Boston Public Health Commission

Biological Laboratory Safety Permit Application

SECTION 7: DISEASE SURVEILLANCE PLAN

Boston University

National Emerging Infectious Diseases Laboratories

March 2014

CONTENTS

APPENDICES:

Boston Public Health Commission

Biological Laboratory Safety Permit Application

SECTION 7: DISEASE SURVEILLANCE PLAN

Boston University

National Emerging Infectious Diseases Laboratories

March 2014

1.0 PURPOSE AND APPLICABILITY

The Boston Public Health Commission's (BPHC) "Guidelines for the Implementation and Enforcement of Boston Public Health Commission's Disease Surveillance and Reporting Regulation" require laboratory registration and a medical surveillance program for research laboratories working with select agents and other high-risk agents that require containment in BSL-3 and BSL-4 facilities. The BPHC compliance guidelines specify practices for ensuring that the BPHC receives timely access to information regarding incidence of disease syndromes, any outbreak or cluster of a disease, and potential exposures to reportable diseases deemed harmful to the public health. The Boston University (BU) and Boston Medical Center's (BMC) Disease Surveillance Plan sets forth the roles and responsibilities of researchers and compliance staff at BU and BMC, as mandated by the BPHC Disease Surveillance and Reporting Regulation.

The Disease Surveillance Plan is an integral component of the BU/BMC's select agent research and occupational health and safety programs. The purpose of the Plan is to prevent laboratory-acquired infections associated with the receipt, storage, handling, and disposal of select agents and high-risk pathogens in BSL-3 and BSL-4 laboratory environments, and to protect workers outside of the BSL-3 and BSL-4 laboratory containment, the environment, and the public from exposure to those agents. The Plan includes policies and provisions for identifying at-risk individuals, maintaining vigilance for the recognition of potential exposures, identifying potentially exposed individuals, and providing a quick and appropriate medical response to an accidental exposure or to symptoms suggestive of a laboratory-acquired infection. The Plan provides the direction, approaches, and responsibilities for maintaining compliance with the Boston Public Health Commission's (BPHC) Disease Surveillance and Reporting Regulation, the Federal

Government's Final Rule on the Possession, Use, and Transfer of Select Agents and Toxins (Select Agent Rule), and the National Institutes of Health's Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines). Adherence to the plan is ensured by the Institutional Biosafety Committee as a requirement for IBC approval and on an ongoing basis through the Research Occupational Health Program. Noncompliance is addressed by the IBC and the Office of Research Compliance and may result in the closing of a research lab. Noncompliance related to post exposure treatment would be addressed by institutional leadership, human resources and possibly public health officials.

An entity required to register under the Select Agent Rule must develop and implement a written biosafety plan that is commensurate with the risk of possessing, using and transferring a select agent. In developing the plan, the entity is charged to consider: 1) the principles of biosafety and guidance described in the Centers and Disease Control and Prevention, and National Institutes of Health publication *Biosafety in Microbiological and Biomedical Laboratories* (BMBL), 5th Edition, including all appendices; and, 2) the NIH Guidelines. The BMBL guidance on occupational health (BMBL-Section VII) serves as the foundation for the comprehensive health and safety management program that will enable the National Emerging Infectious Diseases Laboratories (NEIDL) to operate as a safe and healthy workplace. The BMBL emphasizes that prevention is the most effective strategy for maintaining occupational health; and, that prevention is achievable in a biomedical research setting where the occupational health and safety programs are broadly shared responsibilities involving every group and individual associated with the conduct and support of the research program. At BU/BMC these groups include the Office of the Associate Vice President Research Compliance; Environmental Health and Safety (EHS); the Research Occupational Health Program (ROHP); the BMC emergency care programs; Public Safety; Institutional Biosafety Committee (IBC); and the Institutional Animal Care and Use Committee (IACUC). The principal investigators (PIs), researchers and support staffs who work in the NEIDL all have primary roles in implementing the Disease Surveillance Plan.

The Centers for Disease Control and Prevention and the Boston Public Health Commission Biological Laboratory Regulations require an institution to establish and maintain a health surveillance program for personnel engaged in research involving infectious agents that require BSL-3 or BSL-4 containment in the laboratory. The program must include a system for reporting laboratory accidents, exposures, employee absenteeism, and for the medical surveillance of potential laboratory-associated illnesses. Institutions are required to immediately report spills; accidents that result in overt exposures to organisms containing recombinant DNA molecules are reported to the Biological Safety Officer, Institutional Biosafety Committee, and to the NIH Office of Biotechnology Assessment (OBA).

The development of a successful medical surveillance program must take into consideration the potential hazards to which employees may be exposed and which have the potential to cause adverse health consequences. The surveillance program must evaluate the work processes, tasks performed by individuals, the hazardous agents in use, and the potential exposure that may occur in handling the agents. The outcome of such risk and hazard assessments will determine the overall needs of the individuals with potential for exposure. These needs must then be met through a clearly articulated plan of exposure management that includes clinical care and/or quarantine as well as provision for coverage of associated costs. The Disease Surveillance Program is based on these principals.

2.0 ROLES AND RESPONSIBILITIES

2.1 Environmental Health and Safety (EHS)

Environmental Health and Safety (EHS) is responsible for the management of the NEIDL's Biological Safety Program. This responsibility includes providing safety training for all individuals including staff, students, trainees and contracted employees who have access to a BSL-3 laboratory or BSL-4 suite, individuals who support the facility operations of the NEIDL, and individuals who respond to an exposure incident at the NEIDL. The training program provides specific instructions for recognizing, responding to, and reporting actual and potential exposures. EHS is also responsible for conducting an exposure investigation for each actual or potential exposure incident.

2.2 Director of Research Safety, EHS

The Director of Research Safety serves as the Select Agent Rule Responsible Official (RO) and has responsibility, authority and control to ensure compliance with the DHHS and USDA Rules and Regulations pertaining to the possession, use, and transfer of select agents and toxins. The Responsible Official is responsible for ensuring that BU/BMC immediately notifies CDC or APHIS of a release of a select agent or toxin causing occupational exposure, or a release of a select agent or toxin within the NEIDL containment suites.

2.3 Principal Investigator (PI)

The Principal Investigator (PI) is responsible for the scientific and technical direction of a BSL-3 laboratory or BSL-4 suite research program and for reporting all incidents, accidents, and exposures involving a select agent or other high-risk agent to the Responsible Official and the Occupational Health Officer. This responsibility includes ensuring that all

researchers and technical and support staff under the PI's direction are: 1) aware of hazards associated with the use of select agents and other high risk agents; 2) are proficient in the use of safe laboratory practices and containment equipment and understand how practices and equipment help prevent exposures; 3) are trained to recognize, respond to (including the application of first aid treatments), and report an actual or potential exposure incident to the PI, ROHP and/or EHS; 4) direct workers involved in exposure to ROHP for appropriate medical care; and 5) have a medical assessment by ROHP before starting work or returning to work.

The PI should also collaborate with the IBC, Occupational Health Officer, and the EHS Director of Research Safety in determining the occupational health and disease surveillance requirements that are project-specific, and the medical readiness necessary for individuals to work with the agents. The PI is responsible for reporting any potential for disease caused by a select agent or high-risk pathogen that is stored or handled in the laboratory, and any violation or breach of containment that would likely or did cause a release beyond the work area to the Associate Vice President Research Compliance and the Director of Research Safety/Responsible Official who will then report that violation or breach of containment to the BPHC.

2.4 Associate Vice President Research Compliance (AVPRC)

The Associate Vice President Research Compliance (AVPRC) is responsible for: 1) oversight for the control of hazards in the research laboratories and for ensuring that comprehensive, enterprise-wide programs are in place for the safe handling of all hazardous materials (e.g., biological, chemical, radiological); and, 2) all non-financial research compliance at BU/BMC. The AVPRC has direct functional responsibility for the EHS and biological safety programs, the Institutional Biosafety Committee (IBC), the ROHP, laboratory safety committees, the Institutional Animal Care and Use Committees (IACUC) and laboratory animal use and care programs, the responsible conduct of research, and other research-related oversight committees. In consultation with provosts and deans at the Medical and Charles River campuses, and BMC leadership, the AVPRC appoints committee members. The AVPRC charged the IBC, the Director of Research Safety, the ROHP, and EHS with planning and implementing all institutional programs, including the Disease Surveillance Plan, that ensure the health and safety of all personnel working with biohazardous or infectious agents and recombinant DNA molecules.

The AVPRC serves as the Responsible Official (RO) as described in the BPHC Biological Laboratory Regulations and has responsibility and authority to ensure compliance with the Regulations. The AVPRC also has responsibility for ensuring compliance with the research laboratory reporting requirements specified in BPHC's Disease Surveillance and Reporting Regulation. The AVPRC develops and ensures communication between the IBC, IRB, and IACUC-sponsored research offices, and local, state and federal regulatory agencies regarding the safe conduct of biomedical research and reporting of incidents.

2.5 Occupational Health Officer (OHO) or Designee

The Occupational Health Officer is the Director of the NEIDL Occupational Health Program. The Occupational Health Officer is responsible for the 24 hour a day, 7 day a week, leadership and management of the ROHP at BU/BMC. The Occupational Health Officer may name a designee to perform all duties and functions for planning and operation of the disease surveillance program, including the preparation of project-specific disease surveillance and treatment plans, provided that the designee is also a licensed physician experienced in occupational medicine, a nurse practitioner or registered nurse experienced in occupational health nursing.

The Occupational Health Officer or designee has specific responsibilities for reporting certain findings related to the Disease Surveillance Program to the BPHC. These responsibilities include:

- Reporting findings of a disease surveillance assessment of an individual with access to a BSL-3 or BSL-4 laboratory that was either exposed to a BSL-3 or BSL-4 agent, exhibited symptoms of illness, or was diagnosed with disease. The Occupational Health Officer is responsible for immediately reporting such findings upon discovery of the event, but no later than 24 hours after discovery.

- Reporting the results of a medical evaluation of any BSL-3 or BSL-4 laboratory worker absent from work for two or more consecutive work days where the PI has no other explanation for the absence (such as vacation) and an evaluation indicates that illness may be related to the individual's laboratory work. The Occupational Health Officer is responsible for immediately reporting such findings, but no later than within 24 hours of making that determination.

2.6 BMC Infection Control (IC)

The Associate Director of Infection Control at Boston Medical Center also serves as the Director of Infection Control at NEIDL and acts as liaison between BMC and the NEIDL related to the medical care of those that work in or support the laboratory. The Associate Director of Infection Control coordinates with Occupational and Environmental Medicine at BMC and Research Occupational Health at BU to provide efficient and effective services that address the management of exposures.

2.7 NEIDL Researchers and Technical Staff

NEIDL researchers and technical staff are responsible for consistently following required laboratory practices and containment equipment procedures to prevent an exposure, a potential exposure, or a release of a select agent or high-risk agent. They are responsible for immediately reporting to the PI, Occupational Health Officer or designee, and the Director of Research Safety (Responsible Official [Select Agent Rule]) any accident involving a select agent or high-risk agent that causes an exposure, presents a potential for exposure, or that results in a release of an agent into the BSL-3 laboratory or BSL-4 suite. Researchers and technical staff who are absent from work for two or more consecutive days due to illness must report to the Occupational Health Officer before returning to work. They are also responsible for participating in the annual training courses to keep current on the methods and procedures for recognizing, responding to, applying first aid treatment, and reporting an actual or potential exposure incident.

2.8 NEIDL Facility Operations, Maintenance, and Engineering Staff

The operations, maintenance and engineering staff assigned to the NEIDL are responsible for maintaining the integrity of the facility secondary barriers that are designed to prevent the release of a select agent or high-risk agent from a BSL-3 laboratory or BSL-4 suite into the non-laboratory areas of the NEIDL or the community environment. They are also responsible for reporting to the Associate Vice President Research Compliance and the Director of Research Safety/Responsible Official (Select Agent Rule) any observed facility barrier or operational deficiency that could cause a release into the non-laboratory areas of the NEIDL or the environment.

Upon receipt of the report the following actions should be taken:

- EHS will take immediate action to secure and contain the area.

- The Principal Investigator will take immediate action to suspend the operation until the observed deficiency has been mitigated.
- The Occupational Health Officer will evaluate the deficiency and determine if there was any potential exposure and respond accordingly, including any reporting to the BPHC.
- IBC will initiate its investigation of the reported deficiency according to their procedures

2.9 Healthcare Providers

Healthcare providers will have access to the Boston University Research Occupational Health Program (ROHP) website where agent specific information is available including PPE, containment and treatment information and contact information for ROHP staff. Research staff are issued ROHP Medical Surveillance Cards (Appendix 5) identifying high hazard agents they work with and ROHP contact information. Additionally a select group of BMC healthcare providers will be trained specifically to the BSL-4 Select Agents being researched at the NEIDL in order to provide care if necessary. See 6.2 below.

2.10 BU Emergency Response Staff

Emergency response staff has responsibility for wearing personal protective equipment when responding to an emergency involving an exposure or potential exposure to a select agent or high-risk agent. The staff is also responsible for decontaminating the protective equipment before removal of the equipment at the completion of the response.

2.11 Institutional Biosafety Committee

The Institutional Biosafety Committee (IBC) is responsible for reviewing the occupational health and disease surveillance requirements that are project-specific as part of the IBC's responsibility for evaluating new research projects and ensure that the appropriate medical clearance has been granted to individuals included for approval in such new research projects. The IBC has the responsibility for notifying the BPHC Director of Biological Safety of approved new research projects at least thirty days before granting approval for project initiation.

The IBC is also responsible for the maintenance of the list of biological agents approved for use within the Boston University/Boston Medical Center research community that have the potential to cause laboratory acquired infection (LAI). While LAI is a rare event, the research community continues to take proactive measures to further mitigate risk to

researchers, safety personnel and medical providers. This list was developed at the request of the AVPRC and Agent Information Sheets are developed by representatives of EHS, IBC, ROHP and others. Agent Information Sheets specific to work done at Boston University can be found on the Research Occupational Health Program website at http://www.bu.edu/rohp/agent-information-sheets/agent-information-sheets/

3.0 BASIC CONCEPTS IN THE DEVELOPMENT OF THE NEIDL DISEASE SURVEILLANCE PLAN

The operation of the National Emerging Infectious Diseases Laboratories is based on the principles of a comprehensive health and safety management program built on both engineering features and operational procedures designed to prevent any potential exposure to the individuals working with select agents and other high risk agents, or release to the environment. The NEIDL Disease Surveillance Program is an essential component of the BU/BMC research, environmental health and safety, occupational health, and emergency care management programs. Its purpose is to:

- Implement a preventive care program designed for identifying at risk individuals
- To implement a comprehensive health surveillance program for early identification of potentially exposed individuals (by establishing a baseline medical history and providing appropriate immunizations and testing, reviewing annual medical questionnaires, and participating in the clearance of individuals included in new research projects approved by the IBC)
- To develop a response capacity should an exposure occur.

The NEIDL disease surveillance plan is being built on the existing infrastructure of Environmental Health and Safety, the ROHP, and the Boston Medical Center's emergency care programs. Environmental Health and Safety provides expertise for evaluating and controlling exposure hazards associated with research involving hazardous materials, including select agents and high-risk pathogens. The ROHP currently provides preventive support services to researchers for a variety of routine research related activities, as well as post-exposure support and expertise when needed. The Boston Medical Center – a Level I trauma center – is the primary teaching affiliate for the Boston University School of

Medicine and is the primary medical facility where potentially exposed personnel from BU/BMC are treated.

The development and implementation of a disease surveillance plan requires knowledge of the hazardous characteristics of infectious agents handled in the NEIDL BSL-3 or BSL-4 laboratories; knowledge of work practices that authorized individuals use to prevent exposures when performing protocols and tasks that involve handling select agents and other high risk pathogens; recognition of the types of accidents or events that could cause an exposure of a laboratory worker to an infectious agent, or a release outside of containment; an assessment of the potential for an exposure or release to cause disease in a laboratory worker; and, the capability to provide timely and appropriate medical care following a recognized exposure or in response to symptoms suggestive of a laboratory associated infection. This information enables the Occupational Health Officer to make a determination of medical readiness for an individual to work in a NEIDL BSL-3 or BSL-4 laboratory, and to provide for the medical management of an exposure incident involving a select agent or high-risk pathogen, should such an exposure occur.

The initial scope of research programs in the NEIDL BSL-3 or BSL-4 laboratories will involve several select agents that may include a number of strains of each. The Centers for Disease Control and Prevention, and the National Institutes of Health recommend containment of these agents in BSL-3 or BSL-4 laboratories because they pose a high individual risk of life-threatening disease, and in the case of BSL-4 agents, there are no established prevention or treatment options. Sections 20 and 21 of the BPHC Permit Application addresses specific agents to be researched within NEIDL BSL-3 and BSL-4 laboratories. The federal government may also ask that the NEIDL undertake other research projects involving emerging high-risk pathogens and other select agents as a national priority. Such requests would be addressed through the approvals process in place including approval from the Institutional Biosafety Committee and the Boston Public Health Commission.

Note: No research will involve the use of Variola major virus (Smallpox virus).

The implementation of the Disease Surveillance Plan and its successful outcomes require active collaboration among the NEIDL science program, ROHP, EHS, Animal Facility Operations, and the IBC and IACUC. The Occupational Health Officer or designee, Principal Investigators, Director of Research Safety, and the Director of Animal Facility Operations participate in evaluating each new BSL-3 or BSL-4 research project to: 1) identify possible exposure incidents that may be associated with the research protocol, 2) assess the

potential of each exposure incident to cause disease, and 3) to determine the appropriate first aid measures should the exposure occur. This evaluation occurs prior to project registration with the BPHC, and initiation of work.

The collaboration will aid the Occupational Health Officer in developing plans for preparing: 1) an occupational health assessment of BSL-3 or BSL-4 laboratory workers, and other individuals having access to the laboratory, 2) an exposure management plan for workers who report receiving an actual or potential exposure to a select agent or high risk agent, or having symptoms of infection, and 3) a post-exposure management plan for ensuring the safe provision of emergency medical care for an individual with a confirmed exposure that presents symptoms of disease or is diagnosed with a potential laboratory acquired infection.

This concept for the medical management of potentially exposed personnel from the NEIDL BSL-3 or BSL-4 laboratories is consistent with the same principles that guide the existing Occupational Health programs at BMC. Three elements describe the hierarchy of the ROHP.

- Preventive Management – Measures taken proactively as part of a routine medical surveillance program for the purposes of preventing occupationally acquired disease.

- Exposure Management – Measures taken immediately following a presumptive exposure to reduce the potential for infection and disease, and to support and stabilize the patient until the exposure is confirmed. Successful exposure management requires an aggressive proactive effort in disease surveillance.

- Post Exposure Management – Measures taken after the patient is stabilized, exposure is confirmed, and the patient is placed under longer-term medical care.

4.0 DISEASE PREVENTION (PREVENTIVE MANAGEMENT)

The primary focus of preventive management is to: 1) identify potential occupational hazards and exposure risks that are likely to be associated with the conduct of a proposed research project, 2) select practices and procedures for their control and mitigation, and 3) assess the medical consequences of an exposure. A risk assessment for a proposed research project that involves the use of a select agent or other high-risk pathogen provides the information for developing the

disease prevention measures. Principal investigators have the primary responsibility for performing a risk assessment for each project under their direction that involves the use of a select agent or other high-risk pathogen. The results of a risk assessment will enable the PI to establish necessary safeguards to prevent or reduce the potential for exposures. The identification of hazards and exposure risks will enable the Occupational Health Officer or designee to assess the medical consequences of a potential exposure and prepare an exposure response, health evaluation and treatment plan in advance of project initiation. The Director of Research Safety, Occupational Health Officer or designate, and the Director of Laboratory Animal Facilities when the project involves research animals, assist the PI in developing the project-specific risk assessment and recognizing other hazards that may affect the health and safety of a laboratory employee. A collaborative risk assessment project with these participants is the best way to achieve the disease prevention objective. The outcome may identify requirements for advanced training and mentoring; a need to address a particular health risk in the health assessment, such as the value of an IND vaccine; or a specific physical examination to determine employee fitness to participate in the project, such as a history of immunodeficiency or the physical stamina necessary to wear a positive pressure containment suit.

4.1 Risk Assessment

A risk assessment is the foundation for establishing prudent research practices and habits that enable researchers and technical staff to prevent the occurrence of laboratory-associated disease. A risk assessment is also a valuable tool for determining the necessity for health surveillance of laboratory workers who will be involved in the project. A risk assessment will inform the PI of: 1) hazardous characteristics of an infectious agent or material including the capability of the agent to infect and cause disease in a susceptible human host, the severity of disease, and the availability of preventive measures and effective treatments; 2) laboratory procedures and incidents that can result in laboratory exposure or releases of an agent; 3) training for laboratory workers who may require greater skills in laboratory practices and safe habits; 4) pre-existing health conditions that may increase a worker's susceptibility to infectious disease; 5) a need for health surveillance to maintain fitness to perform certain practices; 6) how to assess an exposure that is more likely to result in disease; 7) first aid response to an exposure; and, 8) reporting requirements to activate the appropriate medical response. The risk assessment will enable the principal investigator to select prudent practices for handling the agent in the conduct of a research project. The risk assessment also provides information of value to occupational health professionals in developing project-specific guidance for disease prevention, surveillance, and medical care.

The principal investigator should follow the latest version of BMBL (currently the 5th edition) risk assessment paradigm in developing a project-specific risk assessment (see Table 1, BMBL 5th Edition Risk Assessment Paradigm). The paradigm involves five steps: 1) review the capability of the agent to cause human disease, the severity of disease, and the availability of preventive measures and effective treatments; 2) identify potential exposure hazards associated with procedures involving the use of the agent; 3) review BSL-3 or BSL-4 practices, containment equipment and facility safeguards described in the BMBL agent summary statement, or one similar to the agent in the absence of an agent summary statement, and consider the need for additional precautions; 4) evaluate the training, technical proficiency, expertise, experience, and good habits, and 5) review the risk assessment with the NEIDL Core Director, Director of Research Safety, Occupational Health Officer, Institutional Biosafety Committee, and the Institutional Animal Care and Use Committee when the research project involves animals. Table 1 summarizes the risk assessment paradigm and includes additional comments that will focus the assessment on critical issues impacting risk.

Table 1. BMBL 5th Edition Risk Assessment Paradigm

Assessment Sequence	Assessment	Comment
Step 1 Disease characterization	▪ Capability of agent to cause disease ▪ Disease severity ▪ Availability of preventive measures ▪ Effective treatments	BSL-4 agents typically cause severe and often fatal disease; there are no effective treatments; protective immunizations are not available
Step 2 Exposure hazard identification	Identify all potential exposure hazards associated with procedures involving agent	**Primary importance for planning occupational health disease surveillance and medical care programs**
Step 3 BSL-4 safe practices and containment requirements	Review BMBL Agent Summary Statement for the agent	Review Statement for a similar agent when a Statement is not available for agent you plan to use Consider need for additional precautions
Step 4 Staff proficiency evaluation	Evaluate training, technical proficiency, expertise, experience, and good habits of all authorized individuals assigned to the laboratory	**Most important indicators of exposure risk**
Step 5 Review assessment with colleagues	▪ NEIDL core director ▪ Director of Laboratory Safety ▪ Occupational Health Officer ▪ Animal care veterinarian	The IBC and IACUC are required to review and approve the risk assessment prior to registering a research project with the BPHC.

The staff proficiency evaluation is as important as the exposure hazard identification for reducing exposure risks. The BSL-3 or BSL-4 Laboratory Core Director, project Principal Investigator, and Director of Research Safety should assess the qualifications of the technical laboratory staff. All authorized users are required to take a series of training courses as a prerequisite for working in a BSL-3 or BSL-4 laboratory suite. The final course

in this series for the research staff is a research practicum. The principal learning objective of the research practicum is to demonstrate proficiency in the use of BSL-4 practices and equipment in the conduct of a planned research protocol.

Table 2, Assessment of Risk Associated with Animal-related Research Involving Select Agents, provides a strategy and guidance for assessing intensity and frequency of exposure hazards. Exposure intensity describes the severity of an exposure hazard and therefore its potential for causing disease. Exposure frequency is an indicator for how often the laboratory worker has contact with a particular exposure hazard. The primary barrier positive pressure containment suits worn by BSL-4 workers provide protection from most exposure hazards related to handling BSL-4 agents and other high-risk pathogens. Nevertheless, there are incidents that could cause a high risk of exposure with subsequent infection. For example, an accidental deep laceration of a researcher's gloved hand during a necropsy procedure involving a nonhuman primate infected with a BSL-4 agent, and a needle stick puncture when inoculating a nonhuman primate with an infectious dose of a BSL-4 agent presents high intensity risk exposures requiring immediate medical attention. Similarly, a researcher carrying out an animal aerosol exposure experiment in BSL-4 cabinet laboratory could accidentally pop out a glove sleeve of the Class III cabinet releasing a highly concentrated infectious aerosol into the laboratory that could cause an aerosol exposure to the researcher. The probability of occurrence is greater for the necropsy and needle puncture exposures than for the aerosol exposure.

The occupational health assessment provides first aid directions for treating the necropsy and puncture wounds. The plan might also address the value of having a second laboratory person present during the necropsy and inoculation procedures to help prevent or mitigate the consequences of these or similar high intensity incidents. It is important to address these types of potential incidents when preparing a project-specific disease surveillance and treatment plan.

Table 2. Assessment of Risk Associated with Animal-related Research Involving BSL-3 and BSL-4 Select Agents [1]

Criterion	Risk Classification	Information Sources
Exposure intensity	High Medium Low	BMBL BSL-4 practices, and primary and secondary barriers; job profile; LASC, LACF, and EHS staff; training and experience of research staff
Exposure frequency	8 h/wk. or more Less than 8 h/wk. No direct contact	Job profile; LASC, LACF, and EHS staffs; training and experience of research staff
Hazards posed by animals	Severe illness Moderate illness Mild illness Illness unlikely	Physical injury; zoonosis, see "Table on Infectious Hazards from Nonhuman Primates"; Institutional veterinarian
Hazards posed by animals experimentally infected with BSL-4 viruses	Severe illness Moderate illness Mild illness Illness unlikely	*Occupational Health and Safety in the Care and Use of Nonhuman Primates*, NRC 2008
Susceptibility of employee	Direct threat[2] Permanent increase Temporary increase	ROHP evaluation, review of personal medical records
Potential incidence or prevalence	High Medium Low	BMBL; published reports[3,4]; LASC, LACF, and OEHS staffs

History of laboratory associated infection or injury	Severe Moderate Mild	BMBL; published reports[3,4]
Regulatory requirements	Required Recommended Judgment permitted	Compliance with Select Agent Rules; NIH Guidelines; OSHA Standards; and BPHC regulations is required

[1] Adapted from: NRC. 1997. *Occupational Health and Safety in the Care and Use of Research Animals*

[2] Reasonable Probability of Substantial Harm. Americans with Disabilities Act of 1990 (PL 101-336)

[3] Harding, A. and K. Byers. 2006. Laboratory Associated Infections, p.53077. In D. Fleming and D. Hunt (ed.) *Biological Safety Principles and Practices*. ASM Press, Washington, D.C.

[4] Rusnak, J., M. Kortepeter, J. Aldis, and E. Boudreau. 2004. Experience in the medical management of potential exposures to agents of bioterrorism on the basis of risk assessment at the USAMRIID. J Occup Environ Med. 46(8):801-11

Table 3, Infectious Hazards from Nonhuman Primates, provides information on zoonotic hazards associated with the handling of Rhesus, Cynomolgus, and African Green monkeys. These species of nonhuman primates are the animals of choice for the scientific programs that researchers will carry out in the NEIDL BSL-4 suites.

Table 3. Infectious Hazards from Nonhuman Primates

Agent Class	Macaques Rhesus and Cynomolgus Monkeys	Quenon African Green Monkey
Viruses	Cercopithecine herpesvirus 1 (B virus) Dengue Ebola Foamy virus Pox viruses Rubeola virus (from human reservoir) Simian retrovirus (Type D) SIV SV40 Yellow fever	B virus (positive titers observed) Rubeola virus (from human reservoir) Foamy virus SIV Pox viruses Yellow fever Dengue
Bacteria	*Burkholderia pseudomallei* *Campylobacter* spp. *Mycobacterium tuberculosis* *Mycobacterium bovis* *Mycobacterium leprae* *Leptospira* spp. *Salmonella* spp. *Shigella* spp.	*Campylobacter* spp. *Leptospira* spp. *Mycobacterium tuberculosis* *Mycobacterium bovis* *Salmonella* spp. *Shigella* spp. *Yersinia pseudotuberculosis* *Yersinia enterocolitica*

	Yersinia pseudotuberculosis *Yersinia enterocolitica*	
Metazoan Parasites	*Hymenolepis nana Oesophagostomum spp.* *Strongyloides spp.* *Trichuris spp.* *Enterobius vermicularis*	*Oesophagostomum spp.* *Strongyloides spp.* *Trichuris spp.*
Protozoan Parasites	*Balantidium coli* *Cryptosporidium spp.* *Entamoeba histolytica* *Giardia intestinalis* *Plasmodium spp.*	*Balantidium coli* *Cryptosporidium spp.* *Entamoeba histolytica* *Giardia intestinalis* *Plasmodium spp.*

Adapted from *Occupational Health and Safety in the Care and Use of Nonhuman Primates*. Institute for Laboratory Animal Research. National Academy of Sciences. 2003.

4.2 Occupational Health Assessment

The Occupational Health Officer or designee will develop a Research Project-specific Disease Surveillance and Treatment Plan (See Appendix 1) that corresponds to the agent hazards and exposure risks identified in the risk assessment. The Plan includes requirements for: 1) initial medical assessment including pre-placement physical examination for all individuals working at the NEIDL (e.g. employees, students, contractors) performing research in the BSL-3 and BSL 4 environment; 2) perform annual health assessment; 3) perform medical assessment for all individuals approved to work in new research projects; 4) post-exposure evaluations that address procedures for immediate response, treatment, and follow-up; 5) illness evaluations for a NEIDL employee having access to a select agent or high-risk agent, or access to materials that contain presumably decontaminated agents and who present with a fever of 100.4° F or higher, with emphasis on infection control procedures; 6) treatment; and, 7) follow-up with either occupational

health or infectious diseases subspecialty clinic as appropriate. Enrollment of an authorized individual in the Disease Surveillance Plan will occur following IBC approval and project registration and approval by the BPHC. ROHP staff will be advised on self monitoring for symptoms after potential exposure to an infectious agent.

Aside from standard staff surveillance through occupational health services at BMC, ROHP will provide additional medical surveillance for its own staff and as required of the BMC staff that are trained to care for patients in the patient isolation unit. This medical surveillance would focus on education regarding and surveillance for symptoms suggesting nosocomial transmission of agent which the researcher was exposed to including agent information sheets and ROHP contact information as it currently does for BSL-3.

4.3 Research Project Plan

The research project plan submitted to the IBC for review and approval needs to address health surveillance requirements that are specific to the possession and use of a listed agent or pathogen. The Principal Investigator (PI) develops the project specific requirements, based on requirements established by the Research Occupational Health Program, in collaboration with the Occupational Health Officer, Responsible Official, IBC, and the Director of Animal Facilities where animals are part of the research protocol. The PI incorporates the health surveillance requirements in the research project plan and submits the plan to the IBC for review and approval. The PI prepares the BPHC registration document after IBC approval of the research project plan and contacts the Associate Vice President Research Compliance (AVP-RC) or designee who will authorize sending the registration document to the BPHC. The BPHC registration form is available online. Registration is the final prerequisite before the PI can initiate the research project.

4.4 Institutional Project Reviews and Approvals

Four institutional oversight committees have responsibility to review and approve research projects where the research activity presents a potential for exposure to hazardous materials. The institutional oversight committees are:

- Institutional Biosafety Committee (IBC). The principal responsibility of the IBC is to review and approve projects using biological materials.
- Institutional Animal Use and Care Committee (IACUC). The principal responsibility of the IACUC is to review and approve projects using animal subjects.
- Radiation Safety Committee (RSC). The principal responsibility of the RSC is to review and approve projects using radioactive materials and sources of ionizing and non-ionizing radiation.
- Laboratory Safety Committee (LSC). The principal responsibility of the LSC is to review and approve projects for hazardous chemicals safety and other laboratory hazards.

All committees have responsibility to review, approve, and monitor:

- Policies and procedures pertaining to research activities at NEIDL
- Research proposals for health and safety
- Potential health effects of the research on employees
- Adherence to project specific disease surveillance plans

4.5 Standard Preventive Management Functions

4.5.1 **Initial Health Questionnaire**

The Initial Health Questionnaire (See Appendix 2) is a risk assessment document that all personnel who work with select agents and high-risk pathogens or animals will complete. The Occupational Health Officer or designee reviews the completed questionnaires and determines what preventive measures, such as vaccinations, respiratory protection, and testing (ROHP is not supportive of utilizing serum banking) might be protective for the individual based on the

laboratory work assignments for the individual. The completed questionnaire may also indicate a need for further evaluation. BSL-3 and BSL-4 authorized users are required to complete the Medical Surveillance Questionnaire annually.

4.5.2 Pre-employment Pathogen Specific Counseling

The Occupational Health Officer or designee reviews the risks associated with the particular pathogen which the personnel will work with. During this session, potential routes of exposure, first aid management after exposures and signs and symptoms of concern are re iterated with the personnel.

4.5.3 Physical Examination

A physical examination is provided for all individuals (e.g. employees, students, contractors) who work in or require access to the NEIDL BSL-3 high and BSL-4 maximum containment suites.

4.5.4 Respiratory Protection

EHS establishes requirements for use of respiratory protective equipment in the BSL-3 laboratory. EHS also provides training and fit testing for employees who wear respirators to ensure for the safe and proper use of this personnel protective equipment. Fit testing is performed annually or as needed in the event of a change in the individual's physical or health status that could affect the proper fit of the respirator. In addition, the employees are required to complete the OSHA Respiratory Medical Evaluation Questionnaire (Appendix 4) before authorization to use respiratory protective equipment and must be completed annually. The form is reviewed by the Research Occupational Health Program.

The Occupational Health Officer or designee reviews the medical evaluation questionnaires and determines if the individuals are capable of working with respiratory protection. Persons not approved for work with a respirator will not be allowed to have access to a BSL-4 suite.

4.5.5 Serum Banking

Traditionally, the purpose of banking baseline serum from employees has been to provide assistance with clinical diagnosis and/or treatment in the event of an occupational exposure. However, there has been a national debate on the utility

of serum banking and the consensus is that it is of limited value. When indicated by the Occupational Health Officer, a serum sample will be drawn from NEIDL BSL-3 or BSL-4 employees who present with a potential or confirmed exposure and stored for further analysis depending on the course of infection and/or disease.

4.5.6 Tuberculosis (TB) Testing

TST is the preferred TB test for any employee. Employees who have had BCG vaccine or BCG used as part of a cancer treatment regimen may also have a follow-up Interferon Gamma Release Assay (IGRA). Immunization-Vaccination

Currently there are no FDA approved vaccines for the BSL-4 select agents that will be used in the NEIDL. There are a number of experimental vaccines offered under an IND for a limited number of such agents. ROHP will conduct a risk assessment and determine availability before recommending use of an IND vaccine. IND use is not mandatory and the exposed individuals have the option to accept or decline any such offers. Researchers working with TB will receive an annual tuberculin skin test or interferon gamma release assay test. Immunizations for measles, mumps, rubella, varicella, hepatitis B, influenza, tetanus and pneumonia are also offered. Immunizations against influenza and pneumonia are also recommended so that they may to help to distinguish flu-like symptoms from possible exposures to a select agent when body temperatures rise above 100.4° F.

TB testing and surveillance may be required for certain at-risk employees who work with non-human primates or Mycobacterium tuberculosis in the NEIDL. For those researchers TST will be the preferred method for screening for latent tuberculosis. IGRA will be used in testing persons who have received BCG either as a vaccine or cancer therapy. If an individual tests positive using a TST or Interferon Gamma Release Assay, the person needs a follow-up clinic evaluation including history, physical exam, chest x-ray, and discussion about treatment. In those already documented to have evidence of infection (positive TST or IGRA) if no written documentation of follow-up as above, they need such follow-up. In those without prior evidence of infection, TST or IGRA (preferably TST) must be done, and if positive, follow-up as above.

4.5.7 **Hearing Conservation**

The NEIDL BSL-3 and BSL-4 laboratory environments generally do not have noise levels requiring a hearing conservation program. The health assessments, however, may identify a person with hearing loss. A medical evaluation will determine whether the loss is too severe for work in the BSL-3 laboratory or BSL-4 suite, or whether the individual could work with certain restrictions or periodic re-examinations.

4.5.8 **Medical Alert Card**

All NEIDL authorized individuals carry Medical Alert Cards (See Appendix 5) that provide succinct medical alert information for each agent the individual uses or may be exposed to within the BSL-3 laboratory or BSL-4 suite. The card directs the worker to contact ROHP immediately for guidance. When the person seeks medical care for an exposure, or symptoms suggestive of an infection with a BSL-3 or BSL-4 agent, or other high-risk pathogen, the individual would present the card upon arrival at the BMC Emergency Department (ED), or other location at which they are seeking medical attention. The card gives information on the symptoms associated with the agent infection and directs the initial caregiver on how to contact the ROHP for guidance.

4.6 Patient Privacy Requirements

The Preventive Management program determines the medical requirements for individuals who work in a BSL-3 or BSL-4 facility and establishes health restrictions and periodic re-examinations when they are required. The BSL-3 and BSL-4 authorized users will be required to complete a new Medical Surveillance Questionnaire annually, and when there are: 1) new hazards introduced to the BSL-3 or BSL-4 laboratory suite that might impact medical surveillance requirements; and, 2) changes in an employee's health status that may impact his or her ability to work under the approved conditions.

Patient confidentiality and privacy requirements apply to all results derived from the medical assessments and examinations. Access to the results of all assessments and examinations are strictly controlled and subject to patient privacy records requirements. ROHP will only notify EHS using the following phrases:

- Cleared to work

- Cleared to work with restrictions (list specific restrictions)
- Not cleared to work

5.0 DISEASE SURVEILLANCE (EXPOSURE MANAGEMENT)

Exposure Management refers to the component of the program that is engaged in the immediate management of any presumptive or actual exposure. The principal challenges for exposure management are: 1) to provide urgent medical care (e.g., cuts, bruises) for the individual; 2) to stabilize the patient; 3) to assess the potential that the incident involved an exposure; 4) to provide prophylaxis if available and appropriate; and, 5) to prepare the patient and facility for the post-exposure management phase.

5.1 Preparedness

A major component of the NEIDL Disease Surveillance Program is its preparedness for dealing with emergencies as they occur. The existing programs at BU/BMC are well established, practiced and routinely updated to ensure they are current. The commitment to preparedness comes from BMC experience as a Level I trauma center with existing management plans for the receipt and treatment of patients who may have been exposed to biological agents or have infectious diseases. BMC prepares for emergencies based on Hazard Vulnerability Analysis that is reviewed annually and identifies the categories of emergencies on which planning should be focused. Epidemic illness, mass casualty, and utility failures rank highest in BMC's vulnerability analysis. The detailed plans for managing emergency incidents are the result of this approach.

BMC manages emergencies using an Incident Command System that coordinates emergency response activities at BMC. In addition, all Boston Hospitals participate in regional planning for emergencies and have similar Incident Command Systems to enable inter-operability of emergency operations and communications. BMC focuses training and preparing front-line employees to ensure they are ready and able to perform their tasks when dealing with incoming emergencies. Staff preparations for managing contagious or epidemic illness occur on several levels.

5.1.1 **Requirements for BMC Managers**

BMC managers are expected to be familiar with the hospital emergency plans and coordinate their departmental response according to those plans. This

responsibility includes both high-risk events with limited casualty numbers, and large scale events.

5.1.2 Requirements for BMC Staff

BMC staff complete annual safety training and a competency exam that includes infection control. BMC screens and offers immunizations for measles, mumps, rubella, varicella, and hepatitis B, when appropriate, to all staff members. BMC offers influenza vaccines to all staff members annually. Each clinical and support staff member is fit-tested for an N-95 mask and offered immunization against pertussis.

A High-risk Airway Procedures Team consists of staff members who have completed the Powered Air Purifying Respirators and PPE training for anesthesia residents and attending physicians. Training is expanded to Respiratory Care personnel and ICU nurses and physicians.

All emergency responders in the Emergency Department, Public Safety, and Facilities Management are trained and approved to wear Powered Air Purifying Respirators.

The emergency response plans address just-in-time training to provide information and direction for infection control and the use of protective equipment to the staffing pool.

More information on the management of emergencies, the composition of emergency response teams and the training and drills associated with preparedness involving both internal and external responders is included in BPHC Permit Section 8 – Comprehensive Emergency Management Plan.

Training plans related to the care of an individual exposed or potentially exposed in BSL-4 are described in section 7 below.

5.2 Exposure Response

All BSL-4 laboratories and BSL-3 laboratories using Select Agents will work under two-person guidance as defined in the BU Personnel Suitability and Reliability Policy (attached).

A BSL-3 laboratory worker, who experiences a non-emergency incident involving a potential exposure such as a puncture wound with a needle, is trained to follow the standard decontamination exit procedures from the laboratory including removing the agent specific personal protective equipment, immediately initiate first aid, and then notify the principal investigator of the occurrence. The laboratory worker would then report to the ROHP for further evaluation and care.

A worker with a similar incident in the BSL4 suite will undergo a similar procedure of decontamination, alert ROHP or the Control Center. ROHP has 24/7 call number and all NEIDL calls will be forwarded to OHO, who will activate the communication protocol outlined below. The BU Emergency Response Team will respond to all emergency incidents requiring medical care that occur within the bio-containment facility. The team will move the individual from the containment area to a designated exit airlock for decontaminating the outer surfaces of the individual's positive pressure suit or agent specific personal protective equipment. The team will move the individual to a space outside of the bio-containment area and immediately provide first aid following Standard Precautions. The team then prepares the patient for transport to BMC.

While the worker is receiving or administering first aid at NEIDL, a communication protocol will alert EHS, ROHP, BPHC, the PI and the BMC response team including an on call infectious diseases attending physician, BMC disaster coordinator, and the nursing coordinator in charge of the patient isolation unit. If a decision is made to admit the patient, the nursing coordinator and ID physician on call will activate the patient isolation unit and call in additional staff for care. Conversely, a researcher who has had a potential exposure to an infectious agent may be escorted home and placed on guided fever watch. If the injury or event poses immediate health risks, the assigned emergency department attending will be included. These decisions will be made by the ROHP official, ID attending physician on call, associated PI, and BMC disaster coordinator in coordination with the local public health departments where the person resides.

The BU Emergency Response Team includes the BSL-3 and BSL-4 research teams, public safety and environmental health and safety staff and is qualified by HAZWOPER training and certified for these tasks.

5.3 Transport of Potentially Exposed Individuals

An incident within a BSL-3 or BSL-4 laboratory that requires transport of a potentially exposed individual to the hospital for medical care will require the exit decontamination of

the suit before removing the individual from the laboratory. This procedure destroys external contamination of the suit that could pose a hazard to the urgent medical caregivers. There remains a hypothetical presence of the agent in the patient from a potential inhalation risk or from an accidental subcutaneous exposure incident. For this reason, the transport of individuals from the NEIDL facility to the BMC for clinical care will fall under the broad categories of Urgent Medical Care and Internally Contaminated.

5.3.1 Urgent Medical Care

This category includes individuals who have suffered a heart attack; have severe wounds that are bleeding; sustained or suspected of having sustained fractured bones; dislocated joints, etc., and are in need of immediate medical care after removal from the BSL-3 laboratory or BSL-4 suite. In this case, an infectious diseases exposure is not suspected.

5.3.2 Internally Contaminated

This category includes individuals who either have or are suspected of having internal contamination from inhalation, mucosal, or subcutaneous exposure, but have not sustained injuries requiring urgent or immediate medical care and who are fully ambulatory.

5.3.3 Rapid Evaluation and Assessment of Exposure Risk

BU Emergency responders will establish an immediate primary and secondary perimeter to isolate the individual and to remove the external clothing. The Emergency Responder will perform a rapid evaluation of the incident to determine if there is a potential for the presence of contamination on the individual (e.g., face, body, hair, inner garments worn under the positive-pressure suits). The assessment would take into consideration the nature and type of incident (e.g., slip or fall verses an explosion); integrity of the positive-pressure suit; location of the incident; type, volume and the nature of agent used (e.g., few milliliters of liquid versus. aerosols).

Based on the assessment, the Emergency Responder will determine: 1) if additional decontamination is needed before transporting the patient; 2) what information they need to provide to the BMC Emergency Department; and, 3) if

the need for urgent care requires immediate transport to the BMC Emergency Department with instructions for isolating the patient and suggestions for increasing personal protection for caregivers.

5.4 Transport of an Unconscious or Injured Individual from a BSL-3 Laboratory

An individual assigned to work in a BSL-3 laboratory who experiences an non-emergency incident involving a potential exposure, such as a puncture wound with a presumably non-contaminated needle, is trained to follow the standard procedure for exiting the BSL-3 laboratory, which includes removal of all PPE. If it becomes necessary to remove an unconscious or otherwise seriously injured individual from a BSL-3 laboratory, laboratory personnel are trained to stabilize the individual; dial the Control Center and report the nature of the incident; use the red extraction vehicle to move the individual to the ante-room entrance; surface decontaminate and remove the individual's PPE; and move the individual into the ante-room to await the arrival of first responders, for treatment, and, if necessary, transport to clinical facilities. In the event of a life threatening emergency first responders will be from the City of Boston and in less acute events response will be from an ambulance service or the NEIDL Emergency Response Team.

5.5 Transport of an Unconscious or Injured Individual from a BSL-4 Laboratory

All NEIDL BSL4 workers work under two-person guidance as defined in the BU Personnel Suitability and Reliability Policy (attached) as a precautionary measure for immediate response. An individual assigned to work in a BSL-4 laboratory who experiences a non-emergency incident involving a potential exposure is again trained to follow standard procedure for exiting BSL4 laboratory and initiate a response as outlined above in section 5.2. Even with a potential exposure to a BSL4 agent, this laboratory worker is not considered infectious at this juncture. However, all BSL4 laboratory workers with no emergent exposures who may require inpatient observation will be transported via public safety to a receiving area at BMC, accompanied by the BMC Response Team, to be led to the patient isolation unit. These workers will be received at the ambulance bay adjacent to the BMC Emergency Department (ED) and will not be brought through the ED.

If it becomes necessary to remove an unconscious or otherwise seriously injured individual from a BSL-4 laboratory, laboratory personnel are trained to stabilize the individual; dial the Control Center and report the nature of the incident; use the red extraction vehicle to move the individual to the ante-room entrance; surface decontaminate and remove the individual's PPE; and move the individual into the ante-room to await the arrival of first

responders, for treatment, and, if necessary, transport to clinical facilities. In the event of a life threatening emergency first responders will be from the City of Boston and in less acute events response will be from an ambulance service or the NEIDL Emergency Response Team. In these cases, patient will receive emergent care at the BMC Emergency Department. City of Boston's first responders have received training and will continue to receive regarding entry and transport of patients from NEIDL.

5.6 Sample Collection and Specimen Handling

Emergency management care requires the collection of samples from the exposed individual. The samples may include articles of clothing removed from the individual, nasal or other swabs taken, fecal or urine samples. All samples should be placed in double plastic bags and clearly labeled as to their source or location on the body.

For a patient with potential exposure to BSL4 agent who has been admitted to the patient isolation unit, an attempt will be made to perform a majority of the clinical laboratory diagnostics on POC tests in that unit. These POC's will include arterial blood gases, comprehensive metabolic panel including electrolytes and liver function tests, HgB. For additional tests, a protocol will be employed by which the specimen is transported with escort and via Department of Transportation approved carrier from the patient isolation unit to the NEIDL core laboratories for either on site evaluation or shipping to an outside laboratory such as CDC. Phlebotomy will be performed by trained nursing or physician staff who are part of the response team selected at BMC.

It is always important to alert laboratory staff to the nature of the specimens prior to sending the specimens to the clinical laboratory. Specimens should remain in the custody of designated laboratory personnel until testing is completed. Due to the potential risks associated with handling infectious materials, laboratory testing should be limited to the minimum necessary for essential diagnostic evaluation and patient care.

5.7 Reporting Exposures

Section 2, Roles and Responsibilities, addresses reporting responsibilities for persons who are exposed to a select agent or high-risk pathogen, and for senior research leaders and institutional officials who manage safety, health and medical care functions. Table 5, Reporting Requirements for Occupational Exposure or Release of a BSL-3 or BSL-4 Agent, summarizes those responsibilities and the required reporting actions.

Table 5. Reporting Requirements for Occupational Exposure or Release of a BSL-3 or BSL-4 Agent

Responsible Person for Reporting	Occupational Exposure, Release, or Symptoms of Disease Event	Requirement for Reporting to BU Official	Requirement for Reporting to BPHC	Requirement for Reporting to CDC/APHIS
Laboratory Researcher	Contaminated sharp injury; bite or scratch from infected animal; inhalation or mucosal exposure to infectious aerosols or droplets; procedure breach resulting in potential or actual exposure or release; absence from work due to illness for two or more days.	Immediately report event to PI, DRS and OHO; Report to OHO prior to returning to work following absence from work or illness	Yes	
Operations and Maintenance Staff	Breach in primary and secondary containment resulting in potential or actual release to the environment; absence from work due to illness for two or more days.	Immediately report breach to the DRS and the AVPRC; Report to OHO prior to returning to work following illness	Yes	
Health Care Providers and BU Emergency Responders	Symptoms of illness associated with a confirmed LAI of a NEIDL employee served by the provider or responder.	Immediately notify the DRS and the AVPRC, and report to the OHO	Yes	
Director of Research Safety (DRS/Select Agent Rule RO)	Occupational exposure, release outside of a primary barrier, or release to the environment of a select agent or an organism containing rDNA molecules.	Informs the AVPRC of incident and reporting actions	Yes	Immediately report: by e-mail, lrsat@cdc.gov upon discovery of a select agent exposure or release; or by phone, 301.496.9838 upon discovery of an rDNA release
Associate Vice President Research Compliance (BPHC RO)	AVPRC is responsible for oversight of the disease surveillance program		Verifies compliance with all reporting requirements	Verifies compliance with all reporting requirements

Occupational Health Officer (OHO) or Designee	Occupational health assessments re: occupational exposure, symptoms of illness, diagnosis of disease, absence from work due to illness	Informs the AVPRC of findings and reporting actions	Report assessment findings by phone 617.534.5611 within 24 hrs. upon completing exposure assessment, or discovery that illness of an absent worker may be occupationally related	In the absence of the DLS report: by e-mail, lrsat@cdc.gov upon discovery of a select agent exposure or release; by phone, 301.496.9838 upon discovery of an rDNA release
Principal Investigator (PI)	PI is responsible for ensuring that workers are trained to recognize, prevent and report exposure incidents	Informs the AVPRC of incident and reporting actions; promptly reports diagnosis of occupational disease, or of an employee absence due to illness for > 2 days to OHO;	In the absence of the OHO, reports diagnosis of disease or release by phone 617.534.5611 within 24 hrs. after discovery	

BPHC defines exposure as meaning “any situation arising from or related to the work operation of an employer where an employee or a community resident may ingest, inhale, absorb through the skin or eyes or otherwise come into contact with any high risk agent.”

5.8 Clinical Safeguards

According to the formal Risk Assessment that was prepared for the NEIDL, the most probable exposures to a laboratory worker in the BSL-3 or BSL-4 laboratory will involve a contaminated needle puncture or a centrifuge accident. These exposures pose minimal risk to caregivers immediately following an exposure and during the early phase of the incubation period for a potential disease. Standard Precautions used when working with human tissue or patients will provide protection during the immediate phase of an emergency where urgent care is provided.

A confirmed or suspected exposure to an individual working with BSL-3 or BSL-4 agents may not be a sufficient reason to quarantine an exposed individual. In the case of BSL4 agent, the US Centers for Disease Control and Prevention (CDC), Interim Guidance for Managing Patients with Suspected Viral Hemorrhagic Fever in U.S. Hospitals (May 19, 2005), states:

> "No viral hemorrhagic fever (VHF) infection has been reported in persons whose contact with an infected person occurred only during the incubation period (i.e., before onset of fever). The incubation period for VHF ranges from 2 days to 3 weeks, depending on the viral agent".

The guidance further states:

> "Persons with percutaneous or mucocutaneous exposures to blood, body fluids, secretions, or excretions from a patient with suspected VHF should immediately wash the affected skin surfaces with soap and water. Mucous membranes (e.g., conjunctiva) should be irrigated with copious amounts of water or eyewash solution. Exposed persons should receive medical evaluation and follow-up care, including fever monitoring twice daily for 21 days after exposure. Consultation with an infectious diseases expert is recommended for exposed persons who develop fever within 21 days of exposure."

Consensus practice at other BSL4 laboratories and medical centers providing support to these facilities is to observe laboratory workers who have been exposed to BSL4 agents in an inpatient setting. Through admission to the patient isolation unit, the laboratory worker is able to receive close monitoring of routine laboratory values and viral PCRs, designed to provide early detection of potential infection. Care in the isolation unit also allows for administration of medical countermeasures where available. BMC patient care protocols

reflect the practices outlined in the "Triage and Management of Accidental Laboratory Exposures to Biosafety Level-3 and -4 Agents" (Biosecurity and Bioterrorism: Biodefense Strategy, Practice, And Science, Volume: 7 Issue 2: July 27, 2009) See summary at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2749272/

However, a decision for isolation or quarantine will require the review and agreement of BPHC in consultation with the NEIDL Core Director, Occupational Health Officer, Director of Research Safety, the attending Physician, and the infectious disease consultant. Similarly, workers returning from unexplained absences due to illness will first be triaged by phone to screen for potentially worrisome infectious symptoms and any possible history of exposure to agents of interest. Worker will either be forwarded to ROHP clinic or other appropriate medical provider, including the Infectious Diseases clinic if symptoms are thought to be infectious but not related to agent in question. If worker has no worrisome history, they will present to ROHP in person prior to clearance to work. If worker has infectious symptoms and there is consensus through discussion with ROHP and ID, local public authorities will be contacted and event will be reported. Patient will be transported via private ambulance to the medical unit at BMC for care. If the patient leaves Boston, the local board of health where the patient resides will provide guidance. Additional guidance regarding patient isolation, contact quarantine, and treatment is presented in Table 6, General Guidelines for Patient Isolation, Contact Quarantine and Treatment Associated with BSL-4 Select Agent Viral Diseases. Decisions related to isolation or quarantine or in the event that the potentially exposed individual refuses hospitalization will be referred to the local board of health where the exposed person resides. If a decision is reached that outpatient isolation or quarantine is required, an appropriate care plan will be developed by the local authority, attending Physician, and ROHP including, but not limited to, the location of the quarantine, arrangements for family members, transportation should the patient become infectious and other necessary services to be provided. Support services or payment for such services mandated by this care plan will be covered by BU unless covered by another payer (medical insurance or worker's compensation)

Table 6. General Guidelines for Patient Isolation, Contact Quarantine and Treatment Associated with BSL-4 Select Agent Viral Diseases

Virus	Patient Isolation	Specific Treatment
Crimean-Congo HF	bloodborne precautions	Supportive care, potentially ribavirin
Ebola	bloodborne precautions; private hospital room away from traffic	Supportive care, potentially monoclonal antibodies against viral targets or vaccine candidates such as rVSV platform vaccine.
Hendra virus	none	Supportive care, potentially monoclonal antibodies
Lassa	bloodborne precautions; private hospital room away from traffic	ribavirin within first 6 days of illness
Marburg	bloodborne precautions; private hospital room away from traffic	Supportive care, potentially monoclonal antibodies
Nipah virus	bloodborne precautions	Supportive care, potentially monoclonal antibodies
Guanarito	bloodborne precautions; strict isolation during acute febrile period; respiratory protection	Supportive care, ribavirin
Junin	bloodborne precautions; strict isolation during acute febrile period; respiratory protection	Supportive care, ribavirin
Machupo	bloodborne precautions; strict isolation during acute febrile period; respiratory protection	Supportive care, ribavirin

Sabia	bloodborne precautions; strict isolation during acute febrile period; respiratory protection	Supportive care, ribavirin
Kyasanur Forest D	bloodborne precautions	Supportive care
Omsk HF	bloodborne precautions	Supportive care
Russian Spring-Summer Encephalitis	bloodborne precautions	Supportive care, ribavirin

6.0 MEDICAL CARE (POST-EXPOSURE MANAGEMENT)

Post-exposure management provides the medical care for long term treatment after the immediate medical emergency has been addressed, the individual has been provided with emergency medical care and stabilized, exposure has been confirmed or is suspected, and the individual is released either from ROHP or the Emergency Department to home with follow up with ROHP and as needed in Clinical Infectious Diseases clinic at BMC. In the case of long term treatment for the exposure to a BSL-4 agent, laboratory workers who are released in good health after inpatient observation will have follow up both at ROHP and at Clinical Infectious Diseases clinic at BMC after the quarantine period is over or after the patient is no longer considered infectious.

6.1 Biological Emergency Plan

BMC has a well-established Biological Emergency Plan that addresses situations where potentially contaminated patients might be arriving at the Medical Center. The Plan addresses four specific Phases (Phases A - D) that range from minor event not impacting routine operations to the full activation of the incident command system that might be declared as a result of response to a widespread known, or suspected, infection due to a biological agent. The Plan includes guidelines for standard hygiene precautions, laboratory specimen precautions, patient placement and movement, quarantine, decontamination, handling of remains and defined roles and responsibilities, PPE, and isolation precautions.

The Occupational Health Officer and the Associate Director of Infection Control, BMC or their designees reach the decision on whether the individual should be treated as an inpatient or outpatient based on the best option for optimal clinical care and infection control. All plans will be subject to approval by BPHC or local authority having jurisdiction. The decision may include a number of other parameters such as:

- Agents involved including incubation period
- Risk of transmission
- Availability of prophylaxis
- Whether the individual lives alone or with others.
- Ability of the individual to care for themselves and follow instructions

- Modes of transportation taken by the individual

If the decision is made to treat the individual as an inpatient, the individual will be hospitalized in the patient isolation unit that is specially designed for patients with exposure to BSL-3 or BSL-4 agents. Inpatient care of researchers exposed to BSL4 agents will be provided by an internal medicine care team under the leadership of an infectious diseases physician, on the Infectious Diseases service at BMC. The care will be administered by a subset of BMC staff who have specifically been trained in protocols relating to serious communicable diseases (see Sections 2.9 and 2.10 above).

The patient isolation unit assigned to care of a researcher with potential exposure or illness from a BSL4 agent will be on the 7W unit of the Menino Pavillion of BMC. Current infrastructure at BMC already provides the facilities necessary for care of patients with highly contagious infections. However, this patient isolation unit would enhance clinical facilities by incorporating some of the engineering and safety measures used in specialized hospital facilities and research containment laboratories specifically designed to minimize nosocomial transmission of highly contagious and hazardous diseases. This unit will consist of two single patient rooms with an ante room and storage space. The unit will be an Infectious Diseases Isolation Unit large enough to store disinfection and some patient care equipment for the duration of the hospitalization. Support space will have space for donning PPE, storage of point of care equipment and hands free sink. The rooms will have double door entries from the hospital corridor and have directional air flow driven by graded negative pressure with the patient room having the greatest negative pressure.

The rooms will be fitted with seamless surface preparations that facilitate topical disinfection of all surfaces. These non-traditional surfaces allow for effective terminal cleaning of the unit. Air exhausted from the room is HEPA filtered before release to the outside via the common hospital ventilation system. There will be 100 % exhaust from these rooms. Each room is equipped with private bathroom facilities. Unit and HVAC system already have an emergency power system.

There will be controlled access to the unit entrance for the security and privacy of researchers/patients and staff involved.

The following medical equipment will be present in isolation unit:

- Personal Protective Equipment including PAPRs will be needed for routine care of patients who are symptomatic.

- Point of Care Tests equipment, which provide at the minimum basic metabolic panel, Hgb, and arterial blood gases.
- Surgical equipment providing capacity to perform minor invasive procedures such as sutures, forceps, surgical scissors and hemostat.
- Basic and Advanced Cardiac Life Support capabilities in the form of a "crash cart" which is either on site or easily accessible.
- Hemodynamic monitoring, telemetry, pulse oximetry equipment.
- Closed mechanical ventilation equipment.
- When there is need, portable digital radiology and ultrasonography will be brought into the room and ascribed as dedicated equipment until terminal cleaning of the room.

BU will cover the cost of necessary inpatient and outpatient medical and other out-of pocket expenses associated with the exposure to the extent such costs are not otherwise covered through medical insurance, worker's compensation coverage, or otherwise.

If a decision is reached that outpatient isolation or quarantine is required, an appropriate care plan will be developed by the local board of health where the person resides, attending Physician, and ROHP including, but not limited to, the location of the quarantine, arrangements for family members, transportation should the patient become infectious and other necessary services to be provided. Support services or payment for such services mandated by this care plan will be covered by BU unless covered by another payer (medical insurance or worker's compensation).

6.2 Healthcare Staff Coverage

A select group of BMC healthcare providers will be trained specifically to respond to potential exposures in the BSL4 suite on campus and work in a patient care isolation unit with design elements supporting the care of patients with highly contagious infectious diseases. This cadre of BMC staff will include:

Physician Staff - A subgroup of the ID physician staff that currently carries the needle stick exposure pager 24/7 will now also provide coverage as back up to research occupational health staff in case of an event in the BSL4 suite. The ID physician carrying this pager will provide the on call support for NEIDL. The physicians on the call pager schedule will receive specialized training in anticipation of this response and will be part of the annual drills. The protocols for response and details regarding training are discussed in detail in section 7.

If a patient is admitted, they will be cared for by one of these trained ID physicians and by the Infectious Diseases team.

Other physician staff in the program will include at least 4 intensivists and 4 emergency medicine attendings. Other subspecialty MDs along with some volunteer surgical attending staff and pathology will receive information regarding the program and if there is need for their services, they will receive ad hoc training. Onsite (in the hospital) coverage by an attending physician who has undergone specific training related to care of individuals exposed to BSL-4 agents will be in place from the time the unit is activated for a BSL-4 incident until the unit is deactivated.

No medical trainees (students, interns, residents) will be part of the clinical team caring for these patients.

Nursing Staff - Nursing staff will be recruited and trained to care for patients on the afore-mentioned unit. At least 6 staff nurses will be trained and available to report to duty. Additionally a nursing coordinator will be assigned to provide nursing oversight of the unit.

Other staff - The other categories of staff required as part of the training program may include: respiratory technicians, laboratory staff, radiology technicians, members of facilities, environmental services and central processing department, security staff, and psychological support.

6.3 Care of Hospitalized Individuals

The specifics of care for each individual is a clinical judgment that will be made by the team health care specialists including the emergency physician, infectious disease specialist, occupational health physician and other specialties as appropriate. In general, the type and extent of care provided will depend on a number of factors such as the severity and nature of any injuries sustained, whether or not an exposure has been confirmed, and the agent involved. The following general recommendations of the *Bioterrorism Readiness Plan: A Template for Healthcare Facilities* (document prepared by APIC Bioterrorism Task Force and CDC Hospital Infections Program Bioterrorism Working Group) will be followed for all cases.

6.3.1 **Isolation Precautions**

All patients in healthcare facilities, including symptomatic patients with suspected or confirmed infectious illnesses, should be managed utilizing a graduated response in precautions. Standard Precautions are designed to reduce transmission from both recognized and unrecognized sources of infection in healthcare facilities, and are recommended for all patients receiving care regardless of their diagnosis or presumed infection status. For certain diseases or syndromes additional precautions may be needed to reduce the likelihood for transmission**.** Policies and practice will follow CDC guidelines on isolation precautions. (http://www.cdc.gov/hicpac/pdf/isolation/isolation2007.pdf).

6.4 Treatment

Treatment decisions are based on factors associated with the exposure, the agent, and a consultation by the Occupational Health Officer, Director of Research Safety, NEIDL Core Director or Principal investigator, and consultant infectious disease specialist. The consultation group should refer to the project-specific Disease Surveillance and Treatment Plan (See Appendix 1) in discussing appropriate treatment strategies.

6.5 Protective Practices

Standard Precautions, including OSHA blood borne pathogens precautions, are mandatory for handling patients presenting with potential or confirmed exposures.

6.5.1 **Hand washing**

Wash hands after touching blood, body fluids, excretions, secretions, or items contaminated by body fluids. Wash hands immediately after gloves are removed, between patient contacts, and as appropriate to avoid transfer of microorganisms to other patients and the environment. Plain or antimicrobial-containing soaps are appropriate for washing hands.

6.5.2 Gloves

Clean, non-sterile gloves are worn when touching blood, body fluids, excretions, secretions, or items contaminated with such body fluids. Clean gloves are put on just before touching mucous membranes and non-intact skin. Gloves are changed between tasks and between procedures on the same patient if contact occurs with contaminated material. Hands are washed promptly after removing gloves and before leaving a patient care area.

6.5.3 Masks/Eye Protection or Face Shields

A mask and eye protection (or face shield) are worn to protect mucous membranes of the eyes, nose, and mouth while performing procedures and patient care activities that may cause splashes of blood, body fluids, excretions, or secretions.

6.5.4 Gowns

A gown is worn to protect skin and prevent soiling of clothing during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, excretions, or secretions. Selection of gowns and gown materials should be suitable for the activity and amount of body fluid likely to be encountered. Soiled gowns are removed promptly and hands are washed to avoid transfer of microorganisms to other patients and environments. The use of other PPE (e.g. masks or PAPR) will evaluated on a case-by-case basis by Infection Control and biosafety experts and provided as necessary.

6.5.5 Facilities and Environmental Disinfection

The patient care unit designated for care of laboratory workers with potential serious communicable diseases at BMC will follow the structural elements such as

air handling and power control as outlined above. Specific protocols will be developed for disposal of infectious waste and disinfection of reusable materials.

6.5.6 Handling of Human Remains

If the patient with confirmed exposure to a BSL-4 agent dies, handling of the body should be minimized. The remains should not be embalmed. Remains should be wrapped in sealed leak-proof material and cremated or buried promptly in a sealed casket. If an autopsy is necessary, the BPHC and CDC will be consulted regarding appropriate precautions. In the event that a patient with a confirmed exposure to a BSL-3 agent dies the remains will be treated consistent with standard practices

7.0 TRAINING

The BSL-3 and BSL-4 Principal Investigators and their research staffs are required to participate in annual laboratory environmental health and safety training courses. The principal focus for this training is on: 1) recognition of potential exposure incidents; 2) a review of exposure incidents that occurred in the previous year, and methods to prevent a reoccurrence; 3) a review of regulatory reporting requirements; 4) a review of emergency procedures and notification requirements; and 5) policy changes and revisions to the BPHC permit documents.

Training related to a subset of BMC staff, and others including private ambulance staff, will include training on an annual basis specifically for the management of potential exposure in BSL-3 or BSL-4 space. A general overview training will be provided to all involved staff including those from private ambulance companies under contract to provide transports. This training will be modeled after the CDC framework for training of laboratory workers in BSL4 suits (http://wwwnc.cdc.gov/eid/article/14/11/08-0741_article.htm) and CDC guidelines for Isolation Precautions (http://www.cdc.gov/hicpac/pdf/isolation/isolation2007.pdf). The general training will be provided by BMC and ROHP physicians as well as BU/BMC emergency response personnel and will include:

- Background expertise regarding general principles of biosafety as well as public health and governmental classification and threat assessment of emerging pathogens.
- Principles of Infection Control surrounding BSL4 agents as described by CDC guidelines.

- Knowledge of occupational health program related to this program as well as training on self monitoring of clinical signs of infection.
- Knowledge of patient transport and incident response protocols in case of an event in BSL4 suite.
- Additional hands-on PPE training in the patient care unit.

Additionally clinical staff will receive hands on training on:

- Use of in-unit point of care tests (which will be maintained and quality checked in accordance with BMC program and per manufacturers recommendations). .
- In-unit room, event based sterilization protocols such as cleanup after spill of bloodily fluids as well as handling of patient clinical specimens. Equipment maintenance for autoclave will be provided by BMC facilities and BU/BMC research safety staff in accordance with 105 CMR 480 addressing annual calibration, quarterly challenges and documentation. .
- Nurses will have additional training to be proficient in ancillary tasks such as EKG, blood draws etc. that would allow the program to limit the introduction of other types of ancillary staff into the situation.
- Provision of advanced life support in heavy PPE gear.

8.0 ANNUAL REVIEW, DRILLS, AND EXERCISES

The emergency response teams conduct drills and exercises annually to maintain their high level of awareness and preparedness. The BSL-3 and BSL-4 research staffs also participate in an annual emergency response drill. The occupational health, infection control and other medical caregivers receive annual briefings reviewing the details of all BSL-3 and BSL-4 research project-specific disease surveillance and treatment plans.

BU and BMC Emergency Management staff will design semi annual drills in accordance with the commitments of the Comprehensive Emergency Management Plan and based on annual Hazard Vulnerability Assessments and will include:

- Activation of communication protocol in setting of event requiring BU and BMC resources.
- Transport of a patient exposed to BSL4 agent.
- Transport of patient with non infectious critical illness.
- Transport of patient exhibiting signs of infection from potential BSL4 agent.

- Activation of patient care unit and gathering of staff and equipment resources.
- Use of PPE or isopod by trained private ambulance service providers
- For clinical staff, in unit provision of patient care, use of POC equipment, and provision of ACLS on a sick patient in PPE.
- On the spot, deactivation of waste and event based sterilization after a spill.
- Practice and protocols related to potential exposure in BMC employee from an infectious patient (who will be followed up at ROHP).

Drills will include all staff that needed to respond to the designed event including but not limited to NEIDL lab workers and operational staff, public safety, City of Boston first responders, Research Occupational Health, Infectious Diseases and other physician staff, nursing and other ancillary staff such as transport, respiratory, radiology, etc.

9.0 DEFINITIONS

Expose or Exposure means any situation arising from or related to the work operation of BU or BMC where an employee or community resident may ingest, inhale, absorb through the skin or eyes, or otherwise come into contact with any high-risk agent.

High–Risk Agent means any select agent, agents in Risk Group (RG) 4 as specified in the National Institute of Health's *Guidelines for Research Involving Recombinant DNA Molecules* and *Biosafety in Microbiological and Biomedical Laboratories*, published by the Centers for Disease Control and Prevention and the National Institutes of Health, and the amendments and rulings made relative thereto from time to time; highly pathogenic avian influenza; SARS Co–V or any other agent identified by the Director of the BPHC's Infectious Disease Bureau to be posted on the BPHC's website at www.bphc.org/labs or appearing on BPHC reporting forms.

Select Agent means microbial and toxic agents listed at 42 CFR 73.4, 42 CFR 73.5, and 9 CFR 121.2 and the rulings made by the CDC and U.S. Department of Agriculture relative thereto as amended from time to time.

10.0 KEY REFERENCES AND RESOURCES

Select Agent Regulations and Resources
http://www.selectagents.gov/selagentRegulation.htm

Barbanel, C., Policy for Evaluation of Potential Laboratory Exposures to Agents of Bioterrorism.

NIH Guidelines for Research Involving Recombinant DNA Molecules
http://oba.od.nih.gov/rdna/nih_guidelines_oba.html

Regulations Governing Laboratories in Boston http://www.bphc.org/labs

Biological Laboratory Regulation (passed September 19, 2006) with accompanying Guidelines.

Disease Surveillance and Reporting Regulation (passed March 30, 2004) with accompanying Guidelines.

Recombinant DNA Technology: Use Regulations (passed March 22, 1994)

Biosafety in Microbiological and Biological Laboratories
http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm

USAMRIID. Medical Management of Biological Casualties Handbook. 6th Edition
http://www.usamriid.army.mil/education/instruct.htm

Wadsworth Center. New York State Department of Health. SARs-Coronaviruses and Highly Pathogenic Influenza Virus. Laboratory Occupational
http://www.wadsworth.org/events/sars/SARSprotocol.html

Kortepeter MG, Martin JW, Rusnak JM, Cieslak TJ, Warfield KL, Anderson EL, et al. Managing potential laboratory exposure to Ebola virus by using a patient biocontainment care unit. Emerg Infect Dis. 2008 Jun

Centers for Disease Control and Prevention. Interim guidance for managing patients with suspected viral hemorrhagic fever in U.S hospitals [cited 2006 Nov 15].
http://www.cdc.gov/ncidod/dhqp/bp_vhf_interimGuidance.html

Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings, June 2007.
http://www.cdc.gov/ncidod/dhqp/pdf/isolation2007.pdf

Risi G, Proposed Algorithm for Evaluation and Management of Possible Exposures to BSL-4 Agents. 1st Revision: May 2008

Appendix 1:

OCCUPATIONAL HEALTH SERVICES

FOR SELECT AGENT AND HIGH-RISK AGENT RESEARCHERS

OUTLINE FOR A PROJECT-SPECIFIC DISEASE SURVEILLANCE AND TREATMENT PLAN

(Select Agent or High-risk Agent Name)

I. Statement of Purpose

- A. Medical Readiness to Work in a BSL-3 or BSL-4 Laboratory
- B. Disease Prevention and Surveillance
- C. Available Medical Care Capability Prior to an Exposure Incident

II. Relevant Occupational Health Procedure Manual Sections

III. Background Information (select agent-specific information)

- A. Disease Occurrence
- B. Mortality Rates
- C. Incubation Period
- D. Presenting Symptoms
- E. Later Symptoms
- F. Diagnostic Procedures
- G. Mode of Transmission
- H. Period of Communicability
- I. Susceptibility
- J. Methods to Prevent Exposures
    1. Protocol-specific laboratory practices

2. Infection control measures

    a. patient management and containment

    b. contacts

IV. Medical Evaluations

A. Enrollment Evaluation

1. Medical history

    a. past illnesses

    b. use of medication associated with immune suppression

    c. other immune compromising conditions

    d. medical contraindications to use of respirators

    e. immunizations

2. Disease surveillance instructions

    a. identifying potential exposures

    b. reporting exposures, injuries and accidents

    c. first aid measures

    d. alerts to early symptoms of infection

    e. disease surveillance resources

B. Annual Evaluation

1. Update medical history

2. Repeat disease surveillance instructions

C. Post Exposure Evaluation

1. Immediate response

    a. exposed worker initiates first aid, contacts PI and contacts ROHP for treatment

    b. ROHP alerts the Occupationa l Health Officer (OHO), Environmental Health & Safety (EHS), the Responsible Official (RO), NEIDL Core

Director, and BMC infectious disease (ID) specialist of the incident for risk consultation as needed. Section 2.6 describes the roles and responsibilities of the ID specialist.

c. The OHO repeats first aid, may obtain a blood sample for future testing, obtains exposure history, updates medical history, and obtains information about potential contacts.

d. Standard precautions used during evaluation.

2. Treatment

a. The decision where quarantine will take place is subject to approval by the local health department where the patient resides. If the exposed worker is not quarantined in the hospital, she or he must stay at home and keep a monitoring log to record his/her temperature and any symptoms twice a day 7 days a week. The worker must contact the PI and/or OHO, or designee to report recorded temperature and any symptoms twice a day. If the worker reports a fever or symptoms, the PI or OHO will work with Infectious Diseases Specialist to report changes to local public health authority and arrange transport via private ambulance service contracted and trained for these purposes to the Patient Isolation Unit at BMC. Patient will be transported in an isopod.

b. Additional treatment may be recommended as appropriate for the individual pathogen and exposure. These treatment options should be available in the research protocol disease surveillance risk assessment

The exposed worker will be instructed to remain at home and to keep a monitoring log to record his/her temperature and symptoms twice a day 7 days a week. The worker must contact the PI and/or OHO (or designee) with the recorded temperatures and any symptoms twice a day. Information on symptoms possibly related to the pathogen involved will be provided to the exposed worker by the ID physician and OHO. If a fever or symptoms are reported, OHO will work with Infectious Diseases Specialist to report changes to local public health authority and arrange transport via private ambulance service contracted and trained for these purposes to the Patient Isolation Unit at BMC. Patient will be transported in an isopod.

NOTE: See Section E for inpatient monitoring specific to BSL-4 exposure.

3. Follow-up

a. Obtain second blood sample for possible testing at a time set by treatment plan.

b. Testing for antibodies when clinically warranted.

D. Illness Evaluation

1. Alert event - fever of 100.4° F or higher and any concurrent symptoms.

2. Immediate response

   a. Exposed worker immediately alerts the Principal Investigator (PI), Occupational Health Officer (OHO), or designee with onset of fever of 100.4° F or greater.

   b. A laboratory worker without knowledge of an exposure also alerts the PI, OHO, or the designee with onset of fever of 100.4° F or greater. PI will review possible exposure incidents that may have occurred in the laboratory during a preceding period equivalent to the incubation period of (select agent).

   c. The designated Research Occupational Health Program (ROHP) physician alerts the OHO, EHS, RO, NEIDL Core Director, and BMC ID specialist of the incident for risk consultation as needed. See Section 2.6

   d. The designated ROHP physician speaks with the ill worker to obtain complete medical, occupational and social histories over the preceding incubation period for the agent.

   e. The designated ROHP physician consults with the OHO, EHS, RO, NEIDL Core Director, and BMC ID specialist to determine need for clinical evaluation of illness.

   f. The designated ROHP physician informs the exposed worker of the course of action and provides instructions for infection control.

3. Physical exam conducted either at the ROHP clinic or BMC.

4. Diagnostic testing

E. Inpatient Treatment or Quarantine

1. Hospitalization at Boston Medical Center

2. Depending on the nature of the case the notification to BPHC will be by OHO or Clinical Infectious Diseases, who will be closely coordinating all aspects of care and reporting throughout the case.. Notifications are required for suspected or confirmed illness, unexplained and unanticipated absence from work for two or more consecutive days, and any significant exposure in the laboratory, regardless of any symptoms or illness.

3. Consideration for identifying, evaluating, monitoring contacts

Note: This is a standard practice under the Research Occupational Health Program regardless of whether the employee works in the NEIDL or other BU or BMC research Laboratory.

F. Follow-up

1. The person will remain hospitalized for the duration of his or her infectious period
2. Will be seen in Infectious Diseases Clinic. Follow-up in outpatient clinic for BSL4 patients will be instituted only for those patients who are no longer infectious.
3. Request a second blood sample six weeks from the onset of symptoms.
4. Confirm illness was result of an occupationally acquired infection.

G. Cost of Care

If a decision is reached that inpatient or outpatient isolation or quarantine is required, an appropriate care plan will be developed by the local authority, attending Physician, and ROHP including, but not limited to, the location of the quarantine, arrangements for family members, transportation should the patient become infectious and other necessary services to be provided. Support services or payment for such services mandated by this care plan will be covered by BU unless covered by another payer (medical insurance or worker's compensation) as described in Section 6.1.

V. Periodic Review and Drills

A. Annual review and revision of the Disease Surveillance and Treatment Plan, or as appropriate based upon relevant scientific discoveries.

B. The Research Occupational Health Program staff receives a briefing reviewing the details of this plan each year.

C. Annual drills to assure ROHP preparedness to respond to an occupational exposure or illness.

VI. References

A. Centers for Disease Control and Prevention. Management of patients with suspected viral hemorrhagic fever: United States. Morbidity and Mortality Weekly Report 1995; 44(25):475-9

B. Interim Guidance for Managing Patients with Suspected Viral Hemorrhagic Fever in U.S. Hospitals. 19 May, 2005 [http://www.cdc.gov/ncidod/dhqp/bp_interimGuidance.html]

C. Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings 2007 [http://www.cdc.gov/ncidod/dhqp/gl_isolation.html]

D. USAMRIID's Medical Management of Biological Casualties Handbook. Sixth Edition. U.S. Army Medical Research Institute of Infectious Diseases. Fort Detrick. Frederick Maryland. April 2005

Acknowledgement: This Outline is a modification of an outline on medical services for select agent researchers developed by the Occupational Medical Service, Division of Occupational Health and Safety, Office of Research Services, NIH.

Appendix 2:

Initial Health Questionnaire for BSL-3 or BSL-4 Medical Surveillance

Initial Health Questionnaire

Appendix 3:

Annual Health Questionnaire for BSL-3 or BSL-4 Medical Surveillance

Annual Health Questionnaire

Appendix 4:

OSHA Respiratory Medical Evaluation Questionnaire

OSHA Respiratory Medical Evaluation Questionnaire

Appendix 5: Medical Alert Card

An illustration of the Medical Surveillance Card issued to laboratory personnel approved to work with high risk biological agents