Vanderbilt Basic Researchers' Guide: Institutional Registration & Review of Recombinant or Synthetic Nucleic Acid Molecule Use

All work involving recombinant or synthetic nucleic acid molecules at Vanderbilt University is subject to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules *(NIH Guidelines)*. These guidelines address the safe conduct of research that involves construction and handling of recombinant or synthetic nucleic acid molecules and cells/organisms containing them. The most recent edition of the *NIH Guidelines* is available here.

NIH's Definition of Recombinant and Synthetic Nucleic Acid Molecules

Under the *NIH Guidelines*, recombinant and synthetic nucleic acid molecules (RDNA) are defined as:

1. molecules that are (a) constructed by joining nucleic acid molecules, and (b) that can replicate in a living cell, i.e., recombinant nucleic acids;
2. 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
3. molecules that result from the replication of those described in 1 or 2 above.

Common examples include bacterial expression plasmids, mammalian expression plasmids, viral vectors and the inserted genes they carry, transgenic animals, synthetically generated microbiological agents, and genetically modified cells.

Vanderbilt University researchers who are using recombinant or synthetic nucleic acid molecules as part of their research are expected to file a registration document with the VU Institutional Biosafety Committee (IBC). The IBC will review all registrations and provide recommendations and approvals as appropriate. The VU EHS Biosafety Team supports the VU IBC by administering the registration and review process. This team also assists researchers with registration preparation or revision, training, and lab inspections, as applicable. Questions related to this process can be directed to VUBiosafety@vanderbilt.edu.

Section III of the *NIH Guidelines* outlines the review categories that apply to RDNA use and biosafety levels for specific activities. Principal Investigators are expected to determine where their proposed RDNA activities "fit" in this section.

Review Category	Review/registration action	Activities
A	Requires NIH Director and IBC approval before initiation	Deliberate transfer of drug resistance to microorganisms (not known to acquire the trait naturally) that can compromise the use of the drug to control the microorganism and its disease in humans, veterinary medicine, or agriculture.
B	Requires NIH (Office of Science Policy) OSP & IBC approval before initiation	Cloning of toxin molecules with LD50 < 100 ng/kg; activities previously approved as Major Actions (III-A-1-a) under certain circumstances.
C	Requires IBC and all other applicable institutional and regulatory authorizations before initiation	Human gene transfer and RDNA vaccine studies.
D	Requires IBC approval BEFORE initiation (NOTE: Initiation of work in this category prior to receiving IBC approval of these activities violates the *NIH Guidelines* and is reportable to that agency.)	Most work involving recombinant or synthetic nucleic acid molecules from Risk Group (RG) 2, 3, and 4 agents/materials; creation of viral vectors; administration of vectors, modified cells **modified infectious agents in any animal model**; creation or use of any non-rodent transgenic animal; large scale work (10 liters or greater in one vessel), regardless of biosafety level.
E	Requires IBC notification SIMULTANEOUS with initiation	Creation and some crossing of transgenic rodents; most experiments involving plants; most work involving RG1 materials.
F	Exempt experiments (but registration with IBC recommended)	Acquisition/transfer of transgenic rodents; specific host-vector systems; applications described in Section III-F-8 of *NIH Guidelines*.

Reminders about Recombinant or Synthetic Nucleic Acid Molecule Use…

- "Commercially-available" does not mean "exempt" under *NIH Guidelines*.
- Synthetically generated microbiological agents (not just synthetic genetic elements) are subject to the *NIH Guidelines* and require IBC registration and approval before use.
- Some funding sources may require review and approval of recombinant or synthetic nucleic acid molecule use, even if it fits under the "exempt" category in the *NIH Guidelines*.
- If you are using (or plan to use) materials that meet the definition of "recombinant or synthetic nucleic acid molecules" as previously defined, register your work with the IBC. The IBC typically meets the 4th Tuesday of the month. Registration materials should be submitted at least 6 weeks prior to be considered for the agenda.
- All RDNA use (and any use of human-derived materials, non-human primate-derived materials, infectious agents, or toxins of biological origin AND the people that work with these materials) is expected to be included in your IBC registration.
- You must assure that you are aware of and take action regarding your responsibilities as a PI under the *NIH Guidelines* as summarized on Page 3 of this document and as outlined in the NIH OSP's *Investigator Responsibilities under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* brochure.

NIH OSP RDNA-related Guidance Documents

- Biosafety Considerations for Research with Lentiviral Vectors
- FAQs for Research on Genetically Modified (Transgenic) Animals
- Animal Experiments Covered under the NIH Guidelines (TABLE)
- FAQs on Toxin Experiments involving RDNA

VU EHS Biosafety Key Resources

(latest version s available at https://www.vanderbilt.edu/ehs/biological-safety/)

- Lab Set-Up Pointers for New Researchers Working with Biological Materials
- RDNA end users' guidance on NIH Guidelines and Standard Microbiological Practices
- Responding to Biological Materials Spills and Exposures

Summary of Principal Investigator's Responsibilities for Recombinant or Synthetic Nucleic Acid Molecule Use

NIH Guidelines for Research Involving the Use of Recombinant or Synthetic Nucleic Acid Molecules (Section IV-B-7)

"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 research."

As part of this general responsibility, the Principal Investigator shall:

- Not initiate or modify any recombinant DNA or synthetic nucleic acid research which requires Institutional Biosafety Committee (IBC) approval prior to initiation until that research or the proposed modification thereof has been approved by the Institutional Biosafety Committee and has met all other requirements of the *NIH Guidelines*;
- Determine whether experiments are covered by Section III-E, *Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation*, and ensure that the appropriate procedures are followed;
- Report any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses to the Biological Safety Officer (where applicable), Greenhouse/Animal Facility Director (where applicable), IBC, NIH Office of Science Policy (OSP), and other appropriate authorities (if applicable) within 30 days;
- Report any new information bearing on the *NIH Guidelines* to the IBC and to NIH OSP;
- Be adequately trained in good microbiological techniques;
- Adhere to IBC-approved emergency plans for handling accidental spills and personnel contamination; and
- Comply with applicable shipping requirements for recombinant or synthetic nucleic acid molecules.

To register recombinant or synthetic nucleic acid molecule use with the IBC, the Principal Investigator shall:

- Make an initial determination of the required levels of physical and biological containment in accordance with the *NIH Guidelines*;
- Select appropriate microbiological practices and laboratory techniques to be used for the research;
- Submit the initial research protocol and any subsequent changes (e.g., changes in the source of nucleic acid or host-vector system), if covered under Sections III-A, III-B, III-C, III-D, or III-E (Experiments Covered by the *NIH Guidelines*), to the IBC for review and approval or disapproval; and
- Remain in communication with the IBC throughout the conduct of the project.

Before initiating research, the Principal Investigator shall:

- Make available to all laboratory staff the protocols that describe the potential biohazards and the precautions to be taken;
- Instruct and train laboratory staff in the practices and techniques required to ensure safety, and the procedures for dealing with accidents; and
- Inform the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection).

While research is under way, the Principal Investigator shall:

- Supervise the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed;
- Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the Biological Safety Officer (where applicable), Greenhouse/Animal Facility Director (where applicable), IBC, NIH OSP, and other appropriate authorities (if applicable);
- Correct work errors and conditions that may result in the release of recombinant or synthetic nucleic acid materials; and
- Ensure the integrity of the physical containment (e.g., biological safety cabinets) and the biological containment (e.g., purity and genotypic and phenotypic characteristics).