



GUIDE TO THE NIH GUIDELINES

Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

Compliance with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* is mandatory for every institution that receives NIH funding for research involving recombinant DNA (rDNA) or synthetic nucleic acids. It is the responsibility of each investigator to make sure that his/her laboratory is in compliance. If your experiments require registration, contact EHS at 372-3587. This outline is intended only to serve as a guide to the *NIH Guidelines*. If you are unsure in which category your experiments may fall, contact EHS.

Section III-A,B,C – Experiments that require NIH and Institutional Biosafety Committee (IBC) approval 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. (Section III-A-1)
2. 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 (Section III-B-1)
3. All human gene transfer experiment (Section III-C-1)

Section III-D - Experiments that require IBC approval PRIOR to initiation:

1. Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems. (Section III-D-1)
2. Experiments in which DNA from Risk Group 2, 3, or 4 agents is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems. (Section III-D-2)
3. 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. (Section III-D-3)
4. Experiments involving whole animals in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic animals) and experiments involving viable recombinant or synthetic nucleic acid molecule-modified microorganisms tested on whole animals. (Section III-D-4)
5. Experiments to genetically engineer plants by recombinant or synthetic nucleic acid molecule methods, to use such plants for other experimental purposes (e.g., response to stress), to propagate such plants, or to use plants together with microorganisms or insects containing recombinant or synthetic nucleic acid molecules that require BL3 or BL4 containment. (Section III-D-5)
6. Experiments involving more than 10 liters of culture. (Section III-D-6)
7. Experiments involving human influenza strains H2N2, 1918 H1N1, and/or highly pathogenic avian influenza H5N1. (Section III-D-7)

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

1. Recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus (with the exception of Risk Group 3 or 4 agents). (Section III-E-1)
2. Experiments involving nucleic acid molecule-modified whole plants, and/or experiments involving recombinant or synthetic nucleic acid molecule-modified organisms associated with whole plants that require BL1 or BL2 containment. (Section III-E-2)

3. Experiments with recombinant or synthetic nucleic acid molecule-modified arthropods or small animals associated with plants, or with arthropods or small animals with recombinant or synthetic nucleic acid molecule-modified microorganisms associated with them if the recombinant or synthetic nucleic acid molecule-modified microorganisms have no recognized potential for serious detrimental impact on managed or natural ecosystems. (Section III-E-2)
4. Experiments involving the generation of rodents in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic rodents). Only experiments that require BL1 containment are covered under this section, (Section III-E-3)
5. Breeding experiments to generate transgenic rodents that contain more than 50% of the genome of an exogenous eukaryotic virus, or in which the transgene is under the control of a gammaretroviral LTR. (Section III-E-3; Appendix C-VIII)

Section III-F - Experiments that are exempt but still require IBC registration:

1. Experiments that use synthetic nucleic acids that can neither replicate nor generate nucleic acids capable of replicating in any living cell; are not designed to integrate into DNA, and do not produce a toxin that is lethal for vertebrates at an LD50 of <100 ng/kg body weight. (Section-III-F)
2. Experiments that use recombinant or synthetic nucleic acids molecules 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. (Section-III-F)
3. Experiments that use recombinant or synthetic nucleic acids molecules that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature. (Section-III-F)
4. Experiments that use recombinant or synthetic nucleic acids molecules 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. (Section-III-F)
5. Experiments that use recombinant or synthetic nucleic acids molecules 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). (Section-III-F)
6. Experiments that use recombinant or synthetic nucleic acids molecules 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. (Section-III-F)
7. Experiments that use recombinant or synthetic nucleic acids molecules genomic DNA molecules that have acquired a transposable element provided the transposable element does not contain any recombinant and/or synthetic DNA. (Section-III-F)