NIH Guidelines Reference Updated 9/2019

Use this Classification Guide to refer to the relevant section of the *NIH Guidelines*. The questions in the left column categorize the experiments into six levels of review specified in the *NIH Guidelines*. Access the complete details from the NIH Office of Biotechnology Activities (OBA), online at http://osp.od.nih.gov/office-biotechnology-activities.

CATEGORY OF EXPERIMENTS	LEVEL OF REVIEW IN THE *NIH GUIDELINES*
A **Does the experiment involve** the transfer of a drug resistant trait to microorganisms that are not known acquire the trait naturally, if this acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture?	**Section III-A: Major Actions** **Experiments require IBC and NIH/RAC review, and NIH Director approval before initiation.** See the *NIH Guidelines* and FAQs at http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.
B **Does the experiment involve** cloning genes for toxin molecules with an LD_{50} of less than 100 ng/kg body weight? OR Has the experiment been approved previously as a Major Action under Section III-A-1-a of the NIH Guidelines?	**Section III-B: Toxins, Previous Major Actions** **Experiments require IBC approval and NIH review for containment determinations before initiation.** Principal Investigator must submit relevant information to NIH/OBA and NMSU IBC.
C **Does the experiment involve** the transfer of recombinant or synthetic nucleic acid molecules into human research participants?	**Section III-C: Human Gene Transfer** **Experiments require NIH/RAC review and NMSU IBC and IRB approval before research participant enrollment.** See Appendix M of the *NIH Guidelines.*

RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES

CATEGORY OF EXPERIMENTS	LEVEL OF REVIEW IN THE *NIH GUIDELINES*
D **Does the experiment involve:** • Using Risk Group (RG) 2 - 4, or restricted agents as host-vector systems? **Section III-D-1** • Cloning DNA from RG 2, RG 3, RG 4, or restricted agents into nonpathogenic prokaryotic or lower eukaryotic host-vector systems..... **Section III-D-2** • Using infectious viruses OR defective DNA or RNA viruses in the presence of helper virus in tissue culture systems? ..... **Section III-D-3** • Whole animals..... **Section III-D-4** ▪ Creating stable germ-line alterations of an animal's genome ▪ Testing viable recombinant-modified microorganisms on whole animals? • Whole plants (e.g., nucleic acid-modified plants or plant-associated organisms with recognized potential for detrimental impacts on ecosystems)? ..... **Section III-D-5** • More than 10 liters of culture?. **Section III-D-6** • Influenza viruses generated by recombinant or synthetic methods? ..... **Section III-D-7**	**Section III-D: Experiments require IBC approval** An IBC application is required, signed by the PI and containing: (i) the source of DNA; (ii) the nature of the inserted DNA sequences; (iii) the host and vector to be used; (iv) if an attempt will be made to obtain expression of a foreign gene, and if so, indicate the protein that will be produced; and (v) the containment conditions. Refer to the *NIH Guidelines* for details of Risk Group classifications and containment: • Appendix B, *Classification of Human Etiologic Agents on the Basis of Hazard* • Appendix B - Table 1. *Basis for the Classification of Biohazardous Agents by Risk Group* • Appendix E, *Certified Host-Vector Systems* • Appendix G, *Physical Containment* • Appendix G - Table 1. *Possible Alternate Combinations Of Physical And Biological Containment Safeguards* • Appendix I, *Biological Containment* • Appendix K, *Large Scale Uses of Organisms* • Appendix K - *Table 1. Comparison of Good Large Scale Practice (GLSP) and Biosafety Level (BL) - Large Scale (LS) Practice* • Appendix L, *Research Involving Plants* • Appendix M, *Research Involving Animals*

RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES

CATEGORY OF EXPERIMENTS	LEVEL OF REVIEW IN THE *NIH GUIDELINES*
E **Does the experiment involve**: • The formation of recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus, propagated and maintained in cells in tissue culture using BL1 containment and demonstrated lack of helper virus? • Whole plants, or modified organisms associated with plants, where plant biosafety level 1 (BL1-P) or BL2-P containment is appropriate? • The generation of BL1 transgenic rodents? • Experiments not included in III-A through III-D or III-F, where BL-1 containment is appropriate?	**Section III-E: NMSU IBC approval at initiation** An IBC application is required, signed by the PI. For many experiments in this category, all components are derived from non-pathogenic prokaryotes and non-pathogenic lower eukaryotes. The experiments can be initiated under a provisional approval until the IBC review is completed (see the *NIH Guidelines* Section IV-A, *Policy*).
F **Is the experiment exempt from the *NIH Guidelines*?** Refer to the full text of the *NIH Guidelines* and FAQs at http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines	**Section III-F Exempt Experiments** Although Section III-F experiments are exempt from the *NIH Guidelines*, other federal and state standards of biosafety may still apply. The final determination of whether a project meets the definition of exempt status rests with the IBC.

Note: If an experiment falls into Section III-F and into either Sections III-D or III-E as well, the experiment is considered exempt from the *NIH Guidelines.*

Section III-F Exempt Experiments

- **Section III-F-1**. Synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell, 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.

RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES

CATEGORY OF EXPERIMENTS	LEVEL OF REVIEW IN THE *NIH GUIDELINES*

- **Section III-F-2**. Recombinant or synthetic nucleic acid 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**. Those 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**. 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.
- **Section 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).
- **Section 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. A list of such exchangers will be prepared and periodically revised by the NIH Director with advice of the RAC after appropriate notice and opportunity for public comment (see Section IV-C-1-b-(1)-(c), *Major Actions*). See Appendices A-I 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*.
- **Section 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.
- **Section III-F-8**. Those that do not present a significant risk to health or the environment (see Section IV-C-1-b-(1)-(c), *Major Actions*), as determined by the NIH Director, with the advice of the RAC, and following appropriate notice and opportunity for public comment. See Appendix C, *Exemptions under Section III-F-8* for other classes of experiments which are exempt from the *NIH Guidelines* (also note that exceptions apply):
  - Recombinant or synthetic nucleic acid molecules containing less than one-half of any eukaryotic viral genome viral genome, that are propagated and maintained in cells in tissue culture
  - ***Escherichia coli K-12*** Host-Vector Systems
  - ***Saccharomyces*** Host-Vector Systems
  - ***Kluyveromyces*** Host-Vector Systems
  - ***Bacillus subtilis*** or ***Bacillus licheniformis*** Host-Vector Systems
  - Extrachromosomal Elements of Gram Positive Organisms
  - The purchase or transfer of transgenic rodents for experiments that require BL1 containment
  - The breeding of transgenic rodents to create a new strain that can be housed at BL1 containment.

Refer to the full text of the *NIH Guidelines* and FAQs at
http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines

RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES

The complete text of the *NIH Guidelines* can be searched by topic, using the TABLE OF CONTENTS to navigate:

RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES