**University of Colorado Colorado Springs**

Worksheet 1

RECOMBINANT OR SYNTHETIC NUCLEIC ACID (rsNA) MOLECULE EXPERIMENTS QUESTIONNAIRE

**CLASSIFICATION OF EXPERIMENTS THAT REQUIRE NIH REVIEW AND APPROVAL**

Source: ***NIH Recombinant or Synthetic Nucleic Acid Molecules Guidelines,*** dated March 2013

This section **MUST** be completed if you are working with ANY recombinant or synthetic nucleic acid molecules. Please check the appropriate **Yes** box if the NIH category accurately describes your experiment. IBC applications are required for experiments that may be classified as Section III-F.

## SECTION III-A

**Experiments that require IBC approval, Recombinant DNA Advisory Committee (RAC) review, and National Institutes of Health (NIH) Director Approval *before* initiation of the experiment.**

**Yes**

**III-A-1** **Major Actions Under the NIH Guidelines**.

**Experiments considered as Major Actions under the NIH Guidelines require submission to the NIH for NIH / RAC Review. The NIH will determine the level of containment at the time of approval.**

**III-A-1-a** Deliberate transfer of a drug resistance trait to microorganisms that are known to acquire it naturally, if such acquisition could compromise the use of the drug to control disease agents in human or veterinary medicine or agriculture.

## SECTION III-B

**Experiments that require NIH / Office of Biotechnology Affairs (OBA) and IBC approval *before* the initiation of the experiment.**

**Yes**

**III-B-1** Deliberate formation of recombinant or synthetic DNA containing genes for the biosynthesis of toxin molecules lethal at an LD50 of less than 100 nanograms per kilogram body weight (e.g., microbial toxins such as tetanus toxin, botulinum toxin).

***SECTION III-C***

**Experiments that require IBC approval, Institutional Review Board (IRB) approval, and NIH /RAC Approval *before* Research Participant Enrollment**

**Yes**

**III-C-1** Experiments Involving the 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 (IBC will determine the containment level on a case by case basis depending on the experimental assessment of risk.)**

**Yes**

## III-D-1 Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems (see [Section II-A](http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines.htm#_Section_II-A._Risk), Risk Assessment)

**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.

**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

**III-D-4** Experiments Involving Whole Animals

This section covers experiments involving deliberate transfer of recombinant or synthetic nucleic acid molecules, DNA or RNA derived from recombinant or synthetic nucleic acid molecules, or recombinant or synthetic nucleic acid molecule-modified microorganisms into whole animals and experiments involving whole animals in which the animal's genome has been altered by recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic animals). Experiments involving gene drive modified animals or experiments involving viable recombinant or synthetic nucleic acid molecule-modified microorganisms, except for viruses that are only vertically transmitted, may not be conducted at BL1-N containment. A minimum containment of BL2 or BL2-N is required (see Section III-D-8).

**III-D-5** Experiments Involving Whole Plants

Experiments to genetically engineer plants by recombinant or synthetic nucleic acid molecule methods, to use such plants for other experimental purposes (e.g.,response to stress), to propagate such plants, or to use plants together with microorganisms or insects containing recombinant or synthetic nucleic acid molecules, may be conducted under the containment conditions described in Sections III-D-5-a through III-D-5-e. If experiments involving whole plants are not described in Section III-D-5 and do not fall under Sections III-A, III-B, III-D or III-F, they are included in Section III-E. Experiments involving the generation or use of gene drive modified organisms require a minimum of BL2 containment and are described under Section III-D-8, Experiments Involving Gene Drive Modified Organisms.

**III-D-6** Experiments Involving More Than 10 Liters of Culture

**III-D-7** Experiments Involving Highly Pathogenic Influenza Viruses

**III-D-8** Experiments Involving Gene Drive Modified Organisms

Experiments involving gene drive modified organisms generated by recombinant or synthetic nucleic acid molecules shall be conducted at a minimum of Biosafety Level (BL) 2, BL2-N (Animals) or BL2-P (plant) containment.

***Section III-E***

**Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation (The recommended containment level is BL1; recombinant or synthetic nucleic acid molecules experiments of higher risk and subsequently higher containment, are categorized in Section III-D)**

**Yes**

**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 Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems.

Recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any

eukaryotic virus (all viruses from a single Family being considered identical [see Section V-J, Footnotes and

References of Sections I-IV]) may be propagated and maintained in cells in tissue culture using BL1

containment. For such experiments, it must be demonstrated that the cells lack helper virus for the specific

Families of defective viruses being used. If helper virus is present, procedures specified under Section III-D-3,

Experiments Involving the Use of Infectious Animal or Plant DNA or RNA Viruses or Defective Animal or Plant

DNA or RNA Viruses in the Presence of Helper Virus in Tissue Culture Systems, should be used. The DNA

may contain fragments of the genome of viruses from more than one Family but each fragment shall be less

than two-thirds of a genome.

**III-E-2** Experiments Involving Whole Plants

**III-E-3** Experiments Involving Transgenic Rodents

This section covers experiments involving the generation or use of rodents in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid molecules, or nucleic acids derived therefrom, into the germ-line (transgenic rodents). Only experiments that require BL1 containment are covered under this section; experiments that require BL2, BL3, or BL4 containment are covered under Section III-D-4, Experiments Involving Whole Animals or Section III-D-8, Experiments Involving Gene Drive Modified Organisms.

Section III-E-3-a. Experiments involving the breeding of certain BL1 transgenic rodents are exempt under

Section III-F, Exempt Experiments (See Appendix C-VIII, Generation of BL1 Transgenic Rodents via Breeding).

***Section III-F***

**The following experiments are exempt from the *NIH Guidelines* but require submission to IBC. The Biosafety Officer will verify that the experiment is exempt from the Guidelines; those that meet the requirements of Section III-A through III-E-3 of the Guidelines will be reviewed at a convened IBC meeting:**

**Yes**

**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., oligonucleotides 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 introduce a stable genetic modification, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight. 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). Page 24 - NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (November 2013.

**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.

**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 (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.