Oklahoma State University
Institutional Biosafety Committee (IBC)
NIH Guidelines Summary

The full text of the *NIH Guidelines for Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* is available HERE.

Section III. Experiments Covered by the *NIH Guidelines*

Section III-A. Experiments Requiring IBC Approval, RAC Review, and NIH Director Approval Before Initiation (A.K.A., Major Actions)

- 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 ability to control disease agents in humans, veterinary medicine, or agriculture.

Section III-B. Experiments That Require NIH/OBA and IBC Approval Before Initiation

- III-B-1 - Cloning of toxin molecules with LD_{50} less than 100 nanograms per kilogram body weight.
- III-B-2 - Experiments that have been approved as Major Actions under the *NIH Guidelines*.
    - **Note: This determination must be made by NIH/OBA.**

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

- III-C-1 - Deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participants.

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

- III-D-1 - Experiments using Risk Group 2, Risk Group 3, Risk Group 4, or restricted agents as host-vector systems.
- III-D-2 - 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.
    - **Note: Many experiments in this category are exempt from the *NIH Guidelines* (see Section III-F).**
- III-D-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.
    - **Note: Recombinant or synthetic nucleic acid molecules or nucleic acid molecules derived therefrom, which contain less than two-thirds of the genome of any eukaryotic virus being considered identical, are considered defective and may be used in the absence of helper under the conditions specified in this section.**
- III-D-4 - Experiments involving whole animals (except experiments involving the generation of transgenic rodents that require BSL-1 containment, which are described in Section III-E).
    - **Note: The purchase or transfer of transgenic rodents is exempt from the *NIH Guidelines* (see Section III-F).**
- III-D-5 - Experiments involving whole plants.
- III-D-6 - Experiments involving more than 10 liters of culture.

- III-D-7 - Experiments involving influenza viruses.

Section III-E. Experiments that Require IBC Notice Simultaneous with Initiation (Note: OSU requires IBC review and approval of all research which falls under the *NIH Guidelines* prior to initiation)

- **Note: Experiments not included in Section III-A, III-B, III-C, III-D, III-F, and their subsections are considered in this section.**
- III-E-1 - Experiments involving the formation of recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus.
    - **Note: For BSL-1 containment, it must be demonstrated that the cells lack helper virus for the specific families of defective viruses being used. If helper virus is present, refer to Section III-D.**
- III-E-2 - Experiments involving whole plants.
- III-E-3 - Experiments involving transgenic rodents that require BSL-1 containment (see Section III-D for experiments that require BSL-2, BSL-3, or BSL-4 containment).

Section III-F. Exempt Experiments (Note: OSU researchers may only self-exempt for activities involving synthetic nucleic acid molecules that cannot replicate or generate nucleic acids that can subsequently replicate in any living cell [e.g., oligonucleotides]. All other exempt activities must be reviewed and approved by the IBC prior to initiation.)

- III-F-1 - Those synthetic nucleic acids that: (1 can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotids 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.
    - **Note: 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.**
- III-F-2 - 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.
- III-F-3 - Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.
- III-F-4 - 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.
- III-F-5 - 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).
- III-F-6 - 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.
- III-F-7 - Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.

- III-F-8 - 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, and following appropriate note and opportunity for public comment.

Determining Risk Group Classification

Appendix B of the *NIH Guidelines* classifies organisms into risk groups based on their ability to cause disease in healthy adult humans (see Table 1 below). However, the OSU IBC also considers an organism's ability to cause disease in animals. Please see Table 2 for the classification scheme currently used by the IBC.

Table 1. Classification of Human Etiologic Agent on the Basis of Hazard

Risk Group 1 (RG1)	Agents that are not associated with disease in healthy adult humans
Risk Group 2 (RG2)	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available
Risk Group 3 (RG3)	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may* be available (high individual risk but low community risk)
Risk Group 4 (RG4)	Agent that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available (high individual risk and high community risk.

Table 2. WHO Classification of Infective Microorganisms by Risk Group

Risk Group 1 (RG1)	A microorganism that is unlikely to cause human or animal disease
Risk Group 2 (RG2)	A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock, or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
Risk Group 3 (RG3)	A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.
Risk Group 4 (RG4)	A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

Please contact the Biosafety Officer (744-3203) if you need assistance with risk group determination or in assessing which sections of the *NIH Guidelines* apply to your experiments.