NIH Guidelines Overview

UF Biosafety Office 2020
Section III-A: Experiments that Require NIH Director Approval and IBC Approval Before Initiation

Section III-A-1-a: Deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally which can compromise treatment or control. Example: *M. tuberculosis* engineered to be resistant to rifampin

IBC Deliberation: Determination of applicability, perhaps through NIH OSP consult

NIH Director Approval: Initiated upon submission of relevant information on the proposed experiment to NIH OSP, preferably by e-mail to: NIHGuidelines@od.nih.gov

IBC Approval before Initiation

Section III-B: Experiments that Require NIH OSP and IBC Approval Before Initiation

Section III-B-1: Experiments Involving the Cloning of Toxin Molecules with LD₅₀ of <100 ng/kg Body Weight. Example: Cloning of botulinum toxins.

IBC Deliberation: Determination of applicability, perhaps through NIH OSP consult

NIH OSP Approval: Initiated upon submission of relevant information on the proposed experiment to NIH OSP.

IBC Approval before Initiation

Section III-B-2: Experiments approved (under Section III-A-1-a) as Major Actions under the NIH Guidelines

IBC Deliberation: Determination of applicability, perhaps through NIH OSP consult

NIH OSP Approval: NIH OSP determines no substantive differences in the proposed study relative to the initial III-A-1-a approval regarding biosafety/public health considerations

IBC Approval before Initiation

Section III-C: Experiments Involving Human Gene Transfer that Require IBC Approval Prior to Initiation

Section III-C-1: Deliberate Transfer of rsNA Molecules, or nucleic acids derived thereof, into One or More Human Research Participants. Example: Clinical trials.

IBC Approval before Initiation: Contingent upon all other applicable institutional and regulatory authorization(s)
Section III-D: (1-4)
Experiments that Require IBC Approval Before Initiation

Section III-D-1:
Using RG2, RG3, RG4, or Restricted Agents as Host-Vector Systems
- III-D-1-a: rsNA molecules into RG2 vector. Example: Using S. Typhi to harbor plasmids.
- III-D-1-b: rsNA molecules into RG3 vector. Example: Formation of lentiviral vectors
- III-D-1-c: rsNA molecules into RG4 vector
- III-D-1-d: rsNA molecules into restricted agent vector

NIH OSP Review
Case-by-case basis

Section III-D-2:
Experiments in which DNA From RG2, RG3, RG4, or Restricted Agents is Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems
- III-D-2-a: DNA from RG2, RG3, and RG4 (granted an irreversibly defective fraction) transferred into nonpathogenic prokaryotes or lower eukaryotes. Example: Cloning Brucella genes into K-12 lineage (nonpathogenic) E. coli.

NIH OSP Review
Case-by-case basis

Section III-D-3:
Use of Infectious DNA or RNA Viruses or Defective DNA or RNA Viruses in the Presence of Helper Virus in Tissue Culture Systems
- III-D-3-a: RG2 viruses in the presence of helper virus. Example: AAV & Adenovirus 5.
- III-D-3-b: RG3 viruses in the presence of helper virus
- III-D-3-c: RG4 viruses in the presence of helper virus
- III-D-3-d: Restricted poxviruses in the presence of helper virus
- III-D-3-e: Viruses in the presence of helper virus, not covered by the prior sections

NIH OSP Review
Case-by-case basis

Section III-D-4:
Experiments Involving Whole Animals
- III-D-4-a: rsNA, except >2/3 eukaryotic viral genome, transferred to any non-human vertebrate or any invertebrate at ABSL-1. Example: AAV in vivo studies.
- III-D-4-b: rsNA, or nucleic acids derived thereof, in whole animals, not covered by III-D-1 or III-D-4-a. Example: Lentivirus in vivo studies.
- III-D-4-c: Exceptions
  - III-D-4-c-(1): Transgenic rodents under ABSL-1 containment
  - III-D-4-c-(2): Purchase or transfer of transgenic rodents

Section III-D-4-c: Exceptions
Section III-D: (5-7)
Experiments that Require IBC Approval Before Initiation

Section III-D-5: Experiments Involving Whole Plants (BSL-2P+, -3P, or -4P)

III-D-5-a: Plants associated with exotic infectious agents associated with serious environmental concerns.

III-D-5-b: Plants containing the genomes of transmissible exotic agents, with serious environmental concerns.

III-D-5-c: Plants containing readily transmissible exotic high-impact pathogens with arthropod vectors.

III-D-5-d: Plants encoding vertebrate toxins with an LD₅₀ of <100 ng/kg body weight.

III-D-5-e: RsNA-modified microbial pathogens of insects or small animals in plants.

Section III-D-6: Experiments Involving >10 Liters of Culture

Section III-D-7: Experiments Involving Influenza Viruses

Refer to Appendix K for containment guidance

III-D-7-a: Human H2N2 (1957-1968)

III-D-7-b: HPAI H5N1

III-D-7-c: 1918 H1N1

III-D-7-d: Antiviral Susceptibility and Containment.
Section III-E:
Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation
(Note: Experiments not included in Sections III-A, III-B, III-C, III-D, III-F are considered III-E)
Examples: Cloning using BL21 (not K-12 lineage) E. coli; CRISPR/Cas9 editing of eukaryotic genomes.

Section III-E-1:
Experiments Involving the Formation of rsNA Molecules Containing <2/3 of the Genome of any Eukaryotic Virus.
Example: Production of AAV.

Section III-E-2:
Experiments Involving Whole Plants (BSL-1P, -1P+, or 2P)

III-E-2-a:
BSL-1P Experiments, not covered in III-E-2-b.

III-E-2-b:
BSL-1P+ or BSL2-P Experiments

III-E-2-b-(1):
rsNA-modified noxious weeds or plants that can interbreed with local noxious weeds

III-E-2-b-(2):
Plants containing the complete genome of a non-exotic infectious agent

III-E-2-b-(3):
Plants associated with rsNA modified non-exotic, yet detrimental, microorganisms

III-E-2-b-(4):
Plants associated with rsNA modified exotic microorganisms that pose no risk to the environment

III-E-2-b-(5):
Experiments with rsNA modified arthropods or small animals. May involve rsNA modified microorganisms that pose no risk to the environment

Section III-E-3:
Experiments Involving the generation of transgenic Rodents at ABSL-1

Section III-E-3-a:
Experiments involving the breeding of transgenic rodents at ABSL-1
Section III-F: Experiments that are exempt from the NIH Guidelines. 

(Note: Per UF Policy, project registration with the BSO/IBC is required)

Section III-F-1: Synthetic nucleic acids that are:
1. Non-replicative
2. Non-integrative
3. Do not encode a toxin that is lethal for vertebrates at an LD50 < 100 ng/kg body weight

Section III-F-2: rsNA not in organisms, cells, or viruses and are incapable of penetrating cellular membranes

Section III-F-3: rsNA derived from a single source that exists contemporaneously in nature

Section III-F-4: rsNA derived 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: rsNA derived 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: DNA segments from different species that exchange DNA by known physiological processes (see listed agents in Appendices A-I through A-VI), though one or more of the segments may be a synthetic equivalent.

Section III-F-7: Genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any rsNA

Section III-F-8: Experiments that do not present a significant risk to health or the environment, as determined by the NIH Director following appropriate notice and opportunity for public comment. Exemptions detailed under Appendix C.