
The Boston University
National Emerging Infectious
Diseases Laboratories
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Finding Cures. Saving Lives.

The Boston University National Emerging Infectious Diseases Laboratories (NEIDL)

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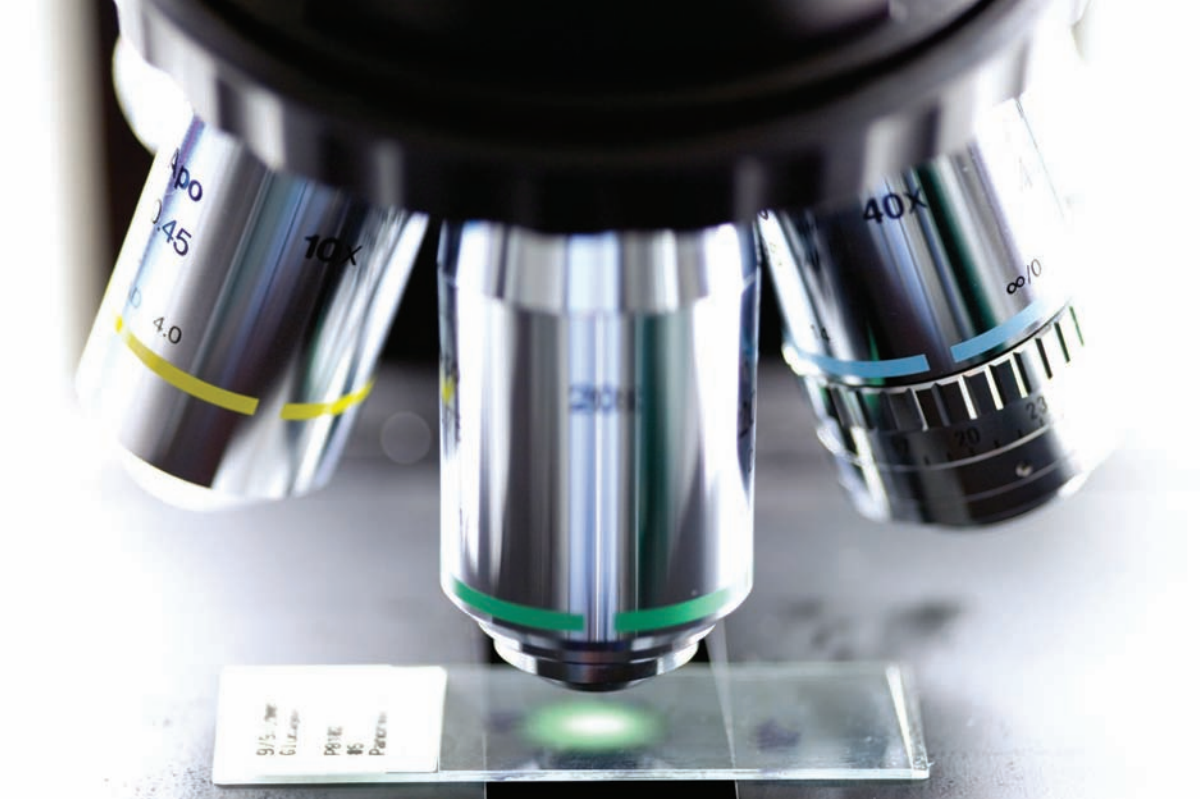


Our mission

The National Emerging Infectious Diseases Laboratories (NEIDL) is part of a national network of secure facilities that study infectious diseases that are of major public health concern—whether they occur naturally or are introduced deliberately through bioterrorism. Our facility is located in BioSquare, a biomedical research and business park adjacent to Boston University Medical Campus.

Our mission is threefold:

- To perform cutting-edge basic and clinical research on emerging infectious diseases and to develop diagnostic tests, treatments, and vaccines to promote the public's health through combating infectious diseases
- To provide training in these areas of research and to support a national response in the event of a biodefense emergency
- To establish a research facility with the highest attention to community and laboratory safety and security

State-of-the-art technologies were employed in the NEIDL's design and will be used to conduct research in safe and secure environments. The comprehensive core research

facilities will enable basic, translational, and clinical research and the development of products related to emerging infectious diseases. World-renowned experts in emerging and re-emerging infectious diseases lead each of our multidisciplinary research programs.

The NEIDL represents a major step forward in advancing public health and complementing the region's reputation as the biomedical research hub of the nation.

Our research cores are state of the art.

The research cores at the NEIDL will facilitate discoveries about emerging infectious diseases for the institution, the region, and the nation.

As a national resource, we must anticipate the research needs of investigators over at least a 20-year period and "add value" to existing and planned facilities. To meet these needs, we will use flexible core facilities devoted to a comprehensive array of research methodologies. Together, these cores contribute to the entire product development continuum from basic science to clinical research.

The NEIDL includes facilities for:

- Basic research to identify mechanisms of pathogenesis and potential targets for new diagnostics, vaccines, biologicals, and therapeutics
- Translational research to identify molecules/reagents/leads that might be useful as diagnostics, immunogens, biologicals, or therapeutics
- Clinical studies involving human volunteers

We strongly emphasize the core facilities that are housed in high-containment areas since these resources are the most urgently needed and least available nationwide. The following are some of the NEIDL's research core facilities. More information on each of the cores is available at www.bu.edu/neidl.

Aerobiology Core

A fully functional, productive infectious diseases aerobiology core is a critical lynchpin in any emerging infectious diseases research laboratory. Since many severe diseases are contracted through the respiratory route, we must develop and study models that mimic the natural transmission of these infections as well as novel drugs, treatments, or prophylactic measures that would be effective via aerosol.

The design of the NEIDL incorporates both BSL-3 and BSL-4 Aerobiology Core laboratories. This design maximizes the efficiency of research to be performed under high containment by minimizing downtime required for conversion of a single flexible laboratory module. Moreover, it allows for concomitant use of both high-containment laboratories, thereby more than doubling the total workflow in this core.

Biomolecule Production Core

For NEIDL researchers, this core provides the necessary infrastructure for the expression and purification of biologic molecules including antigens, proteins, carbohydrates, nucleic acids, and other biologics from the Risk Group 3 and 4 agents. As in the Aerobiology Core, incorporating both BSL-3 and BSL-4 Biomolecule Production Core laboratories maximizes efficiency by reducing downtime and increasing workflow.

The Biomolecule Production Core at BSL-4 will have dedicated facilities and production capabilities to grow Risk Group 4 viruses and isolate biologic molecules of interest under BSL-4 containment. The scope of work for the BSL-4 facility will be strictly governed by the NIH Guidelines for Recombinant DNA Research and by City of Boston regulations.

Cell and Tissue Imaging Core

Because new technologies allow high-resolution imaging of living cells and tissues that may be infected with viable microorganisms, the Cell and Tissue Imaging Core (CTIC) will be in BSL-4 containment. It will offer multiple state-of-the-art imaging systems to analyze specimens. As a result, fine-scale topography of fixed tissues gathered from transmission or scanning electron microscopy can be integrated with information gathered from multi-probe, live-cell analyses using deconvolution or laser confocal microscopy.

Existing facilities for electron and conventional microscopy of fixed, nonviable specimens are part of the research infrastructure at Boston University Medical Campus and will be available to NEIDL investigators.

Clinical Research Core

The Clinical Research Core (CRC) design was based upon extensive experience with clinical research, including studies of the prevention and diagnosis of infectious diseases.

The fundamental goal of this core is to provide a dedicated location and trained staff for the network of researchers in the NEIDL, the Regional Centers of Excellence in Emerging Infectious Diseases, the Regional Biocontainment Laboratories, and the Galveston National Biocontainment Laboratory, as well as private entities doing sponsored research to fulfill the strategic plan of the National Institute of Allergy and Infectious Diseases.

The Clinical Research Core will not provide care for or research on patients with infectious diseases. It will enable investigators to conduct approved studies on normal human volunteers. We anticipate that researchers will conduct studies of vaccines (Phase 1), lot consistency, novel immunogen delivery systems by various routes, candidate vaccine stability, pharmacokinetics of novel therapeutics, delivery of therapeutics through alternative routes (e.g., respiratory, oral, mucosal, transdermal), and Phase 1 safety trials of biologicals (e.g., therapeutic antibodies).

Extramural Investigator Research Collaboration Cores

As a National Biocontainment Laboratory, the NEIDL will give extramural investigators access to BSL-3 and BSL-4 high-containment laboratories as well as scientific and administrative cores. These investigators will come from both academic and commercial entities whose research has reached the stage where high containment is required. For example, *in vivo* challenge studies for determining vaccine and/or therapeutic development efficacy would be an appropriate phase for engaging the Collaborative Research Group Cores.

At least two Collaborative Research Group Cores will be established to host research from extramural investigators. These teams will be employed by the NEIDL and dedicated to the hands-on execution of all extramural research conducted here. Extramural investigators guiding the research may be either on-site for the duration of this work, directing work on a daily basis from their home institutions, or a combination of the two.

Immunology Core

The Immunology Core will provide the infrastructure for characterizing innate and adaptive immune responses to infectious agents. It will also accommodate standardized testing of vaccine candidates, including biologics produced within the NEIDL's Biological Molecule Production Core.

Under most circumstances, the Immunology Core will concentrate on analysis of specimens obtained from animals challenged with agents requiring BSL-3 or BSL-4 containment. To allow investigators to monitor both *in vivo* and *in vitro* immune responses, the core will provide four essential services:

- Basic cell enumeration and separation for human and animal cells using magnetic separation, and cell subset identification by flow cytometry in high containment
- Elucidation of cytokine profiles of responding cells by flow cytometry, and cytokine production in serum and in culture by BioPlex analysis

- Antibody assays by ELISA or ELISPOT for enumerating antibody-producing cells and neutralizing antibodies using automated plaque and colony-counting assays
- Consultation services and help in developing other immunological assays as needed by investigators in the NEIDL.

Core for the Study of Insect Vectors

Many of the most widely distributed infectious diseases are transmitted to humans by insects—mosquitoes, ticks, mites, lice, and biting flies, for example. Some of the most important emerging infectious diseases are examples of vector-borne diseases. These include dengue, West Nile virus, the encephalitis viruses such as eastern equine encephalitis, and bacteria such as *Francisella tularensis* and *Yersinia pestis.*

Arthropod Containment Levels 3 and 4 are required for research on many of these diseases. Critical research involving vector-borne pathogens includes:

- Natural infection studies with hemorrhagic fever viruses
- Vector competence experiments to determine which insects are capable of transmitting the microorganisms
- Testing of immune and non-immune mediated strategies to eliminate pathogens from vectors (so-called vector interruption strategies)

Specimen Processing Core for BSL-4 Research Projects

The Specimen Processing Core and its associated laboratory equipment and capabilities will support NEIDL investigators in the study of emerging infectious diseases, including NIAID Category A, B, and C agents.

Coordination with the Animal Cores (including Pathology/Necropsy) will ensure that specimens are processed immediately following collection and transported to the laboratory quickly and safely. We will have the ability to flash-freeze the specimens and autoclave them or treat with gamma radiation prior to transportation out of the BSL-4 area.

This core will include the following laboratories and equipment:

- A microbiology laboratory equipped for classical non-molecular as well as state-of-the-art molecular diagnostics. This lab will complement the research and serve, if required, in the event of a national emergency.
- A molecular biology laboratory for identifying the presence of select agents in tissue, cell culture, or environmental specimens.
- A clinical chemistry laboratory using the Abaxis VetScan VS2 analyzer for routine analysis of samples obtained from control and experimental animals.
- A hematology laboratory using the Beckman Coulter ACT10 and HEMAVET 950FS for routine analysis of blood cells from control and experimental animals.

Multimodal Whole Animal Imaging Core

The Multimodal Whole Animal Imaging Core will operate a unique animal imaging facility under BSL-4 containment in which the synergies of multiple imaging modalities will be available for discoveries about infectious diseases studied at the NEIDL. Elucidation of *in vivo* kinetics of organism pathogenesis, treatment response, and immune protection studies of agents, such as tuberculosis and the hemorrhagic fever viruses in whole animals, have been severely hampered by the lack of advanced whole animal imaging systems capable of routine operations in a BSL-4. This is particularly true for the assessment of pathogen-induced cellular and structural changes in larger animals, in which cross-sectional post mortem studies had to substitute for the more desirable longitudinal *in vivo* studies.


SOFT WATER
CLEAN STEAM
SOFT WATER
SOFT WATER

The primary objective of this core will be to circumvent technical challenges and utilize recent and anticipated innovations in multimodal imaging technologies, including a custom-designed, one-of-a-kind BSL-4 compatible 4.7 Tesla whole animal MRI scanner, fluorescence optical tomography, and X-ray computed tomography. In-house developed multimodal imaging software packages designed specifically for emerging infectious diseases' needs will facilitate further the quantitative and multimodal analyses of the data to gain insights into the pathogenesis and treatment of major infectious diseases that are public health concerns.

Our work will be critical, comprehensive, and transparent.

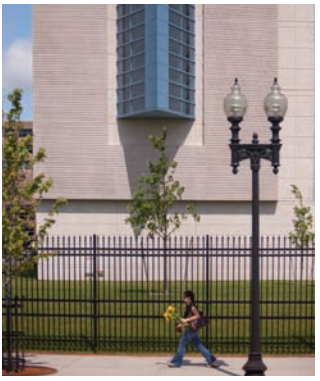
The NEIDL is dedicated to developing diagnostics, vaccines, and therapeutics to combat emerging and re-emerging infectious diseases. To that end, we will study a wide range of NIAID Category A, B, and C agents, including the viruses that require BSL-4 containment:

- Central European tick-borne encephalitis
- Congo-Crimean hemorrhagic fever
- Ebola
- Guanarito
- Hendra
- Junin
- Kyasanur Forest disease
- Lassa
- Machupo
- Marburg
- Nipah
- Omsk hemorrhagic fever
- Russian spring-summer encephalitis
- Sabia

We will also study agents such as mycobacteria, tuberculosis, influenza viruses, West Nile virus, and others that require BSL-3 containment.

A wide variety of safeguards are in place to minimize risks and protect our researchers and the community. In addition to building design and construction, these include the recruitment of experienced researchers; the rigorous observance of standard operating procedures for safety, security, and operations; limited access to the NEIDL; and extensive security checks of persons and property. There will be collaborative training programs with city agencies and integration of our institutional protocols with Boston Medical Center clinicians. We will follow guidelines and regulations of the Boston Public Health Commission, the National Institutes of Health, and the Centers for Disease Control.

Beyond safety, we are committed to providing transparency in our work. Oversight by several committees ensures community access to information about our work and opportunities for open dialogue. The Institutional Biosafety Committee, which has oversight responsibility for all biosafety programs at Boston University and Boston



Medical Center, includes public representation. The Community Liaison Committee was created specifically to promote community outreach and feedback. The five-member NEIDL Institute Executive Committee also includes a public member-at-large as a key representative of public interests.

Furthermore, our External Scientific Advisory Committee, the Boston Public Health Commission, and the Massachusetts Department of Public Safety all provide important links between our activities and our community. Finally, the NEIDL is accountable to independent public health and safety officials in more than a dozen local, state, and federal agencies and organizations.

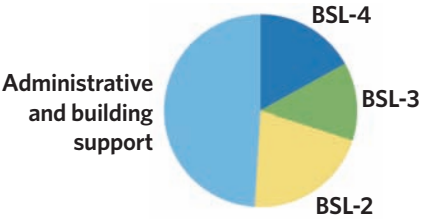
Our facility meets the most stringent guidelines.

The NEIDL is a 192,000-square-foot, 7-story building, designed in accordance with the most stringent and protective measures defined by the National Institutes of Health. It was built on the experience of six existing BSL-4 facilities in North America, none of which has ever had a release or community incident.

Our facility provides BSL-2, -3 and -4 capacities. The containment areas include imaging, aerobiology, insectary, and other specialized cores and support areas. The building also offers a BSL-4 training simulator to provide hands-on training for all research staff.

The NEIDL is constructed to maximize research capacity. Total building area includes:

- 16% BSL-4 research
- 13% BSL-3 research
- 20% BSL-2 research
- 3% BSL-2 clinic
- 48% Administrative and building support



All critical building systems within the NEIDL have a redundant system to ensure safety and uninterrupted operations at all containment levels. Operating procedures will be based on best practices and government standards (CDC/NIH).

For more information about the NEIDL facilities, work, researchers, and safety systems, please visit www.bu.edu/neidl.


SUIT ROOM
MICROSCOPY PREP

The Boston University National Emerging Infectious Diseases Laboratories (NEIDL)

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