

Summary - NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

On behalf of the institution, the Principal Investigator is responsible for full compliance with the NIH Guidelines in the conduct of recombinant DNA research. Under these NIH Guidelines, the PI must:

1. determine the experimental class of the research (III-A through III-F) as identified in **Section III of the Guidelines**;
2. initiate or modify no recombinant DNA research which requires IBC approval prior to initiation (class III-A through III-D) until that research or the proposed modification thereof has been approved by the IBC and has met all other requirements of the NIH Guidelines;
3. Report any significant problems, violations of the NIH Guidelines, or any significant research-related accidents and illnesses to the IBC (using an **Adverse Biosafety Event Report Form** - see below) and Animal Facility Director (where applicable) immediately, and to the National Institutes of Health Office of Biotechnology Activities (NIH/OBA) and other appropriate authorities (if applicable) within 30 days.
4. report any new information bearing on the NIH Guidelines to the IBC and to NIH/OBA;
5. be adequately trained in good microbiological techniques;
6. adhere to IBC approved emergency plans for handling accidental spills and personnel contamination; and
7. comply with shipping requirements for recombinant DNA molecules.

The NIH Guidelines classify recombinant DNA research into several categories, each requiring different levels of review and approval - and in most cases, this review and approval must occur BEFORE the work is performed. A summary of the NIH classifications of recombinant DNA experiments, and the required level(s) of approval are as follows:

Section III-A – Experiments that Require IBC, NIH RAC Review and NIH Director Approval Before Initiation

These protocols are considered “Major Actions” and include the deliberate transfer of a drug resistance trait to a microorganism that is not known to acquire the trait naturally, if the acquisition of the drug resistant trait could affect the use of the drug to control the disease in humans, animals, or agriculture. For example, inserting a chloramphenicol-resistant trait into an infectious agent would fall under this category because chloramphenicol is still widely used in low income countries against a wide variety of microorganisms.

Section III-B – Experiments that Require NIH/OBA and IBC Approval Before Initiation

Protocols involving the cloning of toxin molecules with an LD50 of less than 100 ng/kg body weight fall into this category.

Section III-C – Experiments that Require IBC and IRB and RAC Review Before Research Participant Enrollment

Experiments involving the deliberate transfer of recombinant DNA, or DNA or RNA derived from recombinant DNA, into one or more research participants fall into this category. These protocols, often called human gene transfer protocols, may include the deliberate transfer of the DNA or RNA into humans as a marker in a cell, to compensate for defective genes, to produce a potentially therapeutic substance, or to trigger the immune system to fight disease.

Section III-D – Experiments that Require IBC Approval Before Initiation

Several categories of protocols fall under this section including:

- Experiments involving the introduction of recombinant DNA into risk group 2, 3 or 4 agents (mostly BSL2, BSL3, and BSL4 organisms)
- Experiments in which DNA from risk group 2, 3 or 4 agents (mostly BSL2, BSL3, and BSL4 organisms) is transferred into nonpathogenic prokaryotes or lower eukaryotes
- Experiments involving the use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in tissue culture systems

- Experiments involving whole animals, including the creation of transgenic organisms other than rodents
- Experiments involving viable recombinant or synthetic nucleic acid molecule-modified microorganisms tested on whole animals
- Experiments involving whole plants
- Experiments involving more than 10 liters of culture

Section III-E – Experiments that Require IBC Notice Simultaneous with Initiation

Several categories of protocol fall under this section including:

- Experiments involving the formation of recombinant or synthetic molecules containing no more than 2/3 of the genome of any eukaryotic virus
- Experiments involving the creation or mating of some transgenic rodents (see explanation in III-F)
- Experiments involving the transfection of recombinant DNA molecules into tissue culture
- Experiments that don't fall into any other category, such as experiments involving the introduction of risk group 1 DNA/RNA into risk group 1 organisms such as *E. coli* BL21

Section III-F – Experiments Exempt From NIH Guidelines but Which Require Notification of the OUHSC IBC

- Experiments that consist entirely of DNA from a prokaryotic host when propagated only in that host or those that consist entirely of DNA from a eukaryotic host when propagated only in that host.
- Experiments involving recombinant DNA containing less than ½ of any eukaryotic viral genome propagated and maintained in cells in tissue culture.
- The use of existing tissue culture cell lines created by the introduction of recombinant or synthetic nucleic acid molecules if no further recombinant activities are performed on those cells
- Experiments which use risk group 1 or 2 DNA/RNA inserted into *E. coli* K-12, *Saccharomyces*, or *Bacillus subtilis* or *Bacillus licheniformis* host-vector systems (***E. coli* BL21 does not fall into this category**), which do not involve the cloning of toxin molecules or large-scale experiments (more than 10 liters of culture)
- Experiments involving the mating of two transgenic lines to form a third, unique transgenic line that also meets the following criteria:
 - (1) Both parental rodents can be housed under BL1 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.