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Preliminary Authorization Basis Documentation for the Proposed Bio Safety Level 3 (BSL-3) Facility

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Auspices Statement

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for the

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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
ACGIH	American Conference of Governmental Industrial Hygienists
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	Biological safety cabinet
BSL	Biological safety 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
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
FHA	Fire Hazards Analysis
FSP	Facility Safety Plan
GC-MS	Gas Chromatography-Mass Spectrometry
HAP	Hazardous air pollutant
HEPA	High efficiency particulate air (filter)
HHS	US Department of Health and Human Services
HID	Human infective dose
HID_{50}	Human infective dose - 50 percent
HMIS	Hazardous Material Information System
HVAC	Heating, ventilation, and air conditioning
IACUC	Institutional Animal Care and Use Committee
IBC	Institutional Biosafety Committee
ID_{50}	Infective dose - 50 percent
IRB	Institutional Review Board
ISMS	Integrated Safety Management System
IWS	Integration Worksheet
LBOC	LLNL 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
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
PPE	Personal protective equipment
RCRA	Resource Conservation and Recovery Act
RG	Risk Group
RL	Risk Level
RNA	Ribonucleic acid
SMEs	Subject matter experts
SOP	Standard Operating Procedure
SSCs	Structures, systems and components
TLV	Threshold Limit Value
UC	University of California
USAMRIID	United States Army Medical Research Institute for Infectious Diseases
USC	United States Code
WHO	World Health Organization

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 Center of 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 built in accordance with the required BMBL guidelines. 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 1,100 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). The BSL-3 facility will be designed and operated in accordance with guidelines for BSL-3 laboratories established by the CDC and the NIH.

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 handled in this facility will be limited in quantity, type and form in accordance with the BMBL requirements and 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 using infectious agents or biologically derived toxins (biotoxins). These types of aerosol studies will be strictly confined in a Class II Type B biosafety cabinet.

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 2002) 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 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. Facility space at the site is generally categorized into four types according to use: office and drafting; light laboratories and shops; heavy laboratories; and miscellaneous, including a fire station, medical facility, and several cafeterias.

Many buildings throughout the site contain light laboratories and shops, which account for slightly less than 40% of LLNL's total assignable space. Most light laboratories conduct direct research and can usually be characterized as either wet or dry. Wet laboratories support a wide variety of chemical analyses, whereas dry laboratories support activities such as laser optics research.

Heavy laboratories account for less than 10% of LLNL's assignable space. Heavy laboratories usually have high-bay construction, overhead cranes, and shielding in areas containing radioactive materials.

A thorough description of the LLNL site characteristics is available in the Final Environmental Impact Statement [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 capabilities and, ultimately, to save lives in the event of a chemical or biological attack in support of our national security's nonproliferation mission.

2.3 BSL-3 Facility Location

The proposed location of the BSL-3 facility is in 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 LLNL centrally located. 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).

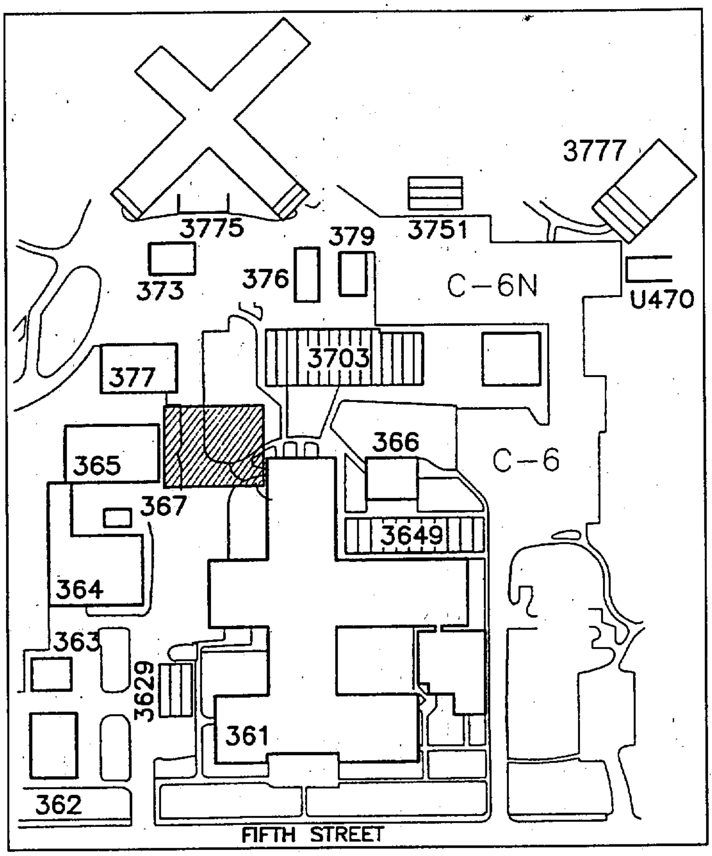

Figure 2-1. Map of the Building 360 Complex Area showing the location of the proposed BSL-3 facility (cross-hatched area)

3. Facility Description

The proposed BSL-3 facility will be a one-story building with about 1,100 ft^2 (102 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. Specifically the seismic design will conform to the 2000 International Building Code, Seismic Use Group III, Criteria 2/3, 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, and equipment will be accessible for cleaning with disinfectants.

Each of the three BSL-3 laboratories will have at least one Class II biological safety cabinet[1] (BSCs) (Figure 3-2). Class II BSCs provide their own airflow, have high efficiency particulate air (HEPA)[2] filtration internally within the cabinet and will be designed to provide personal, environmental, and test material protection. Exhaust air from the BSCs will exit the room via the fixed-duct connection to HEPA filters in the mechanical rooms, then outside the building. 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 B BSCs are designed to operate at a minimum inward flow of 100 linear ft per min (30.5 linear m per min) at the face opening (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,

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

[2] 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.

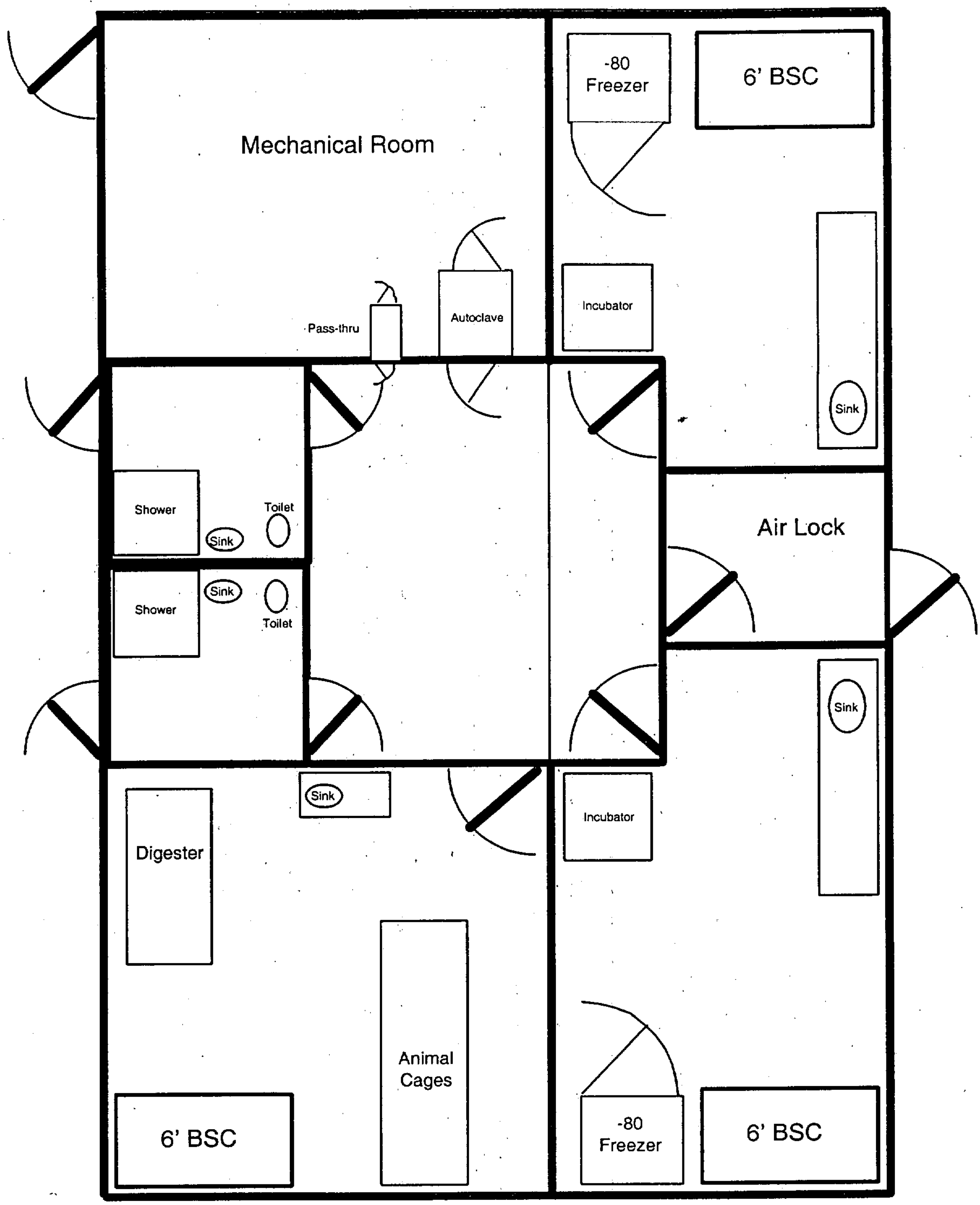

Figure 3-1. Conceptual floor plan for the proposed BSL-3 facility at LLNL (not to scale)

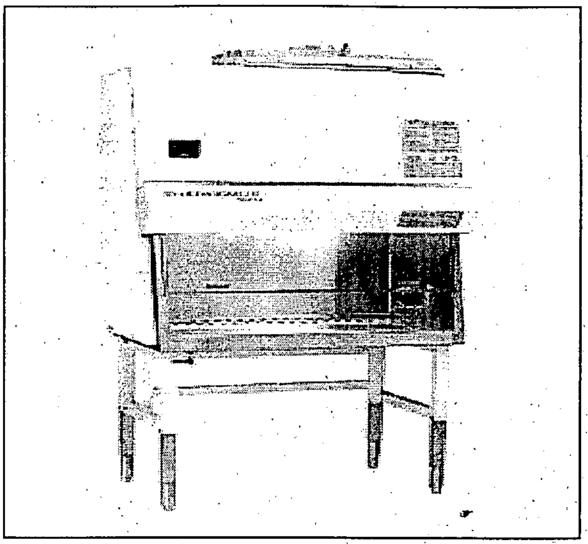

Figure 3-2. Photo of a Baker SterilchemGard III™ - BSC[3]

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 power circuit to maintain airflow through the HEPA filters in the event of power failure to the building.

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 will also contain at least one refrigerator or freezer. Biological materials will be stored either in regular 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.

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 pressurized with HEPA-filtered air, thus reducing both ammonia and carbon dioxide. The negative pressurization will provide

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

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.

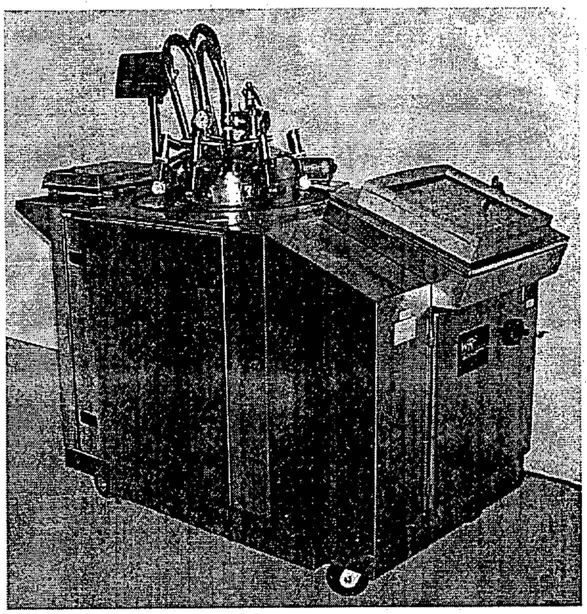

Figure 3-3. Photo of a Waste Reduction Inc. ™ small-capacity tissue digestor[4]

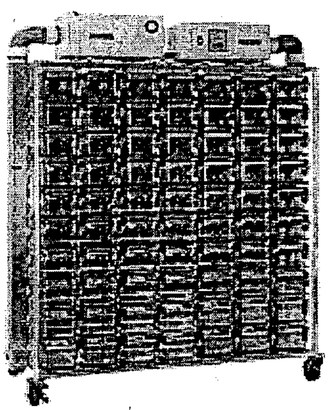

Figure 3-4. Photo of an Allentown Caging Equipment Co. BioContainment Unit for rodents.

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

A maximum of 100 rodents, mainly mice (some rats and possibly guinea pigs), will be used 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[5] 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 a smoke detection system. This system will allow early detection of an incipient stage fire and allow the occupants and the LLNL Fire Department to respond and resolve the situation before the sprinklers operate. This will limit the problem of smoke removal and containment of the sprinkler discharge water. Fire suppression for the BSL-3 facility will be provided by a standard wet-pipe fire sprinkler system. Waterflow alarms will be connected to LLNL's fire alarm monitoring station. 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.

HEPA filter banks in the building exhaust system will filter all room air once-through and provide secondary filtration for exit air from the BSCs. Filter banks could be switched or alternated to permit disinfection and filter replacement. Routine maintenance of the filter banks, including replacement of the filters, will be conducted by certified technicians. 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 laboratories areas with no recirculation from the BSL laboratories to other areas of the building. 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

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

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 60 kilowatts (kW); the building will be attached to an adjacent building that has a diesel generator sized to supply laboratories with electric power in the event of a power failure from the supply grid system. In the event of a power outage, the generator will immediately 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. The HVAC systems will be supplied with backup power from an adjacent facility diesel generator to minimize power supply interruption.

Should 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 entering the BSL-3 laboratories through spigots in the sinks or showerheads will have backflow preventers to protect the potable water distribution system from contamination. Biological cultures could be disposed of in the sinks after undergoing treatment with chemical disinfectants for an appropriate amount of time.

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 are 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 Draft 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, July 2002), 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), 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	Confined gases, compressed gases (nitrogen, air), ruptures, vacuum systems, noise
Chemical	Alcohols (methyl, ethyl, amyl, isopropyl), corrosive chemicals (sodium hydroxide), reactive chemical (hydrogen peroxide, carcinogens (formaldehyde, chloroform), 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).
Cold Sources	Liquid nitrogen, cryogenics

Sample Hazard Source Groups	Examples of Hazard Energy Sources
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 (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:

- Lack of workers ability and attentiveness
- 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 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; more 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.	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; chemical fume hoods; 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 (evacuate facility, shutdown process, 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 devices (x-ray); potential for: (1) severe and permanent radiation injury if exposed to primary beam from x-ray machine; (2) high dose to skin, extremities, or to the lens of eye; (3) exceeding dose standards.	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; seismic events.	Spreading of infectious agents, which may contain 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; 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; sharp controls; rodent pest control program; develop biosafety manual and procedures; trained operators; all laboratory manipulations will be performed in the BSC or enclosed equipment; all biohazardous wastes to be sterilized by autoclaving or digesting method; access control.	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 exposed 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 radioactive materials, propellants, high explosive materials, or open flames. The quantities of hazardous chemicals stored in the facility at any one time will be just a few liters each of chemical disinfectants (such as sodium hypochlorite or potassium hypochlorite) and biologic stabilizers (phenol). Chemicals such as paraformaldehyde will not be stored in the facility but brought in only when required for fumigation (the facility has a minimal amount of storage space). 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 exceeding the lowest value of 40 CFR 302.4 and 40 CFR 355 Reportable Quantities (RQs) or 40 CFR 68.130 and 29 CFR 1910.119 Threshold Quantities (TQs), or 40 CFR 355 Appendix A (List of Extremely Hazardous Substances) Threshold Planning Quantities (TPQs).

All hazardous chemicals used in the proposed facility (such as formaldehyde, chloroform, phenol, ethyl alcohol, isopropyl alcohol, amyl alcohol, and sodium hypochlorite) will not become waste for this facility. Only small quantities of these chemicals (sufficient for operations) will be present in the facility at any time. There will be no chemical storage in the facility. 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 BSL-3 facility 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 may need pH adjustment prior to discharge to the sanitary sewer system if it is too alkaline to meet discharge standards.

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, and viruses 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. While current plans will focus on these biohazards, future programs may require the use of other bacterial or viral infection agents in the BSL-3 category described in Section VII of the 4th edition of the BMBL.

The pathogen library of the proposed BSL-3 facility will consist of up to 25,000 strains, 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 few cells will be transferred to a 50 ml plastic container with growth media and incubated for several days. All work will be performed in a BSC. No bench top work is allowed. 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 amounts of material at risk 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 common industrial hazards/events that are being adequately covered by the OSHA regulations and therefore are not evaluated in this Preliminary Authorization Basis Document. 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, 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 consequences are the same for workers and off-site public. The consequences are categorized as High, Moderate, Low, and 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

	Frequency		
Consequence	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*

	Frequency		
Consequence	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 cut by sharp objects, leaking gas, spill and ignition of flammable liquid, wiring failure)

- 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.

A seismic evaluation of the BSL-3 facility has not been conducted; therefore, it is conservatively assumed that a seismic event will cause some damage to the structure of the facility and some materials (biological in this case) may be released. This event is discussed in Section 4.3.1.

High winds will cause similar but less damage to the facility than a seismic event. Therefore, the seismic event will bound events initiated by high winds (see Section 4.3.1). 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 toppled 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 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 part of routine procedures 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 a wet pipe sprinkler system. Waterflow alarms will be connected to LLNL's fire alarm monitoring station so that designated responders will be notified and Fire Department will respond within 3 minutes.

Accident scenarios involving heat, fire, sunlight or wind would normally be seen to exacerbate or enhance a release or spread of the hazardous or radiological materials, but for the BSL-3 facility these conditions tend to render the infectious agents innocuous. Virulent organisms wouldn't survive a fire or explosion scenario. Similarly, these organisms would be killed by 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. An exception is microbes that undergo sporulation, such as anthrax, that can survive sunlight or wind.

The site of the proposed BSL-3 facility is located near a service road for the BBRP complex of buildings. The scenario 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. The design feature of the facility will be 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; and 8) 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 consequence of the dropping or spilling of a culture container is very similar to those caused by an earthquake or high wind and only BSL-3 workers are exposed to this type of risk.

Two scenarios are evaluated: SD-1 occurred inside the BSC and SD-2 occurred outside the BSC (see Table 4-7). The unmitigated consequence to BSL-3 workers is Moderate for both scenarios. The mitigated frequency or probability of these two scenario is reduced to Unlikely because of preventive actions, such as using unbreakable plasticware instead of glassware; seismic restraint to prevent tipping over of the BSCs and equipment; HEPA filter and 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 clean up easy and to prevent microbial migration; providing respirators to workers; mitigative controls, such as the spillage can be easily sterilized 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. While the mitigated consequence for the SD-1 scenario to BSL-3 workers is Negligible, the mitigated consequence for the SD-2 scenario to BSL-3 workers is Low because no credit is taken for the BSC as one of the controls.

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

For a needle stick or cut from 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 BSL-3 workers are 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 sharp disposal methods, minimizing or eliminating the use of glassware. In addition, intrinsically safe needles (syringes that re-sheathe the needles or needle-less systems) are mostly used in BSL-3 facility. 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 to handle rodents. The BSL-3 facility 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. Even if a laboratory-fed rodent escapes from the ABSL-3 laboratory, its chance of surviving in the natural environment is unlikely.

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 High. 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 and the public are Negligible because of the aforementioned administrative controls and the use of appropriate face/eye and respiratory protection by BSL-3 workers.

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 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 rodent and pest control program is implemented.

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 frequency 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 because there is no standing water around the BSL-3 facility that can be used as a breeding ground for mosquitoes. The unmitigated consequences to BSL-3 worker 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 filter and 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 Low 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 flow rate. The BSCs are also equipped with alarms on low flow conditions. The mitigated consequences to BSL-3 workers and the public are Negligible because of administrative controls.

4.3.8 Centrifuge accident (Scenario CF-1)

A hypothetical centrifuge-accident analysis 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 environmental conditions. 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) (25-50) (inhalation) for Q-fever is 10 organisms. Q-fever is the second most commonly reported laboratory associated-infection (CDC 1999). The CDC and the World Health Organization (WHO) identify Q-fever as a disease most commonly contracted occupationally by those working with livestock handling and processing, and those in laboratory and veterinary practice (CDC 2001b; WHO 1999).

The probability of catastrophic events (due to earthquake) is very low. The low probability of an earthquake capable of rupturing the facility containment, coupled with an additionally low probability of such an event occurring during a daytime activity where microorganism containment is vulnerable, also makes it an unlikely event. The proposed laboratory hypothetical centrifuge accident-release scenario, which itself is very unlikely due to the simultaneous occurrence of several events/conditions that must be combined to produce a release, bounds the catastrophic release scenario. The BSL-3 facility will have only a few operations or activities that will hypothetically place up to 1-liter quantities of material containing infectious organisms at risk at any point in time. These operations or activities will occur at infrequent times and a release to the environment from a catastrophic event will require several simultaneous conditions to coexist: a worker is transferring a quantity of infectious material when the catastrophic event occurs; the containers are not properly sealed; the entire set of containers is dropped; the containers break open; and the catastrophic event simultaneously causes a structural breach in the BSL-3 containment walls. Engineering and procedural controls minimize opportunities for this hypothetical scenario. For example, culture samples are kept in locked freezers or within incubation chambers most of the time and will not become aerosolized in such an event. Therefore, catastrophic events capable of resulting in a substantial release of microorganisms from the confinement of the facility (specifically at greater than infectious dose quantities) are unlikely to occur.

Initial conditions:

- This hypothetical accident scenario occurs at a BSL-3 laboratory in the proposed BSL-3 facility. Details and consequences of this accident scenario are described in the *Final Programmatic Environmental Impact Statement; Biological Defense Research Program* (DA 1989).
- A centrifuge, the key piece of equipment in this scenario, is in a room and not in a BSC.
- The size of the room is 1,080 ft^3 (30,240 liters), but since the room is under negative pressure and airflow is continuous, the volume of the duct from the room leading to the filter is also included (608 ft^3 or 17,024 liters) for a total volume of 1,688 ft^3 (47,264 liters).
- The BSL-3 centrifuge room exhausts air via a HEPA filter system, which is conservatively estimated to have 95% particulate removal efficiency, and air then exits through a roof stack.
- The only microorganism handled in the laboratory is a Rickettsial organism, *Coxiella burnetii,* which causes Q-fever. This organism is hardy and withstands laboratory manipulation with little or no loss in viability, is highly stable in aerosols, and dies at a rate of about one percent per minute over a wide range of humidities (30 to 85 percent relative humidity) and temperature (0 to 30 °C). It is extremely infectious in a small particle aerosol.
- Aerosolization efficiency (the number of infectious doses of *Coxiella burnetii* rendered airborne in a 1-5 micron particle size) was conservatively assumed to be 0.1%.
- A single worker is working with one liter of *Coxiella burnetii* slurry.
- The worker places 165 mL of slurry into each of six 250-mL polypropylene centrifuge tubes AND fails to insert O-rings or tighten the centrifuge caps that are screw-on.

Accident scenario:

The centrifuge is turned on at 10,000 revolutions per minute for 30 minutes.

- All six tubes leak;
  - *Some slurry leaks into the rotor.*
  - *Some slurry leaks into centrifuge compartment.*
  - *Most of the slurry remains in the tubes.*
  - *Most of the slurry that leaked into covered rotor is not aerosolized (99 percent).*
  - *Only a fraction of the slurry that leaked into the centrifuge cabinet is aerosolized and 90 percent of that settles as droplets inside the chamber.*
- A few minutes after the centrifuge stops, the worker opens the centrifuge and reaches in to remove the rotor;
  - *He notices leak.*

- *He gets assistance of two co-workers to help him manage the spill.*
- *Four more workers enter the laboratory not knowing of the accident.*
- *All seven workers may have been exposed to a dose of organisms sufficient to cause infection in unimmunized individuals.*

- The slurry is thixotropic (much like egg white) but due to centrifuging has a reduced viscosity (20 to 25 centipoises) containing about 20 percent dry solids.
- The percent aerosol recovery (aerosol efficiency is defined as the number of infectious doses of *Coxiella burnetii* rendered airborne in a 1- to 5-micron particle size) representing the maximum infectivity for man is determined to conservatively be 0.1 percent.

Result to the Workers:

- The accident immediately produces 9.9×10^9 airborne human infective doses at a 50 percent rate for contracting the disease (HID_{50}) contained in a 3x3x3-foot area above and around the centrifuge (756 liters).
- There are 1.3×10^3 HID_{50} per liter of air in the seconds after the lid was opened.
- The centrifuge operator, excited by the accident, was breathing 15 liters of air per minute and was in the confined aerosol for no more than 5 minutes and could have inhaled about 100,000 HID_{50}.
- The two co-workers coming to the operator's assistance were exposed to only a slightly less dose than the centrifuge operator.
- The other four workers were exposed for less than 1 minute to the aerosol after it was dispersed in the room and are unlikely to have been exposed to more than 100 to 300 HID_{50}.
- Illness lasts from 2 days to 2 weeks and the workers were fully recovered.

Result to the General Population and Surrounding Environment:

The result to the general public was evaluated using a simple Gaussian plume-dispersion air model. In this type of model the downwind distance that a given concentration of microorganisms travels is a direct function of the emission rate and an inverse function of the lateral and vertical dispersion and wind speed. Higher rates of emission result in greater downwind distances for a given concentration. Similarly, lower lateral dispersion, vertical dispersion, or wind speed result in greater downwind concentrations. Downwind concentration is decreased as a consequence of environmental degradation (e.g., from oxygen and ultraviolet light). Modeling assumptions used were:

- The maximum number of aerosolized infectious doses presented to the filters is 9.9×10^5 HID_{50}.
- After passing the 95% efficient filters the accident releases 5×10^4 infectious doses.
- The release is a daytime event since that is when the work is done.

- The breathing rate is 15 L/min.
- The lung retention of respirable particles is determined to be one-half or less of the intake.
- A Pasquill stability class D is used which "is the most stable one that can occur during the day."
- The mixing layer depth is 100 m for stable conditions.
- Lateral and vertical dispersion coefficients used are 9.02 m and 6.5 m, respectively. (Chosen for open level-terrain which is more conservative)
- The wind speed is 4.5 mph.
- The quantity of human infective doses, by simple Gaussian plume dispersion models, is expected to be dissipated to:
  - *Less than 1 HID_{50} in 1 liter (L) of air at a distance of less than 2 m from the stack,*
  - *Less than 0.1 HID_{50} in 1 L of air at a distance of 16 m from the stack, and*
  - *Less than 0.01 HID_{50} in 1 L of air at a distance of 38 m from the stack.*

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 he would contract the illness.

The DA conclusion for its maximum credible event (MCE) showed that the only worker to potentially contract the illness as a consequence of the accident would be the centrifuge worker, and even that individual would likely not become ill.

Under the realistic operating conditions in the proposed BSL-3 facility at LLNL, this hypothetical accident is considered Unlikely according to Table 4-3 because it involves events resulting from two independent failure modes (operator errors for not sealing the centrifuge tubes tightly and the centrifuge rotor's failure).

The unmitigated consequence to BSL-3 workers is Low and the unmitigated consequence to off-site public is Negligible.

By using a containment 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 would be significantly reduced. Aerosolization of the product in a centrifuge can occur when a bottle or tube leaks or ruptures. A containment device can be a secondary gasket to seal the rotor or centrifuge lid or safety cups and canisters that would contain a ruptured tube and/or specimen.

The mitigated consequence to the public of the scenario is further reduced because of the following preventive controls such as the HEPA filter and negative 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 clean up easy and to prevent microbial migration. Mitigated consequences to the BSL-3 workers are Negligible because respirators are provided to workers and other controls such as the spillage can be easily sterilized using sodium hypochlorite solution; the workers can shower and their clothes can be autoclaved to prevent cross-contamination; and the whole room or whole BSL-3 facility can be isolated and sterilized.

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	SSCs: BSC with seismic restraint	Use sealed, unbreakable plasticware, HEPA filter, negative air system, double air lock, sealed surface, PPE, respirators, room sterilization system, 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	Double contain-ment	Use sealed unbreakable plasticware, HEPA filter, negative air system, double air lock, sealed surface, PPE, respirators, room sterilization system, 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			Note
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 intrinsically safe needles	Immunoprophylaxsis, HEPA filter, negative air system, double air lock.	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: High Mitigated: Negligible **Public:** Unmitigated: High 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	Anthrax attacks in Washington, D.C and NYC

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 labora-tory	Infectious agents	Infectious rodents escaped from their cage	Seismic event or operator error	Seismic restraint the animal contain-ment 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, pet & rodent control program, 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			Note
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 requires tested and certified periodically	Negative pressure ventilation system, HEPA filter.	Potential impact to worker **Worker:** Unmitigated: Low Mitigated: Negligible **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Anticipated Mitigated: Unlikely **Public:** Unmitigated: Unlikely Mitigated: Unlikely	**Worker:** Unmitigated: RL III Mitigated: RL IV **Public:** Unmitigated: RL IV Mitigated: RL IV	

Hazard Summary					Controls		Event Rankings			Note
Event	Process Activity	Hazard	Scenario	Cause	Preventive Features	Mitigative Features	Consequence	Frequency	Risk	Note
CF-1	Operator Handles liquid infectious agents	Inhalation of infectious agents	There is leakage from centrifuge tubes and some of the infectious agent is aerosolized	Operator error, defective centrifuge rotor	Use containment centrifuge, safety cup.	HEPA filter, negative air system, double air lock, PPE and respirators, room sterilization system, Immuno-prophylaxsis.	Potential impact to worker **Worker:** Unmitigated: Low Mitigated: Negligible **Public:** Unmitigated: Negligible Mitigated: Negligible	**Worker:** Unmitigated: Unlikely Mitigated: Unlikely **Public:** Unmitigated: Unlikely Mitigated: Unlikely	**Worker:** Unmitigated: RL IV Mitigated: RL IV **Public:** Unmitigated: RL IV Mitigated: RL IV	

5. Controls Selection

The combination of utilizing the guidelines, standards, practices and procedures established by the CDC, NIH, Human Health Services, and public health services together with BSL-3 safety equipment and facility safety barriers significantly reduce 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. Design of PC-2 SSCs will result in limited structural damage from design basis natural phenomena events to ensure minimal interruption to the BSL-3 facility operation and 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 or in some situation, those SSCs can reduce risk rank from higher Risk Level (RL) to a lower one 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) 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 double containers in order to contain a spill if a container leaks or breaks.
c) In the ABSL-3 laboratory, the risk of exposure to the infectious aerosols from infected rodents or their beddings during cage cleanup is Anticipated. The risk of infectious aerosols from infected rodents or their bedding also can be reduced if 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, or other equivalent primary containment systems.
d) Containment centrifuge since it can protect the release of aerosolized infectious agents to the laboratory that reduces the risk of worker contamination.
e) Negative pressure ventilation system because it 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 other 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 filtration on the building exhaust because it provides assurance that infectious agents will not escape from the facility when there is spill outside of the BSC or when rodents escape from the cage.

g) Respirators because operators may inhale infectious aerosols that are generated from infected rodents or their bedding.

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
Biosafety Cabinets (BSCs)[1]	PPE[1]
Double containment of samples when they are outside of BSCs[1]	Sanitation system[1] (structure design of the BSL-3 facility and decontamination/sterilization system)
Particle type cage for rodents[1]	Hands-free or automatically operated sink for hand washing. Eyewash station is readily available in each laboratory.[1]
Containment Centrifuge[1]	Audible alarm for power or ventilation system failure[1]
Negative ventilation systems[1]	Retention tank
HEPA filters[1]	Immunoprophylaxsis [1] (vaccine, antibiotics)
Respirators[1]	Immunization tests[1]
	Access Control[1]
	Autoclaves[1]
	Tissue Digestors[1]
	Physical barriers (bumpers, bollards)

[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 operations 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, 2002a), NAI, having management authority, has delegated this 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) Maintain 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 biological or chemical inventory in the BSL-3 facility or using a pathogen and 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.

For programmatic areas, the failure to meet the intent of a safety program will be considered a violation. An isolated program deficiency would not be considered a violation.

6.3 Minimum Staffing for Safety

Requirements for adequate staffing and minimum staffing for safety are defined in the 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.

Working alone is permitted 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 exceeding the lowest value of 40 CFR 302.4 and 40 CFR 355 Reportable Quantities (RQs) or 40 CFR 68.130 and 29 CFR 1910.119 Threshold Quantities (TQs), or 40 CFR 355 Appendix A (List of Extremely Hazardous Substances) Threshold Planning Quantities (TPQs).

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) are established and implemented to ensure that operations in the BSL-3 facility will be bounded by conditions and assumptions used to performed its safety basis:

a) An FSP shall be prepared and maintained for the BSL-3 facility.
b) *ES&H Manual,* Document 13.6 shall be revised to address the BSL-3 activities. The BSL-3 facility will be operated in accordance with Document 13.6.
c) Specific policies and operating procedures for the BSL-3 facility, such as procedure for the BSCs usage shall be prepared.
d) IBC and IACUC approvals shall be obtained for all activities involving pathogens and rodents in this BSL-3 facility, respectively.
e) Integration Worksheets (IWSs) shall be prepared for each operation in the BSL-3 and ABSL-3 laboratory.
f) BBRP Assessment Plan covering the BSL-3 activities.
g) BBRP Training Plan covering the BSL-3 activities.
h) BBRP Configuration Management Plan covering the BSL-3 activities.
i) BBRP Integrated ES&H Management Plan covering the BSL-3 activities.
j) Register all BSL-3 workers with access to select agents.
k) A permit from CDC for all select agent materials shall be obtained.

l) 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. 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, alarm for power or ventilation system failure.
b) SSCs maintenance records.
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 guidelines and those of the NIH Guidelines for Research Involving Recombinant DNA Molecules. Additionally, before introduction of any bioagent to the BSL-3 facility, requires IBC review and approval.

Part of the administration controls is the institutional oversight committees that are involved with biological research. These include: The Institutional Biosafety Committee (IBC), The Institutional Animal Care and Use Committee (IACUC), and the Institutional Review Board (IRB). All three of these boards are appointed by the Laboratory Director and include members of the community from outside of LLNL. The IBC is chartered by the National Institutes of Health (NIH) and is charged with reviewing all work with 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.

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.

Change control: A safety basis change control program will be developed and implemented for the BSL-3 facility to address planned changes. Management shall authorize planned changes that are outside the approved safety basis. The safety basis document shall be modified to reflect the changes and submitted to DOE. DOE approval for planned 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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BBRP Assessment Plan

BBRP Training Plan

BBRP Configuration Management Plan

BBRP Integrated ES&H Management Plan