UPDATE TO THE NIH GUIDELINES ON RESEARCH INVOLVING RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES

Stanford University Environmental Health & Safety

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Does your research require approval from the Stanford University Administrative Panel on Biosafety (APB) per the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules?

- **At Stanford, ALL research must comply with the NIH Guidelines**. It is the responsibility of each principal investigator to make sure that their laboratory is in compliance with these Guidelines. Research that is non-exempt (see below) under the Guidelines requires APB approval.
- This document provides an overview of the "NIH Guidelines for Research Involving Recombinant DNA or Synthetic Nucleic Acid Molecules". NOTE: **UPDATED GUIDELINES** INCLUDE WORK WITH **rDNA AND SYNTHETIC NUCLEIC ACID MOLECULES** (March 2013).
- For information or questions, contact Biosafety at 650.725.1473 or see the following documents:

NIH FAQs on Guideline Exemptions	Stanford University Biosafety Program
NIH FAQs on Synthetic Nucleic Acids	Working with Viral Vectors (Stanford)
NIH Guidelines	Overview of Covered Experiments (Yale)

If your research requires APB approval, please go to **eprotocol.stanford.edu**.

Approval required for experiments involving: (Specific NIH Guideline Section)	Further Information and Examples:
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 ability to control disease agents in humans, veterinary medicine or agriculture. (III-A-1-a)	• Transferring a drug resistance trait that is used, had previously been used, may be used (including outside the U.S.), or that is related to other drugs that are used to treat or control disease agents. • Examples include transfer of: erythromycin resistance into *Borrelia burgdorferi*; pyrimethamine resistance into *Toxoplasma gondii*; chloramphenicol resistance into *Rickettsia conorii*; tetracycline resistance into *Porphyromonas gingivalis*.
2. Cloning of DNA, RNA or synthetic nucleic acid molecules encoding toxins	• Cloning toxins (or using plasmids that express toxins with low LD50s).

lethal to vertebrates at an LD50 of <100ug/kg body weight. (III-B-1)	● Examples include: botulinum, tetrodotoxin, ricin, T-2, saxitoxin, abrin, tetanus, *Shigella dysenteriae* neurotoxin, pertussis, *Staph aureus* Beta, shigatoxin, and conotoxins.
3. Transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules into human research participants. (III-C-1)	● Use of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, that meet ANY of the following four criteria: o Contain >100nt, or o Possess biological properties that enable genome integration, or o Have the potential to replicate in a cell, or o Can be translated or transcribed. ● Examples include: use of a defective adenoviral vector to deliver the CFTR gene intranasally to patients with Cystic Fibrosis; introduction of an HSV-TK transduced cell line into patients with epithelial ovarian carcinoma; introduction of a shRNA delivered in a plasmid, bacterial or viral vector.
4. Risk Group 2, Risk Group 3, Risk Group 4 or Restricted Agents used as Host-Vector Systems. (III-D-1) (Item 4 cont.) (III-D-1)	● The introduction of recombinant or synthetic nucleic acid molecules into Risk Group 2, 3, 4, or Restricted Agents that meet ANY of the following criteria: o Have the potential to replicate in a cell, or o Possess biological properties that enable genome integration, or o Produce a toxin lethal to vertebrates at an LD50 of <100ug/kg body weight. ● Examples include: Adenovirus, Herpes virus, Lentivirus, Amphotrophic or VSV-g pseudotyped Murine Retrovirus, Human Retrovirus, Vaccinia virus Vesicular Stomatitis virus, and Adeno-Associated virus with helper virus.
5. DNA from Risk Group 2, Risk Group 3, Risk Group 4 or Restricted Agents cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems. (III-D-2)	● Transfer of DNA from Risk Group 2, 3, 4, or Restricted Agents into nonpathogenic prokaryotes or lower eukaryotes. ● Use of pathogens or defective pathogens as vectors. ● Examples include: Adenovirus, Herpes virus, Lentivirus, Amphotrophic or VSV-g pseudotyped Murine Retrovirus, Human Retrovirus, Vaccinia virus Vesicular Stomatitis virus, and Adeno-Associated virus with helper virus.
6. Infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in tissue culture systems. (III-D-3)	● rDNA experiments involving Risk Group 2, 3, or 4 pathogens. ● rDNA experiments involving ≤ 2/3 of the genome from eukaryotic viruses in the presence of a helper virus. ● Examples include: HIV, HTLV-I & II, West Nile Virus, and Lymphocytic Choriomeningitis Virus.
7. Whole animals, including transgenic animals. (III-D-4)	● Experiments utilizing any of the following that may lead to transmissible infection either directly or indirectly as a result of complementation or recombination in the animal: o > 2/3 of eukaryotic viral genome, or o Animals containing sequences from viral vectors, or o Stable integration of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germline.

	• Use of viable recombinant or synthetic nucleic acid molecule-modified Risk Group 2, 3, 4 or Restricted Agent microorganisms tested on whole animals.
8. Whole plants. (III-D-5)	• Experiments involving exotic infectious agents when recombinant or synthetic nucleic acid molecule techniques are associated with whole plants. • Experiments with plants involving cloned genomes of readily transmissible exotic infectious agents. • Experiments with plants involving readily transmissible exotic infectious agents (i.e. soybean rust fungus *Phakopsora pachyrhizi*, maize streak or other viruses) in the presence of their specific arthropod vectors. • Experiments involving plants or their associated organisms and the introduction of sequences encoding potent vertebrate toxins. • Experiments involving microbial pathogens of insects, arthropods or small animals associated with plants if the recombinant or synthetic nucleic acid molecule-modified organism can detrimentally impact the ecosystem.
9. Large-scale DNA work. (III-D-6)	• ≥ 10 liters of culture combined. • Examples include: Use of ≥10 L fermentor; growing up to five 2 L flasks of rDNA culture (i.e. E. coli K-12).
10. Influenza virus. (III-D-7)	• Experiments with Influenza virus shall be conducted at the BSL containment corresponding to the Risk Group of the virus that was the source of the majority of segments. • Experiments that alter antiviral susceptibility may increase containment level requirements. • Examples of BSL3 influenza work: 1957-1968 Human H2N2, Highly pathogenic avian influenza H5N1 strains within the Goose/Guangdong/06-like H5 lineage (HPAI H5N1), 1918 H1N1.