




Developing a Biosafety Risk Assessment for Biological Select Agents and Toxins (BSAT)

Federal Select Agent Program
Responsible Official Workshop

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42 CFR §73.12 Biosafety

An individual or entity required to register under this part must develop and implement a written biosafety plan that is commensurate with the risk of the select agent or toxin, given its intended use….

The biosafety plan must include the provisions:

1) The hazardous characteristics of each agent or toxin listed on the entity's registration and the biosafety risk associated with laboratory procedures related to the select agent

2) Safeguards in place to protect entity personnel, the public and the environment from exposure to the select agent or toxin

Biological Risk Assessment Factors

Biosafety in Microbiological and Biomedical Laboratories, 5th edition (BMBL) also states that the primary factors to consider in risk assessment and selection of precautions fall into two broad categories:

- agent hazards

- laboratory procedure hazards

The agent summary statements contained in the BMBL identify the primary agent and procedure hazards for specific pathogens and recommend precautions for their control. The BMBL lists three other steps for conducting a biological risk assessment

- BMBL 5th ed. pp 9 and 19

Initial Steps

1. Identify agent hazards and perform an initial assessment of risk.
2. Identify laboratory procedure hazards.

Next Steps

3. Make a determination of the appropriate biosafety level and select additional precautions indicated by the initial risk assessment.
4. Evaluate the proficiencies of staff regarding safe practices and the integrity of safety equipment.
5. Review the risk assessment with biosafety professionals, subject matter experts, and management.

- BMBL 5th ed. p 16 -19

Agent Hazards

- **- Pathogenicity**
- **- Agent stability**
- **- Virulence**
- **- Infective dose**
- **- Host range**
- **- Genetic modification**

- Transmission method/route
- Susceptible hosts
- Prophylaxis availability
- Treatment availability
- Concentration and volume of agent

BMBL pp. 10 - 13

Laboratory Procedure Hazards

- - Aerosol generation
- Spills and splashes on skin and mucous membranes
- Ingestion
- Animal bites and scratches
- Sharps injuries

BMBL pp. 10 - 13

Biological Risk Assessment Timing

Ideally, a laboratory should perform an initial risk assessment before any work is started.

Risk assessments should also be reviewed whenever a change occurs in factors that may significantly impact risk such as:

- new infectious agents, toxins, reagents, new animal species, or models
- new route(s) of administration of biological agents
- new procedures and practices or equipment
- aging of equipment
- a relocation or renovation
- personnel changes

Risk assessments should also be performed after a “near-miss” incident or laboratory-acquired infection.

Laboratory Biosafety and Biosecurity Risk Assessment Technical Guidance Document p 12-13

Biological Risk Assessment Exercise Objective

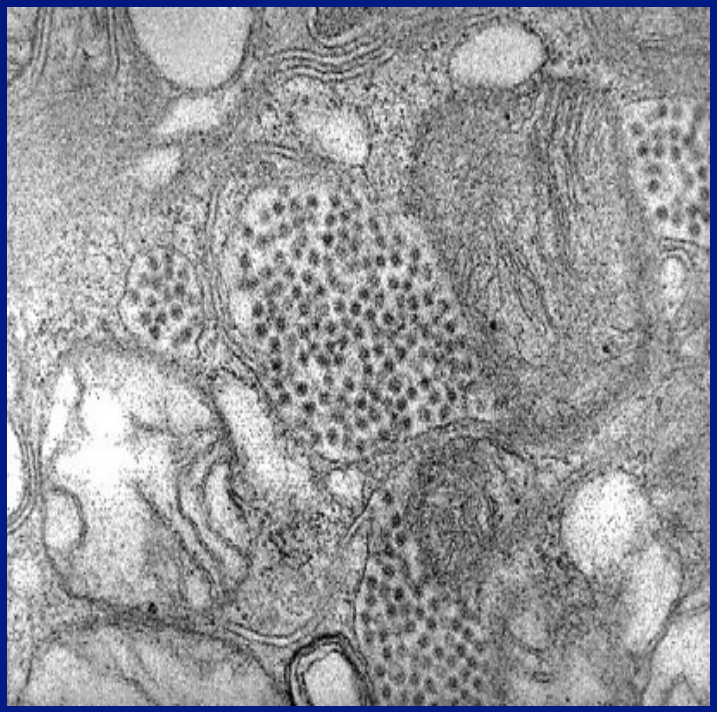
The objective of the exercise is to conduct biological risk assessments after BSAT release events involving Eastern equine encephalitis virus (EEEV).

EEEV Biological Risk Assessment

Eastern equine encephalitis virus (EEEV) is a member of the genus Alphavirus, family Togaviridae. They are small, enveloped viruses with a genome consisting of a single strand of positive-sense RNA. EEEV can cause encephalitis often accompanied by long-term neurological sequelae.

Incubation period ranges from 1-10 days and the duration of acute illness is typically days to weeks depending upon severity of illness. Although not the natural route of transmission, the viruses are highly infectious by the aerosol route and laboratory-acquired infections have been documented.

- BMBL 5th ed. p. 242-244



https://www.cdc.gov/easternequineencephalitis/index.html

EEEV Biological Risk Assessment

Step 1. Identify agent hazards

EEEV can cause encephalitis often accompanied by long-term neurological sequelae. Incubation period ranges from 1-10 days and the duration of acute illness is typically days to weeks depending upon severity of illness.

- BMBL 5th ed. p. 242

EEEV Biological Risk Assessment

Step 2. Identify laboratory procedure hazards

The primary laboratory hazards associated with EEEV are parenteral inoculation, contact of the virus with broken skin or mucus membranes, bites of infected animals or arthropods, or aerosol inhalation.

Alphaviruses may be present in blood, cerebrospinal fluid (CSF), and other tissues (e.g., brain), or throat washings.

Many infections result from procedures involving high virus concentrations and aerosol-generating activities such as centrifugation and mouth pipetting.

Procedures involving animals and mosquitoes also are particularly hazardous.

- BMBL 5th ed. p. 242-243

EEEV Biological Risk Assessment

Step 3. Make a determination of the appropriate biosafety level and select additional precautions indicated by the risk assessment

Diagnostic and research activities involving clinical material, infectious cultures, and infected animals or arthropods should be performed under BSL-3 practices, containment equipment, and facilities.

Due to the high risk of aerosol infection, additional personal protective equipment, including respiratory protection, should be considered for non-immune personnel.

Animal work with EEEV should be performed under ABSL-3 conditions.

- BMBL 5th ed. p. 18 and 243

EEEV Biological Risk Assessment

Step 4. Evaluate the proficiencies of staff regarding safe practices and the integrity of safety equipment

In conducting a risk assessment, the laboratory director or principal investigator should ensure that laboratory workers have acquired the technical proficiency in the use of BSL-3 microbiological practices and safety equipment required for the safe handling of the agent, and have developed good habits that sustain excellence in the performance of those practices.

- BMBL 5th ed. p. 18

EEEV Biological Risk Assessment

Step 5. Review the risk assessment with a biosafety professional, subject matter expert, and the Institutional Biosafety Committee (IBC)

A review of the risk assessment and selected safeguards by knowledgeable individuals is always beneficial and sometimes required by regulatory or funding agencies. Review of potentially high risk protocols by the local IBC should become standard practice. Adopting this step voluntarily will promote the use of safe practices in work with hazardous agents in microbiological and biomedical laboratories.

- BMBL 5th ed. p. 19

Risk Assessment Scenario 1

While working in a BSL-3 laboratory, a technician was bitten by a mouse that had been challenged with a laboratory strain of EEEV. The bite occurred 4 days after the mouse had been challenged with the virus.

Immediately after being bitten, the worker verified that the outer glove was punctured but could see no puncture in the middle puncture-resistant glove. It was concluded that the bite had not punctured the inner and middle gloves and work was continued.

Risk Assessment Scenario 1

After later leaving the laboratory, the gloves were leak tested and pin hole-sized holes were observed in both gloves (inner and middle). The skin had been broken and was bleeding at the site of the bite.

The worker notified supervisors about the bleeding and was directed to inform the Responsible Official (RO) about the incident.

Risk Assessment Scenario 1

Later that day, the worker visited a physician for evaluation. Blood samples were collected and the worker was put on fever and symptom watch.

The worker was also advised to report any symptoms of infection immediately. Samples were collected from the infected animal to evaluate the status of the mouse at the time of the injury.

Risk Assessment Scenario 1

What would you do differently?

The bite injury occurred four days (incubation period between 1-10 days*) after the virus challenge. Should more attention have been given to the post-exposure decontamination of the bite wound immediately after the injury?

Should the worker have left the laboratory immediately and been evaluated and treated by occupational health professionals?

* (BMBL p. 243)

Risk Assessment – Scenario 2

Samples of brain tissue from six horses were sent to a reference laboratory for rabies testing over a five week period. Seven individuals worked with the specimens or were in the laboratory. These workers engaged in aerosol-producing work activities on open benches at BSL-2 wearing only face shields, gloves and laboratory coats.

All samples were negative for rabies.

Risk Assessment Scenario 2

Brain tissue samples from the same six horses were also sent to another reference laboratory for other animal pathogen testing. Workers at this laboratory also engaged in aerosol-producing work activities on open benches at BSL-2

Samples from all six horses were positive for EEEV.

Seven workers were potentially exposed to EEEV at the second reference laboratory.

Risk Assessment Scenario 2

Workers used only face shield, gloves and laboratory coat during open bench work

There was limited availability of biosafety cabinets

The workers at the second reference laboratory had no reason to suspect the presence of EEEV because of a lack of information about this potential risk.

No workers at the either laboratory have developed any illness or symptoms attributable to this event.

Risk Assessment Scenario 2

What would you do differently?

Improve communication between laboratories?

Change procedures to eliminate or limit open bench work with unknowns?

Obtain additional biosafety cabinets?

References

Caskey and Sevilla-Reyes. in laboratory Biorisk Management, p 45 CRC Press 2015.

RC Knudsen. Anthology of Biosafety III. Applications of Principles. Risk assessment for working with Infectious agents in the biological laboratory. pp. 1-10.

Laboratory Biosafety and Biosecurity Risk Assessment Technical Guidance Document.

Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition. Section II—Biological Risk Assessment pp. 9-21

Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition. Section II—Biological Risk Assessment pp 242-244.

Discussion

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