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| REVIEWER USE ONLY:IBC No:       Category: Choose an item. **Approval Date:** **Expiration Date:** | | | | | | | |
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| **General Information** | | | | | | | |
|  | New Application  Periodic Review | | | | | | |
|  | IBC # (to be assigned by research office): | | | | | | |
|  | Protocol Title(s): |  | | | | | |
|  | Principal Investigator (PI): |  | | | | | |
|  | PI Email: |  | | | PI Phone #: | |  |
|  | 1st Lab Contact: |  | | | | | |
| 1st Lab Contact Email: |  | | 1st Lab Contact Phone #: | | |  |
|  | 2nd Lab Contact: |  | | | | | |
| 2nd Lab Contact Email: |  | | 2nd Lab Contact Phone #: | | |  |
|  | List all locations where work will be conducted in the table below: | | | | | | |
|  | ***Campus:*** | | ***Building(s):*** | | | ***Room Number(s):*** | |
| VA Medical Center | |  | | |  | |
| VA Medical Center | |  | | |  | |
| Other (list): | |  | | |  | |

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| IBC Application - Section 2: Project Description | |
| **Disclaimer:**  The Institutional Biosafety Committee (IBC) and the Subcommittee on Research Safety (SRS) is made of a diverse group of people. It is therefore important to use language that will be detailed enough for scientific evaluation as well as general enough to be understood by people with non-scientific backgrounds. Please provide sufficient information for committee members to evaluate the work for purposes of making a biohazard risk assessment. | |
|  | **What are the primary hypothesis and objectives of your research?**  *In lay language, provide a one paragraph summary of your overall research objectives. This short summary will be used in the IBC minutes for publication to the public:* |
|  | **Laboratory Work:** If part of this work will be completed in a BSL-2 and part in a BSL-3 laboratory, describe each part.  N/A |
|  | **Technical Description***: Summarize the purpose and goals and anticipated outcomes of this rDNA research*: |
|  | **If you are submitting a periodic renewal, provide a summary report of working on this protocol for the period covered in this review.** |

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| IBC Application - Section 3: Nanoparticles | | | | | |
|  | **Does your project(s) involve the use of nanoparticles to deliver rDNA?** | | Yes  No | | |
| Section 4: Recombinant & Synthetic Nucleic Acid Molecules | | | | | | | |
| **Purpose:** The purpose of the “NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules” (NIH Guidelines)is to specify the practices for constructing and handling:   * Recombinant nucleic acid molecules, * Synthetic nucleic acid molecules, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, and * Cells, organisms, and viruses containing such molecules.   **Definition:** In the context of the NIH Guidelines, recombinant and synthetic nucleic acids are defined as:   1. Molecules that:    1. Are constructed by joining nucleic acid molecules and    2. That can replicate in a living cell, i.e., recombinant nucleic acids; 2. Nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids, or 3. Molecules that result from the replication of those described in (i) or (ii) above.   **Note:***Your answers to the questions in this section will allow the IBC to determine the level of review that your experiments require.* | | | | | | | |
|  | | Does your protocol involve recombinant or synthetic nucleic acid molecules (rDNA)? | Yes  No | | | | |
| **Relevant Sections of the NIH Guidelines** | | | | | | | |
| ***NIH Guidelines Section III-A:***  ***Experiments that require IBC approval and NIH Director approval before initiation*** | | | | | | | |
|  | | Do any rDNA experiments involve the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (if such acquisition could compromise ability to control disease agents in humans, veterinary medicine, or agriculture)? | | | Yes\* | No | |
| *\*If you answered Yes, the experiment is considered a Major Action and falls under NIH Guidelines Section III-A.* | | | | | |
| ***NIH Guidelines Section III-B:***  ***Experiments that require NIH/OSP and IBC approval before initiation*** | | | | | | | |
|  | | Do any rDNA experiments involve the cloning of toxin molecules with an LD50 of less than 100 ng/kg body weight? | | | Yes\* | No | |
| *\*If you answered Yes, the experiment requires NIH/OSP and IBC approval before initiation. It falls under* *NIH Guidelines Section III-B-1.* | | | | | |
|  | | Does your protocol involve experiments that have been Approved (under Section III-A-1-a) as Major Actions under the NIH Guidelines previously? | | | Yes\* | No | |
| *\*If you answered Yes, the experiment requires NIH/OSP and IBC approval before initiation. It falls under NIH Guidelines Section III-B-2.* | | | | | |
| ***NIH Guidelines Section III-C:***  ***Experiments that require IRB and IBC approval*** | | | | | | | |
|  | | Do any rDNA experiments involve the deliberate transfer of rDNA, into one or more human research participants? | | | Yes\* | No | |
| *\*If you answered Yes, the experiment requires IRB and IBC approval and NIH/ before initiation. It falls under NIH* *Guidelines Section III-C-1.* ***NOTE****: The deliberate transfer of recombinant or synthetic nucleic acids into one human research participant, conducted under an FDA regulated individual patient expanded access IND or protocol, including for emergency use, is not research subject to the NIH Guidelines and thus does not need to be submitted to an IBC for review and approval.* | | | | | |

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| ***NIH Guidelines Section III-D:***  ***Experiments that require IBC approval before initiation*** | |  |  |
| **Do any rDNA experiments involve:** | | | |
|  | Using risk group 2, 3, 4 or restricted agents as host-vector systems? | Yes\* | No |
| *\*If you answered Yes, the experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-1.* ***NOTE:*** *The NIH Guidelines require that introduction of rDNA or sDNA into RG4 agents be performed under BSL-4 (or ABSL-4) containment. VA does not permit experiments that requires BSL-4 or ABSL-4 containment.* | | |
|  | Will any agents described in 4.6 above be used in animals? | Yes\* | No |
| *\*If you answered Yes, the experiment requires IACUC approval before initiation. It falls under NIH Guidelines Section III-D-1.* | | |
|  | DNA from Risk Group 2, 3, 4 or restricted agents is cloned into a nonpathogenic prokaryotic or lower eukaryotic host vector system? | Yes\* | No |
| *\*If you answered Yes, the experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-2.* ***NOTE:*** *The VA does not permit experiments requiring BSL-4 containment.* | | |
|  | The use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in tissue culture systems? | Yes\* | No |
| *\*If you answered Yes, the experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-3.* | | |
|  | The creation of: |  |  |
| * Transgenic rodents (housed at ABSL-2 and above)? | Yes\* | No |
| * Transgenic animals other than rodents? | Yes\* | No |
| * rDNA modified arthropods? | Yes\* | No |
| * Knock-out rodents (housed at ABSL-2 and above)? | Yes\* | No |
| *\*If you answered Yes, the experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-4.* | | |
|  | The breeding of: |  |  |
| * Rodents from one strain for propagation or colony maintenance (housed at ABSL-2 and above)? | Yes\* | No |
| * Rodents from two strains, or the breeding of a transgenic rodent and a non-transgenic rodent with the intent to generate a new strain (housed at ABSL-2 and above)? | Yes\* | No |
| * Transgenic animals other than rodents? | Yes\* | No |
| * Knock-outs from two strains to generate a new strain (housed at ABSL-2 and above)? | Yes\* | No |
| *\* If you answered Yes, the experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-4.* | | |
|  | The experiments with: |  |  |
| * Transgenic rodents (housed at ABSL-2 and above)? | Yes\* | No |
| * Transgenic animals other than rodents? | Yes\* | No |
| *\* This experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-4.* | | |

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|  | Experiments with whole plants that involve: |  |  |
| * Genetically engineering plants by rDNA methods? | Yes\* | No |
| * Using rDNA modified plants for experimental procedures? | Yes\* | No |
| * The propagation of rDNA modified plants? | Yes\* | No |
| * Using microorganisms or arthropods containing rDNA with the potential for detrimental impact to ecosystems? | Yes\* | No |
| * Using exotic infectious agents in the presence of arthropod vectors? | Yes\* | No |
| * Using microbial pathogens of insects or small animals associated with plants with the potential for detrimental impact to ecosystems? | Yes\* | No |
| *\* This experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-5.* | | |
|  | More than 10L of culture? | Yes\* | No |
| *\* This experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-6.* | | |
|  | The use of influenza viruses? | Yes\* | No |
| *\* This experiment requires IBC approval before initiation. It falls under NIH Guidelines Section III-D-7.* | | |
| ***Exempt Experiments in the NIH Guidelines:***  The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Answer the questions in this section to see if any of your experiments are exempt. However, even if the experiment is exempt, it may still be reviewed by the Biosafety Office. | | | |
| **Do the rDNA experiments involve:** | | | |
|  | 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 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?   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 | Yes\* | No |
| *\*This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-1*. | | |
|  | Do any rDNA experiments involve rDNA 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? | Yes\* | No |
| *\*This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-2.* | | |
|  | rDNA molecules that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature ? | Yes\* | No |
| *\* This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-3.* | | |
|  | rDNA molecules that consist entirely of DNA from a prokaryotic host including indigenous plasmids or viruses when propagated only in that host (or closely related strain of the same species), or when transferred to another host by well-established physiological means? | Yes\* | No |
| *\* This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH* *Guidelines Section III-F-4.* | | |
|  | rDNA molecules that consist entirely of DNA 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)? | Yes\* | No |
| *\* This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-5.* | | |
|  | rDNA molecules that consist entirely of DNA segments from different species that exchange DNA by a known physiological process, though one or more segments may be a synthetic equivalent? | Yes\* | No |
| *\* This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-6.* | | |
|  | Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA? | Yes\* | No |
| *\* This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-7.* | | |
|  | Experiments 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 following appropriate notice and opportunity for public comment. | Yes\* | No |
| *\* This experiment is exempt from the NIH Guidelines. The NIH Guidelines provide specific experiments that are exempt from the requirements of the Guidelines. Even though the experiment is exempt, it is still reviewed by the Biosafety Officer. It falls under NIH Guidelines Section III-F-8.* | | |
|  | rDNA molecules that contain less than ½ of any eukaryotic viral genome that are propagated and maintained in cells in tissue culture? In order for these experiments to be exempt, they cannot:   * Fall under section III-B; * Involve DNA from risk groups 3, 4, or restricted organisms or cells known to be infected with these agents; or * Involve the deliberate introduction of genes coding for the biosynthesis of molecules that are toxic for vertebrates.   + NOTE: Whole plants regenerated from plant cells and tissue cultures are covered by this exemption provided they remain axenic cultures even though they differentiated into embryonic tissue and regenerate into plantlets | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-I.* | | |

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|  | *Escherichia coli* K-12 host-vector systems where:   1. The *E. coli* host does not contain conjugation proficient plasmids or generalized transducing phages; or 2. Lambda or lambdoid or Ff bacteriophages or non-conjugative plasmids shall be used as vectors?   However, experiments involving the insertion into *E. coli* K-12 of DNA from prokaryotes that exchange genetic information with *E. coli* may be performed with any *E. coli* K-12 vector (e.g., conjugative plasmid). When a non-conjugative vector is used, the *E. coli* K-12 host may contain conjugation-proficient plasmids either autonomous or integrated, or generalized transducing phages. In order for these experiments to be exempt they cannot:   * + Fall under Section III-B;   + Involve DNA from Risk Groups 3, 4, or restricted organisms or cells known to be infected with these agents;   + Involve large-scale experiment (> 10 L of culture); or   + Involve the deliberate cloning of toxin molecule genes coding for the biosynthesis of molecules that are toxic for vertebrates | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-II.* | | |
|  | Experiments involving *Saccharomyces cerevisiae* and *Saccharomyces uvarum* host-vector systems? In order for these experiments to be exempt they cannot:   * Fall under Section III-B; * Involve DNA from Risk Groups 3, 4, or restricted organisms or cells known to be infected with these agents; * Involve large-scale experiment (> 10 L of culture); or * Involve the deliberate cloning of toxin molecule genes coding for the biosynthesis of molecules that are toxic for vertebrates | Yes\* | No |
| *\*The experiment falls under* NIH Guidelines Appendix C-III. | | |
|  | Experiments involving *Kluyveromyces* *lactis* host-vector system? In order for these experiments to be exempt they cannot:   * Fall under III-B; * Involve DNA from Risk Groups 3, 4, or restricted organisms or cells known to be infected with these agents; * Large scale experiments (> 10 L of culture); or * Involve the deliberate cloning of toxin molecule genes coding for the biosynthesis of molecules that are toxic for vertebrates | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-IV.* | | |
|  | Any asporogenic *Bacillus subtilis* or asporogenic *Bacillus licheniformis* strain which does not revert to a spore-former with a frequency greater than 10-7 used for cloning DNA?  In order for these experiments to be exempt they cannot:   * Fall under Section III-B; * Involve DNA from Risk Groups 3, 4, or restricted organisms or cells known to be infected with these agents; * Involve large-scale experiment (> 10 L of culture); or * Involve the deliberate cloning of toxin molecule genes coding for the biosynthesis of molecules that are toxic for vertebrates | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-V.* | | |

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|  | Recombinant DNA molecules that are derived entirely from extrachromosomal elements of the organisms listed Appendix C-VI (including shuttle vectors constructed from vectors described in [Appendix C](http://oba.od.nih.gov/oba/rac/Guidelines/APPENDIX_C.htm#_APPENDIX_C._EXEMPTIONS)), propagated and maintained in organisms listed in Appendix C-VI?  In order for these experiments to be exempt they cannot:   * Fall under III-B; * Involve DNA from Risk Groups 3, 4, or restricted organisms or cells known to be infected with these agents; * Involve large-scale experiment (> 10 L of culture); or * Involve the deliberate cloning of toxin molecule genes coding for the biosynthesis of molecules that are toxic for vertebrates | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-VI.* | | |
|  | The purchase or transfer of transgenic rodents for experiments that require BL1 containment? | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-VII.* | | |
|  | The breeding of two different transgenic rodents or the breeding of a transgenic rodent and a non-transgenic rodent with the intent of creating a new strain of transgenic rodent that can be housed at BL1 containment? To be considered exempt the following must be true:   * Both parental rodents can be housed under BL1 containment; * Neither parental transgenic rodent contains the following genetic modifications:   + Incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses   + Incorporation of a transgene that is under the control of a gammaretroviral long terminal repeat (LTR); and * The transgenic rodent that results from this breeding is not expected to contain more than one-half of an exogenous viral genome from a single family of viruses. | Yes\* | No |
| *\*The experiment falls under NIH Guidelines Appendix C-VIII.* | | |
| ***NIH Guidelines Section III-E:***  ***Experiments that require IBC notice simultaneous with initiation***  *\*These experiments still require VA IBC review and approval* | | | |
| **Do the rDNA experiments:** | | | |
|  | Not fall under Sections III-A, B, C, D, F or any exemptions thereof? | Yes\* | No |
| *\* The experiment falls under NIH Guidelines Section III-E.* | | |
|  | Involve the formation of rDNA molecules containing no more than 2/3 of the genome of any eukaryotic virus? For such experiments, it must be demonstrated that the cells lack helper virus for the specific Families of defective viruses being used. | Yes\* | No |
| *\* The experiment falls under NIH Guidelines Section III-E-1.* | | |
|  | Involve whole plants, except those that fall under III-A, B, D, or F, including:   * rDNA modified arthropods associated with plants (BSL-2 and above); * Small animals associated with rDNA-modified plants; or * rDNA-modified arthropods or small animals associated with plants? | Yes\* | No |
| *\* The experiment falls under NIH Guidelines Section III-E-2.* | | |
|  | Involve the creation of transgenic or knock-out rodents in which the animal’s genome has been altered by stable introduction of rDNA or DNA derived there from, into the germ-line? Only experiments that require ABSL-1 containment are covered by this section. | Yes\* | No |
| *\* The experiment falls under NIH Guidelines Section III-E-3.* | | |
|  | Involve the breeding of rodents from 2 strains to generate a new strain or a knock-out that can be housed at ABSL-1 and don’t fall under the exemption explained in Appendix C-VIII  (#10.29 in this form)? | Yes\* | No |
| *\* The experiment falls under NIH Guidelines Section III-E-3.* | | |

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| ***General Recombinant DNA Questions*** | | | |
|  | ***Use of VA Facilities:***  Will you be utilizing any VA facilities to conduct any rDNA experiments (i.e., creation of transgenic mice, breeding experiments, creation of lentiviral vectors)? | Yes\* | No |
| *\** *Name of the Core Facility you will be using:* | | |
| *\** *Explain what service(s) the Core Facility will provide for your project:* | | |
|  | ***Use of Replication-Incompetent Virus Derived Vector Systems:***  Will you be using a virus derived vector system that is replication-incompetent? | Yes\* | No |
| *\*If yes, explain how this has been achieved using details, maps, references, etc. Also, describe how you will test to assure that your vector material is and remains free from contamination by replication competent virus.* | | |

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|  | Use the table below to describe your rDNA experiments. Unused rows will be deleted upon submission. | | | | | | | |
| ***Host*** | ***Vector*** | ***Inserted DNA*** | ***Purpose of the Insert*** | ***What is the largest fraction of eukaryotic viral genome contained in the rDNA molecules?*** | ***Will a helper virus be used?*** | ***Is the virus replicative?*** | ***Proposed NIH Category*** | ***Will you expose humans, animals or plants to the rDNA? Check all that apply.*** |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
| ***Host*** | ***Vector*** | ***Inserted DNA*** | ***Purpose of the Insert*** | ***What is the largest fraction of eukaryotic viral genome contained in the rDNA molecules?*** | ***Will a helper virus be used?*** | ***Is the virus replicative?*** | ***Proposed NIH Category*** | ***Will you expose humans, animals or plants to the rDNA? Check all that apply.*** |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
| ***Host*** | ***Vector*** | ***Inserted DNA*** | ***Purpose of the Insert*** | ***What is the largest fraction of eukaryotic viral genome contained in the rDNA molecules?*** | ***Will a helper virus be used?*** | ***Is the virus replicative?*** | ***Proposed NIH Category*** | ***Will you expose humans, animals or plants to the rDNA? Check all that apply.*** |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
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|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |

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| ***Host*** | ***Vector*** | ***Inserted DNA*** | ***Purpose of the Insert*** | ***What is the largest fraction of eukaryotic viral genome contained in the rDNA molecules?*** | ***Will a helper virus be used?*** | ***Is the virus replicative?*** | ***Proposed NIH Category*** | ***Will you expose humans, animals or plants to the rDNA? Check all that apply.*** |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
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| ***Host*** | ***Vector*** | ***Inserted DNA*** | ***Purpose of the Insert*** | ***What is the largest fraction of eukaryotic viral genome contained in the rDNA molecules?*** | ***Will a helper virus be used?*** | ***Is the virus replicative?*** | ***Proposed NIH Category*** | ***Will you expose humans, animals or plants to the rDNA? Check all that apply.*** |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
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|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***Host*** | ***Vector*** | ***Inserted DNA*** | ***Purpose of the Insert*** | ***What is the largest fraction of eukaryotic viral genome contained in the rDNA molecules?*** | ***Will a helper virus be used?*** | ***Is the virus replicative?*** | ***Proposed NIH Category*** | ***Will you expose humans, animals or plants to the rDNA? Check all that apply.*** |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |
|  |  |  |  | Choose an item. | Choose an item. | Choose an item. | Choose an item. | Humans  Animals  (list):  Plants  (list):  N/A |

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| Section 5: CRISPR/ Cas 9 STUDIES | | | |
| **Disclaimer:**  CRISPR/Cas 9 is a unique technology that enables geneticists and medical researchers to edit parts of the genome by removing, adding or altering sections of the DNA sequence.  **The following questions must be answered prior to using this technology in your studies.** | | | |
|  | Will you be using CRISPR/Cas 9 technology in your Studies? If *No* skip to the next Section. | Yes | No |
|  | Which organism(s) do you plan to modify? List the organism(s) below. |  |  |
|  | Is the work in cell culture? If *Yes* list the cell lines below. | Yes | No |
|  | Is the work in a whole organism? If *Yes* list the species below. | Yes | No |
|  | What is the function of the gene(s) being modified? |  |  |
|  | What will be the function of the gene(s) after modification? |  |  |
|  | Will the gene editing technology be used for human gene transfer research? | Yes | No |
|  | Are the guide RNA gene and the Cas 9 gene physically linked on the same DNA? If *Yes,* please describe below. | Yes | No |
|  | Is the guide sequence specific to animals or humans or could it affect both?  If \**Both*, describe any similarity between human and animal guide sequences.  Animals  Humans  \*Both |  |  |
|  | Will direct gene modification or the administration of donor cells that have been genetically modified be used for Human Clinical Studies? If *Yes,* please describe below. | Yes | No |
|  | How is the gene editing technology being delivered? Check all that apply.  Plasmid  Nanoparticles  Lentivirus  Adeno-associated virus  Other\* please give details below |  |  |
|  | For CRISPR research involving viral vectors, a Genome Target Scan (GT-Scan) for off target effects by your gRNA must be completed. This is necessary to determine if there is homology to human DNA and for assessing the risk of potential exposure in the event of an unanticipated incident. An off-target database is available at <http://www.rgenome.net/cas-offinder/>.  N/A (No vectors will be used)  Viral Vectors will be used (Discuss the homology below) |  |  |
|  | | |
|  | **The mutant forms of Cas9 can help significantly decrease off-targeting effects during gene editing (when using CRISPR/Cas9). Researchers should consider using the mutant Cas9 forms to increase the specificity and decrease off-target effects. Will unexpected mutations due to off-target be expected?** If *Yes,* please describe below. | Yes | No |
|  | **Will the genome editing technology target animal/plant embryos or germ cell lines?** | Yes | No |
|  | **Will the research involve the creation of a gene drive experiment (i.e., a system that greatly increases the probability that a trait will be passed on to offspring?** | Yes | No |
|  | **Are any special safety considerations required to perform this study?** If *Yes,* please describe below. | Yes | No |
|  | **What should be done in the event of an accidental exposure (e.g. needlestick).** Please describe below. |  |  |

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| Section 6: Dual-Use Screening | | | |
| **Disclaimer:**  A research project is considered dual-use in nature if the methodologies, materials or results could be used for public harm. **The following questions must be answered prior to the initiation of research.** It should be noted that an affirmative answer will not delay the progress of research but indicates that further review and consideration may be warranted as the research advances. Information regarding the dual-use dilemma in biological research may be found at <http://www.serceb.org/dualuse.htm>. | | | |
|  | Will an intermediate or final product of your research make a vaccine less effective or ineffective? | Yes | No |
|  | Will the intermediate or final product of your research confer resistance to antibiotics or antivirals? | Yes | No |
|  | Will your work enhance the virulence of a pathogen or render a non-pathogen virulent? | Yes | No |
|  | Will the results of your work increase the transmissibility of any pathogen? | Yes | No |
|  | Will your research result in the alteration of the host range of the pathogen? | Yes | No |
|  | Will your research result in an intermediate or final product that may prevent or interfere with the diagnosis of infection or disease? | Yes | No |
|  | Does your research enable weaponization\*\* of an agent or toxin? | Yes | No |
| \*\**In this context, weaponization refers to the enhanced dispersion, deliverability, survivability or pathogenesis of a potentially harmful agent or toxin.* | | |
|  | Will synthetic biology*+* techniques be used to construct a pathogenic organism, toxin or **potentially harmful** intermediate product? | Yes | No |
| +*Synthetic biology includes, but is not limited to, techniques of molecular biology, chemistry and genetics that would allow for the de novo synthesis or reverse engineering of genes, gene products or entire functional organisms.* | | |
|  | **After considering your answers to 6.1 – 6.8, do you believe there is the potential for your research data/product to be readily utilized to cause public harm?** | Yes | No |

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| Section 7: Progress Report | | | | | | |
|  | Have any adverse events occurred in the last approval period? | | | Yes\* | | No |
| \**If yes, please provide details of the events:* | | | | | |
|  | Were these events reported to the BSO (and/or Safety Office) immediately following the incidents?  \**All accidents and injuries must be reported.* | | Yes | No\* | | N/A |
|  | Have there been any accidental exposures related to this protocol, not limited to your lab staff? | | | Yes\* | | No |
| *\*If yes, please provide details of events (including notification being sent to the Safety Office) and what was done to prevent this type of event from recurring:* | | | | | |
|  | Were these events reported to the BSO (and/or Safety Office), SRSS, and NIH-OSP immediately?  \**All accidents and injuries must be reported.* | | Yes | No\* | | N/A |
| Section 8: Investigator’s Assurance | | | | | | |
| 8. 1 | I confirm that all persons involved with this project (including my collaborators) have been adequately trained in good microbiological techniques, have received instruction on any specific hazards associated with the project and worksite, and are aware of any specific safety equipment, practices, and behaviors required while conducting project procedures and using these facilities. The IBC may review my records documenting the instruction. | | | | I Accept | |
| 8. 2 | I will immediately report to the VA Safety Office, SRSS, and, if applicable, ORO, any accident, injury, spill of biohazardous material, equipment or facility failure (i.e. ventilation failure), and/or any breakdown in procedure that could result in potential exposure of laboratory personnel, staff, or the public to biohazardous or toxic material. | | | | I Accept | |
| 8. 3 | I confirm that all proposed changes to my work will be reported to the IBC for evaluation before the change is implemented. | | | | I Accept | |
| 8. 4 | I confirm that no work requiring SRS, IBC or R&D approval will be initiated or modified until approval is received, and all requirements have been met. | | | | I Accept | |
| 8. 5 | I will notify the IBC of all personnel changes or additions through the use of the SRS amendments | | | | I Accept | |
| 8. 6 | I have read and understand my responsibilities of Principal Investigator outlined in [Section IV-B-7 of the NIH Guidelines](http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines.htm#_Toc7261589) and agree to comply with these responsibilities. | | | | I Accept | |
| 8. 7 | I certify that the information provided within this application is accurate to the best of my knowledge. I also understand that, should I use the project described in this application as a basis for a funding proposal (either intramural or extramural), I am responsible for ensuring that the description of procedures in the funding proposal is identical in principle to that contained in this application. | | | | I Accept | |
| 8. 8 | I confirm that all persons involved with this protocol will comply with all applicable environmental laws and regulations and that this project does not significantly impact the environment. | | | | I Accept | |
|  |  |  | | | | |
| *Principal Investigator*  (By electronically entering your name, you are indicating verification that all items are accurate, and you agree to ensure compliance with the above items.) | *Date* | | | | |