UNIVERSITY OF SOUTH FLORIDA

Institutional Biosafety Committee Policy Manual

Research Integrity & Compliance

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Purpose

The University of South Florida (USF) Biosafety Program and the USF Institutional Biosafety Committee (IBC) is committed to incorporating health and safety practices governing all USF personnel working with biohazardous materials in research and/or teaching activities at USF. The USF Biosafety Program is established to reduce the risk of potential occupational exposure to infectious agents, biological toxins, Select Agents/Toxins, and Recombinant or Synthetic Nucleic Molecules Acid (rDNA) in a research and/or teaching environment.

It is the policy of the USF Biosafety Program that all research and/or teaching involving infectious agents, biological toxins, Select Agents/Toxins, and Recombinant or Synthetic Nucleic Acid Molecules must be conducted in a safe manner. Biosafety containment practices protect the faculty, staff, students, volunteers, and visitors from exposure to infectious agents, biological toxins, Select Agents/Toxins, and Recombinant Deoxyribonucleic Acid (rDNA) and prevent the release of biological hazards into the environment. To ensure the safe handling of infectious agents, biological toxins, Select Agents/Toxins, and recombinant or synthetic nucleic acid molecules, USF requires compliance with the National Institute of Health *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*, Centers for Disease Control and Prevention (*Biosafety in Microbiological and Biomedical Laboratories*, 5th Edition), US Department of Health and Human Services, Office of Biotechnology Activities, Office of Health and Safety-Biosafety, USF Biosafety Program Institutional Biosafety Manual, and other applicable federal, state, and local regulations.

SECTION 1.0 IBC Policy Regarding Use of Biohazardous Agents

Section 1.1 Overview

1.1.1 A USF Biosafety protocol is required for all (research and/or teaching) laboratory activities which involve the use or manipulation of infectious agents (including but not limited to bacteria, viruses, fungi, rickettsia, protozoa, or parasites), biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules which are:

a. supervised or conducted by USF faculty or staff;
b. conducted on USF premises, or in a building or location administered by or under the control of USF; and/or
c. supported by funds provided by or through USF.

1.1.2 Principal Investigators (PI) at USF who possess or plan to possess, store, work with, or transport infectious agent(s), biological toxin(s), Select Agent(s)/Toxin(s), and/or recombinant or synthetic nucleic acid molecules must register the infectious agent(s), biological toxin(s), Select Agent(s)/Toxin(s), and/or recombinant or synthetic nucleic acid molecules with the USF Institutional Biosafety Committee (IBC).

1.1.3 It is the policy of the IBC that the Principal Investigator (PI) is responsible for the proper acquisition, use, handling, storage, transportation, and disposal of

biohazardous material (i.e., infectious agent(s), biological toxin(s), Select Agent(s)/Toxin(s), and/or recombinant or synthetic nucleic acid molecules) in research and/or teaching. In addition, all individuals working with these materials must adhere to IBC policy, procedures, and rules.

1.1.4 It is the policy of the IBC that Biosafety Containment Level 4 (BSL-4) agents may not be used or stored at the University of South Florida. See Appendix B-IV of the NIH *Guidelines for Research Involving Recombinant or Synthetic DNA Molecules* (NIH *Guidelines*) for a list of these agents.

1.1.5 All work with infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules will be conducted in compliance with USF IBC policy, the publications *Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition*, and the NIH *Guidelines* published by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), and 42 CFR 73, 9 CFR 121, and 7 CFR 331 for Select Agents.

Section 1.2 Scope of IBC Policy

1.2.1 This policy applies to USF faculty, staff, students, volunteers, and visitors who engage in any university activity within all divisions and departments of USF and/or conducted on university premises (refer to section 1.1.2).

1.2.2 USF faculty, staff, students, volunteers, and visitors use of infectious agents, biological toxins, Select Agents/Toxins, and recombinant or synthetic nucleic acid molecules (as defined per item 2.1) for research and/or teaching.

Section 2.0 Biohazardous Materials

Section 2.1 Types of Biohazardous Materials that Require Registration with the IBC

2.1.1 USF IBC review and approval is required prior to using the following biohazardous agents:

a. The use of recombinant or synthetic nucleic acid molecule (Section III-A-F) as defined by the *NIH Guidelines*.
b. Any microorganism (including but not limited to bacteria, viruses, fungi, rickettsia, protozoa, or parasites), or infectious substance, or naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance that is capable of causing death, disease, or other biological malfunction in a human, an animal, or a plant;
c. Select Biological Agents and Toxins, High Consequence Livestock Pathogens, and Restricted Plant Pathogens as identified by 42 CFR 73, 9 CFR 121, and 7 CFR 331; See the list of HHS and USDA Select Agents and Toxins
d. Any biological toxin: A toxic material or product of plants, animals, microorganisms (including but not limited to bacteria, viruses, fungi,

rickettsia, or protozoa), or infectious substances, or a recombinant or synthesized molecule (whatever the origin and method of production);
e. Any clinical materials that may contain wild poliovirus;
f. The definition also includes projects that involve known biohazards that do not appear to fall into one of the above criteria (e.g., prions or cells lines known to be infected with viruses). If in doubt as to whether a material constitutes a potential biohazard; the USF Institutional Biosafety Officer (IBO) should be consulted.

Exceptions: Research using any materials that require BSL-4 containment will not be considered by the IBC for work at any USF location or facility (dictated by the lack of qualifying facilities at USF).

2.1.2 All use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules as indicated above must be reviewed and approved by the IBC. IBC protocols are submitted through BiosafetyNet (https://arc.research.usf.edu/Safety/) on the ARC platform.

Section 3.0 Assessment and Selection of Appropriate Safeguards

3.1 It is the responsibility of the PI to conduct a preliminary risk assessment to determine the appropriate level of perceived risk and biological and physical containment level prior to possessing or using biohazardous material(s). Evaluating the risk allows the PI to choose the appropriate containment level for the organism.

3.2 The PI is encouraged to consult with the USF Institutional Biosafety Officer (IBO) regarding the risk assessment. However, the IBC will make the final decision as to the level of risk and appropriate biological and physical containment levels for infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules that are subject to its review and approval.

Section 4.0 Regulations and Guidelines

4.1 The IBC Policy is drafted in accordance with the following regulations and guidelines:
a. *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. The NIH *Guidelines* publication is available from the NIH-OSP.
b. Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition, published by the Centers for Disease Control and Prevention (CDC) and NIH. The BMBL is generally considered the standard for biosafety.
c. Code of Federal Regulations (CFR): 42 CFR 73,
d. Agricultural Bioterrorism Protection Act of 2002, 7 CFR 331, and 9 CFR 121,
e. USA Patriot Act (October 2001),
f. Public Health Security and Bioterrorism Preparedness Response Act of 2002.

Section 5.0 Institutional Official

5.1 The Senior Vice President for Research Innovation & Knowledge Enterprise is the Institutional Official responsible for the Biosafety Program.

5.2 The Senior Vice President for Research Innovation & Knowledge Enterprise is responsible for an Institutional Biosafety Committee (IBC).

5.3 The Senior Vice President for Research Innovation & Knowledge Enterprise is responsible for the appointment of IBC members, alternates, ex-officio, ad hoc, and consultants.

5.4 The Senior Vice President for Research Innovation & Knowledge Enterprise shall appoint the members of the IBC and may add, reappoint, or remove members. Qualified successors shall be nominated as required, based on the recommendation of the Institutional Biosafety Officer, the IBC Chairperson, and/or the Director of Research Integrity & Compliance. Procedures for appointment of alternate members, terms of appointment, length of service, and duties are the same as for regular IBC members.

5.5 The Senior Vice President for Research Innovation & Knowledge Enterprise is responsible for notifying the NIH-OSP (Office of Science Policy) and/or CDC of incidents of serious or continuing noncompliance with IBC policy or applicable federal regulations.

Section 6.0 Institutional Biosafety Committee (IBC)

6.0.1 An IBC is an appropriately constituted group that has been formally designated to review and monitor research involving infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules. In accordance with the NIH guidelines and the CDC BMBL requirements, the IBC is responsible for approving, requiring modification to secure approval, deferring, or disapproving research involving infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules.

6.0.2 The IBC is empowered with the authority to suspend or terminate activities involving infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules for activities/practices that jeopardizes the health and safety of any USF faculty, staff, students, volunteers, and visitors at USF, repeated safety violations, and/or continued noncompliance with IBC regulations and policy.

6.0.3 University of South Florida (USF) Research Integrity & Compliance provides professional and administrative support to the IBC.

Section 6.1 Charge of the Committee

6.1.1 The Institutional Biosafety Committee (IBC) is responsible for advising the Senior Vice President for Research Innovation & Knowledge Enterprise on all matters pertaining to the safe use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules in research at USF.

a. The IBC establishes guidelines for USF faculty, staff, students, volunteers, and visitors conducting research and/or teaching programs involving biological agents which are potentially harmful to the environment and/or potentially pathogenic to humans, animals, and/or plants, as well as projects involving recombinant DNA.
b. The IBC guides and supports the work of the university's researchers in conducting research and/or teaching programs involving infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules which are potentially harmful to the environment and/or potentially pathogenic to humans, animals, and/or plants, as well as projects involving recombinant DNA.
c. The IBC assures compliance with appropriate federal/state/local regulations and IBC Policy by reviewing applications and conducting laboratory inspections for the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules.

6.1.2 The IBC establishes policy, practices, and/or procedures for review of all projects involving the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules to assure compliance with federal, state, and local regulations and guidelines.

6.1.3 It is the IBC's responsibility to establish, monitor, and enforce policy and procedures for the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules.

6.1.4 All use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules must be reviewed and approved by the IBC before the possession of and/or the use of the agent.

6.1.5 The IBC shall maintain diverse membership representing the community and a variety of University interests.

6.1.6 Non-committee faculty/ad hoc experts may be asked to advise the IBC when necessary.

Section 6.2 IBC Membership

6.2.1 IBC members and their alternates are selected so that they have collective experience and expertise to fully evaluate the biosafety risks associated with the wide variety of research and/or teaching agents which come under its review.

6.2.2 The IBC is composed of scientists and clinical investigators from USF and its affiliate institutions and representative(s) from the community.

a. The IBC must consist of at least five members that have experience and expertise in biosafety and are able to assess the safety of research involving infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules, including human gene transfer trials, to identify any potential risk to USF faculty, staff, students, volunteers, and visitors, the environment, or public health.
b. These appointments may come from the Colleges of Medicine, Arts and Sciences, Engineering, Public Health, or other appropriate colleges.
c. At least two members shall not be affiliated with the University but should represent the interests of the surrounding community with respect to health and protection of the community and the environment.
d. The Institutional Biosafety Officer (IBO) serves as a voting member of the IBC.
e. A representative from the USF Office of Environmental Health and Safety, with expertise in biomedical waste disposal shall provide ad hoc expertise as needed.

6.2.3 The IBC shall include at least one individual with expertise in plant, plant pathogen, and/or plant pest containment principles when research involving recombinant plants is reviewed by the IBC (Refer to Appendix L, Physical and Biological Containment for Recombinant or Synthetic DNA Research Involving Plants, of the *NIH Guidelines*).

6.2.4 The IBC shall include at least one individual with expertise in animal containment principles when research involving animals and infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules materials is reviewed by the IBC.

6.2.5 The IBC shall include at least one individual with expertise in human gene transfer principles and safety issues when research involving human subjects and recombinant or synthetic nucleic acid molecules materials is conducted by the university.

6.2.6 IBC members are appointed by the Senior Vice President for Research Innovation & Knowledge Enterprise, for a term of three years.

6.2.7 The Senior Vice President for Research Innovation & Knowledge Enterprise and the Director of Research Integrity & Compliance shall serve on the IBC in an ex-officio capacity.

6.2.8 No member of the IBC may be involved (except to provide information requested by the IBC) in the review or approval of a project in which he or she has been or

expects to be engaged in and has a direct financial interest, or any other type of *conflict of interest.*

6.2.9 IBC meetings are held on the third Tuesday of every month. The IBC will not meet on days that USF is "closed for business". The IBC meeting schedule is available at https://www.usf.edu/research-innovation/research-integrity-compliance/committees-meeting-schedules.aspx.

6.2.10 IBC alternates are appointed to ensure that the committee is properly constituted at all times. When a regular member is unavailable to serve an alternate member will be contacted for their participation to ensure that the committee has quorum. The following applies for alternate members:

- Alternate members will have voting rights, except that they may not vote at meetings attended by their respective regular members.
- Alternate members will be included in determining or establishing quorum at meetings when their respective regular members are absent.

6.2.11 All members and alternates of the IBC are provided information on an ongoing basis regarding current biosafety news, topics, and regulations.

6.2.12 IBC members must attend each regular monthly scheduled meeting or send their alternate. IBC members must notify the IBC administrative staff of planned absences prior to protocol review assignments.

6.2.13 Visitors and guests that are non-members of the IBC that attend IBC meetings are not allowed to participate in the discussions unless acknowledged by the IBC Chairperson.

6.2.14 The IBC, at its discretion, may recruit ad hoc consultants whose input to the deliberations at meetings has unique importance. These recruited ad hoc consultants may be University or non-University affiliated scientists, clinical investigators, or community representatives.

Section 6.3 Operational Procedures and Guidelines

6.3.1 The IBC shall adopt and adhere to the operating procedures and principles as described in the National Institutes of Health (NIH) *Guidelines for Research Involving Recombinant or Synthetic DNA Molecules* and the Centers for Disease Control and Prevention (CDC/NIH) *Biosafety in Microbiological and Biomedical Laboratories, 5th edition* (BMBL).

Section 6.4 Institutional Biosafety Committee (IBC) Responsibilities

6.4.1 The committee develops recommendations, operating policy, and procedures regarding the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules, as needed to supplement the federal, state, and local regulations and guidelines.

6.4.2 The IBC reviews the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules research conducted at or sponsored by the USF or its affiliates for compliance with the applicable guidelines and regulations. The review will include:

a. Assessment of potential risks to health and the environment for the proposed research.
b. Assessment of the containment levels of the proposed research.
c. Assessment of the facilities, procedures, practices, and training and expertise of personnel involved in use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules;
d. Providing for the adjustment of containment levels based on risk for experiments as specified in the *NIH Guidelines*, CDC/NIH) *Biosafety in Microbiological and Biomedical Laboratories, 5th edition* (BMBL), USF Biosafety Program Institutional Biosafety Manual, or IBC policy;
e. Providing a forum for the discussion of biosafety concerns and assisting in the resolution of any biosafety issues brought before the IBC.
f. Notifying the PI of the results of the IBC review.

Section 6.5 Quorum

6.5.1 A quorum is required in order to conduct routine IBC business. In order to establish a quorum the number of committee members present must equal greater than 50% of the total committee membership. A passing vote will be a simple majority of members present; minority views will be recorded in the minutes.

Section 6.6 Chairperson/Vice Chairperson

6.6.1 Initially, and thereafter (renewal time, unexpected vacancy, etc.), the Senior Vice President for Research Innovation & Knowledge Enterprise shall appoint the Chairperson of the IBC and may reappoint or remove the Chairperson. A qualified Chairperson shall be nominated as required, based on the recommendation of the Institutional Biosafety Officer, the IBC Chairperson, and/or the Director of Research Integrity & Compliance. Procedures for appointment of the Chairperson, terms of appointment, length of service, and duties are exactly as for regular IBC members.

6.6.2 The IBC Chairperson has the following duties:

a. Conduct each meeting in an orderly manner.
b. The Chairperson is responsible for chairing the meeting, conducting business so that each protocol is fairly and completely reviewed, and that the committee reaches a decision on the disposition of each protocol.
c. Sign correspondence on behalf of the IBC.
d. Appoint a Vice Chairperson. The Vice Chairperson will be an experienced faculty member of the IBC who will assume the responsibilities of the Chairperson during any period of absence.

Section 6.7 Institutional Biosafety Officer (IBO)

6.7.1 Responsibilities of the IBO include:

a. Screening research protocols proposed by investigators for completeness and forwarding them to the IBC for review.
b. Reporting to the IBC significant problems related to accidents and illnesses, operations, or other activities involved with proposed or approved protocols.
c. Assisting laboratories in conforming to pertinent regulatory guidelines and IBC policy by providing training, facility inspection, and communication of program requirements.
d. Overseeing the conduct of inspections, to ensure adherence to federal, state, and University regulations and IBC policy for the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules at USF.
e. Monitoring federal, state, and local regulatory trends and communicate such to the IBC and responsible institutional representatives.
f. Serving as a voting member of the IBC and conducting certain activities on behalf of the IBC in support of the program (e.g., review/inspect individual facilities, biosafety manuals) and confirm compliance with NIH and/or CDC guidelines and/or USF IBC policy, procedures, and requirements.
g. Providing recommendations to the IBC on biosafety matters.
h. Preparation and filing of annual IBC membership report to NIH OSP.
i. Acting as a liaison with University and Institutional Review Boards (IRBs), Institutional Animal Care and Use Committees (IACUC), Infection Control Units, and the Environmental Health and Safety (EHS) office.

Section 6.8 Biosafety Program Support Staff

6.8.1 The USF Research Integrity & Compliance Biosafety Program personnel/staff (IBO, et al) will serve as support staff to the IBC.

6.8.2 IBC support staff supplements the function and operation of the IBC at the direction of and under the supervision of the Institutional Biosafety Officer.

6.8.3 Responsibilities of the Institutional Biosafety Program Staff:

a. Maintain the official roster of IBC members;
b. Schedule IBC meetings;
c. Ensure that all meeting materials are available to members prior to the scheduled meeting;
d. Compile and maintain the minutes of IBC meetings in compliance with regulatory requirements;
e. Maintain all IBC documentation and records;
f. Facilitate communication between investigators and the IBC;
g. Track the progress of each research protocol submitted to the IBC;

h. Maintain a computerized IBC database for tracking purposes and record incoming information into the database;
i. Serve as a resource for investigators on regulatory information, biosafety procedures and practices, and provide guidance regarding submission procedures;
j. Conduct laboratory inspections;
k. Propose, review, and revise IBC documents;
l. Draft reports and correspondence on behalf of the IBC or IBC Chairperson;
m. Review IBC applications.

Section 6.9 Reporting to NIH—Recombinant or Synthetic Nucleic Acids

6.9.1 The IBC on behalf of the institution, shall report to the NIH OSP:

- Per Section IV-B-1-j of the *NIH Guidelines* any significant problems with or violations and any significant research-related accidents or illnesses to the NIH OSP within 30 days; unless the IBC determines that a report has already been filed by the Principal Investigator.
- For BSL-2, per Appendix G–II-B-2-k, any spills and accidents which result in **overt exposures** to organisms containing recombinant or synthetic nucleic acid molecules are **immediately reported** to the Institutional Biosafety Committee and NIH OSP.
- For BSL-3, per Appendix G-II-C-2q any spills and accidents which result in **overt or potential exposures** to organisms containing recombinant or synthetic nucleic acid molecules are **immediately reported** to the Biological Safety Officer, Institutional Biosafety Committee, and NIH OSP

Reports to NIH OSP shall be sent to the Office of Science Policy, National Institutes of Health, preferably by e-mail to: NIHGuidelines@od.nih.gov

6.9.2 The Institutional Biosafety Officer, on behalf of USF and the IBC, shall file an annual report with NIH OSP which includes:
a. A roster of all IBC members clearly indicating the Chairperson, contact person, Institutional Biosafety Officer, plant expert (if applicable), animal expert, human gene therapy expert, or ad hoc consultant (if applicable).
b. Biographical sketches of new IBC members, including community members.

Section 6.10 Director of Research Integrity & Compliance

6.10.1 The Director of Research Integrity & Compliance is designated as overall administrator for the USF IBC and is responsible for ensuring that it functions and operates within USF in compliance with all federal, state, and local laws and regulations and USF IBC policy and procedures that govern the safe use of infectious agents, biological toxins, Select Agents/Toxins, and recombinant or synthetic nucleic acid molecules in the conduct of research and/or teaching activities.

6.10.2 The Director of Research Integrity & Compliance may delegate operational authority to USF Institutional Biosafety Officer as appropriate.

6.10.3 The Director of Research Integrity & Compliance is responsible for immediate notification to the USF Senior Vice President for Research Innovation & Knowledge Enterprise regarding:

- any serious injury/exposure to infectious agents, biological toxins, Select Agents/Toxins, and recombinant or synthetic nucleic acid molecules;
- any serious adverse event related to gene therapy use;
- major biohazardous material spills;
- breach of Biosafety Level 3 agents;
- unanticipated problems;
- any theft of restricted agents;
- any biosecurity issues;
- serious or continuing non-compliance with IBC policy and requirements by research investigators; or
- suspension or termination of IBC approval.

SECTION 7.0 Responsibilities for Safe Use of Biohazardous Materials

Section 7.1 Principal Investigator

7.1.1 The Principal Investigator (PI) is defined as a faculty member at USF and/or its affiliated institutions. The PI is ultimately responsible for the activities in their laboratory.

7.1.2 All uses, storage, and/or possession of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules must be reviewed and approved by the IBC.

7.1.3 The PI should make an initial determination of the required levels of physical, biological containment, and section of the NIH guidelines (III-A-III-F) their rDNA experiments falls under, in accordance with the requirements set in the *NIH Guidelines* and CDC BMBL, 5th edition.

7.1.4 The PI must select appropriate microbiological practices and laboratory techniques to be used for the research intended.

7.1.5 The PI must complete and submit their research protocol to the IBC for review and approval. IBC protocols are submitted through BiosafetyNet on the ARC platform.

7.1.6 Prior to initiation, the PI must submit all proposed modifications to a previously approved IBC study for IBC review and approval.

- For IBC protocols that are in in paper form, must submit a Modification Request form accessed at https://www.usf.edu/research-

innovation/research-integrity-compliance/documents/biosafety/modification.doc .

- IBC protocols that are approved in BiosafetyNet must submit amendments to their approved protocols in BiosafetyNet.

7.1.7 Prior to Initiating Research the Principal Investigator shall:

a. Make available to all laboratory staff and involved facilities staff the protocol that describes the potential biohazards and the precautions to be taken.
b. Instruct and train all research personnel in protocol specific procedures and:
   i. The practices and techniques required to ensure safety;
   ii. The procedures for dealing with accidents and spills; and
   iii. The reasons and provisions for any precautionary practices advised or requested (e.g., vaccinations or personal protective equipment).
c. Ensure that transportation of any biohazardous material comply with all applicable packaging and shipping requirements.

7.1.8 During the Conduct of the Research the Principal Investigator shall:

a. Supervise the safety performance of the laboratory staff to ensure that the required safety practices are employed.
b. Report any significant problems pertaining to the operation and implementation of containment practices and procedures to the IBC.
c. Immediately notify the IBO (813) 974-0954//Biosafety Manager (813) 974-5091 (during normal working hours) or the University Police using 911 (after hours) of any biological spills, accidents, containment failure, or deviations of biosafety practice which result in the release of biohazardous material and/or the exposure of laboratory personnel or members of the public to biohazardous materials.
d. Restrict access to the laboratory when experiments are in progress to those who are aware of the risks associated with the use of biohazardous agents and are trained to safely handle the biohazardous agents.
e. Be responsible for full compliance with the policy, practices, and procedures set forth in this policy manual and as described in the approved IBC protocol. Investigators are required to notify the IBC promptly of any noncompliance regarding applicable regulatory requirements (federal, state, and local) and IBC policy.

7.1.9 As part of the general responsibilities, the Principal Investigator shall:

a. Complete the Biosafety Core Course requirement and triennially thereafter a refresher biosafety training course.
b. Develop and implement written laboratory-specific biosafety procedures and containment practices (for BSL-2 and higher) that are consistent with the nature of current and planned research activities. The PI shall ensure that all laboratory personnel, including other faculty members, understand and comply with these laboratory specific biosafety procedures.
c. Ensure that all laboratory personnel (e.g., faculty, staff, students, volunteers, visitors), and maintenance personnel, who have the potential to be exposed to

any biohazardous materials are informed in advance of their potential risk and of the safety procedures required to minimize that risk.

d. Ensure that all maintenance work in, on, or around contaminated equipment is conducted only after that equipment is thoroughly decontaminated by the laboratory staff or PI.
e. Ensure that research materials are properly decontaminated before disposal and that all employees are familiar with the different methods of waste disposal.
f. Report any significant problems, violations of the policy, practices, and procedures set forth in this manual, or any significant research-related accidents and illnesses, to the Institutional Biosafety Officer (813) 974-0954/Biosafety Manager (813) 974-5091.
g. Report any potential exposures. For information, see our Exposures, Incidents and Near Misses web page
h. If USF employees, follow the USF Risk Management web page regarding instructions to file Workers Compensation claims
i. For all blood borne pathogen USF exposures:
    i. USF Health faculty, staff or volunteers notify the USF Health Medical Health Administration immediately (813) 974-3163, pager: (813) 216-0153, during regular working hours (Monday-Friday 8 am-5 pm) and the on call USF Infectious Disease fellow "Expert Consultation" at (813)974-2201 during non-regular working hours.
    ii. All other USF faculty, staff or volunteers contact USF Environmental Health & Safety (http://www.usf.edu/administrative-services/environmental-health-safety/programs-services/bloodborne-pathogens.aspx)
j. Comply with shipping requirements for infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules.

Section 7.2 Laboratory Worker

7.2.1 Any person working with infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant DNA or who works in a laboratory where these materials are used/stored is defined as a laboratory worker, whether the person is a faculty member, a student, an intern, a visiting scholar, or a volunteer.

7.2.2 It is the laboratory staff's responsibility to:

a. Complete the Biosafety Core Course requirements and triennially thereafter a refresher biosafety training course.
b. Follow laboratory specific biosafety practices and procedures.
c. Inform the PI of any personal health requirements that may require implementation of safety precautions.
d. Report to the PI or the lab supervisor all problems, deviations in procedure, spills involving biohazardous materials, exposures and/or safety/security concerns (e.g., suspicious persons or activities).

Section 7.3 Authorized Maintenance and Janitorial Personnel

7.3.1 USF Physical Plant personnel (housekeeping and maintenance) that are required to enter laboratory facilities where biohazardous materials are being used, stored, and/or disposed of (e.g., BSL-2 labs) should be informed of the potential risks associated with biohazardous materials. USF Biosafety Office conducts annual training for Physical plant personnel to provide general information about biological that may be present in BSL-2 laboratories. If these personnel have concerns regarding biosafety issues, these concerns should be discussed with their supervisor, the Principal Investigator, the Institutional Biosafety Officer, or the Institutional Biosafety Committee members.

7.3.2 USF Physical Plant personnel (housekeeping and maintenance) and other maintenance personnel do not have unrestricted access to Biological Safety Level 3 (BSL-3) laboratories. Housekeeping staff will not be provided access to BSL-3 areas unless approved by the BSL-3 facility director and the IBO. Any maintenance personnel who enter a BSL-3 facility must be supervised at all times by the BSL-3 lab director/lab manger or their designee. No work with biologic agents is allowed during a visit by maintenance personnel. All affected environmental surfaces in the BSL-3 facility need to be decontaminated prior to entry by maintenance personnel. The BSL-3 lab director/lab manger or their designee completes a *Safety Checklist for Maintenance Work in BSL-3 Laboratories* prior to maintenance work being accomplished. BSL-3 personal protection equipment (PPE) is provided to the maintenance personnel. A BSL-3 containment practices training is presented annually to USF Physical Plant personnel. The IBO ensures that USF maintenance personnel have attended BSL-3 training prior to them undertaking any task in a BSL-3 facility.

Section 8.0 Activities Involving Recombinant DNA Material

8.0.1 All research involving recombinant or synthetic nucleic acid molecules at USF must comply with the " NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ," (NIH *Guidelines*) published by the National Institutes of Health (NIH).

8.0.2 Recombinant and Synthetic DNA as defined by the NIH *Guidelines* as:
(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;
(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
(iii.) molecules that result from the replication of those described in (i) or (ii) above.”

Section 8.1 Recombinant or synthetic nucleic acid molecules Experiments

8.1.1 It is the policy of the USF IBC that research involving the use of recombinant or synthetic nucleic acid molecules as defined by the NIH *Guidelines* must be documented by a protocol and be reviewed and approved by the IBC. All research and/or teaching activities involving the use of recombinant or synthetic nucleic acid molecules material must be registered with the IBC.

8.1.2 All recombinant DNA (rDNA) protocols categorized as Section III-A through III-F must be submitted for review and approval by submitting a protocol in BiosafetyNet.

8.1.3 Approval by the IBC is required prior to initiating the research or teaching activity involving recombinant or synthetic nucleic acid molecules work (i.e., prior to handling the agent).

8.1.4 rDNA protocols require full committee review. Recombinant or synthetic nucleic acid molecules protocols are approved for a one-year period at the end of which, an annual renewal may be submitted for years two (2) and three (3) of the protocol. A new protocol must be submitted to and approved by the full committee every three (3) years.

8.1.5 All changes to an approved recombinant or synthetic nucleic acid molecules protocol must be submitted and approved prior to initiation.

- For IBC protocols that are in paper form, must submit a Modification Request form accessed at https://www.usf.edu/research-innovation/research-integrity-compliance/documents/biosafety/modification.doc .
- IBC protocols that are approved in BiosafetyNet must submit amendments to their approved protocols in BiosafetyNet.

No changes can be instituted to a previously approved rDNA protocol until that proposed modification has been submitted to and approved by the IBC.

8.1.6 Types of recombinant DNA experiments that need to be registered with the IBC are as follows;

a. Section III-A: 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
b. Section III-B: Experiments Involving the Cloning of Toxin Molecules with LD50 of Less than 100 ng/kg Body Weight.
c. Section III-C: 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. (see section 8.3 below)

d. Section III-D-1: Experiments Using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as Host-Vector Systems
e. 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
f. 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 Virus in Tissue Culture Systems
g. Section III-D-4: Experiments Involving Whole Animals
h. Section III-D-5: Experiments Involving Whole Plants
i. Section III-D-6: Experiments Involving More than 10 Liters of Culture
j. Section III-D-7:Experiments Involving Influenza Viruses
e. Section III-E-1: Recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus may be propagated and maintained in cells in tissue culture using BL1 containment (with the exception of DNA from Risk Group 3, 4, or Select Agents/Toxins).
f. Section III-E-2: 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.
g. Section III-E-3: 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
k. Section III-F: Exempt Experiments
f. 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 integrate into DNA, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 ng/kg 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.
g. 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.
h. 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.
i. 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.

j. 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).

k. 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 with advice of the RAC after appropriate notice and opportunity for public comment (see Section IV-C-1-b-(1)-(c), Major Actions). See Appendices A-I through A-VI, Exemptions under Section III-F-6--Sublists of Natural Exchangers, for a list of natural exchangers that are exempt from the NIH Guidelines.

l. 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.

m. 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.

Section 8.2 Section III-E and Section III-F recombinant or synthetic nucleic acid molecules Experiments

8.2.1 All Section III-E and Section III-F category research involving recombinant or synthetic nucleic acid molecules shall be conducted in accordance with the current version of the NIH *Guidelines*.

8.2.2 Section III-E and Section III-F category research involving recombinant or synthetic nucleic acid molecules require IBC review and must be submitted for review and approval in BiosafetyNet.

8.2.3 Protocols using rDNA that have been determined as category Section III-E and Section III-F of NIH Guidelines, are approved for the life of the research project with a continuing review every five years. In addition, all changes to these protocols must be reported by submitting an amendment.

Section 8.3 Recombinant DNA Studies Involving Human Research Participants

8.3.1 Principal investigators performing human gene transfer work must adhere to the responsibilities that are detailed in the most current version of the NIH *Guidelines*.

8.3.2 For 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 human research participants (human gene transfer), no human gene transfer experiment shall be initiated (see definition of initiation in Section I-E-4) until Institutional Biosafety Committee (IBC) approval (from the clinical trial site) has been obtained and all applicable regulatory authorization(s) and approvals have been obtained. USF IRB approval must be obtained.

8.3.3 For human gene transfer protocols, the recombinant or synthetic nucleic acid molecules study is assigned to two IBC members (primary and secondary reviewer) for review, with copies of the protocol sent to all members.

a. The primary reviewer assigned the human gene transfer protocol is to be a Clinician/Physician.
b. The primary and secondary reviewer's responsibilities are to provide a thorough review of the protocol and documents and provide their recommendations regarding approval of the study.

8.3.4 For research involving human subjects, the USF IBC may consider a frequency of review more often than once every year due to the degree of risk involved or the vulnerability of the participants.

8.3.5 Based on risk assessment, a human gene transfer research protocol that has reached the point where the research is permanently closed to the enrollment of new participants; where all participants have completed all research-related interventions; and where the research remains active only for long-term follow-up of participants, it no longer requires a six month review. The Continuing Review will subsequently be approved for a twelve month period by the IBC that coincides with the IRB Continuing Review Process.

Section 8.4 Documents Submitted for IBC Gene Transfer Review

8.4.1 **Review Requirements for IBC for review of Human Gene Transfer (HGT) Protocols**

The HGT protocol must be submitted via BiosafetyNet for review and approval by the IBC. As a part of the HGT IBC protocol submission the following documents must be included:

a. Clinical Protocol.
b. Investigational Brochure.
c. Based on a case by case review the IBC may require additional information.

Section 8.5 Reporting Requirements for Human Gene Transfer Protocols

8.5.1 All amendments and continuing reviews that are submitted to the IRB related to the gene transfer study or in support of gene transfer protocol must be submitted to the IBC for review. This includes:

a. All Continuing Review Reports to the IRB.
b. All Change in Procedures/Investigator's brochure reported to the IRB.
C. Report(s) of significant problems, violations of the NIH *Guidelines*, or any significant research-related accidents and illnesses.

Section 8.6 Use of Recombinant Viral Vectors with Animals

8.6.1 Investigators planning to administer recombinant or synthetic nucleic acid molecules to animals should refer to Appendix M and Section III-D-4 of the NIH *Guidelines* for information on biological and physical containment practices. Visit the USF Division of Comparative Medicine Website for additional guidance and to obtain applications to work with animals. Work involving laboratory animals requires USF Institution Animal Care and Use Committee (IACUC) approval and IBC approval before initiation of the study.

8.6.2 A pre-performance meeting must be conducted prior to using animals with potentially infectious recombinant or synthetic nucleic acid molecules materials requiring BSL-2 containment practices. The meeting is scheduled with the PI and his/her staff that represent the applicant's laboratory, Division of Comparative Medicine staff, and the Institutional Biosafety Officer or his/her designee.

a. This pre-performance meeting is required in order to ensure that all involved personnel are aware of the precautions, containment practices, facilities, protective devices, disposal and decontamination procedures, and other necessary safety procedures that must be followed to protect personnel from accidental exposure to the biohazardous material and to prevent cross contamination to other animals.
b. Agent specific information must be provided to all animal husbandry personnel involved in handling animals exposed to potentially infectious recombinant or synthetic nucleic acid molecules materials. Information should cover: the hazards associated with the work; required containment practices and procedures; proper handling of bedding, food, and water; cage washing; and all other husbandry materials associated with the experiment.

8.6.3 Animals that are infected with adenovirus or adeno-associated viral vectors, must utilize an Animal BSL-2 (ABSL-2) containment area for the procedure(s). ABSL-2 housing is required due to the replication-defective virus may revert or recombine *in vivo* thereby causing the vector to become replication competent. In turn this live virus may be shed from the animal and pose a potential exposure to those handling animals, animal bedding, feces, etc.

a. Animals exposed to replication incompetent adenovirus or adeno-associated viral vector(s) as a part of the research protocol, must be housed under Animal BSL-2 (ABSL-2) containment practices for first the 72 hours following infection of the animal.

b. Precautions must be taken to minimize aerosol creation (e.g., emptying animal waste material, washing down cages, cleaning the room with water hoses).

8.6.4 Animals that are infected with lentiviral/retroviral vectors, must utilize an Animal BSL-2 (ABSL-2) containment area for the procedure(s). ABSL-2 housing is required due to the replication-defective virus may revert or recombine *in vivo* thereby causing the vector to become replication competent. In turn this live virus may be shed from the animal and pose a potential exposure to those handling animals, animal bedding, feces, etc.

a. Animals exposed to replication incompetent lentiviral/retroviral vector(s) as a part of the research protocol, must be housed under Animal BSL-2 (ABSL-2) containment practices for:
   - The life of the study for direct administration of other viral vectors (e.g. Lentivirus, retrovirus) that are co-administered with human cells to the animals
   - Seven days for direct administration of other viral vectors (e.g. Lentivirus, retrovirus) that are not co-administered with human cells to the animals

b. Precautions must be taken to minimize aerosol creation (e.g., emptying animal waste material, washing down cages, cleaning the room with water hoses).

Section 8.7 Using recombinant or synthetic nucleic acid molecules to Create Genetically Engineered/Transgenic Animals

8.7.1 Investigators who create genetically engineered animals (either by pronuclear microinjection of DNA, or by blastocyst microinjection of embryonic stem cells that have been electroporated with DNA, or by other methods of genetic engineering involving recombinant DNA) must submit an IBC protocol prior to initiation of the experiment. In addition, the appropriate IACUC documents must be completed and approved.

8.7.2 Experiments involving the purchase of, or the transfer of, transgenic rodents that require Biosafety Level 1(BSL-1) containment practices are exempt from the NIH *Guidelines* and IBC registration

Section 8.8 Using recombinant or synthetic nucleic acid molecules to Create Genetically Engineered /Transgenic Plants

8.8.1 Experiments to genetically engineer plants by recombinant DNA methods require IBC review and approval.

8.8.2 To prevent the release of transgenic plant materials into the environment, the NIH *Guidelines*, Section III-D-5 provides containment recommendations that must be implemented.

Section 8.9 Research Studies and Protocols Involving Oligonucleotides

8.9.1 All human oligonucleotide therapy protocols will be examined on a case by case basis by the IBC chairperson and/or Institutional Biosafety Officer to determine whether they pose any biosafety issues.

Section 9.0 Activities Involving Infectious Agents

Section 9.1 Infectious Agents

9.1.1 All research and teaching activities involving the use of infectious agents must submit an IBC protocol in BiosafetyNet and be approved by the IBC.

9.1.2 The use of agents requiring BSL-4 containment is not permitted at the University of South Florida.

9.1.3 **Definition**: Infectious/Biological Agent refers to any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsia, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, capable of causing death, disease, or other biological malfunction in a human, an animal, a plant, or other living organism.

9.1.4 The use of agents requiring BSL-3 containment will be restricted to laboratories designated as BSL-3 containment laboratories. Protocols requesting the use of BSL-3 containment facility and practices will be reviewed by the IBC.

Section 9.2 Cell Lines

9.2.1 Cell cultures known to contain an infectious/pathogenic agent in the cell line are classified at the same level as that recommended for the agent.

9.2.2 Cell lines which are non-human in origin (excluding non-human primate- NHP ell lines), which do not harbor a primate virus, which are not contaminated with bacteria, mycoplasma or fungi and which are well established are classified as Risk Group 1 cell lines and manipulated at Biosafety Level 1 containment practices.

9.2.3 All cell lines exposed to or transformed by a primate oncogenic virus, and all virus containing primate cell lines are classified as Risk Group 2 cell lines and manipulated at Biosafety Level 2 containment practices.

Section 9.3 Use of Potentially Infectious Pathogens with Animals

9.3.1 Animal Biosafety Level (ABSL) Criteria. ABSL criteria must be adhered to as specified in the CDC BMBL (5th edition) when using infectious agents in animals.

a. All work with animals involving the use of infectious agents must be submitted to the IBC for review and approval in addition to review and approval from the IACUC.
b. Studies involving the use of animals exposed to infectious agents require a pre-performance meeting involving the PI and his/her staff that represent the applicant's laboratory, Division of Comparative Medicine staff, and the Institutional Biosafety Officer or his/her designee.

9.3.2 Appropriate facilities and equipment must be used to provide containment for laboratory animals exposed to or harboring infectious agents which is appropriate to the risk level of the infectious agents involved.

9.3.3 Housing of animals infected with BSL-2 agents must be in accordance with the recommendations of the CDC BMBL, 5th edition for Animal Biosafety Levels. These animals will be housed at ABSL-2 for the life of the study.

(Please Note: There are no Animal Biosafety Level 4 facilities at USF.)

Section 9.4 Transplantation of Human Blood or Blood Products into Research Animals

9.4.1 The IBC in conjunction with the Division of Comparative Medicine has implemented specific practices to be followed to reduce the risk of exposure of research faculty and staff, animal care personnel, and animals to potentially infected human tissues and/or clinical samples.

9.4.2 Samples Characterized For Pathogens Prior To Transplantation

a. Prior to injecting animals with human blood or blood products a copy of the testing results from an accredited laboratory must be submitted to the Division of Comparative Medicine and the USF IBC for each different lot/sample control number.
   i. If the testing results are positive for any pathogen and if the Principal Investigator chooses to transplant them into animals, these animals must be housed in accordance with Animal Biosafety Level 2 (ABSL-2) practices.
   ii. If the testing results are positive for any pathogen the investigator must notify the Institutional Biosafety Officer and the pathogen must be registered with the Institutional Biosafety Committee.

9.4.3 Samples Not Screened For Pathogens Prior To Transplantation

a. The usage of any unscreened sample(s) of human blood or blood products in animals will require the animals to be housed under Animal Biosafety Level 2 (ABSL-2) containment in accordance with the OSHA Blood Borne Pathogen

Standard using Standard Precautions (formerly known as Universal Precautions).

9.4.4 In handling any and all human blood or blood products the IBC recommends that samples be handled with Standard Precautions (OSHA Blood Borne Pathogen Standard). At a minimum, that should include the use of gloves, lab coats, and protective eyewear.

9.4.5 During transport of human blood or blood products, specimens should be doubly contained to prevent spills and/or leakage with adequate absorbent material between the primary and secondary container to absorb all spills and/or leakage.

Section 9.5 Transplantation of Xenografts into Research Animals

9.5.1 The IBC in conjunction with the Division of Comparative Medicine has implemented specific practices to be followed to reduce the risk of exposure of research faculty and staff, animal care personnel, and animals to potentially infected human tissues and/or clinical samples.

9.5.2 Animals administered uncharacterized primary human tumor resections, tissue explants, blood, or other patient-derived xenografts are housed in ABSL-2 containment.

9.5.3 In handling any and all xenografts the IBC recommends that samples be handled with Standard Precautions (OSHA Blood Borne Pathogen Standard). At a minimum that should include the use of gloves, lab coats and protective eyewear.

9.5.4 During transport of xenografts the specimens should be doubly contained to prevent spills and/or leakage with adequate absorbent materials between the primary and secondary container to absorb all spills and/or leakage.

Section 10.0 Work with Biological Toxins

10.1 **Definition**: Biological Toxin refers to the toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, rickettsia, or protozoa), or a recombinant or synthesized molecule.

10.2 Research and teaching activities may involve the use of select agent biological toxins. Protocols for the use of select agent biological toxin is required for all Select Agent Toxins in any amount. The protocols must be reviewed and approved by the IBC. Protocols are submitted in BiosafetyNet. See the permissible amounts of toxin on the CDC web site (http://www.selectagents.gov/PermissibleToxinAmounts.html).

10.3 Researchers and students must follow requirements as specified in the CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories* Manual, Appendix I

Guidelines for Work with Toxins of Biological Origin, as the minimum containment required for this work. Containment requirements are subject to modification by the IBC.

Section 11.0 IBC Review and Approval Process

11.1 The IBC reviews all use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules material. No research or teaching activities involving biohazardous materials may be initiated or continued at USF or by USF's employees without prospective review and approval by the IBC.

11.2 All protocols are submitted in BiosafetyNet.

11.3 IBC meetings are held on the third Tuesday of every month. The IBC will not meet on days that USF is "closed for business". The IBC meeting schedule is available at https://www.usf.edu/research-innovation/research-integrity-compliance/committees-meeting-schedules.aspx#bio. A complete protocol must be submitted by the submission deadline date which is 10 days prior to the meeting date. Protocols received after this date will automatically be put on the next month's agenda for review.

11.4 Prior to the convened meeting, all IBC members are provided with all agenda items. IBC members are charged to review these materials for each protocol.

11.5 The IBC conducts full board initial review of all protocols (Recombinant or synthetic nucleic acid molecules and Infectious Agent/Biological Toxin research/teaching use) at a convened meeting. IBC protocols for infectious agents, biological toxins, and/or recombinant or synthetic nucleic acid molecules materials that are limited to storage of the materials are reviewed by a designated IBC member through an expedited process. The designated member has the discretion to request a full committee review. Prior to agent manipulation or use in research, an IBC protocol must be submitted, reviewed and approved by the IBC.

11.6 A quorum of the IBC members (or their designated alternates) must be present in order to conduct a convened meeting. In order for research to be approved, it must receive the approval of a simple majority of those members present at the meeting.

11.7 The IBC reviews are conducted in accordance with applicable federal, state and local requirements (e.g., NIH *Guidelines* and the CDC/NIH *BMBL 5th edition*).

11.8 The IBC uses a primary reviewer system for the initial review of new protocols (except Human Gene Transfer studies) at a convened meeting. The primary

reviewer for initial reviews is considered the lead reviewer for research proposals assigned to them. They are responsible for:

a. conducting an in-depth review of the application and all supporting materials,
b. presenting a review of the research at the convened meeting,
c. proposing a motion of action (i.e. Approval, Requires Modifications to Secure Approval, Deferred, or Disapprove).

The IBC uses a primary and secondary reviewer system to assist in the initial review of research involving Human Gene transfer studies. The primary and secondary reviewers for the initial review of research involving Human Gene transfer studies are considered the lead reviewers for research proposals assigned to them.

11.9 IBC staff selects a primary reviewer based on the member's scientific or scholarly expertise. IBC staff ascertain that the reviewer chosen as a primary reviewer is not listed as personnel on the IBC protocol to prevent a *Conflict of Interest*. The IBC may rely on ad hoc consultant(s) to review the study in the absence of IBC expertise in a particular area. Consultants will have access to all documents submitted to the USF IBC relevant to the specific project under review. The Consultant may participate in the deliberations and make recommendations, but may not vote.

11.10 The IBC protocol will be available to all IBC members, and all IBC members will be afforded the full opportunity to discuss each research proposal during the convened meeting. It is permissible for the primary reviewer to contact individual investigators for clarification on any point prior to the convened meeting.

11.11 The IBC may take one of the following actions:

a. **Approval** - Full approval will be granted by the IBC if there are no outstanding biosafety issues. The approval is only for materials, personnel, facility, and procedures specifically described and provided in the protocol. The PI may commence the research only *after* receiving approval indicated by an approval letter in BiosafetyNet.
b. **Requires Modifications to Secure Approval** - Such clarification(s) and/or additional information is clearly delineated by the IBC. The additional items of clarification are not a major biosafety concern. The PI must respond by revising their protocol as requested by the Committee and receive final approval prior to initiating the research. The protocol with the requested modifications is to be reviewed by a designated IBC member. The research may be approved by the designated reviewer or the chairperson.
c. **Deferred -** Deferred for consideration at a subsequent meeting. The IBC determines that a deferred study lacks sufficient information about the research procedures or safety practices and a complete risk assessment of the biohazards cannot be performed. The research may not proceed until the convened IBC has reviewed and approved a revised protocol that incorporates

all necessary information as requested by the committee. Additional information may or may not secure approval.

d. **Disapproval -** The IBC has determined that the research proposal has substantive biosafety issues. Protocols that are disapproved require submission of a revised protocol for review by the full IBC. The research may not proceed until the convened IBC has reviewed and approved a revised protocol that incorporates all necessary information as requested by the committee. Additional information may or may not secure approval.

11.12 After committee review, the decision of the committee is communicated to the PI by email notification from BiosafetyNet.

11.13 Infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules material may not be used and/or handled until notification of approval is received by the PI from the IBC.

11.14 **Investigator Assurance for All Approvals**: The principal investigator, by submitting their protocol or amendment request agrees to adhere to the practices, procedures, and information described in the protocol or amendment request as it was written when it was reviewed and approved by the IBC.

11.16 Under an expedited review procedure, the IBC Chairperson and/or the Institutional Biosafety Officer may review and approve on behalf of the IBC.

Section 12.0 Continuing Review of Approved Protocols

12.1 The IBC approves requests for the use of infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules for a period of twelve months. The PI may annually renew an IBC-approved study for up to a total of two additional one-year periods.

- Protocols which have been determined to meet criteria for Section III-E and Section III-F research under the NIH Guidelines are approved for the life of the research project with a continuing review every five years.
- Protocols limited to the storage of infectious agents, biological toxins, and/or recombinant or synthetic nucleic acid molecules materials are approved with a continuing review every five years. Prior to agent manipulation or use in research, an IBC protocol must be submitted, reviewed and approved by the IBC.

12.2 After three years all continuing studies must be completely re-described in a new protocol.

- Protocols which have been determined to meet criteria for Section III-E and Section III-F research under the NIH Guidelines do not require a re-described protocol as they are approved for the life of the study.
- Protocols approved for the storage only of infectious agents, biological toxins, and/or recombinant or synthetic nucleic acid molecules materials

do not require a re-described protocol as they are limited to storage only. Prior to agent manipulation or use in research, an IBC protocol must be submitted, reviewed and approved by the IBC.

12.3 Researchers cannot continue to work with infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules material under an expired protocol. If a PI wishes to continue the research a new protocol must be submitted and approved by the IBC prior to the expiration of the previous protocol.

12.4 Approximately 90 days before the end of the first and second year approval period, the PI will be sent reminder notifications from BiosafetyNet to submit a request for continuing review in BiosafetyNet prior to the end of the approval period. If changes have been made or if changes are proposed to be made to the approved protocol, the PI must submit an amendment request separately from the continuing review.

12.5 The Continuing Review requests are reviewed by the IBC chairperson and/or the Institutional Biosafety Officer (IBO) through an expedited process. The Continuing Review request may be approved by the IBC chairperson and/or the Institutional Biosafety Officer (IBO). The chairperson and/or IBO have the discretion to request a full committee review.

12.6 Approximately 90 days before the end of the three year approval period, the PI will be sent reminder notifications from BiosafetyNet to submit a new protocol or to close the existing study.

Section 13.0 Modifications to an IBC Approved Protocol

13.1 All proposed modifications to an approved research study involving infectious agents, biological toxins, Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules material must be submitted to the IBC for review and receive approval prior to the implementation of the proposed modifications.

13.2 If the proposed modification changes the overall scope, intent of the study, or the risk (e.g., addition of an infectious agent from a higher Risk Group) a new protocol must be submitted.

13.3 The IBC reserves the right to determine whether the proposed modification(s) are substantive and to request further information or a new IBC protocol.

13.4 The IBC may utilize Expedited Review procedures to review a proposed modification to previously approved research. A modification request considered for Expedited Review does not change or alter:
a. the Risk Group or Biosafety Level;
b. the research design or methodology;

c. the use of aerosol generating procedures;
d. the facilities available to support safe conduct of the research.

13.5 Amendments eligible for Expedited Review are follows:
a. Change in Biological Agent (must remain within the same family of agents previously approved-must not change overall BSL)
b. Change in Protocol Title;
c. Change in Protocol Sponsor;
d. Change in Lab Location;
e. Change in Procedure;
f. Change in Personnel; and
g. Changes that do not alter the overall risk of the study.

13.6 The Amendments are reviewed by the IBC chairperson, designated IBC member or Institutional Biosafety Officer through an expedited process. The Modification Request requests are approved by the IBC chairperson, designated IBC member or the Institutional Biosafety Officer (IBO). The reviewer has the discretion to request a full committee review.

13.7 When an amendment does not meet the criteria for Expedited Review (policy item 13.4 & 13.5) then the full IBC must review the proposed change(s) at a convened meeting. The IBC may require a new research protocol to be submitted.

Section 14.0 Biosafety Laboratory Inspections

14.1 Required Laboratory Inspections (to verify the status of safety compliance, evaluate the conditions, and document the review/inspection):
a. If required by the granting agency (e.g., Department of Defense)
b. To establish an account to purchase items (e.g. cell lines) from a vendor (e.g. American Type Culture Collection (ATCC) account)
c. Laboratories registered with the USF IBC utilizing Biosafety Level 2 (BSL 2) and Biosafety Level 3 (BSL-3) containment
d. Courtesy inspections at the request of PIs

14.2 Prior to securing the Institutional Biosafety Officer's signature to establish an ATCC account the PI must schedule a laboratory inspection with the Institutional Biosafety Officer (IBO) and/or the IBO's designee.

14.3 Laboratory inspections for biosafety containment practices, facilities, and equipment are conducted as part of the IBC's review and approval process for protocols requiring a containment level or BSL-2 or higher. Protocols that may require a biosafety inspection are as follows:
a. All new IBC protocols unless an inspection of the lab space has occurred within a year.
b. IBC protocols with a modification to a protocol for addition of lab spaces.
c. IBC protocols involving infectious agents on an annual basis.

d. Post report events.

14.4 All biosafety laboratory inspections will be performed in accordance with requirements published by the CDC/NIH in the Biosafety in Microbiological and Biomedical Laboratories, 5th edition for the required biosafety containment level for the biohazardous materials utilized.

14.5 Lab Inspections are not required for the following applications:
a. Human Gene Transfer studies that occur in a clinical setting. Standard precautions which are the clinical equivalent of BSL-2 are used in these settings. The Biosafety office will not inspect these facilities as they defer to the inspections performed by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) as acceptable standard precautions inspections in lieu of BSL-2 at the current time for these clinical areas.
b. Recombinant DNA application approved at BSL-1

14.6 Grades of Deficiencies:
Serious: Deficiencies that are an immediate threat to human health, and/or security of biological agents and/or toxins and those that indicate a need for systemic improvements. In selected cases, an Immediate Action Report will be submitted within 7 days to PI and IBC Chair following the inspection. Required corrective action may include ceasing work or addressing departures within a shortened period of time. Other departures will be reported in the routine inspection report sent to the PI within 7 days.

Moderate: Deficiencies that have the potential to be a threat to human, plant, or animal health, animal or plant products, and/or security of biological agents and/or toxins. If not corrected, such departures will likely impact the safety of humans and/or security of biological agents and/or toxins and increase the risk of more serious departures. A routine inspection report will be sent to the PI within 7 days of the inspection.

Low: Deficiencies that are unlikely to pose an immediate threat to human health and/or security of biological agents and/or toxins but are not consistent with safe and secure standards of practice. If not corrected, such departures degrade the culture of safety and security. Repetition of departures may be considered more serious and lead to enforcement actions. A routine inspection report will be sent to the PI within 7 days of the inspection.

Section 15.0 Select Agents and Toxins

Section 15.1 Background

15.1.1 The United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) have identified certain bacteria, viruses, toxins, rickettsia, and fungi that pose a potential threat to public health

and welfare. These organisms are considered Select Biological Agents and Toxins (HHS), High Consequence Livestock Pathogens and Toxins (USDA), or HHS/USDA overlap agents.

15.1.2 A select agent may not be possessed or used in the United States, received from outside the United States, or transferred within the United States by any individual(s), academic institution, or other legal entity unless such activities are conducted for a lawful purpose and in accordance with the federal law. (E.g. the select agent/toxin must be registered with HHS and/or the USDA.

15.1.3 The University of South Florida (USF), in order to comply with the USA PATRIOT Act of 2001, and the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, requires PIs to register the possession, use, and transfer of Select Biological Agents and Toxins with the IBC.

15.1.4 PI's who wish to possess, use, and or transfer Select Biological Agents and Toxins must be registered with the USF IBC. Registration with the Centers for Disease Control and Prevention (CDC) and/or the USDA/APHIS is also required.

Section 15.2 Registration with the USF IBC for Use of Select Agents

15.2.1 A PI planning to work with any Select Agent/Toxin material must also submit a protocol in BiosafetyNet to the USF IBC for review and approval.

Section 15.3 CDC/USDA Requirements for Use of Select Agents

15.3.1 Registration is valid only for the specific Select Biological Agents and Toxins, the particular activities and locations involved, and the specific individuals approved to handle or use the regulated materials listed on the application.

15.3.2 The PI must collaborate with the USF Institutional Biosafety Officer to develop and implement agent-specific plans for biosafety, site-specific plans for security (e.g., inventory control, access control, cyber security), and emergency response.

15.3.3 As part of the federal registration process the Responsible Officer, Alternate Responsible Officer, PI, and staff will undergo a security risk assessment that includes a background check and finger printing.

15.3.4 Only those individuals who have documented a legitimate need to handle or use Select Biological Agents and Toxins and who have appropriate training and skills to handle such agents will be granted access to the agents.

15.3.5 There are specific requirements for record keeping, notification of transfer, theft, loss, and/or destruction.

15.3.6 The laboratory will be inspected by the CDC or USDA before final federal approval is granted.

15.3.7 The Responsible Official or his/her alternate, must conduct regular inspections of the laboratory where select agents/toxins are used or stored.

Section 16.0. Coordination with other Compliance Committees/Divisions

Section 16.1 Animal Use

16.1.1 Review by the IBC is independent of review by the Institutional Animal Care and Use Committee (IACUC). However, there is representation on both committees that communicate and coordinate regarding Biosafety issues in animal studies.

16.1.2 Initiation of the animal component of the study is contingent upon the completion of and approval by the Institutional Animal Care and Use Committee (IACUC) process.

Section 16.2 Human Subjects

16.2.1 Review by the IBC is independent of review by the IRB. However, there is representation on both committees that communicate and coordinate regarding Biosafety issues in Human Gene transfer trials.

Section 16.3 Office of Sponsored Research

16.3.1 Biosafety Program staff make available to the Office of Sponsored Research information regarding Approval, Closure, and Continuing Review letters of all studies approved by the IBC.

Section 17.0 Biosafety Education and Training

Section 17.1 Persons Required to Complete Training

17.1.1 Training and education in microbiological techniques is required for anyone working with infectious agent(s), biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules at BSL-2 or who works in a laboratory where these materials are used and/or stored.

a. The PI is responsible for providing training, conducting practical demonstrations, and assessments of competence in the laboratory regarding microbiological techniques.
b. The Biosafety Program requires education in biosafety principles and practices for all faculty, staff, students, volunteers, and visitors directly involved in the conduct of research with infectious agent(s), biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid

molecules or who works in a laboratory where these materials are used and/or stored. USF Research Integrity and Compliance provides this education.

Section 17.2 Training Requirements

17.2.1 There are three types of Biosafety training requirements:

a. **Core Course** – The Biosafety Principles and Practices course. All persons involved in the conduct of research with infectious agent(s), biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules must complete the core course requirements before they directly handle the biological material.
b. **Continuing Education** – Triennial completion of an IBC approved continuing education course by investigators and personnel involved in all IBC approved studies
c. **Special Topics** – Required for persons involved in certain types of work (e.g., BSL-3 training, shipping infectious substances, and diagnostic specimens).

Section 18.0 Non-Compliance

18.1 Information regarding non-compliance and/or deficiencies with the NIH *Guidelines*, *CDC/NIH BMBL 5th edition*, and IBC policy may be brought to the attention of the USF Institutional Biosafety Committee and/or the USF Biosafety Program by any individual.

18.2 Information concerning non-compliance and deficiencies with the NIH *Guidelines*, *CDC/NIH BMBL 5th edition*, and IBC policy is presented in a manner that protects, to the limits possible, the identity of the complainant, investigator, study, or facility.

18.3 Reports regarding biosafety concerns, deficiency, and non-compliance with the NIH *Guidelines*, *CDC/NIH BMBL 5th edition*, and IBC policy are immediately forwarded to the IBC chairperson. The Institutional Biosafety Officer (IBO) in consultation with the IBC chairperson and Director of Research Integrity & Compliance shall have the authority to interrupt (e.g., temporarily suspend the project or practice) any activity involving research or teaching using infectious agents, biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules that jeopardizes the health and safety of any individual or presents a threat to the safety of the environment. Further review following the above alleged non-compliant activity will occur. The IBC will meet within three (3) business days and make a recommendation on how to address the situation before work will be allowed to resume.

18.4 In cases of non-compliance with established safety rules that is discovered during a safety inspection, but where there is no imminent danger to individuals or property, the IBO will notify the PI to correct the deficiencies. In instances where the noncompliance is not corrected, a two-step process will be followed:

Step 1: The IBO will notify the PI (faculty member in charge of the lab) in writing describing the deficiencies and personnel involved. A suggestion for how compliance with University procedures can be achieved will be included and the faculty member will be asked to notify the IBC of the status of his/her efforts to make the correction. The laboratory will be scheduled for a follow-up inspection by the IBO.

Step 2: If the IBO is not able to achieve compliance through efforts outlined in Step 1, the status of the situation will be brought to the attention of the IBC.

18.5 All reports of alleged biosafety concern(s), deficiency, or non-compliance are forwarded to the IBC for investigation and corrective action. The subject Principal Investigator is informed of the allegation in writing by the IBC Chairperson and may be invited to meet with the IBC to respond to questions regarding the alleged deficiency.

18.6 The IBC on behalf of the institution shall report to the NIH OSP:

- Per Section IV-B-1-j of the *NIH Guidelines* any significant problems with or violations and any significant research-related accidents or illnesses to the NIH OSP within 30 days; unless the IBC determines that a report has already been filed by the Principal Investigator.
- For BSL-2, per Appendix G–II-B-2-k, any spills and accidents which result in **overt exposures** to organisms containing recombinant or synthetic nucleic acid molecules are **immediately reported** to the Institutional Biosafety Committee and NIH OSP.
- For BSL-3, per Appendix G-II-C-2q any spills and accidents which result in **overt or potential exposures** to organisms containing recombinant or synthetic nucleic acid molecules are **immediately reported** to the Biological Safety Officer, Institutional Biosafety Committee, and NIH OSP

Reports to NIH OSP shall be sent to the Office of Science Policy, National Institutes of Health, preferably by e-mail to: NIHGuidelines@od.nih.gov

Section 19.0 Suspension or Termination of IBC Approval

19.1 The IBC may suspend an activity that it previously approved if it determines:

- failure to willfully comply with federal/state regulations and/or IBC policy;
- any activities adversely effecting the health and safety of any individual involved in research or teaching using infectious agents, biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules;
- any serious adverse event related to gene therapy study; or
- the activity does not match the description of the activity originally approved by the IBC.

19.2 The IBC deliberates regarding reports of alleged deficiencies at its next regularly scheduled monthly meeting, or the IBC Chairperson can call an emergency quorum to discuss the issue in advance of a regular meeting if deemed necessary. The IBC Chairperson can choose to invite involved personnel to the meeting to whom questions can be directed. The IBC reports the findings of its deliberations to the PI and the Vice President of Research.

19.3 If the IBC suspends an activity involving infectious agents, biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules, the PI will be informed in writing of the suspension, its conditions, and the expectations of the IBC which need to be met before additional activities involving infectious agents, biological toxin(s), Select Agents/Toxins, and/or recombinant or synthetic nucleic acid molecules resume.

19.4 The IBC may vote, at a convened meeting, to suspend or terminate approval of research that has been associated with noncompliance regarding applicable regulatory requirements and/or IBC policy.

Section 20.0 Policy Review

20.1 This policy will be reviewed annually.

APPENDIX I - HHS & USDA Regulated Select Agents and Toxins

HHS SELECT AGENTS AND TOXINS

- Abrin
- Botulinum neurotoxins*
- Botulinum neurotoxin producing species of Clostridium*
- Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$)
- *Coxiella burnetii*
- Crimean-Congo haemorrhagic fever virus
- Diacetoxyscirpenol
- Eastern Equine Encephalitis virus[1]
- Ebola virus*
- *Francisella tularensis**
- Lassa fever virus
- Lujo virus
- Marburg virus*
- Monkeypox virus[1]
- Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)
- Ricin
- Rickettsia prowazekii
- SARS-associated coronavirus (SARS-CoV)
- Saxitoxin
- South American Haemorrhagic Fever viruses:
    - Chapare
    - Guanarito
    - Junin
    - Machupo
    - Sabia
- Staphylococcal enterotoxins A,B,C,D,E subtypes
- T-2 toxin
- Tetrodotoxin
- Tick-borne encephalitis complex (flavi) viruses:
    - Far Eastern subtype
    - Siberian subtype
- Kyasanur Forest disease virus
- Omsk hemorrhagic fever virus
- Variola major virus (Smallpox virus)*
- Variola minor virus (Alastrim)*
- *Yersinia pestis**

OVERLAP SELECT AGENTS AND TOXINS

- *Bacillus anthracis* *
- *Bacillus anthracis Pasteur strain*
- *Brucella abortus*
- *Brucella melitensis*
- *Brucella suis*
- *Burkholderia mallei**
- *Burkholderia pseudomallei**
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus[1]

USDA SELECT AGENTS AND TOXINS

- African horse sickness virus
- African swine fever virus
- Avian influenza virus[1]
- Classical swine fever virus
- Foot-and-mouth disease virus*
- Goat pox virus
- Lumpy skin disease virus
- *Mycoplasma capricolum[1]*
- *Mycoplasma mycoides[1]*
- Newcastle disease virus[1,2]
- Peste des petits ruminants virus
- Rinderpest virus*
- Sheep pox virus
- Swine vesicular disease virus

USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS AND TOXINS

- *Peronosclerospora philippinensis (Peronosclerospora*
- *sacchari)*
- *Phoma glycinicola (formerly Pyrenochaeta glycines)*
- *Ralstonia solanacearum*
- *Rathayibacter toxicus*
- *Sclerophthora rayssiae*
- *Synchytrium endobioticum*
- *Xanthomonas oryzae*

*Denotes Tier 1 Agent
[1]Select agents that meet any of the following criteria are excluded from the requirements of this part: Any low pathogenic strains of avian influenza virus, South American genotype of eastern equine encephalitis virus , west African clade of Monkeypox viruses, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies Mycoplasma capricolum except subspecies capripneumoniae (contagious caprine pleuropneumonia), all subspecies Mycoplasma mycoides except subspecies mycoides small colony (Mmm SC) (contagious bovine pleuropneumonia), any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, and Vesicular stomatitis virus (exotic): Indiana subtypes VSV-IN2, VSV-IN3, provided that the individual or entity can verify that the agent is within the exclusion category.

[2] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (Gallus gallus) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.