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|  | **DREXEL UNIVERSITY’S INSTITUTIONAL BIOSAFETY COMMITTEE**  **BIOSAFETY PROTOCOL APPLICATION**  ***Recombinant DNA Registration Addendum (Form B)*** |
| ***Instructions***   * *All funded and non-funded research involving recombinant DNA (rDNA) must be* ***registered*** *with the Drexel University’s Institutional Biosafety Committee (IBC) using this form, which must also be accompanied by the* ***General Biohazard Form (Form A)****.* * *This registration process establishes and communicates specific biosafety practices and containment principles 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*   + *cells, organisms, and viruses containing such molecules*   + *research involving gene drive modified organisms (GDMOs)* * *In the context of the NIH Guidelines, recombinant and synthetic nucleic acids are defined as:*   1. *(i) molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids;*   2. *(ii) 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. *(iii) molecules that result from the replication of those described in (i) or (ii) above.* * *This registration applies to work that may include or involve:*   + *Plasmid or viral vectors.*   + *Any synthetic DNA, RNA, or synthetic nucleic acid molecules that have been chemically or otherwise modified but can base pair with naturally occurring nucleic acids.*   + *Any RNA produced from rDNA, including messenger RNA (mRNA), small interfering RNA (siRNA), or micro-RNA (miRNA).*   + *Genetically modified organisms (e.g., animals, plants, bacteria, viruses, or fungi). This includes creation, cross-breeding, or manipulation of transgenic animals and plants.*   + *The use of GDMOs. As defined by the NIH Guidelines (April 2024), the definition of “gene drive” is “a technology whereby a particular heritable element biases inheritance in its favor, resulting in the heritable element becoming more prevalent than predicted by Mendelian laws of inheritance in a population over successive generations.”*   + *Any such material obtained for research from another researcher or source.* * *For distinct vectors with different backbones, submit a Form B for each vector (i.e adeno-associated virus (AAV) and lentivirus (LV). If the vectors differ in DNA/RNA insert (e.g., expression cassette) but use the same vector, a single form is sufficient (i.e. AAV-GFP and AAV-luciferase).* * *If your work involves GDMOs, contact the IBC (*[*biosafety@drexel.edu*](mailto:biosafety@drexel.edu)*) for guidance on performing a comprehensive risk assessment and conducting your work using appropriate biological containment practices.* * *All persons involved in this work must complete the BioRAFT rDNA training module (in addition to general laboratory safety training). Training dates should be recorded on the* ***General Biohazard Form (Form A)****.*   + *Your investigations involving rDNA may be exempt from the NIH Guidelines and registration with the IBC. Criteria for exempt rDNA experiments are specified in section III-F of current NIH Guidelines and can also be found at the end of this form. If your experiments involve rDNA molecules that meet these criteria, you are not required to submit an rDNA form.*   + *Information about the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules can be found at* [*https://osp.od.nih.gov/policies/biosafety-and-biosecurity-policy#tab2*](https://osp.od.nih.gov/policies/biosafety-and-biosecurity-policy#tab2)*/.* * *Changes to an approved biosafety protocol must be made by filing a* ***Protocol Amendment Form (Form E)*** *for Institutional Biosafety Committee review.* * *If you have questions about rDNA registration or this form, please contact the IBC by e-mail (*[*biosafety@drexel.edu*](mailto:biosafety@drexel.edu)*).* | |
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| 1. PROJECT AND INVESTIGATOR INFORMATION |
| Project Title (Must exactly match the grant title if externally funded) |
| Principal Investigator’s Name |

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| 2. RESEARCH DESCRIPTION |
| Provide a brief description of the proposed research in the field below. If this is an externally funded project, please attach an abstract or Specific Aims page from your grant application or proposal. |
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| 3. TRAINING | |
| a. Have you read the most recent NIH guidelines on research involving rDNA? (The NIH Guidelines are available in [HTML](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.htm) and [pdf](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf#%5B%7B%22num%22%3A124%2C%22gen%22%3A0%7D%2C%7B%22name%22%3A%22XYZ%22%7D%2C70%2C709%2C0%5D) formats) | Yes  No |
| b. Are you knowledgeable about Biosafety Levels? <https://www.cdc.gov/training/quicklearns/biosafety/> | Yes  No |

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| 4. rDNA REGISTRATION CATEGORIES | |
| Check the registration categories that best describe your experiments involving rDNA. You may need to check more than one category. For more detailed information about the types of rDNA experiments covered under the NIH Guidelines (maintained by the NIH Office of Science Policy), refer to Section III of the Guidelines (The NIH Guidelines are available in [HTML](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.htm#_Toc3457031) and [pdf](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf) formats) | |
| **Section III-A Experiments that Require NIH Director Approval and Institutional Biosafety Committee Approval Before Initiation** (See Section IV-C-1-b-(1), Major Actions)  *Experiments considered as Major Actions as defined in Section III-A-1-a under the NIH Guidelines cannot be initiated without submission of relevant information on the proposed experiment to the Office of Science Policy, National Institutes of Health, preferably by e-mail to: NIHGuidelines@od.nih.gov, the publication of the proposal in the Federal Register for a minimum of 15 days of comment, and specific approval by NIH. The containment conditions or stipulation requirements for such experiments will be set by NIH at the time of approval. Such experiments require Institutional Biosafety Committee approval before initiation.*  *Specific experiments already approved are included in Appendix D, Major Actions Taken under the NIH Guidelines, and serve as examples of the types of experiments covered under this section.* | |
| -1-a. **Major Actions under the NIH Guidelines**. The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (see Section V-B, Footnotes and References of Sections I-IV), if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture, will require NIH Director approval.  **Note**: Consideration should be given as to whether the drug resistance trait to be used in the experiment would render that microorganism resistant to the primary drug available to and/or indicated for certain populations, for example children or pregnant women.  **Note:** At the request of an Institutional Biosafety Committee, NIH OSP will make a determination regarding whether a specific experiment involving the deliberate transfer of a drug resistance trait falls under Section III-A-1-a and therefore requires NIH Director approval. An Institutional Biosafety Committee may also consult with NIH OSP regarding experiments that do not meet the requirements of Section III-A-1-a but nonetheless raise important public health issues. |  |
| **Section III-B Experiments That Require NIH OSP and Institutional Biosafety Committee Approval Before Initiation**  *Experiments in this category cannot be initiated without submission of relevant information on the proposed experiment to NIH OSP. The containment conditions for such experiments will be determined by NIH OSP in consultation with ad hoc experts. Such experiments require Institutional Biosafety Committee approval before initiation.* | |
| -1. **Experiments Involving the Cloning of Toxin Molecules with LD50 of Less than 100 Nanograms per Kilogram Body Weight**. Deliberate formation of recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight (e.g., microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin, and Shigella dysenteriae neurotoxin).  **Note**: Specific approval has been given for the cloning in Escherichia coli K- 12 of DNA containing genes coding for the biosynthesis of toxic molecules which are lethal to vertebrates at 100 nanograms to 100 micrograms per kilogram body weight.  **Note**: Specific experiments already approved under this section may be obtained from the Office of Science Policy, National Institutes of Health, preferably by submitting a request for this information to: NIHGuidelines@od.nih.gov; additional contact information is also available here and on the OSP website (www.osp.od.nih.gov).. |  |
| -2. **Experiments that have been approved (under Section III-A-1-a ) as Major Actions under the NIH Guidelines**. Upon receipt and review of an application from the investigator, NIH OSP may determine that a proposed experiment is equivalent to an experiment that has previously been approved by the NIH Director as a Major Action, including experiments approved prior to implementation of these changes.  **Note**: An experiment will only be considered equivalent if, as determined by NIH OSP, there are no substantive differences and pertinent information has not emerged since submission of the initial III-A-1-a experiment that would change the biosafety and public health considerations for the proposed experiments. If such a determination is made by NIH OSP, these experiments will not require review and approval under Section III-A. |  |
| **Section III-C Experiments Involving Human Gene Transfer that Require Institutional Biosafety Committee Approval Prior to Initiation** | |
| -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**.Human gene transfer is the deliberate transfer into human research participants of either:   1. Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or 2. Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria:    1. Contain more than 100 nucleotides; or    2. Possess biological properties that enable introduction of stable genetic modifications into the genome (e.g., *cis* elements involved in integration, gene editing); or    3. Have the potential to replicate in a cell; or    4. Can be translated or transcribed.   **Note**: Research cannot be initiated until Institutional Biosafety Committee and all other applicable institutional and regulatory authorization(s) and approvals have been obtained.  **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. |  |
| **Section III-D Experiments that Require Institutional Biosafety Committee Approval Before Initiation**  Prior to the initiation of an experiment that falls into this category, the Principal Investigator must submit a registration document to the Institutional Biosafety Committee which contains the following information: (i) the source(s) of DNA; (ii) the nature of the inserted DNA sequences; (iii) the host(s) and vector(s) 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 that will be implemented as specified in the NIH Guidelines. For experiments in this category, the registration document shall be dated, signed by the Principal Investigator, and filed with the Institutional Biosafety Committee. The Institutional Biosafety Committee shall review and approve all experiments in this category prior to their initiation.  **Note**: Requests to decrease the level of containment specified for experiments in this category will be considered by NIH [see Section IV-C-1-b-(2)-(c), Minor Actions].  **Note**: The general definition of Risk Groups can be found in [Section II-A-1](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.htm#_Toc3457027) of the NIH Guidelines. The lists of human etiologic agents classified by Risk Group can be found in [Appendix B](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.htm#_APPENDIX_B._CLASSIFICATION) of the NIH Guidelines. Remember that there is not a strict relationship between an agent’s Risk Group and the recommended biological containment (Biosafety Levels 1-4). The appropriate level of biocontainment is determined after consideration of the agent and procedures to be used in handling the agent. | |
| **Section 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, Risk Assessment)** | |
| -1-a. Experiments involving the introduction of recombinant or synthetic nucleic acid molecules into Risk Group 2 agents will usually be conducted at Biosafety Level (BL) 2 containment. Experiments with such agents will usually be conducted with whole animals at BL2 or BL2-N (Animals) containment. |  |
| -1-b. Experiments involving the introduction of recombinant or synthetic nucleic acid molecules into Risk Group 3 agents will usually be conducted at BL3 containment. Experiments with such agents will usually be conducted with whole animals at BL3 or BL3-N containment. |  |
| -1-c. Experiments involving the introduction of recombinant or synthetic nucleic acid molecules into Risk Group 4 agents shall be conducted at BL4 containment. Experiments with such agents shall be conducted with whole animals at BL4 or BL4-N containment. |  |
| -1-d. Containment conditions for experiments involving the introduction of recombinant or synthetic nucleic acid molecules into restricted agents shall be set on a case-by-case basis following NIH OSP review.  **Note**: A U.S. Department of Agriculture - Animal and Plant Health Inspection Service (USDA/APHIS) permit is required for work with plant or animal pathogens (see Section V-G and V-M, Footnotes and References of Sections I-IV). Experiments with such agents shall be conducted with whole animals at BL4 or BL4-N containment. |  |
| **Section 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** | |
| -2-a. Experiments in which DNA from Risk Group 2 or Risk Group 3 agents (see Section II- A, Risk Assessment) is transferred into nonpathogenic prokaryotes or lower eukaryotes may be performed under BL2 containment. Experiments in which DNA from Risk Group 4 agents is transferred into nonpathogenic prokaryotes or lower eukaryotes may be performed under BL2 containment after demonstration that only a totally and irreversibly defective fraction of the agent's genome is present in a given recombinant. In the absence of such a demonstration, BL4 containment shall be used.  **Note**: The Institutional Biosafety Committee may approve the specific lowering of containment for particular experiments to BL1. Many experiments in this category are exempt from the NIH Guidelines (see Section III-F, Exempt Experiments).  **Note**: Experiments involving the formation of recombinant or synthetic nucleic acid molecules for certain genes coding for molecules toxic for vertebrates require NIH OSP approval (see Section III-B-1, Experiments Involving the Cloning of Toxin Molecules with LD50 of Less than 100 Nanograms Per Kilogram Body Weight) or shall be conducted under NIH specified conditions as described in Appendix F, Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates. |  |
| -2-b. Containment conditions for experiments in which DNA from restricted agents is transferred into nonpathogenic prokaryotes or lower eukaryotes shall be determined by NIH OSP following a case-by-case review (see Section V-L, Footnotes and References of Sections I-IV).  **Note**: A U.S. Department of Agriculture permit is required for work with plant or animal pathogens (see Section V-G, Footnotes and References of Sections I-IV). |  |
| **Section III-D-3**. **Experiments Involving the Use of Infectious DNA or RNA Viruses or Defective DNA or RNA Viruses in the Presence of Helper System in Tissue Culture Systems**  **Caution**: The potential for reversion or generation of replication competent virus should be considered when generating or using defective viruses or vectors in the presence of helper systems (e.g., helper viruses, packaging cell lines, transient transfection systems, replicon systems). Special care should be used in the evaluation of containment levels for experiments which are likely to either enhance the pathogenicity (e.g., insertion of a host oncogene) or to extend the host range (e.g., introduction of novel control elements) of viral vectors under conditions that permit a productive infection. In such cases, serious consideration should be given to increasing physical containment by at least one level.  **Note**: Recombinant or synthetic nucleic acid molecules or nucleic acid molecules derived therefrom, which contain less than two-thirds of the genome of any eukaryotic virus (all viruses from a single Family (see Section V-J, Footnotes and References of Sections I-IV) being considered identical (see Section V-K, Footnotes and References of Sections I-IV)), are considered defective and may be used in the absence of helper systems under the conditions specified in Section III-E-1, Experiments Involving the Formation of Recombinant or Synthetic Molecules Containing No More than Two-Thirds of the Genome of any Eukaryotic Virus.. | |
| -3-a. Experiments involving the use of infectious or defective Risk Group 2 viruses (see Appendix B-II, Risk Group 2 Agents) in the presence of helper system may be conducted at BL2. |  |
| -3-b. Experiments involving the use of infectious or defective Risk Group 3 viruses (see Appendix B-III-D, Risk Group 3 (RG3) - Viruses and Prions) in the presence of helper system may be conducted at BL3. |  |
| -3-c. Experiments involving the use of infectious or defective Risk Group 4 viruses (see Appendix B-IV-D, Risk Group 4 (RG4) - Viral Agents) in the presence of helper system may be conducted at BL4. |  |
| -3-d. Experiments involving the use of infectious or defective restricted poxviruses (see Sections V-A and V-L, Footnotes and References of Sections I-IV) in the presence of helper system shall be determined on a case-by-case basis following NIH OSP review.  **Note**: A U.S. Department of Agriculture permit is required for work with plant or animal pathogens (see Section V-G, Footnotes and References of Sections I-IV). |  |
| -3-e. Experiments involving the use of infectious or defective viruses in the presence of helper system which are not covered in Sections III-D-3-a through III-D-3-d may be conducted at BL1. |  |
| **Section 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).  **Caution -** Special care should be used in the evaluation of containment conditions for some experiments with transgenic animals. For example, such experiments might lead to the creation of novel mechanisms (e.g., a gene drive; refer to Section III-D-8) or increased transmission of a recombinant pathogen or production of undesirable traits in the host animal. In such cases, serious consideration should be given to increasing the containment conditions**.** | |
| -4-a. Recombinant or synthetic nucleic acid molecules, or DNA or RNA molecules derived therefrom, from any source except for greater than two-thirds of eukaryotic viral genome may be transferred to any non-human vertebrate or any invertebrate organism and propagated under conditions of physical containment comparable to BL1 or BL1-N and appropriate to the organism under study (see Section V-B, Footnotes and References of Sections I-IV).  Animals that contain sequences from viral vectors, which do not lead to transmissible infection either directly or indirectly as a result of complementation or recombination in animals, may be propagated under conditions of physical containment comparable to BL1 or BL1-N and appropriate to the organism under study.  Experiments involving the introduction of other sequences from eukaryotic viral genomes into animals are covered under Section III-D-4-b, Experiments Involving Whole Animals. For experiments involving recombinant or synthetic nucleic acid molecule-modified Risk Groups 2, 3, 4, or restricted organisms, see Sections V-A, V-G, and V-L, Footnotes and References of Sections I-IV.  **Note**: It is important that the investigator demonstrate that the fraction of the viral genome being utilized does not lead to productive infection.  **Note**: A U.S. Department of Agriculture permit is required for work with plant or animal pathogens (see Section V- G, Footnotes and References of Sections I-IV). |  |
| -4-b. For experiments involving recombinant or synthetic nucleic acid molecules, or DNA or RNA derived therefrom, involving whole animals, including transgenic animals, and not covered by Section III-D-1, Experiments Using Human or Animal Pathogens (Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems), or Section III-D-4-a, the appropriate containment shall be determined by the Institutional Biosafety Committee.  Experiments involving gene drive modified animals generated by recombinant or synthetic nucleic acid molecules shall be conducted at a minimum of BL2 or BL2-N (see Section III-D-8). |  |
| -4-c. Exceptions under Section III-D-4, Experiments Involving Whole Animals | |
| -4-c-(1). Experiments involving the generation of transgenic rodents that require BL1 containment are described under Section III-E-3, Experiments Involving Transgenic Rodents. |  |
| -4-c-(2). The purchase or transfer of transgenic rodents is exempt from the NIH Guidelines under Section III-F, Exempt Experiments (see Appendix C-VII, The Purchase or Transfer of Transgenic Rodents). |  |
| -4-c-(3). Experiments involving the generation or use of gene drive modified animals require a minimum of BL2 containment and are covered under III-D-8, Experiments Involving Gene Drive Modified Organisms. |  |
| **Section 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.  Note: For recombinant or synthetic nucleic acid molecule experiments falling under Sections III-D-5-a through III-D-5-d, physical containment requirements may be reduced to the next lower level by appropriate biological containment practices, such as conducting experiments on a virus with an obligate insect vector in the absence of that vector or using a genetically attenuated strain. | |
| -5-a. BL3-P (Plants) or BL2-P + biological containment is recommended for experiments involving most exotic (see Section V-M, Footnotes and References of Sections I-IV) infectious agents with recognized potential for serious detrimental impact on managed or natural ecosystems when recombinant or synthetic nucleic acid molecule techniques are associated with whole plants |  |
| -5-b. BL3-P or BL2-P + biological containment is recommended for experiments involving plants containing cloned genomes of readily transmissible exotic (see Section V-M, Footnotes and References of Sections I-IV) infectious agents with recognized potential for serious detrimental effects on managed or natural ecosystems in which there exists the possibility of reconstituting the complete and functional genome of the infectious agent by genomic complementation in planta. |  |
| -5-c. BL4-P containment is recommended for experiments with a small number of readily transmissible exotic (see Section V-M, Footnotes and References of Sections I-IV) infectious agents, such as the soybean rust fungus (*Phakospora pachyrhizi*) and maize streak or other viruses in the presence of their specific arthropod vectors, that have the potential of being serious pathogens of major U.S. crops. |  |
| -5-d. BL3-P containment is recommended for experiments involving sequences encoding potent vertebrate toxins introduced into plants or associated organisms. Recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD50 of <100 nanograms per kilogram body weight fall under Section III-B-1, Experiments Involving the Cloning of Toxin Molecules with LD50 of Less than 100 Nanograms Per Kilogram Body Weight, and require NIH OSP and Institutional Biosafety Committee approval before initiation |  |
| -5-e. BL3-P or BL2-P + biological containment is recommended for experiments with microbial pathogens of insects or small animals associated with plants if the recombinant or synthetic nucleic acid molecule-modified organism has a recognized potential for serious detrimental impact on managed or natural ecosystems. |  |
| **Section III-D-6. Experiments Involving More than 10 Liters of Culture**  The appropriate containment will be decided by the Institutional Biosafety Committee. Where appropriate, Appendix K, Physical Containment for Large Scale Uses of Organisms Containing Recombinant or Synthetic Recombinant or synthetic nucleic acid Molecules, shall be used. Appendix K describes containment conditions Good Large-Scale Practice through BL3-Large Scale. |  |
| **Section III-D-7. Experiments Involving Influenza Viruses**  Experiments with influenza viruses generated by recombinant or synthetic methods (e.g., generation by reverse genetics of chimeric viruses with reassorted segments, introduction of specific mutations) shall be conducted at the biosafety level containment corresponding to the Risk Group of the virus that was the source of the majority of segments in the recombinant or synthetic virus (e.g., experiments with viruses containing a majority of segments from a RG3 virus shall be conducted at BL3).  **Note**: Experiments with influenza viruses containing genes or segments from 1918-1919 H1N1 (1918 H1N1), human H2N2 (1957-1968) and highly pathogenic avian influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1), including, but not limited to, strains of HPAI H5N1 virus that are transmissible among mammals by respiratory droplets, as demonstrated in an appropriate animal model or clinically in humans (hereinafter referred to as mammalian-transmissible HPAI H5N1 virus), shall be conducted at BL3 enhanced containment (see Appendix G-II-C-5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses) unless indicated below. | |
| -7-a. **Human H2N2 (1957-1968)**. Experiments with influenza viruses containing the H2 hemagglutinin (HA) segment shall be conducted at BL3 enhanced (see Appendix G-II-C-5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses). Experiments with the H2 HA gene in cold-adapted, live attenuated vaccine strains (e.g., A/Ann Arbor/6/60 H2N2) may be conducted at BL2 containment provided segments with mutations conferring temperature sensitivity and attenuation are not altered in the recombinant or synthetic virus. Experiments with Risk Group 2 influenza viruses containing genes from human H2N2 other than the HA gene can be worked on at BL2. |  |
| -7-b. **Highly Pathogenic Avian Influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1)**. Experiments involving influenza viruses containing a majority of genes and/or segments from a HPAI H5N1 influenza virus shall be conducted at BL3 enhanced containment, (see Appendix G-II-C-5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses).  Experiments involving influenza viruses containing a minority of genes and/or segments from a HPAI H5N1 influenza virus shall be conducted at BL3 enhanced unless a risk assessment performed by the IBC determines that they can be conducted safely at biosafety level 2 and after they have been excluded pursuant to 9 CFR 121.3(e). NIH OSP is available to IBCs to provide consultation with influenza virus experts when risk assessments are being made to determine the appropriate biocontainment for experiments with influenza viruses containing a minority of gene/segments from HPAI H5N1. Such experiments may be performed at BL3 enhanced containment or containment may be lowered to biosafety level 2, the level of containment for most research with other influenza viruses. (USDA/APHIS regulations and decisions on lowering containment also apply.) In deciding to lower containment, the IBC should consider whether, in at least two animal models (e.g., ferret, mouse, Syrian golden hamster, cotton rat, non-human primates), there is evidence that the resulting influenza virus shows reduced replication and virulence compared to the parental RG3 virus at relevant doses. This should be determined by measuring biological indices appropriate for the specific animal model (e.g., severe weight loss, elevated temperature, mortality or neurological symptoms) |  |
| -7-c. **1918 H1N1**. Experiments involving influenza viruses containing any gene or segment from 1918 H1N1 shall be conducted at BL3 enhanced containment (see Appendix G-II-C-5, Biosafety Level 3 Enhanced for Research Involving Risk Group 3 Influenza Viruses). |  |
| -7-d. **Antiviral Susceptibility and Containment**. The availability of antiviral drugs as preventive and therapeutic measures is an important safeguard for experiments with 1918 H1N1, HPAI H5N1, and human H2N2 (1957-1968). If an influenza virus containing genes from one of these viruses is resistant to both classes of current antiviral agents, adamantanes and neuraminidase inhibitors, higher containment may be required based on the risk assessment considering transmissibility to humans, virulence, pandemic potential, alternative antiviral agents if available, etc.  Experiments with 1918 H1N1, human H2N2 (1957-1968), or HPAI H5N1 that are designed to create resistance to neuraminidase inhibitors or other effective antiviral agents (including investigational antiviral agents being developed for influenza) would be subject to Section III-A-1 (Major Actions). As per Section I-A-1 of the NIH Guidelines, if the agent is a Select Agent, the NIH will defer to the appropriate Federal agency (HHS or USDA Select Agent Divisions) on such experiments. |  |
| **Section 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**  Experiments not included in Sections III-A, III-B, III-C, III-D, III-F, and their subsections are considered in Section III-E. All such experiments may be conducted at BL1 containment.  For experiments in this category, a registration document (see Section III-D, Experiments that Require Institutional Biosafety Committee Approval Before Initiation) shall be dated and signed by the investigator and filed with the local Institutional Biosafety Committee at the time the experiment is initiated. The Institutional Biosafety Committee reviews and approves all such proposals, but Institutional Biosafety Committee review and approval prior to initiation of the experiment is not required (see Section IV-A, Policy). For example, experiments in which all components derived from non-pathogenic prokaryotes and non-pathogenic lower eukaryotes fall under Section III-E and may be conducted at BL1 containment. | |
| -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**. R  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 a helper system for the specific Families of defective viruses being used. If a helper system 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 Systems 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. |  |
| -2. **Experiments Involving Whole Plants**. This section covers experiments involving nucleic acid molecule-modified whole plants, and/or experiments involving recombinant or synthetic nucleic acid molecule-modified organisms associated with whole plants, except those that fall under Section III-A, III-B, III-D, or III-F. It should be emphasized that knowledge of the organisms and judgment based on accepted scientific practices should be used in all cases in selecting the appropriate level of containment. For example, if the genetic modification has the objective of increasing pathogenicity or converting a non-pathogenic organism into a pathogen, then a higher level of containment may be appropriate depending on the organism, its mode of dissemination, and its target organisms. By contrast, a lower level of containment may be appropriate for small animals associated with many types of recombinant or synthetic nucleic acid molecule-modified plants. | |
| -2-a. BL1-P is recommended for all experiments with recombinant or synthetic recombinant or synthetic nucleic acid molecule-containing plants and plant-associated microorganisms not covered in Section III-E-2-b or other sections of the NIH Guidelines. Examples of such experiments are those involving recombinant or synthetic nucleic acid molecule-modified plants that are not noxious weeds or that cannot interbreed with noxious weeds in the immediate geographic area, and experiments involving whole plants and recombinant or synthetic nucleic acid molecule-modified non-exotic (see Section V-M, Footnotes and References of Sections I-IV) microorganisms that have no recognized potential for rapid and widespread dissemination or for serious detrimental impact on managed or natural ecosystems (e.g., *Rhizobium spp*. and *Agrobacterium spp.*). |  |
| -2-b. BL2-P or BL1-P + biological containment is recommended for the following experiments: | |
| -2-b-(1). Plants modified by recombinant or synthetic nucleic acid molecules that are noxious weeds or can interbreed with noxious weeds in the immediate geographic area. |  |
| -2-b-(2). Plants in which the introduced DNA represents the complete genome of a non- exotic infectious agent (see Section V-M, Footnotes and References of Sections I-IV). |  |
| -2-b-(3). Plants associated with recombinant or synthetic nucleic acid molecule-modified non-exotic microorganisms that have a recognized potential for serious detrimental impact on managed or natural ecosystems (see Section V-M, Footnotes and References of Sections I-IV). |  |
| -2-b-(4). Plants associated with recombinant or synthetic nucleic acid molecule-modified exotic microorganisms that have no recognized potential for serious detrimental impact on managed or natural ecosystems (see Section V-M, Footnotes and References of Sections I-IV). |  |
| -2-b-(5). Experiments with recombinant or synthetic nucleic acid molecule-modified arthropods or small animals associated with plants, or with arthropods or small animals with recombinant or synthetic nucleic acid molecule-modified microorganisms associated with them if the recombinant or synthetic nucleic acid molecule-modified microorganisms have no recognized potential for serious detrimental impact on managed or natural ecosystems (see Section V-M, Footnotes and References of Sections I-IV). |  |
| -3. **Experiments Involving Transgenic Rodents**.  This section covers experiments involving the generation 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. | |
| -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). |  |

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| 5. USE OF rDNA IN YOUR EXPERIMENTS | | | | |
| a. Does your project involve the use of rDNA from an outside source? If your answer is **Yes**, specify the source (e.g., a commercial source or collaborator). | | | | Yes  No |
|  | | | | |
| b. Does your project involve the *de novo* generation and use of rDNA constructs? | | | | Yes  No |
| c. Will animals serve as recipients of rDNA? If your answer is **Yes**, indicate the species below (include the strain for mice). **Note**: You must also submit an **Animal Use Addendum (Form D)**. | | | | Yes  No |
|  | | | | |
| d. Will rDNA be used in tissue culture? If your answer is **Yes**, specify the cell line and its source. | | | | Yes  No |
|  | | | | |
| e. Will cell lines modified with rDNA be used in animals? If your answer is **Yes**, specify the cell line name, its source, and the target animal species (include the strain for mice). | | | | Yes  No |
|  | | | | |
| f. Does your project involve the use of one or more recombinant vectors? If your answer is **Yes**, list the name (e.g., pGL4) and indicate the nature (check all that apply) of each vector. **Note**: Please attach a map for each vector. | | | | Yes  No |
|  | | | | |
| Naked DNA/RNA  Bacterial plasmid  Viral vector | | Adeno-Associated Virus  Adenovirus  Retrovirus | | |
| g. Are you using a lentivirus vector? If your answer is **Yes**, describe the generation and use of the vector system. | | | | Yes  No |
|  | | | | |
| h. Does your work require the use of a host cell line or packaging cells for recombinant vector propagation? If your answer is **Yes**, provide a brief description of the required cells. | | | | Yes  No |
|  | | | | |
| i. Is this a virus-based vector? If your answer is **Yes**, indicate the amount (%) of the viral genome remaining in the vector. | | | | Yes  No |
|  | | | | |
| j. Is the vector replication competent? | | | | Yes  No |
| k. Is a helper virus required? If your answer is **Yes**, describe the helper virus. | | | | Yes  No |
|  | | | | |
| l. Are you using a transgene? If your answer is **Yes**, provide the information requested below. **Note**: A transgene is a gene or genetic material that will be transferred from one organism to another. | | | | Yes  No |
| *Promoter and gene name* | *Source of gene* | | *Biological activity of sequence* | |
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|  |  | |  | |
| If any of the above genes are viral and comprise, in total, more than 2/3 of the original viral genome, provide more information about the virus and genes used. | | | | |
|  | | | | |
| m. Will a deliberate transfer attempt be made to obtain expression of the foreign gene encoded in the recombinant DNA or RNA? | | | | Yes  No |
| n. Indicate the biosafety level required for this work. | | | | |
| Laboratory Biosafety Level (check one) | | 1  2  3 | | |
| Animal Biosafety Level (check one) | | 1  2  3 | | |

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| 6. CREATION OF TRANSGENIC RODENTS | | | | |
| Will your research involve the creation of transgenic rodents? If your answer is **Yes**, complete this section. | | | | Yes  No |
| a. Provide the genus, species, and strain of the parent animal. | | | | |
|  | | | | |
| b. Provide the transgenic strain identification. | | | | |
|  | | | | |
| c. Provide information about the transgene(s) to be used in the creation of transgenic rodents. | | | | |
| *Promoter and gene name* | *Source of gene* | | *Biological activity of sequence* | |
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| d. If any of the above genes are viral, do they comprise more than 2/3 of the original viral genome? If your answer is **Yes**, provide additional information about the virus and genes used. | | | | Yes  No |
|  | | | | |
| e. Will a deliberate transfer attempt be made to obtain expression of the foreign gene encoded in the recombinant DNA or RNA? | | | | Yes  No |
| f. Describe the method of gene transfer. | | | | |
|  | | | | |
| g. Indicate the biosafety level required for this work. | | | | |
| Laboratory Biosafety Level (check one) | | 1  2  3 | | |
| Animal Biosafety Level (check one) | | 1  2  3 | | |

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| --- | --- | --- | --- | --- |
| 7. CROSSING TRANSGENIC ORGANISMS | | | | |
| Does this work involve crossing transgenic organisms? If your answer is **Yes**, continue to the next questions. If your answer is **No**, you may skip the remainder of this section. | | | | Yes  No |
| The following questions pertain to breeding two different transgenic or mutant organism strains to generate a new strain. Answer the following questions about plans to cross transgenic organisms. If you answer **Yes** to any question, provide the information requested in this section. If you answer **No** to all four questions, you can skip the remainder of this section. | | | | |
| Parent strains or offspring require ABSL-2 or higher containment (Example: Breeding knockout mice from two different transgenic strains, one of which requires ABSL-2 containment) | | | | Yes  No |
| Parent strains or offspring contain a transgene encoding more than 50% of an exogenous eukaryotic virus | | | | Yes  No |
| Parent strains or offspring contain a transgene under the control of a gamma retroviral virus | | | | Yes  No |
| Crosses involve transgenic organisms other than mice (Example: Crossing two different transgenic fruit fly lines) | | | | Yes  No |
| a. Provide the genus, species, and strain of the parent animal(s). | | | | |
|  | | | | |
| b. Provide information about the transgenic rodents to be crossed. | | | | |
| *Designation of transgenic line “A”* | *Designation of transgenic line “B”* | | *Designation and genotype of resulting cross-bred line “C”* | |
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|  |  | |  | |
| c. If any of the above genes are viral, do they comprise more than 2/3 of the original viral genome? If your answer is **Yes**, provide additional information about the virus and genes used. | | | | Yes  No |
|  | | | | |
| d. Indicate the biosafety level required for this work. | | | | |
| Laboratory Biosafety Level (check one) | | 1  2  3 | | |
| Animal Biosafety Level (check one) | | 1  2  3 | | |

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| 8. ADDITIONAL INFORMATION |
| Use this text field to provide any additional information pertinent to your work and this biosafety protocol form. |
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| CERTIFICATION BY THE PRINCIPAL INVESTIGATOR | |
| I affirm that, to the best of my knowledge, the information I have provided is complete and accurate. I understand my responsibilities as noted in this form. No changes will be made without prior approval of the Institutional Biosafety Committee. | |
| Signature of Principal Investigator | Date |
| Name of preparer (if prepared by someone other than the PI) | Position |

*SUBMISSION INSTRUCTIONS:*

*Once you have completed this form, convert the completed form directly to an Adobe PDF file and electronically sign the form using the E-signature feature of Adobe Acrobat. Alternatively, print the completed form, add your signature, and scan it to create an Adobe PDF file. Send the completed form by e-mail as an attachment to* [*biosafety@drexel.edu*](mailto:biosafety@drexel.edu)*.*

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| --- |
| ***Criteria for Exempt rDNA Experiments***  *As indicated in Section III-F of the NIH Guidelines, some investigations involving rDNA may be* ***exempt*** *from the NIH Guidelines and registration with Institutional Biosafety Committee. The eight categories of recombinant or synthetic molecules below are considered exempt.*  *If your investigations can be categorized as exempt, you are not required to complete and submit a Form B.*  ***Note****: Other federal and state standards of biosafety may still apply to such research (e.g., standards outlined in the* [*CDC/NIH publication Biosafety in Microbiological and Biomedical Laboratories*](https://www.cdc.gov/labs/BMBL.html)*).*   * ***Section 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.* * ***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.* * ***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 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 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.*   *Source:* [*NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.htm#_Toc3457051) *(April 2024)* |