Compliance Note

Guide to NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules

Compliance with *NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules* is mandatory for all institutions receiving any NIH funding for research involving recombinant DNA (rDNA) or synthetic nucleic acids. Locally, the university Institutional Biosafety Committee has compliance oversight.

Each investigator has the responsibility to ensure their laboratory in in compliance. The Compliance Note is intended only to serve as a guide to the *NIH Guidelines.* Questions regarding the nature of specific experiments or materials should be directed to the Institutional Biosafety Officer.

Section III-A & B, NIH Guidelines – Experiments that require registration and approval of the NIH director and local IBC *prior* to initiation

1. Deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease.
2. Cloning of toxin molecules with LC_{50} of less than 100 ng / kilogram body weight.

Section III-C, NIH Guidelines – Experiments Involving Human Subjects require registration with NIH Recombinant Advisory Committee, and review and approval by the local IBC and COMIRB *prior* to initiation

This section covers the use or “transfer” of any rDNA, or DNA or RNA derived from rDNA, into one or more human subjects, to include certain DNA vaccine trials designed to trigger the immune response to fight diseases. This includes having the vaccine trial reviewed and approved by the IBC in conjunction with COMIRB.

1. Human gene transfer is the process of transferring genetic material (DNA or RNA) into a person with the intent of compensating for defective genes, producing a potentially therapeutic substance, or triggering the immune system to fight disease. At present, human gene transfer is experimental.
2. There are not expedited review or compassionate use exceptions for IBC review and approval.

Section III-D – Experiments that require registration and IBC approval *prior* to initiation

This section describes several categories or experiments involving rDNA for which the laboratory PI must submit a university application form and complete the full local review and approval process prior to initiating these components of their research.

1. Experiments using Risk Group 2, 3, or 4 or Restricted Agents as host-vector systems.
2. Experiments in which DNA from Risk Group 2, 3, or 4 or Restricted Agents is closed into nonpathogenic prokaryotic or lower eukaryotic host-vector systems.

3. Experiments involving the use of recombinant viruses in tissue culture systems; or defective recombinant viruses in the presence of helper-virus or packaging cells in tissue culture systems **(including all eukaryotic viruses)**.
4. Experiments that generate transgenic animals, including insects, with certain exemptions for transgenic rodents meeting ABSL1 criteria.
5. Experiments involving viable rDNA-modified microorganisms tested on whole animals.
6. Experiments involving genetically modified whole plants, or using plants together with microorganisms or insects containing rDNA, with certain exemptions for materials meeting BSL1(P) criteria.
7. Experiments involving large-scale (10 L or more) culture of organisms containing rDNA molecules.
8. Experiments involving human influenza strains H2N2, 1918 H1N1, or highly pathogenic H5N1.

Section III-E – Experiments that require IBC registration simultaneous with initiation

This section describes several categories of experiments involving rDNA that are fully contained at BSL1, and which **may be initiated while undergoing the full review and approval process with the IBC**.

1. Propagation and maintenance of cells in culture, containing rDNA molecules with no more than two-thirds of the genome of any eukaryotic virus, which are safely contained meeting BSL1 criteria (with the exception of DNA from RG 3 or 4 or Restricted Agents).
2. Experiments involving rDNA-modified whole plants, or experiments involving rDNA-modified organisms associated with whole plants, which may be safety contained meeting BSL2(P) or BSL2(P) criteria.
3. The generation of transgenic rodents by stable introduction into the germ-line of rDNA, or DNA derived therefrom, which are safely contained at ABSL1 criteria.
4. Cloning experiments in non-pathogenic prokaryotes and non-pathogenic lower eukaryotes, which are safely contained meeting BSL1 criteria.
5. Experiments involving whole plants that require BSL1 or BSL2 containment.

Section III-F – Experiments that require IBC registration, which are exempt from the full IBC review and approval process

1. Cloning or DNA in *E. coli* K12*, S. cerevisiae*, and *B. subtilis* host-vector systems, with the exception of DNA from RG3, 4 pathogens or other Restricted Agents.
2. Introduction into cultured cells or an rDNA **containing less than half** of a eukaryotic viral genome, with the exception of DNA from RG 3, 4 pathogens or other Restricted Agents.
3. Breeding two different transgenic strains of rodents to generate novel transgenic strains requiring BSL1 containment.