Recombinant DNA Categories vs. Review Bodies

As described in Section 3 of the NIH Guidelines, the Institutional Biosafety Committee functions on behalf of the Institution, with responsibility for overseeing all experimentation that involves the use of recombinant and synthetic nucleic acid molecules.

Recombinant and synthetic nucleic acid molecule experiments have been grouped into the following six categories by NIH. The first five (non-exempt) categories are subject to IBC oversight.

1. **Experiments that Require Institutional Biosafety Committee Approval, RAC Review, and NIH Director Approval Before Initiation**
   - The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally, if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture, will be reviewed by RAC.

2. **Experiments that Require NIH/OBA and Institutional Biosafety Committee Approval Before Initiation**
   - Experiments involving the deliberate formation of recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight (e.g., microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin, and *shigella dysenteriae* neurotoxin).

3. **Experiments that Require Institutional Biosafety Committee Approval, and Institutional Review Board Approvals and RAC Review before Research Participant Enrollment**
   - Experiments involving the deliberate transfer of recombinant or synthetic nucleic acid molecules, DNA or RNA Derived from Recombinant or synthetic nucleic acid molecules into one or more human research participants. *Note that RAC approval must be granted before the IBC can approve any such protocol.*

4. **Experiments that Require Institutional Biosafety Committee Approval, Before Initiation**
   - Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems
   - Experiments in Which DNA From Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents is Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems
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

Experiments Involving Whole Plants (involving use of pathogenic plant microorganisms/insects, or recombinant plants with potentially hazardous properties)

Experiments Involving More than 10 Liters of Culture

Experiments Involving Influenza Viruses

5. **Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation**

- Experiments not included in categories 1-4 or 6, are considered in category 5. All such experiments may be conducted at BL1 containment. *For example, experiments in which all components derived from non-pathogenic prokaryotes and non-pathogenic lower eukaryotes may be conducted at BL1 containment.*

- Experiments Involving the Formation of Recombinant DNA Molecules Containing No More than Two- Thirds of the Genome of any Eukaryotic Virus

- Experiments Involving Whole Plants (involving use of non-pathogenic plant microorganisms, or recombinant plants with non-hazardous properties)

- Experiments Involving Transgenic Rodents - BSL1 ONLY (involving the generation of rodents in which the animal's genome has been altered by the stable introduction of recombinant or synthetic nucleic acid molecules or nucleic acids derived there from into the germ-line).

6. **Exempt Experiments**

The following recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines and registration with the IBC is **not required**:

- Those synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to integrate into DNA, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight. If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III-C, it is not exempt under this Section.

- Those that are not in organisms, cells, or viruses and that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes.

- Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.
- Those that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means.
- Those that consist entirely of nucleic acids from a eukaryotic host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species).
- Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent. See Appendices A-1 through A-VI, *Exemptions under Section III F-6-Sublists of Natural Exchangers*, for a list of natural exchangers that are exempt from the NIH Guidelines.
- Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.
- Those that do not present a significant risk to health or the environment as determined by the NIH Director, with the advice of the RAC. See *Appendix C, Exemptions under Section III F-8* for other classes of experiments which are exempt.
- Additional information is available from NIH though their FAQ document for Exempt Experiments.