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

Compliance with the *NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules* (http://oba.od.nih.gov/rdna/nih_guidelines_oba.html) 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. This outline is intended only to serve as a guide to the *NIH Guidelines*.

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

- "Major Action" – 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 use of the drug to control disease agents in humans, veterinary medicine, or agriculture

*Section III-B – Experiments that require NIH/OBA and IBC Approval **PRIOR** to Initiation:*

- Experiments involving the cloning of toxin molecules with LD_{50} of less than 100 nanograms per kilogram body weight.

*Section III-C – Experiments the require RAC Review, IBC Approval and IRB Approval **PRIOR** to Initiation:*

- Experiments involving the deliberate transfer of recombinant DNA, or DNA or RNA derived from recombinant DNA, into one or more human research participants

*Section III-D - Experiments that require IBC Approval **PRIOR** to Initiation:*

1. Experiments using Risk Group 2, 3, or 4 agents as host-vector systems.
2. Experiments in which DNA from Risk Group 2, 3, or 4 agents is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems.
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.
4. Experiments involving whole animals in which the animal's genome has been altered by stable introduction of recombinant DNA into germline (transgenic animals).
5. Experiments involving whole animals in which viable recombinant DNA-modified microorganisms are tested on whole animals.
6. Experiments involving whole animals where BL2 and BL2-N or higher is required.
7. Experiments involving whole plants in which plants are genetically engineered by recombinant DNA methods.
8. Experiments involving whole plants in which plants are used with recombinant DNA-modified insects.
9. Experiments involving whole plants in which generally BL2-P through BL4-P, depending on risk is required.
10. Experiments involving more than 10 liters of culture.
11. Experiments involving influenza viruses generated by recombinant methods (e.g., reverse genetics of chimeric viruses with reassorted segments, introduction of specific mutations) shall be conducted at the biosafety level containment corresponding to the risk group of the virus that was the source of the majority of segments in the recombinant virus.
12. Experiments involving influenza viruses containing genes or segments from 1918-1919 H1N1 (1918 H1N1), human H2N2 (1957-1968) and highly pathogenic avian influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1) shall be conducted at BL3 enhanced containment.

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

1. Experiments involving the formation of recombinant DNA molecules containing no more than 2/3 of the genome of any eukaryotic virus.
2. Experiments involving whole plants.
3. Experiments involving transgenic rodents.
4. Experiments not included in III-A – III-D or III-F.
5. Experiments involving the generation of transgenic rodents in which rodent's genome has been altered by stable introduction of recombinant DNA into germline.
6. Experiments involving the generation of transgenic rodents in which BL1 containment is appropriate.

Section III-F - Experiments that are exempt:

1. Experiments that are not in organisms or viruses.
2. Experiments 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.
3. Experiments 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.
4. Experiments that consist entirely of DNA from an 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).
5. Experiments 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 (meaning recombinant DNA molecules that are composed entirely of DNA segments from one or more of the organisms within as submist, and to be propagated in any of the organisms within the same sublist).
6. 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.
7. Recombinant DNA molecules containing less than one-half of any eukaryotic viral genome [all viruses from a single family being considered identical that are propagated and maintained in cells in tissue culture are exempt (with the exceptions listed in Appendix C-1-A)].
8. Experiments which use *Escherichia coli* K-12 host-vector systems (with the exception of those experiments listed in Appendix C-1-A).
9. Experiments involving *S. cerevisiae* and *S. uvarum* host-vector systems (with the exception of experiments listed in Appendix C-III-A
10. Any asporogenic *Bacillus subtilis* or asporogenic *Bacillus licheniformis* strain which does not revert to a sporeformer with a frequency greater than 10^7 may be used for cloning DNA (with the exception of those experiments listed in Appendix C-IV-A, *Exceptions*).
11. Recombinant DNA molecules derived entirely from extrachromosomal elements of the organisms listed in the *NIH Guidelines*, propagated and maintained in organisms listed in the *NIH Guidelines*
12. The purchase or transfer of transgenic rodents for experiments that require BL1 containment.