ENVIRONMENTAL HEALTH AND SAFETY
University of Nebraska-Lincoln

Safe Operating Procedure

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BIOLOGICAL MATERIAL RESEARCH COMPLIANCE AND IBC OVERSIGHT

SCOPE

This SOP addresses clinical, diagnostic, research, and teaching activities that are subject to *UNL Biosafety Guidelines*, including review and approval by the Institutional Biosafety Committee (IBC). Specifically, work with any of the following biological materials is subject to IBC review and approval:

- human, animal, or plant pathogens;
- recombinant or synthetic nucleic acids;
- genetically-modified animals or plants;
- certain biologically-derived toxins;
- human blood or other potentially infectious body fluid;
- human and non-human primate cells and organ/tissue cultures; and
- field collection or sampling of wild animals.

This SOP does not address regulatory requirements associated with field trials, field releases, clinical trials, or other experimental work regulated by other authorities (FDA, USDA, etc.).

RESOURCES

This document is derived from the following guidelines and documents, available on the EHS website:

- **NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules** (*NIH Guidelines*). Dept. of Health and Human Services, Office of Science Policy, National Institute of Health.
- **University of Nebraska-Lincoln Biosafety Guidelines.** UNL Office of Research and UNL Environmental Health and Safety.

INTRODUCTION

Clinical, diagnostic, research, and teaching activities that fall under the purview of the UNL IBC are described below. Described activities require submission of a protocol for review and approval by the IBC. Protocols are managed through NUgrant, UNL's secure electronic research administration system. Access to NUgrant is granted by using your My.UNL login credentials.

A. PATHOGEN USE

Principal Investigators working with human, animal, or plant pathogens must submit a registration protocol to the IBC protocol and describe the specific pathogen(s) and proposed experiments. In addition, a pathogen inventory must be submitted to EHS and updated on an annual basis (see EHS SOP, **Pathogen Inventories**). When preparing a protocol for IBC review involving pathogens, researchers must be aware of the following:

- Applicable risk group*;
- Pathogen host range;
- Presence of recombinant or synthetic nucleic acids;
- Proposed containment level (BSL-1, BSL-2, etc.);
- Suitable disinfectant;
- Decontamination and disposal requirements and procedures;
- Applicable medical surveillance for lab staff;
- Emergency procedures and spill response;

*Currently, risk groups are only assigned to *human* pathogens. The 4 risk groups, along with member species in each risk group can be found in ***Appendix B*** of the *NIH Guidelines*.

> **NOTE:** Researchers who wish to manipulate Risk-Group 3 pathogens or Select Agents must contact the Biosafety Officer **prior to** initiating a protocol. Additional regulatory and training requirements are required for manipulation of such agents. Manipulation of Risk Group 4 agents is not permitted at UNL.

B. RECOMBINANT OR SYNTHETIC NUCLEIC ACID (r/sNA) USE

According to the *NIH Guidelines*, r/sNA are defined as molecules that:

a) are constructed by joining nucleic acid molecules and that can replicate in a living cell, i.e., recombinant nucleic acids;

b) 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

c) Molecules that result from the replication of those described in (a) or (b) above.

All experiments involving r/sNA molecules or r/sNA-containing materials and organisms must be registered with the IBC regardless of source, risk group, proposed use, or status under the NIH Guidelines.

Principal Investigators (PIs) registering a protocol with the IBC must reference the appropriate section(s) of the *NIH Guidelines* when manipulating r/s NA. To accomplish this, the PI must designate which sections of the guidelines best describe the proposed experiments. The applicable sections can be found in Section III-A through III-F of the *NIH Guidelines*, which are summarized on Page 1 of the IBC protocol. The applicable sections of the guidelines establish when proposed work may begin.

Research at UNL usually falls into Sections III-D, III-E, or III-F of the *NIH Guidelines*. Often, multiple sections of the *NIH Guid*elines apply to a given protocol.

- **Section III-D**: Experiments **may not** begin until a protocol is submitted **and** committee approval is received;
- **Section III-E**: Experiments **may not** begin until a protocol is submitted to the IBC. Work must stop if the protocol is not subsequently approved by the committee.
- **Section III-F**: Although considered exempt from the *NIH Guidelines*, these experiments **must be registered** in an IBC protocol. Work must stop if the protocol is not subsequently approved by the committee.

NOTE: Please notify the BSO if any proposed experiments are described in sections III-A, III-B, or III-C, or involve cloning/expression of genes encoding biological toxins. Additional registration and review requirements may be applicable.

C. USE OF GENETICALLY-MODIFIED ORGANISMS (GMO)

PIs must register all work (use, creation, breeding, etc.) with genetically-modified organisms, (animals, plants, arthropods, etc.). Registration is required regardless of source. Work with genetically-modified organisms is described in certain sections of the *NIH Guidelines*. Guidance on applicable sections of the *NIH Guidelines* for animal work can be found here: https://osp.od.nih.gov/wp-content/uploads/Animal_Activities_Table.pdf

Work with transgenic organisms may require additional research compliance protocols or permits (IACUC, USDA-APHIS, etc.). Additional protocols or permits must be referenced in the IBC protocol. Applicable permits may also be attached to the protocol as a separate file.

IBC review and approval of genetically-modified plant experiments (including growing of transgenic plants; administration of any pathogenic microorganism, arthropod or nematode to genetically-modified plants, etc.) conducted in laboratory, growth chamber or greenhouse settings is required (See Sections III-D-5, III-E and III-E-2 of the *NIH Guidelines*).

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. Field trials of this type are not under the purview of the UNL IBC; the UNL BQMS committee is responsible for review of these applications. The IBC is notified of the actions of the BQMS committee on a regular basis.

D. USE OF CERTAIN BIOLOGICALLY-DERIVED TOXINS

Work with toxins of biological origin is 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. Cloning and expression of toxins with an LD50 in vertebrates of less than 100 micrograms/kilogram may require additional approval or registration with NIH.

Toxins obtained in pure form from commercial sources are not covered by the *UNL Biosafety Guidelines*, except those that are on the Select Toxin List. Work with 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.

E. USE OF HUMAN BLOOD, BLOOD PRODUCTS, OR POTENTIALLY INFECTIOUS MATERIAL

Clinical, diagnostic, research, and/or teaching activities involving collection/manipulation of human blood or potentially infectious material must be registered with the IBC, and work can be initiated only after review and approval of the IBC. This is in addition to enrollment in the UNL Bloodborne Pathogen (BBP) Program. Consult the *UNL Biosafety Guidelines* and *UNL Bloodborne Pathogen Exposure Control Plan (ECP)* for additional information.

Depending on the source, work with human blood, cells, or tissue may require an Institutional Review Board (IRB) protocol, also managed through NUgrant. Please consult UNL Research Compliance Services for additional requirements.

F. 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 subject to the *UNL Bloodborne Pathogen Exposure Control Plan (ECP)* and require 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. ***See Appendix C of the UNL ECP for further details.***

G. FIELD COLLECTION OR SAMPLING OF WILD ANIMALS

Certain field work with wild animals requires review and approval by the IBC when there is risk of exposure to zoonotic diseases. See Section 4.7 of the ***UNL Biosafety Guidelines***.

PROTOCOL PRE-REVIEW

After a protocol is submitted by the PI, the initial review process involves thorough evaluation by EHS Biosafety Staff. Revisions to the protocol may be requested from the PI during this process. Prompt response to revision requests by the PI will facilitate timely submission of the protocol to the IBC for review.

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

LABORATORY SAFETY SURVEYS

New PIs will be contacted to schedule a “pre-approval” safety survey of their laboratory to ensure the space is adequate for the proposed research. Results of “pre-approval” safety surveys are reported to the IBC during protocol review. In addition, EHS conducts periodic safety surveys of laboratory spaces to ensure compliance with biosafety guidelines and other applicable safety regulations and standards (OSHA, NFPA, etc.). Results of EHS safety surveys are communicated to the IBC when protocol amendments are submitted for review by the committee.

IBC REVIEW

As indicated in the *NIH Guidelines* and *UNL Biosafety Guidelines*, the IBC is charged with reviewing submitted protocols, establishing final biosafety containment levels as applicable, and helping ensure compliance with the *NIH Guidelines*. PIs are responsible to address questions, concerns, or other issues identified by EHS or the IBC promptly. PIs are

encouraged to attend IBC meetings when their protocols are being reviewed to answer any questions posed by the committee. The IBC meets monthly on the second Monday of the month and protocol submissions must be submitted at least 3 weeks prior to the meeting date in order to be eligible for review at the upcoming meeting. The average time from protocol submission to final committee approval is 4 weeks.

TRAINING REQUIREMENTS

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 on IBC approved protocols. The following biosafety-specific EHS training courses are required:

- Biosafety 100: Research Compliance
- Biosafety 101
- Biosafety 201, if working at BSL2 or higher containment
- Autoclave Operation is strongly encouraged

This training must be completed **prior** to working on experiments/protocols that require IBC approval. Additionally, the PI must ensure that laboratory workers receive annual refresher training on biosafety. Biosafety training requirements are further detailed in the EHS SOP, ***Biosafety Training.***

POST-APPROVAL MONITORING (PAM) VISITS

To help PIs maintain compliance with *UNL Biosafety Guidelines* and *NIH Guidelines*, an informal visit will be conducted by members of the EHS Biosafety team. This visit is separate from the periodic laboratory safety surveys or IBC protocol pre-review evaluation and is designed to discuss any future research plans of the PI and assist in submitting any applicable IBC forms if needed. Post-approval monitoring is conducted on a variety of timelines (annual, biannual), at the discretion of the IBC with most PIs being visited at least every two years.

NON-COMPLIANCE

Any manipulation of or experiments with r/s NA (including transgenic organisms) without submission and approval of an IBC protocol describing the work could be considered non-compliant with the *NIH Guidelines* and may be reportable to the NIH Office of Science Policy (OSP). Information submitted to the NIH-OSP includes:

- Name of researcher and title;
- Description of unauthorized experiments performed;
- Applicable sections of the guidelines which were violated;
- Funding source (NIH, NSF, etc.).

Non-compliance incidents will be reported to the IBC. Corrective actions prescribed by the IBC may include:

- Retraining of PI and lab staff on the *NIH Guidelines* and roles/responsibilities;
- Strict oversight of PI and laboratory experiments by the IBC, enforced and reported by the Biosafety Officer;
- Suspension of experiments;
- Suspension of funding.

In the event of a non-compliance incident, a new protocol or protocol amendment must be filed ***immediately*****,** delineating all experiments and materials not previously disclosed.

Non-compliance with the *NIH Guidelines* may jeopardize federal funding eligibility of both the PI and the institution as a whole.