Boston Public Health Commission

Biological Laboratory Safety Permit Application

# SECTION 9: BSL-3/BSL-4 HAZARD EVALUATION AND RISK MANAGEMENT PLAN

Boston University

National Emerging Infectious Diseases Laboratories

April 2014

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## 1.0 INTRODUCTION

Laboratory hazard evaluation and risk management consists of the examination of potential hazards in laboratory operations that could cause harm to people in the immediate area, in the entire facility, or the external environment. Once these hazards are identified, the facility design, safety equipment, personal protective equipment, and operational procedures are reviewed to ensure that adequate precautions are in place to prevent harm.

In order to determine potential hazards, it is important to establish a comprehensive knowledge of:

- Biological, chemical, and/or physical hazards present in the laboratory;
- The principles of biological, chemical, and physical safety;
- The modes of transmission and routes of exposure for the various infectious agents encountered in the laboratory;
- The procedures performed, the hazards they could introduce, and their mitigation methods (e.g., aerosol production);
- Engineering safety features of the laboratory and the equipment (e.g., ventilation, filter systems, Biosafety Cabinets);
- The nature of medical surveillance needed for each employee's job;
- Institutional requirements under which the laboratory operates (e.g., University, local, state, and federal regulations).

These hazard evaluations, and any risk management and mitigation measures required to eliminate or reduce the hazards, are conducted *prior to the commencement* of any study. Additionally, each amendment to the research protocol undergoes similar evaluation to ensure that the risk management strategies that are in place continue to provide adequate protection.

## 2.0 ROLES AND RESPONSIBILITIES

### 2.1 Associate Vice President for Research Compliance

The Associate Vice President for Research Compliance (AVP-RC) is responsible for: 1) oversight of the control of hazards in the research laboratories and 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 and Boston Medical Center (BMC). The AVP-RC has direct functional responsibility for Environmental Health &Safety (EHS) and the Biosafety Program, the Institutional Biosafety Committee (IBC), laboratory safety committees, the Institutional Animal Care & Use Committee (IACUC) and laboratory animal use and care programs, other research-related oversight committees, and the responsible conduct of research. The AVP-RC reports to the Vice President and Associate Provost for Research who has overall responsibility to Boston University's Research Enterprise.

### 2.2 Responsible Official

The Responsible Official (RO) is an authorized individual with responsibility, authority, and control to ensure compliance with the Centers for Disease Control and Prevention (CDC) and Animal and Plant Health Inspection Services (APHIS) Rules and Regulations pertaining to the possession, use, and transfer of Select Agents and Toxins. The Director of Research Safety is designated to serve as the CDC Select Agent RO. In the event of an incident, the CDC Select Agent RO will immediately inform the AVP-RC, oversee the proper implementation of required procedures, and report the results of these efforts to the CDC and APHIS.

### 2.3 Environmental Health & Safety

Environmental Health & Safety (EHS), in support of the IBC, conducts the hazard assessments and assists the PI to ensure that the mitigation factors initially identified and proposed by the PI appropriately address the hazards associated with the materials and procedures.

### 2.4 Principal Investigator

The Principal Investigator (PI) is an authorized individual approved by the RO. The PI is responsible for the scientific and technical direction of a Select Agent or Toxin project or program. The PI, who is knowledgeable about the agent and procedures to be performed, makes the initial

assessment of risk and submits detailed information to the IBC in an application form, as described in 4.0 Biological Hazard Evaluation of this section. The PI is responsible to ensure that all incidents are reported to the RO and EHS upon discovery.

### 2.5 Core Supervisors

The supervisor for each of the NEIDL scientific cores shall be responsible for daily operations for that core, including oversight of hazard evaluation and risk management.

### 2.6 BSL-4 Laboratory Authorized Individuals

All authorized individuals of BSL-4 laboratories will abide by all requirements set forth by the PI, RO, AVP-RC, and EHS and work according to all appropriate standard operating procedures.

## 3.0 HAZARD EVALUATION AT THE NEIDL

In evaluating the potential hazards of a research project, Environmental Health & Safety (EHS) and the appropriate oversight committees review each protocol for the following hazards:

- biological materials and agents used
- chemicals used in the laboratory
- radiological materials used
- physical hazards
- special hazards, such as the use of animals in research

During the hazards evaluation process, evaluators review each protocol and consider factors such as:

- types of hazards
- mode of transmission for biological agents
- individuals who are potentially at risk, and how
- specific procedures performed and the risks associated with them
- availability of containment equipment and/or personal protective equipment (PPE)
- other laboratory equipment used

- personnel involved in the study and their training and expertise in the procedures
- location of use and its adequacy for the procedures performed
- other factors that might contribute to potential hazards

## 4.0 BIOLOGICAL HAZARD EVALUATIONS

The hazard of a biological material is the set of its inherent properties that give it the potential to cause harm. Assessing risk involves examining the extent of the likelihood of a material causing harm in the actual circumstances of the work. The initial assessment of risk is determined by the Principal Investigator (PI), who is knowledgeable about the agent and procedures to be performed. The initial assessment also includes the safety equipment to be used, personal protective equipment, method for inactivating the agent, and special practices that must be followed. The Institutional Biosafety Committee (IBC) evaluates the hazard and the EHS assessment for BSL-4 laboratories during the review of the research protocols, which includes the PI's risk assessment as part of his or her routine approval of protocols involving the use of biological materials and toxins.

Specifically, the IBC evaluates research projects that use recombinant or synthetic nucleic acid molecules, hazardous biological agents (e.g., viruses, bacteria, fungi, parasites, rickettsia, prion, human and non-human primate primary or cell lines), other potentially infectious materials (e.g., blood, plasma, serum, unfixed tissue, organs, unfixed cells from human and non-human primates, unfixed tissues from sheep), human embryonic stem cells, select biological toxins, inactivated biological samples derived from BSL-3 or higher agents, genetically modified animals, field studies with wild animals and animal tissues inherently infected or which would be experimentally infected with agents that must be studied at BSL-2 or at a higher containment level.

In order to conduct any research project involving the use of biological materials or toxins, the PI must obtain approval from the IBC. The application form requires that the PI provide detailed information on the personnel involved in the study including their training and experience, materials used, procedures performed, equipment used, locations where the study will be conducted, an experimental summary, procedures and manipulations performed, and must identify high risk procedures listed in the application (e.g., tissue grinding, centrifuge use, sonication), chemical agents used, any radioactive materials used, whether or not the study involves the use of animals, labeling of the areas, storage practices, waste disposal procedures, engineering controls in place, etc.

EHS reviews the protocol(s) and visits the laboratory to perform a detailed review of the laboratory and proposed study. This evaluation is based on the following:

- Training and experience of the individuals listed on the protocol;

- Appropriateness of the locations of use for the proposed research (e.g., adequate ventilation, suitability for the BSL of the materials used, adequacy of storage space, availability of sinks, access to autoclaves, etc.);
- Equipment used as part of the research and any potential hazards from the use of such equipment (e.g., centrifuges, cryostats);
- Personal protective equipment that will be used and availability;
- Availability of primary containment device including Biosafety Cabinets;
- Procedures performed in the laboratory and adequacy of the proposed safety precautions proposed in the protocol;
- Proper labeling of signage of storage and usage areas;
- The biosafety level that should be assigned to the facility;
- Waste streams generated and their segregation, storage, and disposal practices;
- Adequacy of chemical safety practices based on the criteria established by the BSL-3 and BSL-4 Chemical Hygiene Plans;
- Other hazards, such as use of cryogenics and compressed gas cylinders, and appropriateness of the safety precautions established;
- Compliance history of the laboratory.

The results of this review are submitted to the IBC and become part of the hazard evaluation or the protocols during their routine meetings.

## 5.0 PROTOCOL REVIEW OUTCOMES

At the conclusion of discussion during its scheduled meeting, the Institutional Biosafety Committee (IBC) determines the outcome of its review, which will be one of the following:

### 5.1 Approved

A protocol that receives full approval requires no (additional) changes or clarifications to comply with IBC policies. Work may commence immediately upon full approval of a protocol. Approval is valid for the study as described in the protocol form for a period of three years from the approval date. PIs must complete a renewal form annually after the first and second year following initial

approval and must submit a new application to continue the work beyond the approved three year time period.

The Boston Public Health Commission (BPHC) requires notification and submission of documents for review upon IBC approval of any new BSL-3 and BSL-4 project at least thirty (30) days before initiating any project experimentation activity requiring the IBC's approval pursuant to section 2.04.b of the Boston Public Health Commission Biological Laboratory Regulations.

### 5.2 Approved Pending

"Approval pending" is used when a protocol requires some relatively minor changes to bring the protocol into compliance with IBC policies but does not need to be re-reviewed. The PI must respond in writing to the particular issue(s), allowing for administrative modification of the application without requiring review by the primary reviewer.

### 5.3 Conditionally Approved

The IBC votes for "conditional approval" when minor changes or clarifications are required to bring the protocol into compliance with IBC policies. The investigator must respond in writing to the IBC's notice of conditional approval outlining proposed modifications needed prior to full approval. The primary reviewer of the protocol will review the response.

### 5.4 Tabled

The IBC votes to "table" a protocol when numerous and/or major changes or clarifications are required to bring the protocol into compliance with Committee policies. A "tabled" protocol must be entirely rewritten by the PI. The modified protocol will be reviewed at the next regular IBC meeting.

### 5.5 Rejected

The IBC may reject a protocol if it contains serious violations of Committee policy and/or if repeated attempts to bring the protocol into compliance with Committee policy have failed.

### 5.6 Deferred

A protocol may be deferred when there is insufficient time at the IBC meeting to conduct a thorough review.

## 6.0 ADDITIONAL REVIEWS

The NEIDL External Advisory Committee is charged with reviewing the strategic direction of the research at the NEIDL, while the NEIDL Internal Advisory Committee is charged with reviewing

specific projects that are under consideration for performing work at the NEIDL. Both committees serve as advisory committees to the NEIDL Director and Associate Directors.

If the protocol involves the use of animals, radioactive materials, sources of radiation (e.g., X-rays, lasers) and/or high-hazard chemicals, additional approvals must be obtained from the Institutional Animal Care and Use Committee (IACUC), Radiation Safety Committee (RSC), and Laboratory Safety Committee (LSC), respectively, as appropriate. These committees follow procedures similar to that of the IBC.

BSL-3 and BSL-4 research protocols that are approved by the IBC are submitted to the BPHC for review and approval. These protocols cannot be initiated until approved by BPHC.

## 7.0 RISK MANAGEMENT

Once the oversight committees have completed their evaluations of the proposed protocol, protocols that are approved can be initiated. EHS conducts a routine review of approved laboratories to verify that the conditions required by the IBC are continuously adhered to by the laboratory personnel.

### 7.1 Engineering

Engineering controls are the primary method of risk management. The design of the NEIDL BSL-3 and BSL-4 laboratories are state of the art with safety features such as High Efficiency Particulate Air (HEPA) filtered air exhaust and redundant power supply systems, as described in Section 1: Introduction of the BPHC's Biological Laboratory Safety Permit Application. The BSL-4 has two HEPA filters in series installed in the exhaust and a HEPA filter in the air supply system.

### 7.2 Operational

EHS works with the laboratory in ensuring that safety is a primary component of all laboratory operational processes. Proposed laboratory procedures are reviewed by both the IBC and EHS and once the protocol is approved, safety processes identified during the review are implemented and maintained. The research protocol also incorporates the training of personnel; appropriate personal protective equipment used for the agents and procedures performed; medical surveillance requirements; safety equipment requirements (e.g., Biosafety Cabinets) and the required quality assurance practices for each; procedures for transport, receipt, storage, and use of agents as necessary; waste treatment and disposal requirements; and any additional requirements that EHS, oversight committees, and the BPHC have requested as a condition of approval.

The conditions set by the IBC upon review of the protocol are sent to the PI and considered as part of the "approval" that must be met and followed. The PI and research personnel must understand and follow the protocol-specific requirements.

### 7.3 Medical Surveillance

The medical surveillance program, which is detailed in Section 7: BSL-3 and BSL-4 Disease Surveillance Plan, meets regulatory standards and establishes minimum guidelines to prevent, monitor, and respond to occupational injuries and exposures. This process requires the screening of newly hired individuals at risk for required baseline pre-placement, occupational and medical history evaluations, vaccinations, and clinical testing (e.g., TB testing) offered by the Research Occupational Health Program (ROHP).

As part of the review process:

- All laboratory staff, including the PI, complete and submit a medical health questionnaire form. The medical evaluation of personnel is based on the agents and procedures performed in the laboratory. The ROHP's clinical staff reviews the Medical Surveillance Form as part of the Hazard Evaluation and Risk Management Plan..
- Newly hired individuals must be screened for required baseline pre-placement, occupational and medical history evaluations, vaccinations, and clinical testing (e.g., TB testing) offered by the ROHP.
- The employee undergoes occupational and medical history review, as well as a physical examination, testing, and vaccination performed by ROHP medical staff, which includes a Nurse Practitioner and a Board Certified Occupational Medicine physician (Occupational Health Officer) responsible for providing Medical Director Program oversight and clinical leadership.
- All staff who work with human materials, including blood, tissue, cells, and bodily fluids, must be offered the hepatitis B vaccine and antibody testing.
- These elements are used to establish a pre-employment baseline of employee health condition and future monitoring of employee health.

At the conclusion of their assessment, ROHP staff provides the results of their findings by informing the IBC if the individual is:

- Cleared to work on the proposed research.
- Cleared to work on the proposed research with specific requirements (e.g., additional PPE).

- Not cleared.

*Note*: HIPAA privacy requirements dictate limits for any clinical information that may be shared with the IBC or other oversight committees.

Individuals are also provided with agent-specific training on: 1) maintaining vigilance for the recognition of potential exposures; 2) recognition of the symptoms associated with disease resulting from exposure to the agents with which they work, and 3) reporting requirements.

### 7.4 Security Risk Assessment

The details of the security risk assessment are provided in Section 12: BSL-3/BSL-4 Security Plan, of the NEIDL Biological Laboratory Safety Permit Application submitted to the BPHC and the Personnel Suitability and Reliability Policy.

- All employees with access to BSL-3 and BSL-4 laboratories using Select Agents and Toxins are subject to the select agent security clearance requirements.
- The security training content for authorized individuals will address: 1) identification of and methods for reporting safety and security emergencies and security breaches; 2) mandatory reporting requirements; 3) security procedures for entering the NEIDL; 4) security procedures for controlling access to Select Agents and Toxins; 5) responsibilities for escorting unauthorized individuals while they are in the NEIDL; 6) inspection of approved packages for all items entering the NEIDL; 7) safeguards that secure electronic inventory records of Select Agents and Toxins and protect the confidentiality of sensitive information; and 8) procedures for responding to a breach of a Select Agent or Toxin.
- The safeguards are based on security risk assessments of the NEIDL and risk assessments for Select Agents that require containment in BSL-3 and BSL-4 laboratories. The security risk assessment includes: 1) a threat and vulnerability analysis; 2) an evaluation of methods to secure Select Agents and Toxins commensurate with their risks to the public health; and 3) a review of approaches to secure critical relevant information.
- NEIDL employees must display their IDs when entering the NEIDL grounds and at all times when on NEIDL grounds. Sharing of BU/BMC IDs with anyone is prohibited.
- Access to the BSL-4 suit rooms and laboratories is limited to authorized individuals who have the appropriate training and clearances, as defined in the Personnel Suitability and Reliability Policy.

- Access control to the NEIDL facility and BSL-4 suit rooms is layered, consisting of a combination of proximity card readers and biometric iris scans. Biometric iris scanners control access to all areas where Select Agents and Toxins are used and stored.
- Access control to the NEIDL facility and BSL-3 and BSL-4 laboratories is layered, consisting of a combination of proximity card readers and biometric iris scans. Biometric iris scanners control access to all areas where select agents and toxins are used and stored.