SOP Title:	**Exempt Experiments**	SOP No.	**4**
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Purpose: This standard operating procedure (SOP) explains the procedure for submitting experiments exempt from the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (*NIH Guidelines*).

Reference:
NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (*NIH Guidelines*), https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.htm.

Conditions:

1. Per Section III-F of the NIH Guidelines, experiments are exempt when they involve recombinant DNA that are:
    a. **Section III-F-1:** For synthetic nucleic acids, those 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.
    b. **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.
    c. **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.
    d. **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.
    e. **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).
    f. **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.
    g. **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.
    h. **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, 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.

PIs and IBCs cannot make the determination that a class of experiments other than the ones listed below poses no significant risk.

The following classes of experiments are exempt under Section III-F-8:

1. **Appendix C-I:** Certain recombinant or synthetic nucleic acid molecules that contain less than one-half of any eukaryotic viral genome when propagated and maintained in cells in tissue culture.
2. **Appendix C-II:** *Escherichia coli K-12* host-vector systems
3. **Appendix C-III:** *Saccharomyces cerevisiae* or *Saccharomyces uvarum* host-vector systems
4. **Appendix C-IV:** *Kluyveromyces* lactis host-vector Systems
5. **Appendix C-V:** *Bacillus subtilis* or *Bacillus licheniformis* host-vector systems
6. **Appendix C-VI:** Extrachromosomal elements of gram positive organisms [see specific list of organisms in C-VI]
7. **Appendix C-VII:** The purchase or transfer of transgenic rodents
8. **Appendix C-VIII:** Generation of certain BL1 Transgenic Rodents via Breeding

2. If an experiment falls under Sections III-A, III-B, or III-C and also III-F, then the research is **not** exempt (see the note Under Section III of the NIH Guidelines). The three types of experiments that would not be exempt under this provision are:
    a. **Section III-A:** The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine or agriculture;
    b. **Section III-B:** 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); or
    c. **Section III-C:** The deliberate transfer into human research participants of either:
        i. Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
        ii. 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 integration into the genome (e.g., cis elements involved in integration); or
            3. Have the potential to replicate in a cell; or

4. Can be translated or transcribed.

3. There are certain exceptions to the exemptions described in Appendix C of the NIH Guidelines. [See Appendix C-1-A, through C-V1-A]. In addition to the three types of experiments listed above, these exceptions include experiments involving:
    a. DNA from Risk Group 3, 4, or restricted organisms or cells known to be infected with these agents
    b. Whole plants regenerated from plant cells and tissues cultures that do not remain axenic cultures
    c. Large scale experiments (more than 10 liters of volume in a single culture vessel)
    d. Deliberate introduction of genes coding for the biosynthesis of molecules that are toxic for vertebrates with an LD50 greater than 100 nanograms/kg but less than or equal to100 micrograms/kg (see Appendix F)
4. Although Appendix C-1 does exempt the use of recombinant or synthetic nucleic acid molecules in tissue culture, there are exceptions to this exemption. Existing tissue culture cell lines created by the introduction of recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines **unless**, the cell line:
    a. **Section III-D:** DNA from Risk Group 3, 4, or restricted organisms or cells known to be infected with these agents;
    b. **Section III-B-1:** contains a toxin with an LD50 of less than 100 nanograms per kilogram/kg bodyweight;
    c. **Appendix C-I:** contains viral DNA in a quantity exceeding 50% of any viral genome;
    d. **Section III-D- 3:** is used in conjunction with defective viruses in the presence of helper virus
    e. **Section III-C-1:** is used in an experiment involving the deliberate transfer of the cell line into humans; or
    f. **Section III-D- 6:** is grown in a volume exceeding 10 liters of culture.
5. If an experiment falls into Section III-D or III-E of the *NIH Guidelines* and **also** falls into section III-F, it is exempt. An example of such an experiment is the following: *Staphylococcus aureus* (a Risk Group 2 bacterium) contains a recombinant plasmid. The plasmid is indigenous to *S. aureus*, was created in vitro, and contains only DNA from *S. aureus* (i.e., the DNA inserted into the plasmid was *S. aureus* DNA).
6. Experiments involving rDNA molecules exempt from the NIH Guidelines must still be reported to the IBC for approval.
7. Consult with a member of the IBC to determine if research qualifies for exemption.

Procedures:

1. Login into Cayuse using your JMU eID and password
2. Open the Products drop at top right and change it to Hazard Safety
3. Select Start a New IBC Application
4. When asked to describe the planned activities, for Exempt protocols, choose the appropriate activity described in Section III-F. Any choices made outside of this will result in the protocol being non-

exempt.

5. Submit the completed protocol with AUH approval to the IBC.
6. The Exempt Form will be reviewed by the IBC Chair and the Biosafety Officer to determine if it falls under the eight categories of exemption as described in the *NIH Guidelines*, Section III –F (Exempt Experiments).
    a. Additional members or the full IBC may be consulted for input as necessary.
7. If the protocol has been determined to be an exempt, an Exempt Determination notice will be sent by the IBC Chair or IBC Administrative Support. No continuing review or modification is necessary unless there are any changes to the procedures that could pose a threat to health or the environment.
8. If the protocol has been determined to be nonexempt, a protocol registration will need to be submitted. Please see SOP No. 5 regarding Non-Exempt Protocol Registrations.

Revision History		
Version No.	**Brief Description of Changes**	**Created on Date**
01	Updated hyperlinks. Revised Procedures to reflect new electronic Research Administration (eRA) software system.	2/26/2025