ENVIRONMENTAL HEALTH AND SAFETY

University of Nebraska-Lincoln

UNIVERSITY OF NEBRASKA - LINCOLN

BIOSAFETY GUIDELINES

Revised

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v. 2.4

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https://ehs.unl.edu/safety-committees/institutional-biosafety-committee-ibc/

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Previous Review Dates

October 2014	v. 1.0
July 2018	v. 2.0
June 2020	v. 2.1
January 2024	v. 2.2
April 2024	v. 2.3
April 2025	v. 2.4

1 Introduction

Hazards associated with pathogens and recombinant or synthetic nucleic acids may be encountered in many UNL research, clinical/diagnostic, and/or teaching activities. The University must comply with certain regulatory requirements, generally recognized consensus standards, and/or funding agency guidelines to remain in good standing and retain funding eligibility, particularly as it relates to eligibility for funding from the National Institutes of Health (NIH) and other federal agencies.

The UNL Biosafety Guidelines describe the methods, means, procedures, and policies that govern the conduct of work by UNL employees and/or within UNL facilities, that presents possible biohazard risks to employees, visitors, the public, or the environment. These Guidelines also delineate roles and responsibilities for Principal Investigators (PI), Laboratory Workers, the University Biosafety Officer (BSO), the Institutional Biosafety Committee (IBC), the Institutional Review Entity (IRE), and certain Administrative Officials.

1.1 Scope

The UNL Biosafety Guidelines apply to clinical/diagnostic, research, and teaching activities involving any of the following items individually or in combination with each other:

- **Recombinant or Synthetic Nucleic Acid molecules** that are constructed by joining nucleic acid molecules and that can replicate in a living cell and are chemically (or by other means) synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules or molecules that result from the replication of those described above (*see definitions in Section 1.2*).
    - **Exception:** Experiments conducted in academic teaching lab courses for demonstrative purposes and not considered "research projects" are not subject to IBC Review
- **Human, animal, arthropod, and plant pathogens** (bacteria, virus, yeast, fungus, prions, & parasitic agents) to include growth, manipulation and/or other handling and use *in vitro* or *in vivo*.
- **Toxins of biological origin***,* when the originating organism is grown for the purpose of obtaining toxin. Toxins obtained in pure form commercially are not covered, except for Select Agent toxins. Any amount of a Select Toxin requires submission of an IBC protocol.
- **Human blood and other potentially infectious materials**, as defined by the United States Occupational Safety and Health Administration (OSHA) and the **UNL Exposure Control Plan**.
- **Human and non-human primate cells and organ/tissue cultures**
- **Select Agents and Toxins**, as defined by the United States Departments of Agriculture or Health and Human Services.
- **Dual Use Research of Concern (DURC)** and **Pathogens with Enhanced Pandemic Potential** (See Appendix A of this document).

- **Genetically modified animals (including arthropods) or plants** including growth, breeding, manipulation or other use of the organism in a lab, animal room, growth/ environmental chamber or greenhouse space. A genetically modified organism (GMO) has integration in the genome of foreign nucleic acids or permanent modification via gene editing technologies, making the organism genetically modified (transgenic).

  NOTE: Seed/ plants that are genetically modified (contains recombinant or synthetic nucleic acid that can replicate in a living cell, chemically or by other means synthesized or amplified that can base pair with naturally occurring nucleic acid molecules or molecules that result in replication of those just described) AND is/are viable (even if it is commercially purchased/ sold commercially) AND is received and worked with in the lab/greenhouse/space at UNL, IS subject to the *NIH Guidelines* and requires an IBC protocol. **Field trials** of transgenic plants authorized by the United States Department of Agriculture - Animal and Plant Health Inspection Service (USDA-APHIS) are not subject to review by the IBC and do not require an IBC protocol.

- **Field Collection or Sampling of Wild Animals**, when there is risk of exposure to zoonotic diseases. See section 4.7 for detailed parameters regarding these types of studies.

NOTE: The following activities are not subject to IBC review:

Clinical/diagnostic, research, and teaching activities that:

- are properly conducted at biosafety containment level 1 (BSL-1); **and**
- **do not** involve human, animal, arthropod or plant pathogens capable of causing disease in healthy organisms; **and/or**
- involve only the *in vitro* use of nucleic acids (e.g., PCR, sequencing) **and do not** involve the cloning and propagation of recombinant or synthetic nucleic acid molecules in cells or organisms; **and**
- the nucleic acid molecules are not able to produce infectious forms of a biological select agent or encode for the functional form of a select agent toxin. (See EHS SOP “Select Agents” for details.)

Important: Contact the BSO (ibc@unl.edu) if you are unsure if you need an IBC protocol.

1.2 Definitions

The following terms are used throughout this document and their meaning is defined here.

Biologics – any compound or material of biological origin. This includes but is not limited to recombinant nucleic acid molecules, plasmids, microorganisms, viral vectors, toxins, cells, human blood or body fluids, plant parts, etc.

Dual Use Research of Concern (DURC) – is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to do harm with no, or only minor, modification

to pose a significant threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

Genetically-modified – artificial modification of the genome of an organism (plant, animal, arthropod, microorganism) by any means, other than regular breeding methods, in an attempt to alter the characteristic of that organism. This includes germline (transgenic) and somatic/transient modifications, gene knock-out/knock-in, gene silencing, gene editing, etc.

Gene drive – a technology whereby a particular heritable element biases inheritance in its favor, resulting in the heritable element becoming more prevalent than predicted by Mendelian laws of inheritance in a population over successive generations. An organism modified by this mechanism is a Gene Drive Modified Organism (GDMO).

Pathogenic agents – any microbiological (bacteria, virus, yeast, fungus, prion, parasite) agent or biological toxin that is capable of causing disease in humans, animals, arthropods or plants.

Pathogen with Pandemic Potential (PPP) – a pathogen that is likely capable of wide and uncontrollable spread in a human population and would likely cause moderate to severe disease and/or mortality in humans. Pathogens with pandemic potential are often those with little to no pre-existing immunity in the human population.

Pathogen with Enhanced Pandemic Potential (PEPP) – a type of pathogen with pandemic potential (PPP) resulting from experiments that enhance a pathogen's transmissibility or virulence, or disrupt the effectiveness of pre-existing immunity, regardless of its progenitor agent, such that it may pose a significant threat to public health, the capacity of health systems to function, or national security. Wild-type pathogens that are circulating in or have been recovered from nature are not PEPPs but may be considered PPPs because of their pandemic potential.

Principal investigator (PI) – any person with primary authority over the work conducted, whether the work is research-, clinical/diagnostic- or teaching-related.

Recombinant or Synthetic Nucleic Acids (r/sNA) – (i) molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids; (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids, or (iii) molecules that result from the replication of those described in (i) or (ii) above. *This definition encompasses recombinant or synthetically derived nucleic acids, including those that are chemically or otherwise modified analogs of nucleotides (e.g., morpholinos), or both.*

Work activities – any activity involving conducting experiments on or with, testing, sampling, or analyzing any biological material or sample from a human, animal, arthropod, or plant that falls into one of the categories outlined in Section 4.

1.3 Regulatory Authority

The UNL Biosafety Guidelines are based on several regulatory requirements, as well as nationally recognized consensus standards and guidelines. The following list is illustrative; not exhaustive. Other regulations, standards, or funding agency requirements may apply to specific work activities. PIs must identify and familiarize themselves with all applicable requirements pertaining to their work activities.

- *NIH Guidelines* for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (Herein referred to as "*NIH Guidelines*"), U.S. Department of Health and Human Services, National Institutes of Health. 59 FR 34496 (Final Rule) and subsequent amendments. https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf
- *Biosafety in Microbiological and Biomedical Laboratories*, (latest edition). (Herein referred to as "BMBL" or "CDC Guidelines"), U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. https://www.cdc.gov/labs/bmbl/?CDC_AAref_Val=https://www.cdc.gov/labs/BMBL.html
- Possession, Use, and Transfer of Select Agents and Toxins, 42 CFR 73, U.S. Department of Health and Human Services, Public Health Service; 7 CFR 331 and 9 CFR 121, U. S. Department of Agriculture, Animal and Plant Health and Inspection Service. https://www.selectagents.gov/
- 49 CFR 171-178, Hazardous Materials Transportation regulations, incorporating by reference the International Air Transport Association (IATA), Dangerous Goods Regulations (DGR), *Latest edition*
- 29 CFR 1910.1030, Occupational Exposure to Bloodborne Pathogens, U.S. Department of Labor, Occupational Safety and Health Administration
- 42 CFR Particularly 71.54, Importations
- 9 CFR Parts 91 – 99, Exportation and Importation of Animals (including Poultry) and Animal Products
- 9 CFR Parts 121-124, Viruses, Serums, Toxins, and Analogous Products; Organisms and Vectors
- 7 CFR Part 330, Federal Plant Pest Regulations; General; Plant Pests, Biological Control Organisms, and Associated Articles; Garbage
- 7 CFR Part 340, Movement of Organisms Modified or Produced through Genetic Engineering
- 15 CFR Parts 730 to 774, Export Administration Regulations
- United States Government (USG) Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential[1]; referred to as DURC and PEPP Policy in this document. https://ehs.unl.edu/sites/unl.edu.business-and-finance.university-operations.ehs/files/media/file/USG-Policy-for-Oversight-of-DURC-and-PEPP-May2024-508.pdf

[1] The USG policy was updated in May 2024, with an effective date of May 6, 2025. The new policy expands the types of experiments and biological agents subject to the policy.

- Framework for Nucleic Acid Synthesis Screening, White House Office of Science and Technology Policy (OSTP). https://aspr.hhs.gov/S3/Documents/OSTP-Nucleic-Acid-Synthesis-Screening-Framework-Sep2024.pdf

Biological materials such as reagents, cell lines, plasmids, and vectors are also often subject to the terms of a Material Transfer Agreement (MTA), which governs the transfer of tangible research materials between two organizations, when the recipient intends to use it for his or her own research purposes. The MTA defines the rights of the provider and the recipient with respect to the materials and any derivatives. The UNL Offices of Sponsored Programs have primary authority related to MTAs; therefore, the specific procedures and policies related to MTAs are beyond the scope of these Guidelines. Nevertheless, PIs must understand MTA implications that may impact their work.

1.4 Violations

Non-conformance with *NIH Guidelines* and nationally recognized standards may endanger human, animal, arthropod, or plant health. Violations of *NIH Guidelines* regardless of the specific funding source can jeopardize funding from the NIH and other granting agencies for **all of UNL**. Non-conformance may result in civil and/or criminal penalties.

Violations of the *NIH Guidelines*, Select Agent Regulations, DURC/ PEPP policy, and adverse incidents at UNL in regards to biological material, must be reported to the appropriate Federal and State agencies, as applicable.

The PI, BSO, Institutional Biosafety Committee (IBC), Institutional Review Entity (IRE), and Office of Research and Innovation (R&I) will coordinate, as applicable, to investigate and the BSO will file the incident report with the federal agency of the incident identified. The R&I will communicate with the Senior Administrative Official. The Senior Administrative Official will determine and administer appropriate disciplinary actions, if any, in accordance with existing UNL human resources and responsible conduct of research policies and procedures.

2 Roles and Responsibilities

2.1 Senior Administrative Oversight

The UNL Chancellor is the Senior Administrative Officer overseeing biosafety activities at the University of Nebraska-Lincoln. The UNL Chancellor has delegated this authority to the Vice Chancellor for Research and Innovation (VCRI). The VCRI has further delegated oversight of biosafety to the Institutional Official (IO). (Figure 2-1)

2.1.1 *The Institutional Official (IO) or delegate is responsible for:*

- Acting as the Administrative Advisor to the EHS Biosafety Office and IBC (and IRE) in matters of administrative action and representing the interests of the University community.

- Requesting resources required to carry out the provisions of UNL Biosafety Guidelines. (*Resources are allocated through the Office of Research and the Department of Environmental Health and Safety).*
- Appointing the IBC (and IRE) committee members, designating committee chairperson(s), and ensuring that those selected are appropriately qualified and trained regarding laboratory safety and implementation of the *corresponding policies and guidelines.*
- Determining and administering disciplinary action for willful violation of *NIH Guidelines*, Select Agent Program, DURC/PEPP policy, BMBL, UNL Biosafety Guidelines or other authoritative safety documents.
- Keeping the VCRI apprised of issues regarding operation of the UNL Biosafety Program and protocol termination/suspension for serious non-compliance/non-conformance to regulatory requirements and/or UNL policies.
- In coordination with the BSO and IBC/ IRE Committees, reporting incidents to the appropriate federal agency(s), as applicable.
- In coordination with the Biosafety Officer, forwarding public comments on IBC (and IRE) actions to the appropriate funding agency, as applicable.

2.2 Department Head/Chair or Dean/Director

Department Heads/Chairs and/or Deans/Directors are responsible for:

- Indicating support of a PI's protocol prior to consideration by the IBC.
- Ensuring that adequate facilities are available and maintained to support the proposed protocol.
- Ensuring that biosafety requirements and safety policies and procedures are in place and maintained at the departmental level.
- Ensuring that faculty using biological materials follow laboratory onboarding or decommissioning procedures when they are arriving to UNL, leaving UNL or relocating their lab.

2.3 Institutional Biosafety Committee (IBC)

The IBC is responsible for:

- Investigating potential violations in coordination with the BSO and the IO.
- Reviewing protocols and amendments, including independent assessment of the containment levels required for the proposed research; and consideration of information provided in the protocol or by the BSO regarding facilities, procedures, practices, training and expertise of personnel involved in the protocol.
- Setting final containment levels for certain experiments as described in the *NIH Guidelines* and the BMBL.
    - Minimum of BSL2/ ABSL2/ BSL2-P containment level is required for research involving gene drive technology, due to greater uncertainty of ecological impact and may require additional subject matter expertise when performing the risk assessment for the gene drive projected work.

    - Section III-D-2-a (Experiments in which DNA from Risk Group (RG) 2-3 or *Restricted Ag*ents are Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems); Section III-D-4-b (Experiments Involving Whole Animals); and III-D-5 (Experiments Involving Whole Plants).
- Adopting standard emergency procedures covering accidental spills and personnel contamination resulting from activities subject to the BMBL, *NIH Guidelines* and the UNL Biosafety Guidelines. This includes reviewing and approving alternate procedures proposed by individual PIs, as applicable.

NOTE: The UNL IBC members also function as the IRE committee members for protocols that fall under the United States Government (USG) DURC and PEPP Policy (See Appendix A). Responsibilities of the IRE committee are to:

- Assess whether research is within the scope of the USG DURC and PEPP Policy when a PI makes an initial assessment that their proposed or on-going research may be subject to the Policy.
- Collaborate with the PIs, the Institutional Contact for Dual Use Research of Concern (ICDUR=Biosafety Officer) and Research Compliance staff to conduct a risk-benefit assessment and develop risk mitigation plans accordingly.
- Communicate with the PIs, the ICDUR/ BSO, and the federal funding agencies as required under the USG DURC/PEPP Policy.
- Ensure that risk mitigation plans are approved and fully implemented prior to initiation of research subject to the Policy.
- Review risk mitigation plans and modify the mitigation plan as necessary throughout the duration of the project.
- Ensure maintenance of records required under the Policy.

2.4 The IBC Chair and ICDUR (BSO) are responsible for:

- Ensuring that IBC/ IRE members are appropriately trained regarding laboratory safety and implementation of the *NIH Guidelines (NIH Guidelines, Section IV-B-1-h),* DURC/ PEPP policy, BMBL and the UNL Biosafety Guidelines.

2.5 Research Compliance Services, Export Control

- Inform the IBC/ IRE and BSO of export control requirements that apply to a particular protocol.
- Serve as a subject matter expert and advise the IBC/ IRE, applicable to research compliance and export control.
- Collaborate with the PI, IRE, and ICDUR in developing a risk mitigation plan.
- Conduct a separate export control review if the protocol is determined to be subject to the USG DURC and PEPP Policy.

2.6 Biosafety Officer (BSO)/ Biosafety Office Staff

The UNL Biosafety Officer/ Office is responsible for:

- Evaluating adequacy of facilities, equipment, procedures and techniques and reporting findings to the committee for their consideration in support of initial protocol review, amendment, and on-going evaluation/institutional oversight.
- Notifying PIs of the meeting date, time and location at which their protocol will be considered by the committee and notifying the PI of the results of the IBC review and basis for approval, contingencies or denial of the proposed project.
- Following up with PIs concerning contingencies and other issues identified by the IBC following protocol review.
- Investigating and reporting to the IBC/ IRE and IO:
    - significant problems related to accidents and illnesses
    - operational issues
    - non-compliance with guidelines or other policies, or
    - other adverse circumstances related to biological research and proposed or approved protocols.
- In cooperation with the IBC Chair and IO, reporting incidents to appropriate agencies as specified in the regulations, guidelines and policies.
- Providing technical services/advice and training to the IBC/ IRE and PIs regarding *NIH Guidelines*, standard written safety, emergency, and security procedures and assisting them to train PIs and laboratory staff, as requested.
- Serving as a voting member of the IBC
- Providing administrative support to the IBC, including:
    - assisting the PI's in preparing their IBC protocols for IBC review,
    - assisting with annual updates and minor modifications of the protocols,
    - routing protocols to the IBC chair and/ or IBC as applicable,
    - establishing and distributing agendas and minutes,
    - maintaining records and files of protocols, registration documents, etc.,
    - responding to FOIA requests; and other similar duties, and
    - providing incident report drafts, as applicable.
- Serving as the contact person on the annual NIH Office of Science Policy (OSP) roster of IBC members.
- Filing the IBC membership roster with NIH/OSP, including
    - (i) a roster of IBC members clearly indicating the chair, contact person, BSO, plant expert, and animal expert;
    - (ii) biographical sketches of all IBC members, including community members.
        - This roster must be filed when changes occur in membership and at least annually, as applicable.
- In cooperation with the IO, forwarding public comments on IBC/ IRE actions to NIH/OSP or funding agency, as applicable.

- Serving as the Institutional Contact for Dual Use Research (ICDUR) and act as the liaison between UNL and federal funding agencies. The ICDUR supports all activities of the IRE related to the policy including submittal of annual assurances, maintaining records, providing education and training relevant to the Policy, and coordinating with the IRE and PI in assessing risk-benefit of research subject to the Policy, and developing risk mitigation plans accordingly (See Appendix A).

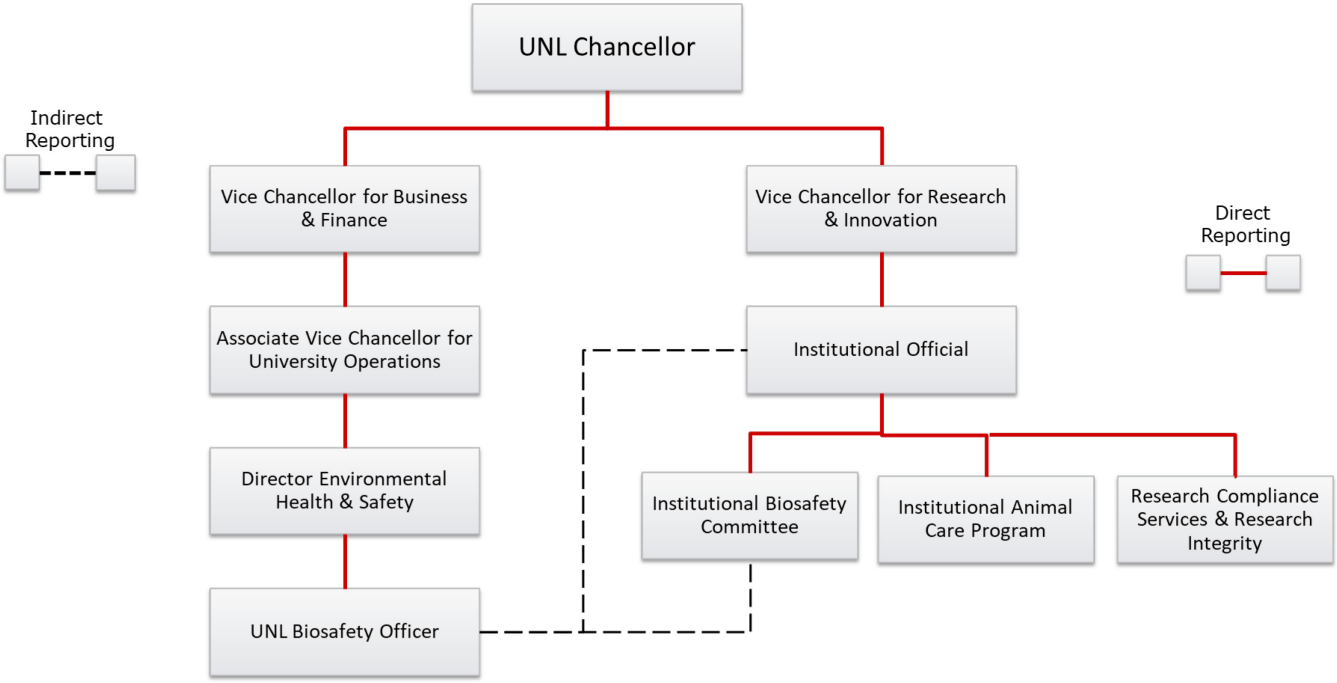


Figure 2-1 Organizational Chart for the UNL Biosafety Program

2.7 Principal Investigator (PI)

PIs are responsible for:

- Adhering to all responsibilities and expectations articulated by the BMBL, Select Agent Program, *NIH Guidelines* (Section IV-B-7);
- Adhering to and training all personnel in all applicable rules, regulations and standard practices, including but not limited to NIH and CDC (BMBL) guidelines.
- Making an initial risk assessment of the agents in use and the work being performed and work with the IBC, biosafety staff, and other knowledgeable experts to determine adequate containment and safety measures for the proposed work. Note: When gene drive technology is utilized, evaluation of environmental impacts may require additional expertise.
- Maintaining IBC protocol forms by submitting **Amendments, Minor Modifications, Annual Update Forms** and **Termination Forms** for protocols that are no longer active. (See subsection 5.5.4 Protocol Terminations for details)
- Adhering fully to UNL policies and procedures for work activities subject to the UNL Biosafety Guidelines.
- Restricting activities to those that are approved by the IBC and abstaining from initiating or modifying research/experiments, as applicable under these Guidelines.
- Making available to all laboratory personnel a copy of the lab specific biosafety manual; training and supervising laboratory workers in good microbial techniques and other practices and procedures related to safety, security, personal protective equipment (use, limitations, and maintenance), accidents, and emergency preparation/response.
    - See the EHS SOP, ***Biosafety Training***, for further training guidance/ requirements. NIH encourages PIs to retain training records.
- Routinely supervising the performance of laboratory workers to assure a safe workplace and correct work errors and conditions that are a risk to the worker, their lab mates and/or the environment.
- Maintaining a current and accurate inventory of all pathogenic agents in his/her possession at UNL and submitting inventory documentation as described in the EHS SOP, ***Pathogen Inventories*** to the UNL Biosafety Officer at least annually.
- Immediately reporting violations of the *Guidelines*, injuries and illnesses attributable to occurrences in the laboratory, personnel contamination, spills, and/ or loss of containment to the Biosafety Officer or Chair of the IBC. See EHS SOP, ***Biohazard Incident Reporting*** for more information.
- Complying with applicable shipping regulations, permit requirements, and Material Transfer Agreements.
- Ensuring that facilities and equipment are maintained to support the required biosafety containment level and enforcing laboratory access limitations to maintain adequate security.

- Informing laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection).
- Notifying the IRE and federal funding agency when proposed or on-going research is or is reasonably anticipated to be subject to the USG DURC and PEPP Policy and collaborating with the IRE and federal funding agencies in assessing risk-benefit of such work and developing and implementing risk mitigation plans.
- Ensuring that laboratory personnel conducting life science research have received and maintained education and training on all research oversight policies and processes and demonstrate competency.
- Provide annual (Category 1) or semi-annual (Category 2) progress reports for research that is subject to the USG DURC and PEPP Policy.
- Responsibly communicate research findings (all communication; not just publication) in accordance with USG DURC and PEPP Policy risk mitigation plans.

2.8 Laboratory Workers

Laboratory workers are responsible for:

- Completing relevant training as required by the IBC/ IRE and provided by EHS, BSO and the PI.
- Restricting activities/experiments subject to the UNL Biosafety Guidelines to those that are authorized under an approved IBC protocol.
- Being familiar with hazards posed by all agents used in the laboratory regardless of whether he/she directly works with them.
- Keeping a current and accurate inventory of the pathogenic agents used and notifying the PI of any inventory changes.
- Knowing and adhering to all emergency procedures established by the PI.
- Reporting all occupational accidents, illnesses, and injuries to the PI and EHS in accordance with UNL policy, as described in the EHS SOP, ***On-the-Job and Student Injuries***.
- Following all laboratory practices established by the PI, EHS, and the IBC.

3 Institutional Biosafety Committee

3.1 Membership

As mandated by the *NIH Guidelines*, at a minimum the IBC is composed of no fewer than five (5) members selected for their collective expertise in recombinant and/or synthetic nucleic acids. A list of current members is maintained on the IBC webpage at: https://ehs.unl.edu/safety-committees/institutional-biosafety-committee-ibc/

- Two (2) members of the IBC are not affiliated with UNL (do not have faculty appointments).
- At least one (1) member has expertise in plant, plant pathogen, or pest containment procedures.

- At least one (1) member has expertise in animal containment procedures.
- One (1) member represents laboratory technical staff.
- One (1) member is the Biosafety Officer.

The *NIH Guidelines* further state that when the institution conducts research involving gene drive modified organisms, the institution must ensure that the Institutional Biosafety Committee has adequate expertise (e.g., specific species containment, ecological or environmental risk assessment) using ad hoc consultants if necessary.

The IO appoints the committee chair and members for a term of three (3) years. The term of the Biosafety Officer is consistent with the term of employment. The members listed above are vested with voting rights. However, they must abstain from voting if they are engaged or have a vested interest in a project proposal that is before the committee for consideration.

A quorum consists of at least 50% of the total membership of the committee and a vote of approval requires at least a simple majority of the members in attendance. The Chair or designee must be present. The Biosafety Officer or designee must be present for approval of BSL-3, large scale, and gene drive protocols.

3.2 Authority

3.2.1 *Suspension/Termination of Existing Protocols*

The committee has authority to withdraw or suspend protocol approval in response to violations to the *NIH Guidelines* or UNL biosafety policies and procedures, including but not limited to:

- Failure to have or maintain an approved protocol;
- Failure to complete required training;
- Failure to adhere to safety and containment design and principles.

In general, the PI is expected to implement corrective actions in a timely manner (upon notice of a deficiency). The IO may also administer additional consequences, up to and including suspension of access to research funds.

Refer to the supplemental IBC policy on remediation of non-compliance with UNL Biosafety Guidelines for additional detail. This policy is available on the IBC website (https://ehs.unl.edu/violations-unl-biosafety-guidelines/).

3.2.2 *Reinstatement of Suspended Protocols*

A suspended protocol can be reinstated when the following occurs:

1) The violation has been addressed/corrected to the satisfaction of the IBC/IRE and IO and;

2) The PI has submitted an explanation, in writing, to the IBC of his/her reasons for non-compliance with the UNL Biosafety Guidelines and actions taken to prevent reoccurrence.

The IBC will discuss reinstatement at the next meeting following completion of the items above and a decision will be made about reinstating full approval of the protocol. The PI will receive a letter notifying him/her as to the IBC's decision.

3.2.3 *Unapproved Work Activities*

If it is discovered that a PI is conducting work activities for which he/she is not approved, the IBC or BSO on behalf of the committee will notify the PI and require immediate submittal of a protocol or protocol amendment and suspension of work activities if the activities are subject to review by the committee prior to initiation. The IO may also administer additional consequences, up to and including suspension of access to research funds. Refer to the supplemental IBC policy on remediation of non-compliance with UNL Biosafety Guidelines for additional detail. This policy is available on the UNL IBC website (https://ehs.unl.edu/violations-unl-biosafety-guidelines/).

3.3 Meetings

IBC meetings are scheduled once per month during the academic year from September through May and as needed during the summer months. Meetings are conducted in a manner that facilitates discussion, public attendance, and PI participation. Committee business is typically conducted in virtual/ live meetings. The schedule and meeting location is available on the EHS website at https://ehs.unl.edu/safety-committees/institutional-biosafety-committee-ibc/. PIs are notified of the meeting date at which their protocol will be discussed and are invited to attend at their discretion.

Minutes of the IBC Meetings will contain sufficient detail to serve as a record of the major points of discussion and the committee's rationale for decisions made and contain the following information:

- Date and time of meeting
- Approval status of prior meeting minutes
- Individuals in attendance
- Whether and why the meeting was closed
- All major motions, including rationale
- Major points of order and discussion
- Whether motions were approved
- Time of meeting adjournment

Additionally, the following information related to the protocol is included in the meeting minutes:

- Principal Investigator (PI) name
- Project title
- Brief summary of research description, in layman's terms, as applicable

- Verification that the PI and laboratory staff performing the research have been appropriately trained in the safe conduct of the research
- The applicable section(s) of the NIH Guidelines the research falls under (e.g. Section III-D-1, Section III-E-3, etc.)
- Containment conditions to be implemented (biosafety level and any special provisions)

Minutes of the committee are maintained by the BSO staff and distributed at the next meeting for review and approval by the IBC. Minutes are then posted electronically https://ehs.unl.edu/safety-committees/institutional-biosafety-committee-ibc/ per *NIH Guidelines*. Minutes of the committee meetings may be redacted. NU legal counsel will be consulted when necessary. Redaction of personal information (such as home phone numbers, addresses, etc.) does not require review by NU legal counsel. Redaction is usually reserved for information that is necessary to protect trade secret information, unpublished data, confidential commercial information, information that, if disclosed, could directly compromise institutional or national security, and similar information.

In accordance with the *NIH Guidelines* Section IV-B-2-a-(7), all public comments made on IBC actions and the IBC's response will be forwarded to NIH/OSP.

IRE meetings will be held separately from IBC meetings and will be held on an as needed basis based on the notification from a PI or Office of Sponsored Programs (OSP) of a project that falls within the scope of the IRE's purview. The IRE will consult with the PIs, Research Compliance staff, OSP and any other subject matter expert to conduct a risk-benefit assessment and develop risk mitigation plans accordingly.

4 Specific Requirements for IBC Protocols

More than one of the following subsections may apply to a given protocol; in which case, the most stringent reporting and initiation requirements apply.

4.1 Recombinant or Synthetic Nucleic Acid Molecules

PIs are required to submit a completed IBC protocol registry form when conducting research experiments involving recombinant or synthetic nucleic acids or materials containing recombinant or synthetic nucleic acids, regardless of whether the experiment is given exempt status under the *NIH Guidelines*. The review, approval and initiation requirements for work that falls under the *NIH Guidelines* are listed below.

4.1.1 *NIH Guidelines, Section III-F (NIH Exempt Experiments)*

Those protocols involving experiments described in Section III-F of the *NIH Guidelines* (Exempt Experiments) and which are appropriately conducted at biosafety level 1 (BSL-1) containment are reviewed only by the BSO and Chair of the IBC. The purpose of this review is to verify exemption status and to generate documentation for the PI that may be required by funding and federal agencies. Experiments described in a protocol of this

nature **may** be initiated simultaneously with submittal of the completed protocol registry form.

Work with the following recombinant or synthetic nucleic acid molecules is exempt from the *NIH Guidelines, but still requires review and approval by UNL's IBC*:

III-F-1: Those synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to introduce a stable genetic modification, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight.

- If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III-C, it is not exempt under this Section.

III-F-2: Those that are not in organisms, cells, or viruses and that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes.

III-F-3: Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.

III-F-4: Those that consist entirely of nucleic acids from a **prokaryotic** host (indigenous plasmids or viruses included) when propagated in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means.

III-F-5: Those that consist entirely of nucleic acids from a **eukaryotic** host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated in that host (or a closely related strain of the same species).

III-F-6: Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent. A list of such exchangers will be prepared and periodically revised by the NIH Director with advice of the RAC after appropriate notice and opportunity for public. See Appendices A-I through A-VI of the *NIH Guidelines* for a list.

III-F-7: Those genomic DNA molecules that have acquired a transposable element provided the transposable element does not contain any recombinant and/or synthetic DNA.

III-F-8: Those that do not present a significant risk to health or the environment..., as listed in Appendix C of the *Guidelines*:

- **Appendix C-I**
  - The recombinant or synthetic nucleic acid molecules are propagated and maintained in cells in tissue culture and contain less than 50% of any eukaryotic viral genome (all viruses from a single family being considered identical). *There are other exceptions to this rule (**Appendix C-I-A**). Check with the BSO.*
- **Appendix C-II**

- Experiments using an *E. coli* K-12 host-vector system except those listed in Appendix C-II-A, provided that: (i) the host does not contain conjugation proficient plasmids or generalized transducing phages; or (ii) lambda or lambdoid or Ff bacteriophages or non-conjugative plasmids shall be used as vectors. (**Note: strain BL21 is not a K-12 strain.**) There are some restrictions on the vectors used (***Appendix C-II-A***). BSL-1 containment is suggested.

- **Appendix C-III**
  - Experiments with *Saccharomyces* host-vector systems. BSL-1 containment is suggested. There are some restrictions (***Appendix C-III, C-III-A***). Among the exceptions that cannot be considered under Appendix C-III are experiments involving GDMOs.
- **Appendix C-IV**

  Experiments involving *Kluyveromyces lactis* host-vector systems. BSL-1 containment is suggested. There are some restrictions (***Appendix C-IV, C-IV-A***). Among the exceptions that cannot be considered under Appendix C-III are experiments involving GDMOs.
- **Appendix C-V**
  - Experiments with *Bacillus subtilis* or *B. licheniformis* host-vector systems and in which reversion to spore formation is $< 10^{-7}$. There are some other restrictions (***Appendix C-V, C-V-A***). BSL-1 containment is suggested.
- **Appendix C-VI**
  - Experiments with r/sNA derived entirely from extrachromosomal elements of gram-positive organisms listed in ***Appendix C-VI*** and propagated in those same organisms. There are some restrictions (***Appendix C-VI-A***).
- **Appendix C-VII**
  - The domestic purchase or transfer of transgenic rodents (e.g., not constructed at UNL) for experiments that require BSL-1 containment are exempt from the *NIH recombinant DNA Guidelines*. (***Appendix C-VII***)
- **Appendix C-VIII**
  - The breeding of two different transgenic rodents or the breeding of a transgenic rodent and a non-transgenic rodent with the intent of creating a new strain of transgenic rodent that can be housed at BSL-1 containment will be exempt from the *NIH Guidelines* if:
    - (1) Both parental rodents can be housed under BSL-1 containment; and
    - (2) neither parental transgenic rodent contains the following genetic modifications: (i) incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or (ii) incorporation of a transgene that is under the control of a gammaretroviral long terminal repeat (LTR); and
    - (3) the transgenic rodent that results from this breeding is not expected to contain more than one-half of an exogenous viral genome from a single family of viruses. (***Appendix C-VIII***)

4.1.2 *NIH Guidelines, Section III-E*

Those protocols involving experiments described in Section III-E of the *NIH Guidelines* are reviewed by the full IBC. Experiments described in a protocol that fall under this section, and which are appropriately conducted at BSL-1 **may be initiated**

simultaneously with submittal of the completed protocol registration form. This section also includes experiments that do not fall into any other section of the *NIH Guidelines*, for example:

- Experiments involving the introduction of Risk Group 1 (RG1) 2 nucleic acid molecules into RG1 organisms such as E. coli BL21
- *N*on-viral RG1 or Risk Group 2 (RG2) r/sNA used in tissue culture systems, or
- *Use of Baculovirus vectors*

Section III-E also includes several subsections, and they are described briefly below:

- ***Experiments involving the formation of r/sNA molecules that contain no more than two-thirds of the genome of any eukaryotic virus [III-E-1]***
- ***Experiments involving whole plants, Section III-E-2***
  - Experiments with r/sNA modified whole plants and plant-associated microorganisms safely conducted at BL1-P containment. Example: *Agrobacterium spp.* and *Rhizobium spp.* [III-E-2-a]
  - BL2-P or BL1-P + biological containment is recommended for the following experiments [III-E-2-b]
  - Plants modified by recombinant or synthetic nucleic acid molecules that are noxious weeds or can interbreed with noxious weeds in the immediate geographic area. [III-E-2-b-(1)]
  - Plants in which the introduced DNA represents the complete genome of a non-exotic infectious agent. [III-E-2-b-(2)]
  - Plants associated with r/sNA-modified non-exotic microorganisms that have a recognized potential for serious detrimental impact on managed or natural ecosystems. [III-E-2-b-(3)]
  - Plants associated with r/sNA-modified exotic microorganisms that have no recognized potential for serious detrimental impact on managed or natural ecosystems. [III-E-2-b-(4)]
  - Experiments with r/sNA-modified arthropods or small animals associated with plants or with arthropods or small animals with r/sNA-modified microorganisms associated with them if the r/sNA-modified microorganisms have no recognized potential for serious detrimental impact on managed or natural ecosystems. [III-E-2-b-(5)]
- ***Experiments involving transgenic rodents, Section III-E-3***
  This section covers the creation of genetically modified rodents (including knock-out animals) that can be safely housed at BSL-1 containment. Animals that require BSL-2 or higher containment are covered under Section III-D-4, or Section III-D-8, Experiments Involving Gene Drive Modified Organisms.

[2] See Appendix B of the *NIH Guidelines* for a list of organisms divided into Risk Groups

4.1.3 *NIH Guidelines, Section III-D*

Those protocols involving experiments described in Section III-D of the *NIH Guidelines* are reviewed by the full IBC. Experiments described in a protocol of this nature **cannot be initiated without IBC approval**. The subsections of III-D are listed below and include experiments involving:

- ***Human or animal pathogens (Risk group 2 or greater) as host-vector systems (III-D-1)***
- ***DNA from human or animal pathogens (Risk group 2 or greater) cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems (III-D-2)***

  Note: Work with Cas9 genes from S. pyogenes in these organisms fall into this section unless the organisms fall under Section III-F (e.g. *E. coli* K-12, *Saccharomyces*, *Kluyveromyces*, *Bacillus subtilis*, *Bacillus licheniformis* host vector systems).
- ***Using infectious viruses (including replication defective viruses) or helper systems (III-D-3)***
- ***Certain whole animal experiments (III-D-4)***
  This section covers the administration of recombinant nucleic acid-containing materials to animals as well as the creation of genetically modified rodents (including knock-out animals) that require being housed at BSL-2, BSL-3 or BSL-4 containment.
- ***Certain whole plant experiments (III-D-5)***
- ***Large scale culture preparations (> 10 liters) (III-D-6)***
- ***Experiments with Influenza viruses (III-D-7)***
- ***Experiments involving GDMOs (III-D-8). Experiments involving gene drive modified organisms generated by recombinant or synthetic nucleic acid molecules shall be conducted at a minimum of Biosafety Level (BL) 2, BL2-N (Animals) or BL2-P (plant) containment.***

4.1.4 *NIH Sections III- A and B (Major Actions)*

Those protocols involving experiments described in Section III- A, or -B of the *NIH Guidelines* are reviewed by the full IBC. Experiments described in a protocol of this nature **cannot** be initiated without approval by the IBC **and** NIH. Experiments that fall into Sections III-A and III-B may also trigger the USG Policy for Dual Use Research of Concern (DURC), please refer to Appendix A for more information on DURC experiments.

- ***III-A-1-a (The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (see Section V-B), if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture.***
- ***III-B-1 (Experiments Involving the Cloning of Toxin Molecules with LD50 of Less than 100 Nanograms per Kilogram Body Weight) Deliberate formation***

of recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight (e.g., microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin, and Shigella dysenteriae neurotoxin). Specific approval has been given for the cloning in Escherichia coli K-12 of DNA containing genes coding for the biosynthesis of toxic molecules which are lethal to vertebrates at 100 nanograms to 100 micrograms per kilogram body weight.

- Experiments that involve cloning genes coding for toxin molecules toxic for vertebrates that have an LD50 of > 100 nanograms per kilogram bodyweight and < 100 micrograms per kilogram body weight require **IBC approval and registration with NIH OSP prior to initiation** per Appendix F of the *NIH Guidelines*.

4.2 Human, Animal, and Plant Pathogens

As defined in Section 1.2, pathogenic agents are those that are infectious to humans, animals, arthropods and/or plants and include bacteria, viruses, yeast, fungi, prions, and parasites. Work of **any kind** with a pathogenic agent requires review and approval by the IBC. Additionally, clinical, diagnostic, research, or teaching activities normally and appropriately conducted at BSL-2 or higher containment; and any work requiring relevant USDA, CDC or other federal permits and regulations, will be subject to review and approval by the IBC. This category of work may be initiated **only after submission** of a completed IBC protocol registration form **and** approval by the IBC. Use of recombinant nucleic acid molecules and technology in conjunction with pathogenic agents may result in additional review and approval requirements specified in the *NIH Guidelines*.

4.3 Toxins of Biological Origin

Work with toxins of biological origin is also subject to review and approval by the IBC when the toxin used is expressed in or produced by biological organisms and isolated for use in the lab. Toxins obtained in pure form from commercial sources are not covered by these guidelines, **except** those that are on the Select Toxin List (see Section 4.6 for more information about work with select toxins). Work with permissible/unregulated quantities of Select Toxins (see EHS SOP, **Select Agents and Toxins**) requires registration with the IBC and use of a log to track inventory and use of the toxin.

4.4 Human Blood and Other Potentially Infectious Materials (OPIM)

Work activities with materials potentially containing Bloodborne pathogens (BBP), as defined below, requires compliance with OSHA's Bloodborne Pathogens Standard as described in UNL's ***Bloodborne Pathogen/ Exposure Control Plan (BBP/ECP)***. This includes, but is not limited to, initial and annual refresher Bloodborne Pathogen training and recommended vaccinations.

Clinical, diagnostic, research, or teaching activities involving human blood or OPIM are subject to review and approval by the IBC. Work may be initiated only after submission of a completed IBC protocol registration form and approval by the IBC. These materials include:

- Human blood, blood components, and products made from human blood.
- The following human body fluids: semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, amniotic fluid, saliva in dental procedures, any body fluid that is visibly contaminated with blood, and all body fluids in situations where it is difficult or impossible to differentiate between body fluids.
- Any unfixed tissue or organ (other than intact skin) from a human (living or dead).
- HIV-containing cells or tissue cultures, organ cultures, and HIV- or HBV-containing culture medium or other solutions.
- Blood, organs, or other tissues from experimental animals infected with pathogens present in blood that can cause disease in humans.

4.4.1 *HIV, HBV and other Bloodborne Pathogens Research Labs*

Research and teaching laboratory activities involving the culture, production, concentration, experimentation, and manipulation of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), or other bloodborne pathogens may be initiated only after submission of a completed IBC protocol registry form and approval from the IBC.

4.5 Human and Non-Human Primate Cells and Organ/Tissue Cultures

Work with all human or non-human primate cells and organ/tissue cultures including those that are potentially infectious or contaminated with bloodborne pathogens, well-established cell lines, human embryonic stem cells and pluripotent cells and their derivatives are covered by the UNL ***BBP/ECP*** and subject to review and approval by the IBC. Work may be initiated only after submission of a completed IBC protocol registry form and approval by the IBC.

Work activities with established human cell lines that are characterized to be free of contamination from HBV, HIV, and other recognized bloodborne pathogens **are not** subject to BBP requirements, but review and approval by the IBC **is** still required. Documentation of the tests verifying the cells to be pathogen free is required and a copy attached to the submitted IBC protocol.
See Appendix C of the UNL BBP/ECP for further details related to human cell lines covered by the BBP/ECP.

4.6 Select Biological Agents and Toxins

Some biological agents and toxins, referred to as Select Agents and Toxins by the U.S. Departments of Health and Human Services (HHS) or Agriculture (USDA), have potential to pose severe threat to public, animal, or plant health or to animal or plant products.

Possession* **of select agents (including select toxins over a certain amount) requires a certificate of registration and security risk assessment (SRA) clearance by the appropriate federal agency (USDA/APHIS or HHS/CDC).**

Note: The only exception to this requirement relates to received diagnostic specimens suspected or found to contain select agent organisms or toxins. When a select agent is positively identified, notification must be sent to CDC/APHIS by the identifying lab within 24 hours. The lab then has 7 days to complete the Form 4 document and destroy or transfer the sample(s) to a registered facility. See EHS SOP,* ***Select Agents and Toxins – Clinical and/or Diagnostic Laboratory Activities**.*

Work with or possession of select agents and toxins can be initiated only after consultation with the BSO and Institutional Responsible Official, submission of a completed IBC protocol registry form, approval from the IBC, and completion of the registration process with the appropriate federal agency (HHS/CDC or APHIS). Possessing Select Toxins in less than certain permissible amounts does not require registration with a federal agency but does require registration with the IBC and consultation with the BSO. See the EHS SOP, ***Select Agents and Toxins*** for more details about work with select agents.

4.7 Genetically Modified Animals, Arthropods and Plants

The *NIH Guidelines* do not permit experiments involving deliberate release of genetically modified organisms into the environment unless, as provided in Section I-A-1 of the *NIH Guidelines*, another federal agency has jurisdiction over the experiment and approves the proposed release.

4.7.1 *Animals (within the kingdom Animalia)*

All live vertebrate animal research at UNL is subject to review by the Institutional Animal Care and Use Committee (IACUC) regardless of IBC review requirements. The following is a summary of general requirements pertaining to genetically modified animals. Refer to the EHS SOP, ***Recombinant and/or Synthetic Nucleic Acid Molecule Experiments Requiring IBC Review*** for a full description and to determine if your project must be approved by the IBC prior to initiation. For the purposes of these guidelines, activities involving genetically modified animals are divided into two categories:

- **Rodents**
  The purchase or transfer of genetically modified rodents (with the exception of Gene Drive Modified Organisms) is exempt from the *NIH Guidelines*, but experiments involving creation or administration of r/s NA to rodents may not be exempt (See sections III-E-3 and III-D-4 of the *NIH Guidelines*). Those activities exempt from the *NIH Guidelines* require submission of an IBC protocol registry form with review by the BSO and Chair of the IBC. Rodent activities that are not exempt from the *NIH Guidelines* must be reviewed and approved by the full IBC prior to initiation.
- **Other Vertebrates and Invertebrates**
  Except as described above, nearly all activities involving genetically modified animals must be reviewed and approved by the full IBC prior to initiating work. This includes all species within the kingdom Animalia.

4.7.2 *Plants*

Review and approval of genetically modified plant experiments conducted in laboratory, growth chamber or greenhouse settings (including growing of transgenic plants even if commercially available); administration of any pathogenic microorganism, arthropod or nematode to genetically modified plants, etc.) is required to be in compliance with Sections III-D-5, III-E and III-E-2 of the *NIH Guidelines* as described in Subsection 4.1 above. The use of gene drive technology in plant research must comply with the minimum containment (BSL2) indicated in III-D-8.

PIs planning genetically modified plant field trials pursuant to a valid and current APHIS permit must submit their application to the UNL Biotechnology Quality Management System (BQMS) committee. The BQMS committee is responsible for reviewing these applications. The IBC is notified of the actions of the BQMS committee on a regular basis.

4.8 Field Collection or Sampling of Wild Animals

The following activities involving the field collection or sampling of wild animals requires submission of an IBC protocol registry form and approval by the IBC prior to initiation of work activities due to the risk of zoonotic diseases. People conducting such research should be familiar with potential implications associated with the Select Agent regulations, as summarized in the ***EHS Guidance: Reporting Requirements for Select Agents and Toxins Identified in Field-collected Samples*** (https://ehs.unl.edu/sites/unl.edu.business-and-finance.university-operations.ehs/files/media/file/EHS%20Guidance_SAReportingReqforFieldSamples.pdf)

- Trapping and handling of wild animals for surveillance of zoonotic agents (infectious to humans and animals) designated at Risk Group 2 or higher.
- Trapping and handling of wild animals that may transmit significant or life-threatening zoonotic diseases (e.g. rabies, Hantavirus Pulmonary Syndrome) as determined by risk assessment of the target species and proposed procedures.
- Laboratory processing of diagnostic samples collected from the above studies.

5 Protocol Development, Approval, and Maintenance

An IBC protocol will be required for each PI working with materials described in Section 2; it should cover **all** research activities requiring registration with the IBC. If you are working with multiple model systems or microorganisms but the basic techniques and procedures are the same, the IBC encourages you to enter all the information in one protocol form with a generalized title. The individual projects can be described separately in the “Research Description” section of the protocol form. A separate protocol will be required for PI’s directing/managing teaching labs and/or core/diagnostic facilities that exist outside of the PI’s research activities; and for experiments or work activities that are not closely related in objectives, techniques, or procedures, or need to be performed in higher containment.

The IBC approval process begins with the PI providing all required documentation and supporting material necessary for thorough review by the IBC and Biosafety Officer (BSO). Documentation and support materials consist of the following items:

- A completed NuRamp IBC New Protocol form, and
- A lab-specific biosafety manual (See EHS SOP, ***Preparing a Laboratory Biosafety Manual***).
- CV/ bio sketch/ experience
- Pathogen Inventory
- Applicable permits
- Any requested documentation from the IBC

In addition, IBC approval will require:

- Completion of required training (See Section 5.2.2) by all personnel listed in the protocol.
- Satisfactory completion of a Pre-approval lab safety survey by the EHS Biosafety Staff.

Protocols approved by the IBC are valid contingent on the PI following the requirements for protocol maintenance described in Subsection 5.5, including providing annual updates to their protocols.

5.1 Protocol Development and Submission

Protocols are registered electronically using the NuRamp research administration system found at https://nuramp.nebraska.edu/login (Log-in credentials default to the PI's *My.UNL* username and password. Further details and instruction about IBC protocol development and the information needed to complete the IBC New Protocol Form can be found on the IBC webpage (https://ehs.unl.edu/safety-committees/institutional-biosafety-committee-ibc/). The information requested in the protocol form is required to support the following:

- Dual use and PEPP considerations (as further described in Appendix A)
- *NIH guidelines*
- Proper selection of appropriate containment level/ facilities, safety equipment, laboratory practices and procedures for the protection of the people working with or around the research and the families, pets and environment of those working in and around the lab research.
- Training and expertise of the PI and laboratory workers

5.2 Pre-approval Requirements

In addition to preparing and submitting the New Protocol Form, there are several additional requirements to be completed prior to IBC review or there will be contingencies of approval following IBC review.

5.2.1 *Preparing a Laboratory Biosafety Manual*

A biosafety manual is an important piece of documentation for every laboratory. The manual is not submitted for IBC review; however, it is evaluated by the BSO as part of the administrative review process described below. EHS provides several standard Safe Operating Procedures (SOPs) related to accidents/injuries, spills, emergency preparedness/response that the PI can include in their manual. If the PI opts to develop individual procedures in lieu of these standard procedures provided on the following link: EHS web page (https://ehs.unl.edu/biosafety/), then those lab-specific procedures must be submitted with the protocol for review and approval by the IBC. The EHS SOP, ***Preparing a Laboratory Biosafety Manual*** provides guidance on the content required for a biosafety manual. The ***Biosafety Manual Table of Contents Form*** described in the SOP should be completed and submitted with the protocol form through NuRamp. The form can be downloaded from http://ehs.unl.edu/forms/ (under the Biosafety section).

5.2.2 *Training*

Training in the principles and practices of general biosafety is essential to maintaining a safe work environment and it is the responsibility of each PI to ensure that his/her lab personnel are properly trained. All employees of UNL are required to take the following EHS courses:

- *Core – Injury and Illness Prevention Plan*
- *Core – Emergency Preparedness Training*
- *Chemical Safety Training* (if assigned tasks with potential for exposure to hazardous chemicals)

Biosafety training is required of all PIs and laboratory personnel working with biological material. This training must be completed **prior** to working on experiments/protocols that require IBC approval. Additionally, laboratory workers must receive annual refresher training on biosafety. Biosafety training requirements are further detailed in the EHS SOP, ***Biosafety Training***. Below is a list of training materials that apply to most biological labs.

- **Biosafety Research Compliance** (required for all UNL employees working with biological materials subject to UNL's Biosafety Guidelines). Training covers the oversight of biological research at UNL, risk assessment, protocol development, the *NIH Guidelines* and the *USG DURC/PEPP Policy* implementation).
    - All UNL employees working with biological materials- web-based- ***Biosafety 100: Research Compliance*** (http://ehs.unl.edu)
- **Biosafety Procedures and Practices** (as applicable)
    - All biosafety levels– ***Biosafety 101***- web-based – http://ehs.unl.edu
    - BSL-2/ABSL-2– ***Biosafety 101*** and ***Biosafety 201***- web-based – http://ehs.unl.edu
    - BSL-3– ***Biosafety 101*** and ***Biosafety 201***- web-based- http://ehs.unl.edu AND additional training provided by BSO/ Responsible Official and BSL3 Facility Directors.

- **Bloodborne Pathogens Training -** PIs and their staff working with bloodborne pathogens or other potentially infectious materials (OPIM), including human cell lines, are required to take training **annually** in addition to other required training.
    - ***Bloodborne Pathogens for Laboratory Workers*** - web-based - http://ehs.unl.edu
- Additional web-based and hands-on training as applicable to the research and containment level. Examples include biosafety cabinet training, autoclave operation training, radiation safety training, chemical safety units, export control awareness, animal handling, equipment use, etc.

IMPORTANT: Completion of training is a condition of continued IBC protocol approval and failure to comply may result in suspension or termination of an IBC protocol.

5.3 Protocol Administrative Review

The protocol review process is depicted in Appendix B of these Guidelines. A unique Protocol ID number is assigned to each protocol when a New Protocol Form is started. All future correspondence related to an approved protocol must reference this protocol number. The initial review process involves thorough evaluation by EHS Biosafety Staff. Revisions to the protocol may be requested during this process. Prompt response to revision requests will facilitate timely submission of the protocol to the IBC for review.

A protocol is released by the IBC Administrative staff to the IBC or IBC Chair for review only after it has been accepted as substantially complete by thebiosafety staff, the PI has electronically signed the form, and the department head/chair has indicated his/her support of the protocol by electronic signature.

After the biosafety staff determines the protocol form to be complete, it is sent back to the PI for his/her electronic signature. When “signing” the document, the PI must agree to the following:

To the best of my knowledge, the information in this document is a true and accurate description of the research that will be conducted in my lab. I understand my responsibilities under the NIH Guidelines and other national standards or regulations as summarized below:

- *I must adhere to all sections of the **UNL Biosafety Guidelines** relevant to my project(s) and ensure that all personnel involved in this project are aware of their responsibilities in the conduct of this research.*
- *I must adhere to the **NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules**, the current edition of the CDC/NIH **Biosafety in Microbiological and Biomedical Laboratories** manual, the **Select Agent Rules** (42 CFR Part 73, 7 CFR Part 331, 9 CFR Part 121), **United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens of Pandemic Potential** and other authoritative and/or regulatory sources as appropriate.*

- *I must amend my protocol and seek IBC approval prior to implementing major changes to my approved protocol; further, I must complete the annual update within 30 days of the designated due date provided on the annual update notification email. Provide notification of minor changes that do not require submission of a formal amendment to my protocol.*
- *I am responsible for the safe conduct of the experiments to be conducted and must ensure that all associated personnel complete required training relative to this work, as described in the **UNL Biosafety Guidelines** and the **NIH Publication, "Investigator Responsibilities".***

After the PI has signed off on the protocol form, notification is sent to the Department Head/Chair/Director (DH/C/D) that the protocol is ready for review. **NOTE**: A PI conducting research and currently serving as a DH/C/D cannot sign off on their own protocol and a Dean/Director/Vice Chancellor will need to be indicated as the DH/C/D on the protocol form. The DH/C/D will review and sign off on the protocol unless they deem revisions are necessary, if so, it will be sent back to the PI for revisions. On the routing page of the form, the DH/C/D must agree to the following statements before signing off on the protocol:

I fully support the research project(s) described in this protocol form. I acknowledge the following:

- *I will ensure that the PI adheres to all sections of the **UNL Biosafety Guidelines** relevant to their project(s) and all biosafety requirements and safety policies and procedures are enforced at the departmental level*
- *I will ensure that adequate facilities are available to the PI for the safe conduct of the proposed experiments.*
- *I will ensure that all associated personnel complete required training relative to this work, as described in the **UNL Biosafety Guidelines** and the **NIH Publication, "Investigator Responsibilities".***

Once the DH/C/D signs off on the protocol it is released for view to the IBC and placed on the agenda for discussion at the next IBC meeting. The BSO will supplement the information in the protocol with a report to the IBC on the facilities, laboratory biosafety manual, personnel training and other relevant information.

5.3.1 *Laboratory Safety Surveys*

For all new IBC protocols, EHS biosafety staff will conduct a pre-approval safety survey of the facilities and review lab-specific procedures and the biosafety manual to verify compliance with safety guidelines. Findings will be communicated to the IBC at the time of protocol consideration and/or prior to issuance of the final approval notification.

For protocol Amendment Forms, results from the most previous EHS Laboratory Safety and Compliance survey are reported to the IBC when the protocol amendment form is reviewed.

5.4 IBC Review

The IBC meets monthly, when there is pending committee business. Committee meeting schedules are published on the EHS web page. Protocols must be submitted **for pre-review at least three (3) weeks before the upcoming meeting** .

IBC meetings are open to the public and after committee approval, the IBC minutes are placed on the UNL IBC website. If the PI requests a closed meeting, or redaction of information from the publicly available protocol or meeting minutes, the BSO will arrange for review of the request by NU legal counsel prior to consideration by the committee. NU legal counsel will determine the appropriate level of public restriction or redaction.

Protocols requiring review by the full committee **must be complete no less than 10 days prior to the next scheduled meeting** (this includes all requested revisions and signatures by the PI and DH/C/D). In some cases, a longer period may be necessary to allow for scheduling and completion of a pre-approval safety survey by the EHS biosafety staff.

The entire protocol review and approval process takes 6-8 weeks on average from initial submission to final committee approval with the minimum processing time being 3-4 weeks. PIs are encouraged to communicate with the BSO early in their planning stages to avoid delays in approval.

The meeting agenda and minutes from the previous meeting are sent to the IBC approximately one (1) week prior to the scheduled meeting date. Protocols will not be included on an upcoming meeting agenda unless the PI and DH/C/D have signed off on the new protocol or amendment form. Following discussion and review, possible actions by the IBC are:

(1) a vote to approve as submitted;
(2) a vote to approve the protocol contingent upon specific conditions set forth by the committee;
(3) a vote to table the protocol for discussion at the next meeting pending revision or submission of additional information by the PI to address specific concerns of the committee;
(4) denial of approval

Following committee action, the biosafety staff will notify the PI of the Committee's decision by formal e-mail. A formal approval email will be issued only after the PI has satisfied all contingencies imposed by the IBC. Timing of initiation of work activities are contingent upon the *NIH Guidelines*, for example, III-E work can begin before the final approval letter, whereas work that falls under III-D cannot (Refer to Section 4 of the "UNL Biosafety Guidelines").

5.4.1 *Review of Protocols Exempt from the NIH Guidelines*

New protocols determined to be "Exempt" from the *NIH Guidelines* (Experiments in Section III-F) and conducted at BSL-1 are reviewed and approved solely by the BSO and IBC Chair. This determination is made during the administrative review process.

5.4.2 *Contingencies of Approval*

Sometimes protocols are approved contingent/ with minor stipulations that need to be addressed before a final approval email is sent to the PI. Following the IBC meeting, the biosafety staff will send an email to the PI explaining the outcome of the IBC review and detail what issues need to be addressed. At this point, the protocol form or amendment form is marked as "Revisions Requested" and opened for editing by the PI. This allows the PI to make any requested edits to the form or to upload any missing attachments. Contingencies that do not require editing of the IBC form include:

- Training needed for personnel
- Missing components of a biosafety manual, or
- Outstanding issues from the last laboratory safety survey.

When contingency items are addressed, their completion can be conveyed to the committee by submitting comments through the submit revisions button in NuRamp.

5.4.3 *Tabled Protocols*

When a protocol is tabled until the next IBC meeting, an email outlining the issues to be resolved is sent to the lead PI listed on the protocol. At this point the protocol form, or amendment form, is marked as "Revisions Requested" and opened for editing by the PI. This allows the PI to make any requested edits to the form or to upload any missing attachments. Protocols are not tabled unless substantial questions are raised during review by the committee or essential information is missing from the protocol to assess the risk and safety of the proposed procedures.

It is the PI's responsibility to address the issues to ensure re-review can be completed at the next scheduled IBC meeting. The PI will also be invited to attend the IBC meeting at which his/her protocol will be re-reviewed by the committee.

5.5 Protocol Forms

5.5.1 *New Protocol Form*

New Protocol Forms and Amendment Forms are identical in what is asked to be completed on the form. The information collected in the protocol forms allows the IBC to perform a risk assessment on the proposed work and document biosafety controls, including containment level(s), to protect the worker and the environment. When describing proposed research on the first page of the form, include the following information:

- Agent characteristics (e.g. virulence, pathogenicity, environmental stability)
- Types of manipulations planned
- Source(s) of the nucleic sequences (e.g., species)
- Nature of the nucleic acid sequences (e.g., structural gene, oncogene)

- Host(s) and vector(s) to be used
- Whether an attempt will be made to obtain expression of a transgene, and if so, the function of the protein that will be produced

5.5.2 *Annual Update Form (AUF)/ Annual Updates to Protocol(s)*

The purpose of the Annual Update Form (AUF) is to inform the IBC of the continuing status of already approved research project(s)/ description(s) and to allow the PI to update certain information. The information that can be edited/ updated on this form includes:

- Changes to personnel (except the PI; this change requires a full Amendment)
- Changes to facilities (Facility inspection by the biosafety staff is required.)
- Changes to funding
- Changes to disinfectants
- Changes to decontamination/disposal procedures
- Updates to pathogen inventory (if it is the same genus and species)

Note: Protocols that describe work performed at BSL-3 require an Amendment Form for any and all changes.

Note: There are questions in the Annual Update Form aimed at helping a PI determine if an Amendment Form is required instead. NOTE: An Amendment Form is needed for "major" modifications. See Amendment Form Section below.

Annual updates must be submitted (except for Select Agent and Select Toxin protocols which require an amendment form). The PI is required to submit an **Annual Update Form (AUF) within one month of the anniversary of the approval of the New Protocol Form.** The PI will be notified by email to login to the NuRamp system and submit the AUF.

Reminders will be sent at the following intervals:

- 30 days before the anniversary date,
- One week before the anniversary date, and
- On the anniversary date.

NOTE: Submission of an AUF is a condition of continued protocol approval and **failure to submit annual update forms or amendments within one month of the protocols anniversary may result in the IBC taking action to suspend or withdraw approval of the protocol until the requested information/documents are received.** See Section 3.2.1 for details about protocol suspension.

Annual Update Forms are reviewed and approved by EHS biosafety staff. The IBC is given a summary of approved Annual Update Forms at each IBC meeting.

5.5.3 *Minor Modification Form*

The Minor Modification Form is almost identical to the Annual Update Form. The Minor Modification Form does NOT allow updates to the pathogen inventory like the Annual Update Form, but DOES allow PIs to provide modifications to:

- Personnel (except the PI; this change requires a full Amendment Form)
- Lab space **in the same building** (Facility inspection by EHS Biosafety staff is required.)
- Funding source
- Disinfectants
- Decontamination/disposal procedures

and can be submitted at any time and approved by Biosafety staff after initial new protocol approval.

These "minor" changes to a protocol can be requested through submittal of a Minor Modification Form OR as part of an Annual Update Form through NuRamp.

Minor modifications are reviewed and approved by the biosafety staff without IBC review. The biosafety staff approves the forms and notifies the PI of any necessary follow up actions. The IBC is given a summary of approved minor modifications at each IBC meeting.

If the proposed changes do not fall into the categories above, then an Amendment Form must be submitted.

NOTE: the Minor Modification Form does not replace the requirement for submission of the Annual Update Form.

Note: No changes to a protocol involving work at BSL-3 qualifies under the minor modification provision.

5.5.4 *Protocol Termination Form*

When approved IBC research projects are no longer active due to faculty retirement, leaving the university, or the project is closed/ completed/ no longer funded or for other reasons, the IBC protocol must be terminated by submitting a Termination Form. The Termination Form asks about the final disposition of the materials described in the protocol (e.g., materials are destroyed, transferred to another PI at UNL or externally, taken with the PI to another university, etc.). Submission of this form must be completed immediately (within 1 month) upon project completion/termination and prior to faculty leaving UNL*.

***Note**: Exceptions to this can be made if lab staff are not leaving with the faculty member and will remain at UNL to finish a project or experiments. If this should occur, the protocol can remain active, but the faculty member must remain in contact with the IBC or designate another faculty member to serve as a representative and responsible person*

for the protocol. Contact the EHS Biosafety staff for help with this process (ibc@unl.edu or 402.472.4925).

If a faculty member is leaving UNL and shutting down his/her lab, other requirements for lab decommissioning apply and are detailed in the EHS SOP, ***Laboratory Decommissioning***.

5.6 Post-Approval Monitoring (PAM)

5.6.1 *Laboratory Safety Surveys*

EHS is tasked by the IBC to conduct regular inspections of all IBC approved facilities to ensure continued observance of safety procedures, adequacy of facilities and equipment, adherence to the approved protocol, and compliance with the *NIH Guidelines*.

5.6.2 *Post Approval Monitoring (PAM) Visits*

EHS biosafety staff will conduct post-approval monitoring (PAM) visits with the lead PI on an IBC protocol at an appropriate interval. The frequency of visits will be based on several factors including but not limited to:

- IBC compliance history
- Infectious agents in use
- Human genes manipulated as well as methods used (CRISPR, etc.);
- Viral vectors used;
- Regulatory requirements (APHIS/ CDC permit, etc.);

EHS may conduct frequent PAM visits with PIs of new protocols as means of providing lab start up assistance to the PI related to safety procedures and practices and to offer assistance with lab personnel training.

5.6.3 *Pathogenic Agent Inventory*

Pursuant to best practices in biosafety stewardship and in order to avoid stockpiles of unknown or abandoned pathogenic agents at UNL, it is institutional policy for all faculty and staff to maintain an inventory of all pathogenic agents in their possession at UNL.

The inventory must be kept current and accurate. An updated copy of the inventory must be submitted to EHS biosafety staff whenever new agents are added/removed or verified at least annually. For PIs with active IBC protocols, the inventory is submitted as part of the IBC protocol form and will be verified annually via the Annual Update Form submitted through NuRamp. The inventory must at a minimum contain the following information:

- Genus and species of microbiological agents; or name and species of origin for biological toxins
- Strain information: list all strains of the agents possessed. (*If known, include the genotype of the microbe indicating all antibiotic resistance genes and any mutations that may increase virulence, host range or pathogenicity*)
- Location of agent (BSL; building and room number)
- Status of agent (e.g. storage only, active use, etc.)

The procedure and other details about submitting and maintaining these inventories can be found in the EHS SOP, ***Pathogen Inventories***.

5.6.4 *Biosafety Refresher Training*

Annual refresher training is required for all workers on active IBC protocols. This training does not need to be comprehensive but should at least cover a basic biosafety topic or specific topic that pertains to the research in the lab. Several options exist to meet this required training.

A. Complete ***Biosafety Refresher Training*** module online at ehs.unl.edu
    - *This online module covers common safety issues observed in labs as well as special topics.*
B. Request EHS biosafety staff to conduct instructor-led training at a location of your choice in a biosafety topic that is relevant to your laboratory.
C. Hold a lab meeting and review relevant lab-specific or EHS procedures, discuss a relevant near miss incident or laboratory acquired infection and lessons learned (this could be an incident that occurred somewhere else), and/or watch a safety video as a lab. A curated YouTube playlist of biosafety-related videos is available at this link: https://go.unl.edu/zp39.

If option A or B is chosen, EHS biosafety staff will keep records of the training and provide those records to the PI upon request. If option C is chosen, the training ***must be documented*** *by recording the date of training, the attendees and the content of the training. A sample refresher-training log is available in the EHS SOP,* ***Biosafety Training****.*

Additional training may be necessary as applicable to the research approved. Examples include autoclave operation training, radiation safety training, export control awareness, animal handling, select agent awareness, etc.

5.6.5 *Medical Surveillance*

The BSO, in consultation with the PI and a medical professional, is responsible for recommending medical surveillance requirements specific to a protocol for consideration by the IBC. The medical surveillance regime generally includes the following components, as appropriate:

- Vaccination and vaccination titers
- Medical history and counseling including previous exposure(s) and the need for preventative immunization or pre-exposure prophylaxis including the related risks of vaccination
- Level of immunity for an employee and whether the employee may be immunocompromised
- Other tests and procedures as applicable (e.g., TB surveillance, post-exposure management, baseline blood draw, etc.)

The Biosafety Officer will assist the PI in arranging for immunizations and medical counseling for all indicated employees when deemed necessary by the IBC.

Appendix A: United States Government Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential Policy

The United States Government (USG) issued a Policy for Oversight of Life Sciences Dual Use Research of Concern on September 24, 2014 that required institutional oversight of DURC research. Effective May 6, 2025, this policy is superseded by an expanded policy referred to as the USG Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential. The new policy extends the list of agents and categories of research subject to the policy and establishes oversight requirements for the institution and federal funding agencies and departments. This appendix provides an overview, but the full policy (https://ehs.unl.edu/united-states-government-policy-oversight-dual-use-research-concern-and-pathogens-enhanced-pandemic/) and implementation guide (https://ehs.unl.edu/united-states-government-policy-oversight-dual-use-research-concern-and-pathogens-enhanced-pandemic/) should be reviewed in their entirety by PIs potentially affected by the policy.

The Policy establishes two categories of research that are subject to the policy, as summarized in the table below

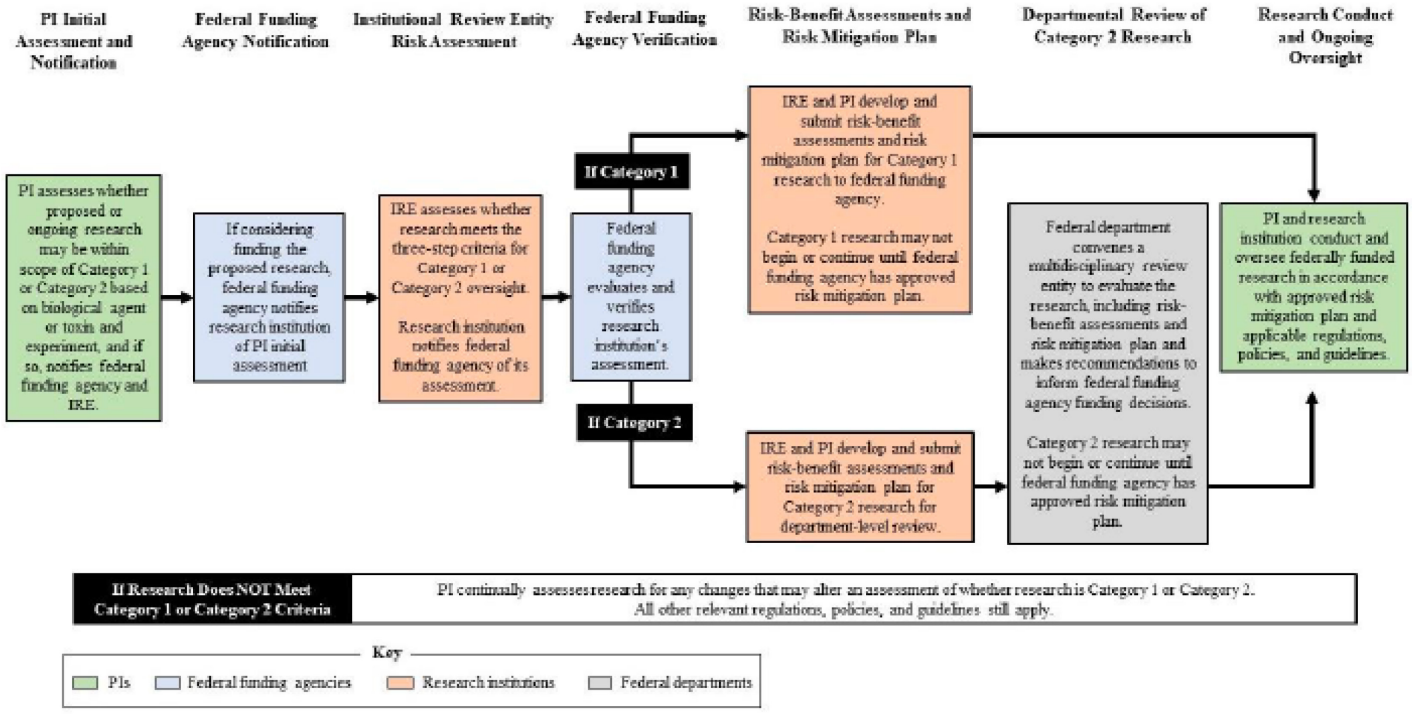
	Category 1 Research	Category 2 Research
Primary risk	The research can be reasonably anticipated to provide, or does provide, knowledge, information, products, or technologies that could be misapplied to do harm with no, or only minor, modification to pose a significant threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security. Category 1 research may also have biosafety risks.	The research can be reasonably anticipated to result in the development, use, or transfer of a pathogen with enhanced pandemic potential (PEPP) or an eradicated or extinct pathogen with pandemic potential (PPP) that may pose a significant threat to public health, the capacity of health systems to function, or national security, through the potential accidental or deliberate introduction of a PEPP or an eradicated or extinct PPP into a human population. Category 2 research may also have dual use risks.
Types of pathogens in scope of the policy	• All Biological Select Agents and Toxins, as listed in 9 CFR 121.3 -121.4, 42 CFR 73.3 – 73.4, and 7 CFR 331.3 and regulated by USDA and/or HHS. • All Risk Group 4 pathogens listed in Appendix B of the *NIH Guidelines* for Research Involving Recombinant or Synthetic Nucleic Acid	• Any pathogen that is modified in such a way that is reasonably anticipated to result in the development, use, or transfer of a PEPP. This includes the development of new PPPs from non-PPPs as well as the enhancement of existing PPPs. • Eradicated or extinct PPPs that may pose significant threat to

	Molecules – Classification of Human Etiologic Agents on the Basis of Hazard. • A subset of Risk Group 3 pathogens listed in Appendix B of the *NIH Guidelines** • For biological agents affecting humans that have not been assigned a Risk Group in the *NIH Guidelines*, agents affecting humans that are recommended to be handled at BSL-3 or BSL-4 per the BMBL guidance are subject to the policy.	public health, the capacity of health systems to function, or national security.
Types of experimental outcomes in scope of the policy	1. Increase transmissibility of a pathogen within or between host species; 2. Increase the virulence (ability to cause disease) of a pathogen or convey virulence to a non-pathogen; 3. Increase the toxicity of a known toxin or produce a novel toxin; 4. Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin (e.g., environmental stability and aero solubility); 5. Alter the host range or tropism of a pathogen or toxin; 6. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods; 7. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions; 8. Alter a human or veterinary pathogen or toxin to disrupt the effectiveness of preexisting immunity, via immunization or natural infection, against the pathogen or toxin; or	1. Enhance transmissibility of the pathogen in humans; 2. Enhance the virulence of the pathogen in humans; 3. Enhance the immune evasion of the pathogen in humans such as by modifying the pathogen to disrupt the effectiveness of pre-existing immunity via immunization or natural infection; or 4. Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP.

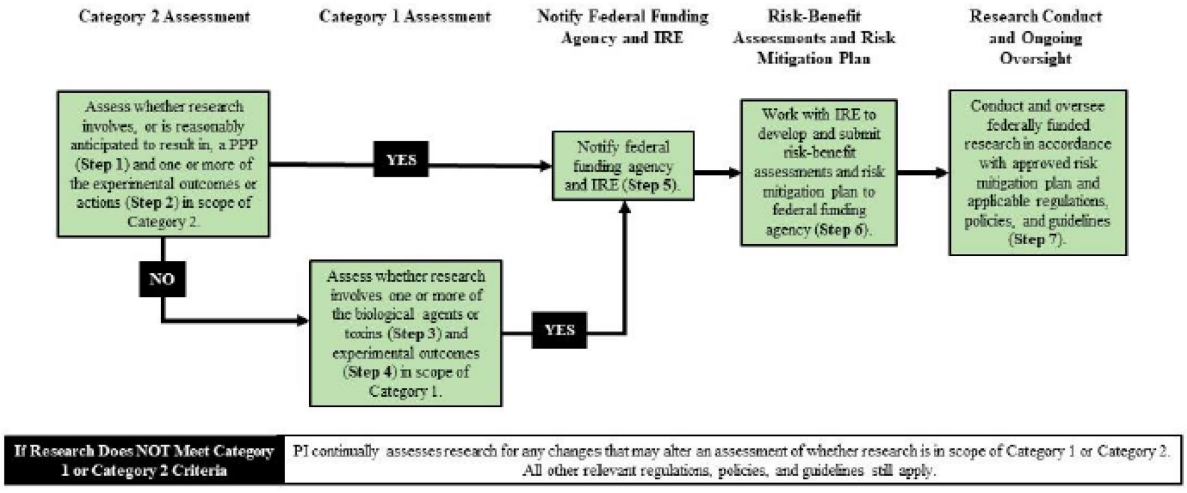
	9. Enhance the susceptibility of a host population to a pathogen or toxin.	
Level of federal review	Funding agency review	Funding agency and department-level review

*The subset of Risk Group 3 pathogens does not include HIV, HTLV, SIV, Mtb (including mycobacterium bovis), Clade II of MPVX viruses unless containing nucleic acids coding for clade I MPVX virus virulence factors, vesicular stomatitis virus, Coccidioides immitis, C. posadasii, Histoplasma capsulatum, and H. capsulatum var. duboisii.

The figure below depicts the PI review process for Category 1 or Category 2 Research. PI specific training can be found on the EHS website under training:



The figure below depicts the IRE review process for Category 1 or Category 2 Research



DURC/ PEPP Policy training for PI's can be found at: https://ehs.unl.edu/web-based-training/#DURCPEPP-PI and DURC/ PEPP Policy training IRE members can be found at: https://ehs.unl.edu/web-based-training/#DURCPEPP-IRE.

Definitions

Experiments that enhance a pathogen's transmissibility include those that enhance environmental stability of the pathogen or toxin or change the tropism or host range of the pathogen or toxin in a way that enables an increased ability to infect and transmit between humans, among others.

[1]**Harmful Consequences:** The ability of a biological agent or toxin to critically alter normal biological functions, inflicting damage on public health resources, material, and public safety. This would include augmenting properties such as virulence, infectivity, stability, transmissibility, or the ability of the biological agent or toxin to be disseminated.

[2]**Biological agent:** As is consistent with 18 U.S.C. § 178, any microorganism (including, but not limited to, bacteria, viruses, fungi, or protozoa), or infectious substance, or any naturally occurring, bioengineered or synthesized component of any such organism or infectious substance, capable of causing (A) death, disease, or other biological malfunction in a human, an animal, a plant, or other living organism; (B) deterioration of food, water, equipment, supplies, or material of any kind; or (C) deleterious alteration of the environment.

[3]**Toxin:** As is consistent with 18 U.S.C. § 178, any toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, or protozoa), or infectious substances, or a recombinant or synthesized molecule, whatever their origin and method of production, and includes (A) any poisonous substance or biological product that may be engineered as a result of biotechnology produced by a living organism; or (B) any poisonous isomer or biological product, homolog, or derivative of such a substance.

[4]**Immunity:** Encompasses all aspects of host immunity (e.g., active, adaptive, adoptive, passive, innate, and immune modulators).

[5]**Immunization:** Refers to the active or passive induction of immunity through inoculation (e.g., natural inoculation or vaccination) with an immunizing agent or with antibodies; this includes antitoxins and toxoids.

[6]**Clinically and/or agriculturally useful prophylactic or therapeutic interventions;** Includes first or second line prevention and treatment measures or alternative therapeutics used with special populations (e.g., pregnant women and pediatric patients), in the form of vaccines, antibiotics, antivirals, antiparasitics, antibodies, herbicides, fungicides, algaecides, insecticides, etc.

[7]**Stability:** The ability of a biological agent to remain viable when exposed to various environmental factors, including temperature, relative humidity, atmospheric pollution, and sunlight. Stability also includes persistence in a host.

[8]**Transmissibility:** The ease with which an agent spreads from host to host or from vector to host (e.g., via arthropod vectors).

[9]**Disseminate:** The process by which infectious diseases or toxins are dispersed. The same routes of entry pertinent to natural spread of diseases are also relevant when their etiologic agents are delivered intentionally (e.g., inhalation of biological agent disseminated as an aerosol, or ingestion of a biological agent disseminated through a water supply.

[10]**Host range:** The number of different species or populations that can become infected by a biological agent, causing disease in the host or allowing it to become a carrier.

[11]**Tropism:** The specificity of a biological agent or toxin for a particular host tissue or cell.

[12]**Host population:** A collective of organisms that constitutes a specific group or occur in a specified habitat. In the context of the criteria, the use of this phrase implies that the misapplication of the knowledge, products, or technologies derived from the research has the potential to broadly impact a population of host organisms.

[13]**Eradicated agent:** A biological agent that has been exterminated through surveillance and containment resulting in the permanent reduction to zero in the worldwide incidence in the transmission of the agent and the infection/disease it causes; intervention measures are no longer needed. Eradicated agents are thought to no longer exist in circulation in plants, animals, and the environment. J Note: Reconstituted eradicated agents of concern are those for which there are no known or widely available prophylactic or therapeutic interventions, those that could evade diagnostics, or those for which there is no known immunity.

[14]**Extinct agent:** These agents are thought to no longer exist in nature or in the laboratory.

Appendix B: IBC Protocol Approval Process