Volume IV

Recombinant or Synthetic Nucleic Acid Molecule Research: Institutional Biosafety Committee Procedures (IBC)

Chapter 1: Purpose, Mission & Organization of the Institutional Biosafety Committee (IBC)

Introduction-Defining Recombinant or Synthetic Nucleic Acid Molecule (RSNAM)

Institutions supporting research using recombinant or synthetic nucleic acid molecules (further abbreviated as RSNAM) are responsible for conforming to and following the *NIH Guidelines.* According to the *NIH Guidelines*, recombinant and synthetic nucleic acids are defined as:

- Molecules that are constructed by joining nucleic acid molecules and can replicate in a living cell (i.e., recombinant nucleic acids)
- 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)
- Molecules that result from the replication of those described in both points above.

1.1 Purpose

The University of Central Missouri (UCM) Institutional Biosafety Committee (IBC) provides oversight for all research involving recombinant or synthetic nucleic acid molecule (RSNAM) technology in compliance with the National Institute of Health (NIH) Guidelines. The IBC also maintains oversight of research involving biohazardous material to protect public health and the environment. This applies to all activities related to research and teaching conducted at UCM or by individuals associated with the university.

1.2 Mission

The IBC is guided by federal regulations and ethical principles intended to ensure the oversight of recombinant or synthetic nucleic acid molecules in research and teaching.

1.3 Organizational Structure

UCM's IBC reports to the Institutional Official (IO). The IBC includes the committee, the Research Compliance Officer (who serves as the Biosafety Administrator), and clerical support.

1.3.1 Institutional Official

The Institutional Official has the authority to legally commit, on behalf of UCM, that regulatory requirements will be met under the National Institute of Health (NIH) guidelines. The IO is responsible for appointing members to IBC, and as the IO, will be the approved signatory authority when necessary.

1.3.2 IBC Committee

The IBC must assess the safety of research and identify potential risks to public health and safety. Therefore, the committee should consist of members that collectively meet the requirements below as outlined in the *NIH Guidelines*.

Any one member can represent more than one area of experience and expertise.

The IBC consists of at least five members that collectively have expertise in RSNAM technology, capable of assessing the safety of RSNAM research, and the ability to identify any potential risk to public health or the environment. The committee should consist of members that match one or more of the requirements below:

- Expertise in biological safety and physical containment, in addition to RSNAM technology.
- Expertise in animal containment principles IF research is conducted with RSNAM involving animals.
- Expertise in plant, plant pathogen, or plant pest containment principles IF RSNAM research involves plants.
- A member or available consultant(s) knowledgeable in institutional commitments and policies, applicable law, standards of professional conduct and practice, community attitudes, and the environment.
- One member should represent the laboratory technical staff.
- Two members should represent the interest of the surrounding community with respect to health and protection of the environment and not be affiliated with UCM
- Research Compliance Officer, ex-officio.

If a member of the IBC will be engaged in or have direct financial interest in proposed research, that member cannot be involved (except to provide information requested by IBC) in the review or approval of the project Section IV-B-2-a-(4).

The committee chair is responsible for ensuring IBC committee members are appropriately trained.

1.3.3 IBC Role and Responsibilities

- Assist Principal Investigators conducting research at the institution in ensuring compliance to NIH Guidelines.
- Ensure appropriate training is provided and available for the IBC chair and members, PIs, and laboratory personnel.
- Review RSNAM research and ensure all research that is covered under Section III of the NIH Guidelines is compliant. The presence of committee members with appropriate experience specific to the research protocol being reviewed is necessary. This review and associated experiments include:
    - Assessment of the containment levels required by NIH for the proposed research.
    - Assessment of facilities, procedures, practices, training, and expertise of personnel involved in RSNAM research.

    - Experiments needing IBC approval (at the BSL-1 or BSL-2 level):
        - Any research or experiments involving Risk Group 2 agents, with

increased priority for the following types of research

- When used as host-vector systems.
- DNA is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems.
- Use of infectious or defective viruses in presence of helper virus.

▪ Research involving transgenic animals (alteration of genome by stable introduction of recombinant or synthetic nucleic acid molecules or nucleic acids derived therefrom into the germline)

▪ Experiments involving viable RSNAM modified microorganisms tested on whole animals.

▪ Experiments to genetically engineer plants by RSNAM methods, to use for experimental purposes, propagate such plants, or use plants with microorganisms or insects containing recombinant or synthetic nucleic acid molecules.

- Determine if the experiment requires approval beyond the IBC.
  - Transfer of a drug resistant trait into a microorganism known to acquire the trait naturally requires approval from NIH Director.
  - Cloning of toxin molecules with LD50 of less than 100 nanograms per kg of body weight will need NIH OSP AND IBC approval.
  - Experiments approved as Major Actions under NIH Guidelines (Appendix D) will need NIH OSP AND IBC approval.
- Inform PI of results of IBC review and approval.
- Ensure that containment levels are set and appropriate for the research according to the NIH Guidelines (Section III D-4-b). Lower containment levels may be set for certain experiments.

(Section III-D-2-a) such as cloning nonpathogenic microorganisms.

- Review RSNAM research conducted at the institution to ensure compliance with NIH Guidelines biannually.
- Adopting emergency plans covering accidental spills and personnel containment resulting from RSNAM research.
- Report any significant problems with or violations of NIH Guidelines and any significant research-related accidents or illnesses to appropriate institutional official and NIH OSP within 30 days. Ensure that the institution or PI has not already filed a report. NIHGuidelines@od.nih.gov.
- File an annual report with NIH OSP which includes:
  - Roster of all IBC members clearly indicating the Chair, contact person, BSO if applicable, plant expert if applicable, animal expert if applicable, human gene therapy expertise or ad hoc consultant if applicable,
  - Biographical sketches of all IBC members including community members.

1.3.4 Research Compliance Officer

The Research Compliance Officer is administrative personnel that ensures compliance with federal mandates and serves as the Biosafety Administrator.

Chapter 2: Protocol Review Process and Procedures

2.1 Functions of IBC

1. Review and approve of procedures outlining the proposal review and approval process. This will include the approval of forms associated with training, incident reporting, registration, and research oversight.
2. Completion of Biosafety training through CITI.
3. Provide a biographical sketch that will be submitted to NIH upon registration of the IBC and/or submission of the annual report.
4. Review all new and modified protocols involving the use of recombinant or synthetic nucleic acid molecules, infectious agents, and select agents (as defined by CDC and USDA). Different levels of review will be used depending on the potential hazards.
5. Conduct periodic reviews of all research protocols involving the non-exempt use of RSNAM to ensure compliance with the NIH Guidelines.
6. Adopt emergency plans covering accidental spills and personnel contamination resulting from RSNAM research.
7. Investigate any research-related accidents or illnesses involving potential biological hazards and file reports, as required, with the NIH.
8. Investigate allegations on noncompliance with NIH Guidelines or other unsafe acts.
9. Participation in meetings.
    a. Meetings will be held when a new research protocol is submitted to the IBC.
    b. Meetings will be held for periodic review of recombinant and synthetic nucleic acid research to ensure compliance.
    c. If there are sufficient protocols submitted, the periodic review of ongoing research will occur during the same meetings. If there are zero to minimal protocols submitted, a quarterly or biannual meeting will be held for compliance oversight depending on the amount of research using recombinant and synthetic nucleic acid being conducted at the University during that year.
    d. The presence of >50% of the voting committee members is considered a quorum. The experience of the attending members much be considered to ensure the appropriate review of the protocol(s) and/or compliance.

2.1.1 Review process

The IBC will review any research involving recombinant or synthetic nucleic acid molecules for compliance with NIH Guidelines and any research involving infectious agents at the BSL-2 level. In addition, the approval and registration of all agents housed on campus is required, including BSL-1 agents used in teaching or for any recombinant work regardless of pathogenicity of the end product. Review of research and teaching protocols will include the following:

1.) Determination of appropriate containment levels (Appendices B, G, K, L, and M from NIH Guidelines.
2.) Protocols shall be reviewed by the full committee and discussed at an IBC meeting or approved by Designated Member Review (DMR). Protocol results

from the full committee review include approved, return for modifications, send to DMR, or disapproved. Approval is by majority vote of those present if a quorum is met.

3.) Laboratory inspections and review of facilities.
4.) Review of institutional procedures and practices and the verification that these are being implemented in the proposed research.
5.) Ensure the training and expertise of the personnel involved in the research proposal.
6.) Once approved by the IBC, the protocol is valid for three years. If the PI wished to make any changes, an amendment must be submitted and approved by the IBC before implementation. If the project may run past the three years, a renewal application must be submitted and approved by the IBC before continuing past the expiration date.

To ensure consideration of time that may be influenced by funding, teaching schedules, and researcher established dates for meeting objectives, members should review research proposals within 2 weeks of reception.

2.1.2 Post Review process

After the review process, the IBC will be responsible for the following:

1.) Notify the PI of IBC review and results.
2.) The IBC may set or modify containment levels for ongoing experiments as warranted.
3.) Implement contingency plans for handling accidental spills and personnel contamination resulting from research.
4.) Report any substantial issues or violations of the NIH Guidelines and any significant research related accidents or illness to both NIH and UCM OSP.
5.) Add any biological agents approved for use in teaching or research to the inventory of biological agents managed by the IBC.

Chapter 3: Responsibilities of the Principal Investigator (PI)

On behalf of the institution, the Principal Investigator is responsible for full compliance with the NIH Guidelines in the conduct of recombinant or synthetic nucleic acid molecule research.

- Do not initiate any research requiring prior approval from the IBC before approval has been granted (Sections III-A, Sections III-B, III-C, III-D, III-E).
- Submit new and modified (renewal or amendment) research protocols to the committee as required.
- Participate in the annual review of each of their research protocols involving the use of recombinant or synthetic nucleic acid molecules.
- Report any significant problems, violations of *NIH Guidelines*, any significant research-related accidents, and illnesses to the Greenhouse/Animal Facility Director (if applicable), IBC, NIH OSP, UCM OSP and other appropriate authorities within 30 days. Send to NIHGuidelines@od.nih.gov.

- Report any new information relating to the research to the IBC, which will report to NIH OSP.
- Be adequately trained in good microbiological techniques.
- Adhere to IBC approved emergency plans for handling accidental spills and personnel contamination.
- If the PI wants certification of a new-host vector system (Appendix I-II), to petition for proposed exemptions to *NIH Guidelines*, or petition for containment regulations, or propose research that require prior authorization from NIH OSP, this information should be submitted to NIH OSP.
- Complete risk assessments on all biological agents to be used.
- When the PI submits proposed research to IBC, include the following information.
    - A research proposal with appropriate microbiological practices and laboratory techniques to be used for the research.
    - An initial determination of required levels of physical and biological containment that follows *NIH Guidelines*.
    - A signed and dated registration document that includes all appropriate and relevant information as outlined in the document. This document is required for BSL-1 and BSL-2 level agents and containment levels.
    - Experiments that are exempt from *NIH Guidelines* and registration with the IBC are in Section III-F. The PI must provide their reasoning for exemption and refer to the appropriate subsection to support their reasoning.
    - Risk assessments.
- Prior to initiating research, ensure all laboratory staff have access to protocols that describe the potential biohazards, the necessary precautions to be taken, and are appropriately trained in practices and techniques required for the research and procedures for accidents.
- During research the PI is responsible for the following:
    - Supervision of safety practices, techniques, and safety performance of laboratory personnel.
    - Correct any actions or conditions that have the potential to release RSNAM materials.
    - Monitor and ensure the integrity of BSCs and biological containment (e.g. purity and genotypic and phenotypic characteristics).
    - Remain in communication with the IBC.
    - If there are concerns or problems relating to operation and implementation of containment, investigate and report these to the Greenhouse/Animal Facility Director, IBC, NIH OSP, and other appropriate authorities. Reports sent to NIHGuidelines@od.nih.gov.

Chapter 4: Compliance

For all RSNAM research that is NIH-funded and research that is not NIH-funded but conducted at an institution that receives NIH funding for research involving such techniques, noncompliance may result in:

a) suspension, limitation, or termination of financial assistance for the noncompliant NIH-funded research project and of NIH funds for other RSNAM research at the institution, or

b) a requirement for prior NIH approval of any or all RSNAM projects at the institution

Through compliance, the institution ensures safe conduct of the research. This will be overseen and carried out by the Institutional Biosafety Committee which does not need to be restricted to RSNAM research (Section IV-B-2).

Chapter 5: IBC Meetings

Email may be used to disseminate information but any voting on protocol approvals or official business requires a meeting to be held in a manner where minutes can be recorded. NIH does not define a quorum; it is the responsibility of the institution to define a quorum in the policies and procedures. However, the presence of at least one unaffiliated member should be required. There is no minimum threshold for meeting frequency. The IBC should conduct enough meetings to ensure compliance with NIH Guidelines Section IV-B-2-b-(5).

Oversight of research is expected to be transparent and accessible to the public. Meeting minutes should meet multiple purposes included institutional records, documentation for the NIH, and documentation for the public that IBC is fulfilling its obligations and expectations. The minutes should provide enough detail that the committee's rationale for decisions is clear, though an extensive level of detail is not needed (e.g. indicated the individual for each remark). (Section IV-B-2-a-(7)).

Resources

NIH Guidelines For Research Involving Recombinant or Synthetic Nucleic Acid Molecules
https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf

Research Compliance Officer/
Biosafety Administrator
Phone: 660-543-8562
E-mail: researchreview@ucmo.edu