

**NIH Guidelines** ([http://oba.od.nih.gov/oba/rac/guidelines\\_02/NIH\\_Guidelines\\_Apr\\_02.htm](http://oba.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm)):

Please use the below guidelines as a reference to accurately assign the proper section of the NIH Guidelines that is applicable to your rDNA work. The proper NIH Guideline section should be indicated on the application form.

**Section III-A Experiments that require Institutional Biosafety Committee (IBC) approval and NIH Director approval before initiation of experiments.**

- III-A-1-a 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 the disease agents in humans, veterinary medicine or agriculture.

**Section III-B Experiments that require NIH/OBA and IBC approval before initiation.**

- III-B-1 Deliberate formation of rDNA containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD50 of less than 100 nanograms per kg body weight (e.g. microbial toxins such as tetanus toxin).

**Section III-C Experiments that require IBC and Institutional Review Board (IRB) approvals, and NIH/OBA registration before initiation.**

- III-C-1 Experiments involving the deliberate transfer of (1) recombinant DNA or (2) DNA or RNA derived from recombinant DNA into one or more human subjects.

**Section III-D Experiments that require IBC approval before initiation of experiments.**

- III-D-1-a Introduction of recombinant DNA into Risk Group 2 (RG-2) agents is usually conducted at BL2 containment. Experiments with such agents will usually be conducted with whole animals at BL2 or BL2-N containment.
- III-D-1-b Introduction of recombinant DNA into Risk Group 3 (RG-3) agents is usually conducted at BL3 containment. Experiments with such agents will usually be conducted with whole animals at BL3 or BL3-N containment.
- III-D-2-a Experiments in which DNA from Risk Group 2 or Risk Group 3 agents is transferred into nonpathogenic prokaryotes or lower eukaryotes may be performed under BL2 containment. Experiments in which DNA from Risk Group 4 agents is transferred into nonpathogenic prokaryotes or lower eukaryotes may be performed under BL2 containment after demonstration that only a totally and irreversibly defective fraction of the agent's genome is present in a given recombinant. In the absence of such a demonstration, BL4 containment shall be used. The Institutional Biosafety Committee may approve the specific lowering of containment for particular experiments to BL1. Many experiments in this category are exempt from the NIH Guidelines.
- III-D-3-a Experiments involving the use of infectious or defective Risk Group 2 viruses in the presence of helper virus may be conducted at BL2.
- III-D-3-b Experiments involving the use of infectious or defective Risk Group 3 viruses in the presence of helper virus may be conducted at BL3.
- III-D-3-d Experiments involving the use of infectious or defective restricted poxviruses in the presence of helper virus shall be determined on a case-by-case basis following NIH/OBA review. A U.S. Department of Agriculture permit is required for work with plant or animal pathogens.
- III-D-3-e Experiments involving the use of infectious or defective viruses in the presence of helper virus which are not covered in [Sections III-D-3-a](#) through III-D-3-d may be conducted at BL1.
- III-D-4-a Recombinant DNA, or DNA or RNA molecules derived therefrom, from any source except for greater than two-thirds of eukaryotic viral genome may be transferred to any non-human vertebrate or any invertebrate organism and propagated under conditions of physical containment comparable to BL1 or BL1-N and appropriate to the organism under study. Animals that contain sequences from viral vectors, which do not lead to transmissible infection either directly or indirectly as a result of complementation or recombination in animals, may be propagated under conditions of physical containment comparable to BL1 or BL1-N and appropriate to the organism under study. Experiments involving the introduction of other sequences from eukaryotic viral genomes into animals are covered under [Section III-D-4-b, Experiments Involving Whole](#)

*Animals.* For experiments involving recombinant DNA-modified Risk Groups 2, 3, 4, or restricted organisms, see [Sections V-A, V-G, and V-L](#), *Footnotes and References of Sections I-IV*. It is important that the investigator demonstrate that the fraction of the viral genome being utilized does not lead to productive infection. A U.S. Department of Agriculture permit is required for work with plant or animal pathogens.

- III-D-4-b For experiments involving recombinant DNA, or DNA or RNA derived therefrom, involving whole animals, including transgenic animals, and not covered by [Sections III-D-1](#), *Experiments Using Human or Animal Pathogens (Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems)*, or [III-D-4-a](#), *Experiments Involving Whole Animals*, the appropriate containment shall be determined by the Institutional Biosafety Committee.
- III-D-4-c-1 Experiments involving the generation of transgenic rodents that require BL1 containment are described under [Section III-E-3](#)
- III-D-4-c-2 The purchase or transfer of transgenic rodents is exempt from the *NIH Guidelines* under [Section III-F](#), *Exempt Experiments*
- III-D-5 Experiments to genetically engineer plants by recombinant DNA 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 DNA, may be conducted under the containment conditions described in Sections III-D-5-a through III-D-5-e. If experiments involving whole plants are not described in Section III-D-5 and do not fall under Sections III-A, III-B, III-D or III-F, they are included in Section III-E.
- III-D-6 Experiments involving more than 10 liters of culture. The appropriate containment will be decided by the IBC. Where appropriate Appendix K of the guidelines will be used to determine containment.

### **Section III-E Experiments that require IBC notification simultaneously with initiation.**

- III-E Experiments not included in Sections [III-A](#), [III-B](#), [III-C](#), [III-D](#), [III-F](#), and their subsections are considered in [Section III-E](#). All such experiments may be conducted at BL1 containment.
- III-E-1 Recombinant DNA molecules containing no more than two-thirds of the genome of any eukaryotic virus (all viruses from a single Family being considered identical) may be propagated and maintained in cells in tissue culture using BL1 containment. For such experiments, it must be demonstrated that the cells lack helper virus for the specific Families of defective viruses being used. If helper virus is present, procedures specified under [Section III-D-3](#), *Experiments Involving the Use of Infectious Animal or Plant DNA or RNA Viruses or Defective Animal or Plant DNA or RNA Viruses in the Presence of Helper Virus in Tissue Culture Systems*, should be used. The DNA may contain fragments of the genome of viruses from more than one Family but each fragment shall be less than two-thirds of a genome.
- III-E-2 Experiments involving recombinant DNA-modified whole plants, and/or experiments involving recombinant DNA-modified organisms associated with whole plants, except those that fall under [Section III-A](#), [III-B](#), [III-D](#), or [III-F](#). See [Section III-E-2](#) for recommendation of containment level.
- III-E-3 Experiments involving the generation of rodents in which the animal's genome has been altered by stable introduction of recombinant DNA, or DNA derived therefrom, into the germ-line (transgenic rodents). Only experiments that require BL1 containment are covered under this section; experiments that require BL2, BL3, or BL4 containment are covered under [Section III-D-4](#)

### **Section III-F Experiments that are exempt from NIH Guidelines. Registration with the IBC is not necessary except for transgenic rodents.**

- III-F-1 Recombinant DNA molecules are not in organisms or viruses.
- III-F-2 Recombinant DNA molecules that consist entirely of DNA segments from a single nonchromosomal or viral DNA source, though one or more of the segments may be a synthetic equivalent.
- III-F-3 Recombinant DNA molecules that consist entirely of DNA 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.
- III-F-4 Recombinant DNA molecules that consist entirely of DNA 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).

- III-F-5 Recombinant DNA 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 synthetic equivalent.
- III-F-6 Recombinant DNA experiments that do not present a significant risk to health or the environment, as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment.