboratories to the non-BSL-3 areas of the building. The

BSL-3 laboratories will be under the most negative pressure with respect to all other areas of the building.

f) HEPA filters: The HEPA filtration on the building exhaust provides assurance that infectious agents will not escape from the facility if there is a spill outside of the BSC or if rodents escape from their cages.
g) Respirators: These protect operators from inhaling infectious aerosols that are generated from infected rodents or their bedding.
h) Packaging/shipping requirements: Packaging and shipping the infectious agents in full conformance with DOT and IATA requirements to prevent any release.

The function of the Defense in Depth SSCs is to add redundancy in protecting workers. The Defense in Depth SSCs are considered as secondary barriers.

Table 7. SSCs used in the proposed BSL-3 facility

Important to Safety		**Defense in Depth**	
SSC	**Scenarios**	**SSC**	**Scenarios**
Biosafety Cabinets[1](includes testing and certification)	SD-1, MD-1	PPE [1]	SD-1, SD-2, IAI-1, RBS-1, RE-1, MIV-1, CF-1
Double containment of samples when they are outside of BSCs[1]	SD-2	Sanitation system[1] (structure design of the BSL-3 facility and decontamination/sterilization system)	SD-1, SD-2, CF-1
Rodent caging system[1]	IAI-1, RE-1, MIV-1	Hands-free or automatically operated sink for hand washing. Eyewash station is readily available in each laboratory.[1]	NS-1
Containment Centrifuge[1] (with safety cups)	CF-1	Audible alarm for power or ventilation system failure[1]	MD-1, SD-1, SD-2
Negative ventilation systems[1]	SD-1, SD-2, NS-1, IAI-1, RBS-1, MIV-1, MD-1, CF-1	Retention tank	SD-1, SD-2
HEPA filters[1]	SD-1, SD-2, NS-1, IAI-1, RBS-1, MIV-1,	Immunoprophylaxsis [1] (vaccine, antibiotics)	SD-1, SD-2, NS-1, IAI-1, RBS-1, RE-1,

	MD-1, CF-1		CF-1, TT-1
Respirators[1]	SD-1, SD-2, IAI-1, RBS-1, RE-1, CF-1	Access Control[1]	IAI-1, RBS-1, RE-1
Packaging and shipping the infectious agents in full conformance with DOT and IATA requirements	TT-1	Autoclaves[1]	SD-1, SD-2
		Tissue Digestors[1]	SD-1, SD-2
		Physical barriers (bumpers, bollards)	SD-1, SD-2, RE-1, TT-1.
		Sealed & unbreakable plasticware	SD-1, SD-2, TT-1
		Double air lock	SD-1, SD-2, NS-1, IAI-1, RBS-1, CF-1
		Sealed surfaces	SD-1, SD-2
		Safe needles	NS-1
		Seismic restraints on animal cages	RE-1
		ABSL-3 laboratory design	RE-1, MIV-1
		Pest and rodent control program	RE-1, MIV-1

[1] Described as controls in the BMBL.

6. Operational Safety Requirements

The following operational safety requirements (OSRs) are the minimum safety requirements necessary to ensure operational safety for the BSL-3 facility. Listed below are OSRs that shall be met prior to operation of the BSL-3 facility.

6.1 Management Role and Responsibilities

The BSL-3 facility is funded through Nonproliferation, Arms Control, and International Security (NAI). In accordance with the *LLNL ISM System Description* (LLNL, 2002), NAI, having management authority, has delegated the authority to construct and operate this facility to Biomedical and Biotechnology Research Program (BBRP). BBRP will have primary responsibility for operations and safety oversight. Staff from multiple organizations will use the facility including Chemistry and Materials Science (C&MS), BBRP, and NAI. The BSL-3 Facility Manager is responsible for ensuring that the requirements of the OSRs are met. This responsibility is demonstrated by establishing, implementing and maintaining OSRs and associated administrative controls (ACs) identified in this Preliminary Authorization Basis Document and in LLNL policies, manuals and procedures.

6.2 Noncompliance and Violations

BBRP and the BSL-3 Facility Manager ensure that the safety requirements for the BSL-3 facility are met. Compliance is demonstrated through the following:

a) Maintaining the facility operation within its safety envelope and performing the surveillance requirements (SRs) defined in Section 6.6.
b) Establishing, implementing and maintaining the administrative controls (ACs) defined in Section 6.5.
c) Taking actions to correct safety basis deficiencies.

A violation of an OSR is determined to be a reportable occurrence to DOE because the safety envelope of the BSL-3 facility has not been maintained. Exceeding CDC select agent permit conditions, exceeding biological or chemical inventory in the BSL-3 facility, or using a pathogen or rodent without approval of IBC and IACUC, is considered a violation. Spills and accidents that result in actual or significant potential exposure to infectious materials including organisms containing recombinant DNA molecules are immediately reported to the Biological Safety Officer. Additional reporting may be required per LLNL Occurrence Reporting Procedures. Appropriate medical evaluation, surveillance, and treatment are provided and written records are maintained.

The failure to meet the intent of a safety program will be considered a violation. An isolated program deficiency would not usually be considered a violation. However, if the isolated program deficiency is significant, malicious and egregious, it may be considered a violation.

6.3 Minimum Staffing for Safety

Requirements for adequate staffing and minimum staffing for safety will be defined in the Facility Safety Plan (FSP) for the proposed BSL-3 facility. Employees and supporting organizations are continuously monitored for adherence to ES&H requirements. The Facility Manager of the BSL-3 facility continuously works with the management of the support organizations to ensure a high level of commitment to ES&H activities.

A requirement that at least two operators shall be present in the BSL-3 laboratory may be imposed by the Institutional Biosafety Committee (IBC) whenever conditions or activities warrant. Unattended activities such as overnight culture growth in the BSCs and/or the overnight incubation are allowed in this BSL-3 facility.

6.4 Operability Limitations

Maximum inventory of BSL-3 microbes and toxins shall not exceed those described in Section 4.2.

Maximum inventory of hazardous materials in the BSL-3 facility shall not exceed their screening thresholds. For chemicals, a screening threshold based upon calculations of TEEL values for each chemical. The chemical thresholds for B368 are the limits imposed on the Low hazard facility.

No radioactive materials, flammable gasses, or explosives will be used in this facility.

A program shall be in place to ensure functional operations of all Important to Safety Controls as described in Table 5-1.

A program for access control shall be implemented and maintained. Only qualified, trained operators can work in the BSL-3 and ABSL-3 laboratories.

6.5 Administrative Controls

The following administrative controls (ACs) will be established and implemented to ensure that operations in the BSL-3 facility will be bounded by conditions and assumptions used to define its safety basis:

a) An FSP shall be prepared and maintained for the BSL-3 facility.
b) *ES&H Manual,* Document 13.6 was revised to address the BSL-3 activities. The BSL-3 facility will be operated in accordance with Document 13.6. A Biosafety Manual shall be assembled consisting of ES&H Documents 13.1 – 13.6, and kept in B368.
c) Specific policies and operating procedures for the BSL-3 facility, such as a procedure for BSC usage shall be prepared.
d) IACUC approval shall be obtained for all activities involving rodents in the facility.

e) The Institutional Biosafety Committee (IBC) shall review all new biological research projects proposed by LLNL staff for compliance with safety principles, regulations and relevant guidelines and references. IBC approval shall be obtained for all activities involving pathogens or toxins in this BSL-3 facility.
f) Integration Worksheets (IWSs) shall be prepared for each operation in the BSL-3 and ABSL-3 laboratory.
g) A BBRP Assessment Plan covering the BSL-3 activities shall be prepared.
h) A BBRP Training Plan covering the BSL-3 activities shall be prepared.
i) A BBRP Configuration Management Plan covering the BSL-3 activities shall be prepared.
j) A BBRP Integrated ES&H Management Plan covering the BSL-3 activities shall be prepared.
k) All BSL-3 workers with access to Select Agents will be registered in accord with the LLNL Select Agent requirements.
l) A permit from CDC for all Select Agents shall be maintained.
m) All personnel working in the BSL-3 facility will be enrolled in the Biohazards Medical Surveillance Program. They will receive appropriate immunizations and testing for the agents handled or potentially present, and serum banking will be done. In general, persons who may be at increased risk of acquiring infection, or for whom infection might have serious consequences, will not be allowed to work in the BSL-3 facility unless special procedures can eliminate the extra risk. An assessment will be made by an occupational health physician.

6.6 Surveillance Requirements

Surveillance requirements (SRs) establish requirements and specific frequencies to verify the operability of the SSCs and their variables are within specified limits to ensure safe operation of the BSL-3 facility.

The SRs for the BSL-3 facility include:

a) The testing/inspection for SSCs used in the proposed BSL-3 facility, such as BSCs, autoclaves, tissue digestors, HEPA filters, ventilation system, decontamination/sterilization system, alarms for power or ventilation system failure;
b) Maintenance records for SSCs;
c) The testing and inspection of the BSL-3 security access system.

6.7 Safety Management Programs

All written operating procedures and operation within the BSL-3 will be fully compliant and consistent with the BMBL (CDC 1999) guidelines and those of the NIH Guidelines for Research

Involving Recombinant DNA Molecules (NIH 2001). Additionally, the introduction of any agent or toxin to the BSL-3 facility requires prior IBC review and approval.

Administrative controls such as the institutional oversight committees that are involved with biological research include: The LLNL Biosafety Operations Committee (LBOC), The Institutional Biosafety Committee (IBC), The Institutional Animal Care and Use Committee (IACUC), and the Institutional Review Board (IRB). All of these boards are appointed by the Laboratory Director and include members of the community from outside of LLNL. The LBOC provides experimenters an initial single point of contact, determines the level of review needed, identifies the associated hazards, and provides recommendations for training, medical surveillance, and changes to the ES&H Manual. The IBC is chartered by the National Institutes of Health (NIH) and is charged with reviewing all work with biological materials, including pathogens, recombinant DNA and select agents. They review proposed research protocols to verify that they can be safely and productively implemented. The IACUC is chartered by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) and is charged with reviewing all use of vertebrate animals in research activities. They review proposed research protocols to assure that animals are employed in a humane and productive manner. The IRB is charged with reviewing the use of human-derived data or cultures of human cells.

Maintenance of BSCs, rodent cage, ventilation system, HEPA filter, etc: BSCs (semiannual) and HEPA filter system will be tested and certified annually and ventilation systems will undergo routine maintenance required by the manufacturer and LLNL operating and maintenance plans. Other safety features in the BSL-3 facility will undergo routine maintenance recommended by the manufacturers.

Support and Services Responsibilities:

Listed below are the organizations and their functions responsible for ensuring a safe work environment in the BSL-3 facility.

a) Plant Engineering and UTel Departments: Plant Engineering and UTel personnel perform preventive maintenance and on-demand repair of building structures, systems, and components (SSCs) as requested by the BSL-3 Facility Manager.

b) Hazards Control Department (HCD): The ES&H Team 2 of the HCD and its members from various disciplines, such as Industrial Hygiene (IH), Industrial Safety (IS), Fire Protection Engineer and Biosafety Officer assist the BSL-3 Facility Manager in establishing and maintaining a safe work environment. The ES&H Team 2 is available to evaluate any proposed or existing operation for possible hazards and to recommend suitable controls. Individual duties and responsibilities of the ES&H Team 2 members are listed in the Team Action Plan issued by the ES&H Team. The fire protection assessment of the BSL-3 facility is carried out in the form of a fire hazard analysis (FHA). The Biosafety Officer is available to provide technical consultation and guidance regarding biosafety practices, procedures and program management. The Authorization Basis Section of the HCD assists the BSL-3 Facility Manager to prepare safety basis documentation for the BSL-3 facility. In addition, the Authorization Basis Section provides independent institutional review and concurrence on the safety basis documentation.

c) Environmental Protection Department (EPD): EPD provides environmental guidance and support to the BSL-3 facility. Any BSL-3 worker can request assistance from EPD through the ES&H Environmental Analyst.

d) Health Services Department: The Health Services Department, which houses a decontamination facility, provides both emergency and non-emergency treatment services and regular physical examination and medical surveillance for BSL-3 workers and LLNL employees.

Change control: A safety basis change control program will be developed and implemented for the BSL-3 facility to address planned changes. Management may propose planned changes that are outside the approved safety basis. The safety basis document shall be modified to reflect those changes and submitted to DOE. DOE approval for those changes is required prior to implementation.

6.8 Design Features for Safety:

The design features for safety are described in Section 5.

7. References

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DOE 2002a: Task Plan for the Preparation of Authorization Basis Documentation for the Proposed Bio-Safety Level 3 Laboratory At Lawrence Livermore National Laboratory, August 2002.

DOE 2002b: Final Environmental Assessment (EA) for the Proposed Construction and Operation of a Biosafety Level 3 Facility at Lawrence Livermore National Laboratory, Livermore, CA (DOE/EA-1442, December 2002).

DOE-STD-1020-2002, Natural Phenomena Hazards Design Evaluation Criteria for Department of Energy Facilities

LLNL Documents:

LLNL *ES&H Manual*, Document 3.1, Non-nuclear Safety Basis Program.

LLNL *ES&H Manual*, Supplement 13.1, Biological Controls and Operations.

LLNL *ES&H Manual*, Supplement 13.2, Exposure Control Plan- Working Safely with Blood and Bloodborne Pathogens.

LLNL *ES&H Manual*, Supplement 13.3, Sanitation.

LLNL *ES&H Manual*, Supplement 13.4, Research Involving Human Subjects.

LLNL *ES&H Manual*, Supplement 13.5, Vertebrate Animals Used in Research.

LLNL *ES&H Manual*, Supplement 13.6, -Safe Handling and Use of Biological Research Materials.
LLNL *ES&H Manual*, Supplement 22.4, Earthquakes.

LLNL BSL-3 Laboratory Blue Book.

LLNL 2000: Lawrence Livermore National Laboratory, "Building 360 Complex; Biology and Biotechnology Research Program (BBRP)," University of California, Livermore, CA, FSP 360, Triennial Review (August 2002).

LLNL 2001a: Lawrence Livermore National Laboratory, "Building 360 Complex, Biohazardous Operations," University of California, Livermore, CA, FSP-360 Addendum 1, Triennial Review (April 2001).

LLNL 2001b: Lawrence Livermore National Laboratory, "LLNL Chemical Hygiene Plan for Laboratories", Document 14.2 of the *ES&H Manual*, University of California, Livermore, CA, (August 18, 2002).

LLNL 2002: LLNL Integrated Safety Management System Description—Version 5.0, University of California, Livermore, CA, UCRL-AR-132791, March 19, 2002.

Preliminary Fire Hazards Analysis Building 368, Revision 0, February 12, 2004.

BBRP Assessment Plan

BBRP Training Plan

BBRP Configuration Management Plan

BBRP Integrated ES&H Management Plan

Appendix A. Responses to the Review Comment Record (RCR)

REVIEW COMMENT RECORD (RCR)	1. Date	2. Review No.
	3. Project No.	4. Page

5. Document Number(s)/Title(s)	6. Program/Project/ Building Number	7. Reviewer	8. Organization/Group	9. Location/Phone
Preliminary Authorization Basis Documentation for the Proposed Biological Safety Level 3 (BSL-3) Facility at LLNL		Mortensen Spagnolo Remick Martin Marcisz	NNSA/LSO	3-3250

17. Comment Submittal Approval:

Organization Manager (Optional)

Date

10. Agreement with indicated comment disposition(s)

Reviewer/Point of Contact

Date

Author/Originator

11. CLOSED

Review/Point of Contact

Author/Originator

12. Item	13. Comment(s)/Discrepancy(s) (Provide technical justification for the comment and detailed recommendation of the action required to correct/ resolve the discrepancy/problem indicated.)	14. Hold Point	15. Disposition (Provide justification if NOT accepted.)	16. Status
1	General – There are many assumptions throughout this document that must be protected to ensure the validity of the conclusions. Suggest developing an Authorization Basis Assumption list now and placing under configuration control.		This will be part of the Final AB Document.	
2	General – The terminology "mitigated" probability tends to confuse since "mitigation" is typically associated with reducing consequence. Suggest rewording		We will consider an appropriate rewording for the Final AB	

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	when discussing frequency to "reduced" probability or something similar.		Document.	
3	General – Ensure that all basic terminology for the BSL-3 facility is consistent within the document and with the EA.		Agreed.	
4	General: Packaging and transportation must also be evaluated as an activity supporting the operation of the BSL-3 facility. Ensure that appropriate scenarios have been evaluated and that controls are in place.	X	Scenario TT-1 was added.	
5	Pg. 7 – Editorials, - Center 'for' Disease Control.		Correction made.	
6	Pg. 9 – Define "light" and "heavy" laboratories.		Excessive detail in this discussion was removed.	
7	Pg. 9, 2.2 – suggest deleting the last sentence concerning the mission. This could imply we are doing chemical work in the facility. Or if the sentence is necessary to define mission then tie it to the CBNP.		Sentence changed to read: "This information is used to develop, demonstrate, and deliver technologies and systems to improve domestic defense capabilities and, ultimately, to save lives in the event of a biological attack in support of our national security's nonproliferation mission."	
8	Pg. 10 – 2nd paragraph – 1st sentence – "centrally located at LLNL".		Change made.	
9	Pg. 15 – 4th paragraph – this section discusses the ability of the LLNL FD to respond and resolve the situation before actuation of the sprinklers. Please explain what the heat detectors for the wet pipe sprinklers will be set at…It does not seem prudent to assume that the FD can resolve an incipient stage fire…where there is smoke, oftentimes there is fire.	X	The BSL-3 facility will be equipped with an LLNL standard fire alarm and emergency paging system that is connected to the LLNL emergency operations center. Activation of pull stations, water flow alarms, or mechanical room smoke detectors will be detected and responded to by the LLNL Fire Department.	

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			The sprinkler head temperature rating will be in the 155° to 165°F range. This rating was added to the text.	
10	Pg. 15 – 5th paragraph – will the maintenance schedule of the HEPA filters be the same as nuclear HEPA change outs? I.e. 18 months.		Definition of the maintenance schedule is deferred to the Final AB Document.	
11	Pg. 15, Paragraph 5 – Will the ventilation system be interlocked to the smoke alarm, i.e., trip on activation of a smoke alarm.	X	The supply fan will provide more than 2,500 cfm and will be interlocked with the smoke alarms to shut down if smoke is sensed. It is not typical practice to interlock the building exhaust and there is no plan to shut down the BSC's in the event of a smoke alarm. Change made in the text.	
12	Pg. 16, 2nd paragraph – does this diesel generator supply other buildings currently and will it when the BSL-3 facility is completed. If so, has drain on the system been evaluated?		Paragraph changed to read: The electrical power requirements for the BSL-3 facility will be about 145 kilowatts (kW). Of this total load, approximately 75 kilowatts (kW) of power is used for the building air handling, fire alarms, freezers, and lighting. A diesel generator in an adjacent building will supply the laboratories with electric power in the event of a power failure from the supply grid system for these systems. The diesel generator supplies B366 and part of B361. The	

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			existing loads were evaluated during preliminary design and there is adequate capacity for the BSL-3 load. In the event of a power outage, the generator will respond in 10 seconds to supply electricity to the laboratories so that workers could shut down the laboratories safely.	
13	Pg. 16, paragraph 2 – Define what is meant by diesel generator response "immediately"… Quantify and ensure that worker evacuation or response is within this timeframe.		Text changed to "10 seconds". See above.	
14	Pg. 16, paragraph 5 – How does LLNL plan to dispose of the biological cultures?		The last sentence was deleted to avoid confusion on this issue.	
15	Pg. 17, Table 4-1 – Include Asphyxiants. Also explain what is meant by "confined gases".		Asphyxiants were added.	
16	Pg. 18, bullets – suggest rewording 1st bullet to simply state "Human Error".		Change made.	
17	Pg. 19 - 21, Table 4-2 - Several items need to be discussed for clarity. Have marked up copy and will provide.	X	Items deferred to the Final AB Document.	
18	Pg. 22 – Explain if a tracking system for the BSL-3 material will be established and a control.		The following was added: "A tracking system will be established for all biohazardous materials used in the BSL-3 facility."	
19	Pg. 22, 4th paragraph – this section notes that future programs may require the use or other bacterial or viral infection agents…are there any new events associated with the introduction of these additional agents…you may want to state that change control is in place to address the future introduction of these agents. Also explain	X	The text is modified to include: "The controls identified in Section 5 will be adequate to handle all BSL-3 infectious	

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			fabricated structure will be designed and constructed using the International Building Code 2000 requirements. There will not be a separate seismic evaluation."	
23	Pg. 25, 3rd paragraph – missile generation should be considered not just toppling… Confirm if PC-2 requires this.	X	Per DOE-STD-1020-94 (CH-1), the wind driven missile criteria is not required for PC-2 structures and no optional design criteria are listed for PC-2 structures.	
24	Pg. 25, 4th paragraph – combustible loading is assumed to be low – provide the method by which this will be protected…will there be combustible loading limits and requirements, i.e., no transient combustibles. See General Comment		The definition of specific controls on combustible loading are deferred to the Final AB Document.	
25	Pg. 25, 4th paragraph – earlier in the document it is stated that no open flames will be in the BSL-3 facility, this statement implies that it may be possible eventho "non-routine". Clarify intent on open flame allowance.	X	This paragraph will be revised as: For fire-related hazards, a Fire Hazards Analysis (FHA) is being developed to identify the initiators of postulated fires and the controls to minimize the risk caused by the fires. Combustible loading in the BSL-3 facility will be low and a major fire will be unlikely. Open flames, sparks or other sources of ignition are not allowed in the BSL-3 facility. Flammable gases are not permitted and natural gas lines are not present (electricity is used for heating).	
26	Pg. 25, 4th paragraph – how will we protect the assumption that the FD can respond within 3 minutes. Is there a needs analysis and evaluation that shows that there are enough personnel available at all times to respond with the necessary tools and resources with 3 minutes. I suggest re-evaluating this statement.	X	This was reworded so that we will not be taking credit for the response time of the Fire Department.	
27	Pg. 26, 1st paragraph – if anthrax is an exception, ensure that this will be appropriately carried forward into hazards and accident analysis.	X	Bacillus anthracis (anthrax) is not an exception to conditions specified in the current revision	

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			specified in the current revision of the PABD.	
28	Pg. 26, 4.3.1 – HEPAs, air locks, sealed surfaces, and respirators are all mitigative features…they do not change the frequency associated with dropping or spilling a container. Correct.		The text was changed to clarify this.	
29	Pg. 27, 4.3.2 – Explain if exposure can occur to maintenance and custodial personnel that are not BSL-3 workers. Or note if they are considered BSL-3 workers and appropriately trained.		The following text was added: "All maintenance and custodial personnel are BSL-3 workers and will be trained."	
30	Pg. 27, 4.3.3 – Please justify why the mitigated consequences to the worker would be negligible…I agree to the public, but the worker would seem to reduce to low at best.		Agree. The mitigated worker consequences were changed to Low.	
31	Pg. 28, 4.3.4 – The assumption that the room is designed to minimize rodent hiding places must be protected and maintained. See General Comment.		This is a part of the rodent and pest control program.	
32	Pg. 28, 4.3.4 – last sentence – reword… "due to implementation of the rodent and pest control program."		Change made.	
33	Pg. 28, 4.3.6 – Explain how the assumption that there is no standing water around the BSL-3 facility to breed mosquitoes will be protected and maintained. See General Comment.		The text was changed so that no credit is being taken for the control of standing water.	
34	Pg. 28, 4.3.6, the use of PPE doesn't reduce the probability only, it also reduces the consequences.		No change needed.	
35	Pg. 29, 4.3.7 – this scenario does fancy accident analysis without even realizing it…I assume these administrative controls credited with reducing the frequency and consequence will be in the OSR or somewhere else.		Agreed. All credited controls will be preserved.	
36	Pg. 29, 4.3.8, the probability of NPH is unlikely, not "very low" ensure that this scenario is consistent with the criteria LLNL uses for its hazards and accident analyses. Additionally, as commented on before, this needs to be significantly reduced in detail unless I am to expect that all of the scenarios will get the same level of sophistication.	X	Change made from "Very Low" to "Unlikely" to maintain consistency of terminology. We also reduced the details of this accident scenario to a level commensurate with the other accidents discussed.	
37	Pgs. 34-38, see earlier comments on text associated with table and let's discuss.	X	Items deferred to Final AB Document.	

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38	Chapter 5 - This section does not clearly discuss all the controls noted throughout the document. It needs to include the Design Features for Safety, and administrative controls (credited). Suggest we as a team go through the PAB and discuss what we believe are the set of currently credited controls, assumptions and design features.		Agreed. Changes deferred to the Final AB Document.	
39	Pg. 40, Table 7, It would be a good idea to cross-reference the SSCs in this table with the scenarios they are associated with.		Cross-reference was added.	
40	Pg. 41, 6.1, typographical error – "…has delegated the authority to construct…"		Change made.	
41	Pg. 41, 6.2 – last sentence – An isolated program deficiency may be a violation if significant, malicious and egregious…Suggest rewording.		Text changed to read: "An isolated program deficiency would not usually be considered a violation. However, if the isolated program deficiency is significant, malicious and egregious, it may be considered a violation."	
42	Pg. 41, 6.3 – this section should discuss if there is any necessary minimum staffing for safety to support the OSR and AB document. I believe you have implied the Facility Manager and LLNL FD are necessary to ensure that you stay within your AB document. Also, are unattended activities allowed within the facility, i.e. – overnight incubation and culture growth? Please reword.		The following was added: "Unattended activities such as overnight incubation and culture growth in the BSCs are allowed in BSL-3 facility." Other details on staffing requirements will be included in the Final AB Document.	
43	Pg. 42, AC – confirm that this listing is comprehensive… I suggest as mentioned earlier that as a team we walk through the PAB to determine what we believe are the necessary ACs…		Changes deferred to the Final AB Document.	
44	Pg. 42, Section 6.4 – Add: "No radioactive materials, flammable gasses, or explosives will be used in this facility."		Change made.	
45	Pg. 43, Section 6.6 – In the Final AB document the surveillance requirements may need to be clarified and with more detail.		Agreed.	
46	Pg. 43, 6.7 – this is not a comprehensive listing of the safety management programs		A list was added of the	

5. Document Number(s)/Title(s)	6. Program/Project/ Building Number	7. Reviewer	8. Organization/Group	9. Location/Phone
Level 3 (BSL-3) Facility contract drawings		Chwang	NNSA/LSO	2-0758

17. Comment Submittal Approval:

Organization Manager (Optional)
Reviewer/Point of Contact

Author/Originator

10. Agreement with indicated comment disposition(s)

Date

Reviewer/Point of Contact

<u>Son N. Nguyen and Tom Altenbach</u>

Author/Originator

11. CLOSED

1/6/04

Date

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1	Has the LLNL fire protection engineer review the revised PABD??		Yes. Mike Jones, ES&H Team 2 Fire Protection Engineer, has reviewed the PABD. He has prepared the Preliminary FHA for the facility.	
2	What is the size of the water retention tank? Should be sized for sprinkler system flow for 20 minutes. Consult with LLNL FPE.		The retention tank can contain up to 1000 gallons. There are 2 water tanks that are inter-connected. One tank is generally empty at all times. Total tank capacity is 2000 gallons. These tanks are enclosed on a concrete pad with a concrete dike. Total dike capacity is 1370 gallons. Thus the	

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			total usable capacity (with the tanks intact) is 3,370 gallons. Assuming a 20 minute discharge (again a very unlikely event as the fire department response time is in the 3 to 5 minute range and would confirm extinguishment and shut down of the sprinkler system in the 5 to 10 minute range) we could have in the range of 1200 to 1500 gallons maximum. The tanks and containment can handle this amount of discharge.	
3	At my last meeting, I thought we agreed to provide a second exit for this building, the second exit is not shown on the floor plan.		There are actually three exits from the laboratory area and one from the mechanical room.	
4	When will LSO/DOE see the FHA for this building ??		When the building is here (LLNL) and after the inspection of the Fire Protection Engineer from the ES&H Team 2, the FHA will be subsequently issued.	
5	p.5 BSL should read Biosafety Level consistent w/p.7 p.7 "challenges to rodents" needs elaboration p.9 bldg not located in parking area, but adjacent p.13 need updated sketch p.16 what happens to the electrical/exhaust system when the sprinklers activate?		5.1) p.5 and p.7. Agree that BSL should read Biosafety Level. 5.2) P.7: "challenge to rodents" means the rodents are infected with a microorganism and then observed for signs of illness. 5.3) P.9: Agree. B368 is located	

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	p.43 implies that incubator is in the BSC, yet sketch shows it as a self-standing unit		adjacent to the parking area. 5.4) P.13: Agree. Will update the sketch. 5.5) P.16: the electrical/exhaust system will function normally when the sprinklers activate. 5.6) P.43: Will correct to indicate that incubators will be placed outside of the BSCs.	