Creighton University

Institutional Biosafety Committee

POLICIES AND PROCEDURES
FOR THE USE OF BIOHAZARDOUS MATERIALS

(Recombinant or Synthetic Nucleic Acid Molecules, Infectious Biological Agents and Select Agents and Select Agent Toxins)

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1.0 Introduction

1.1 Purpose

The purpose of the *Creighton University Institutional Biosafety Committee* (IBC) is to minimize the risks to faculty, staff, students, facilities, the community and the environment while using biohazardous materials during teaching and research activities at Creighton University; or while storing biohazardous materials and to ensure compliance with relevant laws and regulations pertaining to the receipt, use, storage or transfer of biohazardous materials. The IBC *Policies and Procedures for the Use of Biohazardous Materials* (IBC Policies) outlines the processes that must be followed when obtaining, using, storing, transferring or destroying biohazardous materials and provides a review of the relevant regulatory requirements. Since laboratory work can involve exposure not only to biohazardous materials, but also to chemical and radiological hazards, these policies should be used in conjunction with any pertinent University manuals (e.g., the *Users' Manual for Radioactive Materials*).

1.2 Policy

The IBC is responsible for ensuring that biohazardous materials at Creighton University campuses or facilities are received, used, stored, transferred and disposed of in accordance with applicable laws and regulations. The Responsible Official (RO) (See Section 2.3.3) and IBC are jointly responsible for any activity involving Select Agents and Select Agent Toxins.

The IBC shall review and approve any activity involving any known or potential biohazardous materials unless otherwise exempted under federal regulations and these procedures. The RO has final authority over any activity involving Select Agents or Select Agent Toxins.

1.3 Scope

The IBC Policies apply to the receipt, use, storage, transfer or disposal of known or potential biohazardous materials, as defined in Section 1.7.1. It applies to activity and/or research involving biohazardous materials that is:

- Sponsored by Creighton University;
- Conducted by Creighton faculty members;

- Conducted using Creighton University's property, facilities, or non-public information; or
- Stored at any of Creighton University campuses or facilities.

These policies apply to all faculty, staff, students, visitors, and agents and their employees.

1.4 IBC Registration with National Institutes of Health for Research Involving Recombinant or Synthetic nucleic Acid Molecules (r/s NA)

The IBC is registered with the National Institutes of Health (NIH), Office of Biotechnology Activities (OBA) for purposes of Recombinant or Synthetic Nucleic Acid Molecule (r/s NA) research. An annual report is filed with OBA, which includes an updated list of IBC members indicating the role of each member and biographical sketches for each member. The OBA is notified of any changes in IBC membership when they occur. Such notice shall include a revised list of members, contact information for each new member, and biographical sketches for each new member.

1.5 Select Agent and Select Agent Toxin Registration and Individual Security Risk Assessment

Creighton University does not currently have a certificate of registration from either the Centers for Disease Control (CDC) or the United States Department of Agriculture (USDA) for the possession, use, receipt or transfer of listed Select Agents or Select Agent Toxins on the CDC and USDA lists. No individual at Creighton University shall possess, use, receive or transfer any listed Select Agent or toxin, not otherwise exempted or excluded by the CDC and/or USDA, until such time as Creighton University has received a certificate of registration. In addition, no individual shall possess, use, receive or transfer any listed Select Agent or Select Agent Toxin, not otherwise exempted or excluded by the CDC and/or USDA, until such time as that individual has obtained a security risk assessment from the United States Attorney General.

1.6 Responsibilities

The responsibility for biosafety at Creighton University involves a team effort of the IBC, the RO and faculty members (Principal Investigators) who obtain, possess or use biohazardous materials. The IBC's role is to provide oversight and guidance to those at

Creighton University who seek to possess and/or use biohazardous materials and to approve those r/s NA experiments subject to IBC review under NIH Guidelines. Only Creighton faculty members are eligible to seek approval from the IBC to obtain, possess and/or use biohazardous materials. Any staff member, who is a Principal Investigator, may only submit an IBC registration under the auspices of a faculty member who is the director of the laboratory. Any possession and/or use of biohazardous materials at Creighton University must be conducted with appropriate safeguards against environmental release and for the protection of University students, employees, and the community.

1.7 DEFINITIONS

1.7.1 Biohazardous Materials

For purposes of the IBC Policies, biohazardous materials include, but are not limited to, the materials defined in this section.

1.7.1.1 Recombinant or Synthetic Nucleic Acid Molecules

The *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* define recombinant or synthetic nucleic acid molecules as:

(i) molecules that a) are constructed by joining nucleic acid molecules and b) 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.

1.7.1.2 Infectious Biological Agents

Infectious biological agents include biological agents and biologically derived materials that present a risk or potential risk to the health of humans or animals, either directly through infection or indirectly through damage to the environment. Categories of potentially infectious biological materials include the following:

- Human, animal, and plant pathogens (bacteria, parasites, fungi, viruses);

- All human blood, blood products, tissues, and certain body fluids (excluding routine use for clinical purposes) known to contain infectious agents (excluding normal flora);
- Cultured cells known to contain infectious agents; or
- Animals and animal tissues known to contain infectious agents (excluding normal flora).

1.7.1.3 Select Agents and Select Agent Toxins

Select Agents and Select Agent Toxins are those biological agents and Select Agent Toxins that are deemed to pose a threat to public, animal or plant health, or animal or plant products that have not been excluded or exempted from federal regulatory control. The Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC) and the United States Department of Agriculture (USDA) have identified those Select Agents and Select Agent Toxins ("listed Select Agent or Toxin") that are subject to registration and regulatory oversight. The HHS/CDC lists of select agents and Select Agent Toxins (including those that overlap with the USDA) are identified at 42 CFR 73.3 (HHS list) and 42 CFR 73.4 (Overlap List). The USDA list of Select Agents and Select Agent Toxins are identified at 9 CFR 121.3. IBC Appendix C provides direction on obtaining the lists of the CDC and USDA Select Agents and Select Agent Toxins as well as those Select Agents and Select Agent Toxins that are excluded or exempt from registration.

1.7.2 Restricted Person

Restricted persons are prohibited by law from having access to the listed Select Agents or Select Agent Toxins. IBC review of registrations that include a Select Agent or Select Agent Toxin will include a check of the personnel involved in the project against a national database; such review to be conducted by the Institutional General Counsel's Office. A "Restricted Person" means any individual who:

- Is under indictment for a crime punishable by imprisonment for a term exceeding 1 year;
- Has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year;
- Is a fugitive from justice;
- Is an unlawful user of any controlled substance (as defined in 21 USC 802);
- Is an alien illegally or unlawfully in the United States;
- Has been adjudicated as a mental defective or has been committed to any mental institution;

- Is an alien (other than an alien lawfully admitted for permanent residence) who is a national of Iran, Sudan or Syria, or any other country to which the Secretary of State, pursuant to applicable law, has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism; or
- Has been discharged from the Armed Services of the United States under dishonorable conditions.
- Is a member of, acts for or on behalf of, operates subject to the direction or control of, a terrorist organization as defined in section 212(a)(3)(B)(vi) of the Immigration and Nationality Act (8 USC 1182(a)(3)(B((iv).

1.8 Risk Assessment and Selection of Appropriate Safeguards

Research involving biohazardous material is classified on the basis of perceived risk to humans. The risk classification assists in determining the type of biological and physical containment level. There are currently no laboratories at Creighton University certified to conduct Biosafety Level 4 (BL-4) research. It is the responsibility of the faculty member to conduct a risk assessment to determine the appropriate level of perceived risk and biological and physical containment level prior to possessing or using biohazardous material(s) (See Section 3.0, Principal Investigator's Responsibilities, for more information on risk group classifications and biosafety level classifications). The IBC will make the final decision as to the level of risk and appropriate biological and physical containment levels for biohazardous materials (other than Select Agents and Select Agent Toxins) subject to IBC review and approval. The RO shall make the final decision as to the level of risk and appropriate biological and physical containment levels for Select Agents and Select Agent Toxins.

1.9 Biosafety Regulations and Guidelines

The IBC Policies are based upon the following regulations and guidelines:

- ***NIH Guidelines for Research Involving Recombinant Or Synthetic Nucleic Acid Molecules*** **(NIH Guidelines)** – This document provides guidelines for constructing and handling recombinant or synthetic nucleic acid molecules and cells, organisms and viruses containing recombinant or synthetic nucleic acid molecules. Institutions conducting or sponsoring r/s NA research covered by the NIH Guidelines are responsible, through established policies and its IBC, for ensuring that such research is conducted in compliance with the NIH Guidelines (see IBC Appendix E);

- ***Biosafety in Microbiological and Biomedical Laboratories* (BMBL), published by Centers for Disease Control and Prevention (CDC) and NIH** – This document contains guidelines for microbiological practices, safety equipment, and facilities that constitute the four established biosafety levels. The BMBL is generally considered the standard for biosafety (see IBC Appendix E);
- ***Select Agents and Select Agent Toxins*** – The Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC) regulations, 42 CFR Part 73 and the United States Department of Agriculture (USDA) regulations, 9 CFR Part 121, establish requirements regarding the possession, use, receipt and transfer of listed Select Agents and Select Agent Toxins. The regulations set forth the requirements for registration of listed Select Agents and Select Agent Toxins, security risk assessments, safety plans, security plans, emergency response plans, training, transfers, record keeping, inspections and notifications;
- ***Occupational Health and Safety Act (OSHA) Regulations*** – These regulations address such items as Occupational Exposure to Hazardous Chemicals in Laboratories (29 CFR 1910.1450); Hazard Communications (29 CFR 1910.1200) and Hazardous Waste Operations and Emergency Response Standards (29 CFR 1910.120) (see IBC Appendix E). Questions regarding compliance with OSHA requirements should be directed to the Director of Environmental Health and Safety (402 546-6269) or the IBC Chair (402 449-4953).

1.10 University Biological Safety Officer

The Director of Environmental Health and Safety shall serve as the University's Biological Safety Officer for purposes of r/s NA research activity.

1.10.1 Duties of the University Biological Safety Officer

In addition to the duties outlined in the *Laboratory Safety Monograph* for Biological Safety Officers, the Biological Safety Officer's duties include, but are not limited to:

- Periodic inspections of laboratories conducting r/s NA research to ensure that laboratory standards are rigorously followed;
- Reporting to the IBC and the Institution any significant problems, violations of NIH Guidelines, and any significant research-related accidents or illnesses of which he/she becomes aware of, unless the Principal Investigator has already filed a report;

- Developing emergency plans for handling accidental spills and personnel contamination and investigating laboratory accidents involving r/s NA research;
- Providing advice on laboratory security; and
- Providing technical advice to Principal Investigators and the IBC on research safety procedures.

2.0 Institutional Biosafety Committee

2.1 IBC Responsibilities

The IBC is responsible for establishing and implementing policies that (1) provide for the safe use of biohazardous materials at Creighton University, including the possession of and conduct of research with such materials, and (2) ensure compliance with appropriate federal requirements including, but not limited to, the NIH Guidelines, the BMBL and Select Agents and Select Agent Toxins regulations.

The responsibilities of the IBC include, but are not limited to, the following:

- Assist in the development of appropriate procedures as required by NIH, BMBL and/or Select Agents and Select Agent Toxins regulations to oversee the possession and/or use of biohazardous materials.
- Suspend or terminate registration for the possession or use of biohazardous materials, including research, where the IBC finds noncompliance or that such use or possession poses a threat to the health and safety of the community. Routinely review the policies and procedures of the IBC and modify them as necessary to ensure appropriate biosafety measures and compliance with federal and state requirements.
- Review registrations for the possession and/or use of biohazardous materials for compliance with NIH Guidelines, the BMBL and Select Agents and Select Agent Toxins regulations, and approve those requests that are found to conform with NIH Guidelines, the BMBL and Select Agents and Select Agent Toxins regulations, as applicable. As part of the review process, the IBC and/or the Biological Safety Officer will do the following:
  - Conduct an independent assessment of the containment levels (BL-1 to BL-3), as required by Section II-A-3 of the NIH Guidelines for research involving recombinant or synthetic nucleic acid molecules.
  - Conduct an assessment of the facilities, procedures, practices, training, and expertise of personnel involved in r/s NA research. In the event facilities in which r/s NA research is conducted undergo renovation or new facilities are constructed, the IBC shall coordinate with the Department of Environmental Health and Safety to ensure the facility comports with the conditions and containment measures described in the NIH Guidelines.
  - Ensure compliance with all surveillance, data reporting, and adverse event reporting requirements set forth in the NIH Guidelines for r/s NA research.

- Set containment levels as specified in the NIH Guidelines for r/s NA research involving experiments with whole animals or whole plants.
- Conduct periodic review of the possession and/or use of biohazardous materials to ensure compliance with federal and state requirements.
- Notify Principal Investigator of the results of the IBC's review and approval or disapproval of registration.
- Assist the University's Department of Environmental Health and Safety in developing and adopting emergency plans covering accidental spills and personnel contamination resulting from use or possession of biohazardous materials.
- For human gene transfer protocols, review the informed consent document with respect to risks associated with the use of recombinant or synthetic nucleic acid molecules, referring to NIH/OBA guidance on informed consent for human gene transfer in the review process.
- Communicate with other institutional oversight committees, in particular the Institutional Review Board (IRB) and Institutional Animal Care and Use Committee (IACUC), to ensure that all research involving biohazardous materials including, but not limited to, r/s NA molecules and infectious agents, are subject to appropriate registration and oversight. For registrations using non-exempt r/s NA and/or infectious agents that involve humans and/or animals, and thus also require review and approval by the IRB and/or IACUC, IBC review and approval shall generally be the initial step in the process.
- In situations of noncompliance and/or use or possession of an agent that threatens the health or safety of the investigators, institutional personnel, and/or the community, and when all avenues to remediate the issue have been exhausted or the issue is urgent, the IBC may suspend or terminate a registration and shall report such findings to the Department Chair or supervisor of the registrant, the supervisor or Department Chair of any other involved responsible employee and Human Resources. See section 2.8.

2.2 IBC MEMBERSHIP

2.2.1 General

The IBC is composed of at least five members who are appointed by the Creighton University Institutional Official (research) from the faculty and from the community at large. The members will collectively have experience and expertise in recombinant or

synthetic nucleic acid molecules and the capability to assess the safety of research involving recombinant or synthetic nucleic acid molecules and infectious agents and identify any potential risk to public health, animal and plant health or products, or the environment posed by such research. The IBC will be composed of the following:

- At least one individual with expertise in recombinant or synthetic nucleic acid molecules technology, and/or biological safety, and/or physical containment, including human gene transfer;
- At least one scientist with expertise in biological safety and physical containment;
- At least one individual with expertise in the use, storage, transfer and disposal of Select Agents and Select Agent Toxins;
- At least one scientist with expertise in plant, plant pathogen or plant pest containment principles;
- At least one scientist with expertise in animal containment principles;
- An individual representing laboratory technical staff;
- Creighton University's Biological Safety Officer; and
- At least two members who are not affiliated with Creighton University (including family members) and who represent the interests of the surrounding community with respect to health and protection of the environment.

A member can represent more than one of the above criteria, except that the Biological Safety Officer must be affiliated with Creighton University.

The IBC shall consult with General Counsel to address issues pertaining to institutional policies, applicable law, and standards of conduct and practice. The IBC may also invite consultants knowledgeable in community attitudes and the environment to its meetings as necessary to assist in any review, but such consultants shall not vote.

IBC members and Chair(s) serve at the pleasure of the Institutional Official. The University provides liability coverage for Creighton's IBC members for any legal action arising from their actions and decisions while serving as a member of Creighton University's IBC.

2.3 IBC CHAIR

2.3.1 Appointment

The IBC Chair is appointed by the Institutional Official generally from among the IBC members. The Chair shall be an experienced scientific investigator with expertise in biohazardous materials.

2.3.2 Responsibilities

The Chair shall preside over IBC meetings, serve as the contact for all regulatory agencies, and act as liaison between the academic community and the IBC. The Chair shall designate a member of the IBC to serve as Vice-Chair. The Vice-Chair performs all the duties of the Chair in the Chair's absence and other such duties as may be assigned by the IBC or the Chair. The Chair shall review all instances of noncompliance and present them to the IBC for appropriate corrective action, which may include suspension of the registration for possession and/or use of biohazardous materials.

2.3.3 Responsible Official (RO)

The IBC Chair shall serve as the University's Responsible Official (RO) related to non-exempt Select Agents and Select Agent Toxins if such agents are present on campus. If applicable, the RO shall select an appropriate member of the IBC to serve and qualify as the Alternative Responsible Official, to conduct the duties of the RO in his/her absence. All activities involving federal registration of Select Agents or Select Agent Toxins, exclusion or exemption from registration, and intramural or extramural receipt, transfer or disposal of any Select Agent or Select Agent Toxin must be reviewed and approved by the RO before it can be reviewed and approved by the IBC. It should be noted that at this time there are no registrations involving the **non-exempt** use of Select Agents or Select Agents Toxins and none are permitted at Creighton University (see section 1.5).

2.3.3.1 Responsibilities of RO

The RO is responsible for ensuring compliance with the federal regulations governing Select Agents and Select Agent Toxins, including:

- Determining whether or not any Select Agent or Select Agent Toxin request is exempt or excluded from federal registration requirements;
- Submitting all applications for registration of Select Agents and Select Agent Toxins to the CDC and/or USDA;

- Submitting all information to the Attorney General to conduct a security risk assessment to obtain approval for individuals to have access to listed Select Agents or Select Agent Toxins;
- Developing and implementing safety, security and emergency response plans in accordance with regulatory requirements for listed Select Agents and Select Agent Toxins;
- Providing appropriate training for safety, security and emergency response to individuals who handle, use or store Select Agents or Select Agent Toxins;
- Transferring listed Select Agents or Select Agent Toxins only to registered individuals or entities in accordance with regulatory requirements;
- Review all requests for possession and use (including receipt and transfer) of Select Agents and Select Agent Toxins and grant approval in those instances where regulatory requirements, as applicable, have been met.

2.4 IBC MEETINGS

2.4.1 Regular Meetings

The IBC usually meets at least once each year and more often as necessary to review and approve registrations and conduct continuing review of approved registrations. The IBC meeting dates are posted at:
http://www.creighton.edu/researchservices/rcocommittees/ibc/schedule/

2.4.2 Emergency Meetings

The IBC Chair may call an emergency meeting of the IBC as necessary to address noncompliance or serious and/or unexpected events involving biohazardous materials at Creighton University.

2.4.3 IBC Materials

Prior to the regular meeting, each member shall have access (electronic or hard copy) to each registration and other materials to be reviewed at the meeting.

2.4.4 Quorum

A majority of members, including at least one community representative, must be present to conduct business of the IBC, except for expedited reviews. The final approval or

disapproval of registration of biohazardous materials requires a majority vote of IBC members present and voting.

IBC members who have an interest in the project (e.g. are acting as a research investigator, have financial interest in the project, etc.) shall not be present during the IBC's initial or continuing review (i.e. deliberations and voting) of the registration. Those members with a conflict of interest with respect to the review of a registration must acknowledge the conflict, and provide any pertinent information requested by the IBC. The IBC Chair will then decide if the conflict of interest warrants recusal of the member from deliberations and voting by the IBC on the registration in question.

If a quorum is lost at any time during the meeting, the meeting shall be adjourned and no further action shall be taken by the IBC until a quorum is attained.

2.4.5 Attendance

Members are expected to attend a majority of IBC meetings. Members who attend less than 50% of meetings will be contacted and encouraged to increase their attendance. Anticipated absences from an IBC meeting should be communicated to the IBC Chair at least 24 hours before the meeting.

2.4.6 Investigators

An Investigator submitting an application for a new registration is encouraged but not required to attend the relevant portion of the IBC meeting at which his or her application will be discussed. The Investigator may provide information and answer questions posed by the IBC but may not be present during the final discussion and vote on his or her application. Any Investigator who wishes to attend an IBC meeting to present information about an existing registration (e.g. on renewal or modification) may do so upon request to the IBC Chair.

2.5 MINUTES OF MEETINGS

Minutes of IBC meetings shall including the following information:

- Attendance of members and guests;
- IBC actions taken on each registration reviewed and any required modifications for IBC approval;

- Notation of members who were not present during deliberations and voting on registrations with which they have a conflict of interest;
- The basis for disapproving any registration for possession and/or use of biohazardous materials.

2.6 IBC RECORDS

2.6.1 Retention

The IBC shall retain the following records for at least three years after completion of the research/project:

- IBC meeting minutes;
- IBC Principal Investigator Registrations and attachments thereto;
- List of IBC members;
- IBC procedures.

The IBC shall retain its initial NIH/OBA Registration, annual reports, and notices of new members until such time as the IBC is no longer registered with NIH/OBA.

2.6.2 Access

All IBC records, as outlined above, shall be available for inspection and copying by the Institutional Official or his/her designees and designated federal agencies. Upon request, Creighton University shall make available to the public all IBC meeting minutes and any documents submitted to or received from funding agencies for which public access is required. If public comments are made on IBC actions, the University will forward both the public comments and the IBC's response to NIH/OBA at the address set forth in Section 2.7 below.

2.7 REPORTING TO NIH—RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES (R/S NA)

The IBC shall report any significant problems with or violations of the NIH Guidelines and any significant research-related accidents or illnesses related to recombinant or synthetic nucleic acid molecules to the Research Compliance Officer and NIH/OBA within 7 days of learning that a reportable incident has occurred, unless the IBC

determines that a report has already been filed by the Principal Investigator or research sponsor. Reports to NIH/OBA shall be sent to the following address:

Office of Biotechnology Activities
National Institutes of Health
6705 Rockledge Drive, Suite 750, MSC 7985
Bethesda, MD 20892-7985 (20817 for non-USPS mail)
Phone: 301-496-9838
Fax: 301-496-9839

2.8 Compliance Oversight and Corrective Action

The IBC has authority to address non-compliance with these procedures, the NIH Guidelines, the BMBL, Select Agents and Select Agent Toxins regulations or other legal requirements. Non-compliance can result in the IBC taking one or more of the following actions:

- Suspending use of the biohazardous material;
- Termination of the registration for the biohazardous material;
- Confiscation of the biohazardous material;
- Destruction of the biohazardous material;
- Any other action necessary to protect the public and/or the University.

3.0 Principal Investigator's Responsibilities

3.1 Risk Assessment

The Principal Investigator registering to obtain, possess and/or use biohazardous materials must make an initial risk assessment of the biohazardous materials based on the Risk Group (RG) of the agent in order to establish the proper physical and biological containment level (e.g. Biosafety Level). "Risk" implies the probability that harm, injury, or disease will occur. The primary focus of a risk assessment is to prevent or reduce the risk of laboratory-associated infections or accidental or unintentional release of biohazardous agents into the environment.

3.1.1 Risk Group Classification

Agents are classified into four Risk Groups according to their relative pathogenicity for healthy adult humans as follows:

- **Risk Group 1 (RG-1)** agents are not associated with disease in healthy adult humans;
- **Risk Group 2 (RG-2)** agents are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available;
- **Risk Group 3 (RG-3)** agents are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available;
- **Risk Group 4 (RG-4)** agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available.

Various resources are available for reference when assessing the risk of a particular biohazardous agent, including the following:

- NIH Guidelines, Appendix B, *Classification of Human Etiologic Agents on Basis of Hazards;*
- BMBL, Section VII, Agent Summary Statements;
- Canadian Laboratory Biosafety Guidelines;
- World Health Organization Biosafety Guidelines;
- American Biological Safety Association's Risk Group Classification for Infectious Agents;
- Information from field data or from subject matter experts.

3.1.2 Consideration of Agent Factors and Intended Research Use

The agent's Risk Group is one component in assigning the appropriate level of physical and biological containment to reduce the risk of exposure to an agent by employees and the population in general. In addition to the agent's Risk Group, the following factors should also be considered in assessing the risk and determining the level of physical and biological containment for the biohazardous agent(s):

- **Pathogenicity of the biohazardous material(s) –** Consideration should include disease incidence and severity;
- **Virulence –** Consideration should include the relative pathogenicity of the agent and various virulence factors;
- **Operations –** Consideration should be given to how the agent will be utilized during the research;
- **Route of transmission (e.g. parenteral, airborne, ingestion) –** When planning to work with a relatively uncharacterized agent with an uncertain mode of transmission, the potential for aerosol transmission should be strongly considered;
- **Agent stability –** Should include a consideration of factors such as desiccation, exposure to sunlight or ultraviolet light, or exposure to chemical disinfectants**;**
- **Infectious dose of the agent and communicability –** Consideration should include the range from the healthiest immunized worker to the worker with lesser resistance;
- **Concentration –** Include consideration of the milieu containing the organism (e.g., solid tissue, viscous blood or sputum, liquid medium) and the activity planned;
- **Origin of the biohazardous material(s) –** Consideration should include factors such as geographic location, host, and nature of the source;
- **Availability of data from animal studies –** This information may be useful in the risk assessment process in the absence of human data**;**
- **Established availability of immunization/vaccine or treatment –** The unavailability of immunization/vaccine or treatment may impact the risk involved in the use of biohazardous material(s);
- **Gene product effects, such as toxicity, physiological activity, and allergenicity**.

When working with recombinant or synthetic nucleic acid molecules, any strain that is known to be more hazardous than the parent (wild-type) strain, consideration should be given for handling it at a higher containment level. Certain attenuated strains or strains

that have been demonstrated to have irreversibly lost known virulence factors may qualify for a reduction of the containment level compared to the Risk Group assigned to the parent strain. See NIH Guidelines, Section V-B, Footnotes and References of Section I-IV.

When an organism contains genetic sequences from multiple sources such that the parent agent may not be obvious, the risk assessment should include at least two levels of analysis. First, the Principal Investigator should consider the Risk Group(s) of the source(s) of the sequences. Second, the Principal Investigator should assess the functions that may be encoded by these sequences (e.g., virulence or transmissibility). It may be prudent to first consider the highest Risk Group classification of all agents that are the source of sequences included in the construct. The Principal Investigator should also consider the percentage of the genome contributed by each parent agent and the predicted function or intended purpose of each contributing sequence. The initial assumption should be that all sequences would function as they did in the original host context.

The Principal Investigator and the IBC must also be cognizant that the combination of certain sequences in a new biological context may result in an organism whose risk profile could be higher than that of the contributing organisms or sequences. The synergistic function of these sequences may be one of the key attributes to consider in deciding whether a higher containment level is warranted, at least until further assessments can be carried out. A new biosafety risk may occur with an organism formed through combination of sequences from a number of organisms or due to the synergistic effect of combining transgenes that result in a new phenotype.

3.2 BIOSAFETY LEVEL (BIOLOGICAL AND PHYSICAL CONTAINMENT)

The Principal Investigator shall identify the proposed biosafety level for the biohazardous agents. The final assessment of risk, based on the agent's Risk Group and other risk factors, should be utilized to determine the appropriate Biosafety Level (BL-1 to BL-4) for the biohazardous material(s). The Biosafety Level describes the degree of physical and/or biological containment required to confine biohazardous materials and to reduce the potential for exposure of laboratory workers, persons outside the laboratory, and the environment. Experiments involving recombinant or synthetic nucleic acid molecules lend themselves to a third containment mechanism that involves the application of highly specific biological barriers. **Creighton University does not have any laboratories certified for BL-4, therefore no use or possession of biohazardous materials requiring BL-4 is allowed at Creighton.**

The following is a general description of the acceptable biosafety levels at Creighton:

- **Biosafety Level 1 (BL-1) –** The BL-1 containment level is suitable for work involving biohazardous materials of a minimal potential hazard to laboratory personnel and the environment.
- **Biosafety Level 2 (BL-2) –** The BL-2 containment level is suitable for work involving biohazardous materials of a moderate potential hazard to personnel and the environment. The biohazardous materials are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often reliable.
- **Biosafety Level 3 (BL-3) –** The BL-3 containment level is suitable for work involving biohazardous materials that are associated with human disease which may have serious or lethal consequences or that has a potential for aerosol transmission.
- **NOTE: There is no laboratory at Creighton that has been certified as BL-4. Therefore, projects involving biohazardous materials that require BL-4 cannot be conducted at Creighton and will not be approved by the IBC.**

These biosafety levels consist of combinations of laboratory practices and techniques, biosafety equipment, personal protective equipment, and laboratory facilities appropriate for the research to be performed and are based on the potential hazards imposed by the agents used and for the laboratory function and activity.

There are specific biosafety levels for work with biohazardous agents involving plants or animals. Additional information can be found in the BMBL, and NIH Guidelines, Section III and Appendix P (plants) and Q (animals).

Various resources are available when assessing containment levels, including Appendices B, G, I, K, P, and Q of the NIH Guidelines; the BMBL; American Biological Safety Association's Risk Group Classification for Infectious Agents; institutional policies and procedures; and training programs for personnel.

The biosafety level may be equivalent to the Risk Group classification of the agent or it may be raised or lowered based on the comprehensive risk assessment. If you have any questions regarding the risk assessment or appropriate containment level, you may consult with the IBC Chair. Except for certain r/s NA experiments whose biosafety level is established by the NIH, the IBC makes the final determination as to the appropriate Biosafety Level.

3.3 OTHER RESPONSIBILITIES

The Principal Investigator is responsible for full compliance with all federal requirements when conducting research involving biohazardous materials and with the NIH Guidelines when conducting research with recombinant or synthetic nucleic acid molecules. The Principal Investigator is responsible for ensuring that the reporting requirements under the NIH Guidelines for recombinant or synthetic nucleic acid molecules are fulfilled. Additional information and guidance may be found in the CDC/NIH guidelines in the BMBL.

3.3.1 General Responsibilities

The Principal Investigator shall:

- Initiate or modify any research involving biohazardous materials subject to IBC approval under these IBC Policies or NIH Guidelines only after the research or proposed modification has been approved by the IBC;
- Immediately report any significant problems or any significant research-related accidents and illnesses to the Biological Safety Officer, the IBC (using IBC Form 3) and any other Creighton Committee that has reviewed and approved the research activity;
- Be adequately trained in good microbiologic techniques;
- Adhere to IBC approved emergency plans for handling accidental spills and personnel contamination; and
- Comply with shipping requirements for biohazardous materials. For technical guidance see the NIH Guidelines, Appendix H, Shipment for recombinant or synthetic nucleic acid molecules and the *Laboratory Safety Monograph* for all biohazardous materials.

3.3.2 Prior to Initiation of Research Involving Biohazardous Materials

Prior to initiation of research involving biohazardous materials and as appropriate for the biohazardous materials being used, the Principal Investigator shall:

- Complete IBC training (CITI Biosafety training; every 3 years) and ensure that all personnel involved in the registration complete IBC training (CITI Biosafety training; every 3 years). See section 5.2.

- Review the applicable guidelines and regulations and become familiar with the safety procedures and requirements related to the biohazardous materials involved in the research activity;
- Develop standard operating procedures incorporating biosafety procedures or a biosafety manual prepared specifically for the laboratory describing the potential biohazards and the precautions to be taken (e.g., hazards and risks, immunizations, personal protective equipment required, decontamination, storage and disposal, spill procedures).
- Advise laboratory personnel of special hazards, and require them to read and follow instructions on practices and procedures;
- Establish policies and procedures to limit access to those individuals who have been advised on the potential hazards and meet specific entry requirements (e.g., completed training, immunization, use of protective clothing);
- Instruct laboratory and support personnel on the potential hazards associated with the research, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Ensure that personnel receive annual training updates or additional training as necessary for procedural or policy changes;
- Instruct staff in aseptic techniques and in the biology of the organisms used in the experiments so that the potential biohazards can be understood and appreciated;
- Instruct and train laboratory staff in the practices and techniques required to ensure safety and the procedures for dealing with accidents;
- Inform laboratory staff of the reasons and provisions for precautionary medical practices implemented and ensure that they are offered, at no cost, appropriate immunizations or tests for the biohazardous materials handled or potentially present in the laboratory (i.e., hepatitis B vaccine, tuberculosis skin testing).

3.3.3 During the Conduct of Research Involving Biohazardous Materials

During research or any other use of biohazardous materials, and as appropriate for the biohazardous materials being used, the Principal Investigator shall:

- Limit or restrict access to the laboratory when work with the biohazardous material is in progress, including a determination of who may be at increased risk;
- Provide personal protective equipment required for work with the specific biohazardous material (See Creighton University Laboratory Safety policies and procedures)*;*
- Supervise the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed;

- Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the Biological Safety Officer, IBC, NIH/OBA, and/or other appropriate regulatory authorities. Reports to NIH/OBA shall be sent to the following:

  Office of Biotechnology Activities
  National Institutes of Health
  6705 Rockledge Drive, Suite 750, MSC 7985
  Bethesda, MD 20892-7985 (20817 for non-USPS mail)
  (301)-496-9838 (phone)
  (30)-496-9839 (fax)

- Report any adverse events in connection with the use of biohazardous materials utilizing IBC Form 3, Adverse Biosafety Event Report Form (Appendix A);
- Correct work errors and conditions that may result in the release of biohazardous materials;
- Ensure the integrity of the biological and physical containment (Biosafety Level);
- Ensure the security of biohazardous materials at all times.

3.4 Specific Responsibilities—Recombinant or Synthetic Nucleic Acid Molecules

The NIH Guidelines are applicable to all r/s NA research conducted within the United States. Creighton University must ensure that r/s NA research conducted at or sponsored by Creighton University, irrespective of the funding source, complies with the NIH Guidelines as a condition for NIH funding of such research at Creighton University. All r/s NA research conducted at Creighton University, regardless of the funding source, must comply with the NIH Guidelines. Failure to comply with the NIH Guidelines may result in (1) suspension, limitation, or termination of NIH funds for r/s NA research at Creighton University, or (2) a requirement for prior NIH approval of any or all r/s NA projects at Creighton University.

3.4.1 General Responsibilities

In addition to the Responsibilities outlined in Section 3.3 above, the Principal Investigator shall:

- Initiate or modify any r/s NA research, which requires prior IBC approval prior to initiation, only after that research or the proposed modification has been approved by the IBC and has met all other requirements of the NIH Guidelines;

- Determine whether experiments are covered by Section III-E, *Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation*, of the NIH Guidelines, and ensure that the appropriate procedures are followed;
- Report any significant problems, non-compliance with the NIH Guidelines, or any significant research related accidents and illnesses to the Biological Safety Officer, the IBC (using IBC Form 3) and any other appropriate Creighton University Committees that have approved the research, the NIH/OBA, and other appropriate authorities, as applicable, within 30 days. Reports to NIH/OBA shall be sent to the following address:

  Office of Biotechnology Activities
  National Institutes of Health
  6705 Rockledge Drive, Suite 750, MSC 7985
  Bethesda, Maryland 20892-7985 (2087 for non-USPS mail)
  Phone: (301) 496-9838
  Fax: (301) 496-9839.

- Report any new information bearing on the NIH Guidelines to the IBC and to NIH/OBA.

3.4.2 Submissions to NIH OBA

Pursuant to Section IV-B-7-b of the NIH Guidelines, the Principal Investigator shall:

- Submit information to NIH/OBA for certification of new host-vector systems;
- Petition NIH/OBA, with notice to the IBC, for proposed exemptions to the NIH Guidelines;
- Petition NIH/OBA, with concurrence of the IBC, for approval to conduct experiments specified in NIH Guidelines Sections III-A-1, *Major Actions Under the NIH Guidelines,* and Section III-B, *Experiments that Require NIH/OBA and Institutional Biosafety Committee Approval Before Initiation;*
- Petition NIH/OBA for determination of containment for experiments requiring case-by-case review; and
- Petition NIH/OBA for determination of containment for experiments not covered by the NIH Guidelines.

3.5 CDC/USDA Requirements – Select Agents and Select Agent Toxins

Under federal law, Creighton University must register any Select Agents or Select Agent Toxins listed by the CDC and/or USDA (that are not otherwise exempt or excluded) prior to the receipt, use, storage or transfer of those listed Select Agents or Select Agent Toxins. In addition, any principal investigator requesting the receipt or use of listed Select Agents or Select Agent Toxins must first undergo a security risk assessment (including fingerprinting) by the Attorney General and Federal Bureau of Investigation (FBI) before his/her request can be reviewed by the RO and IBC. Restricted persons (See Section 1.7.2 above) are prohibited from having access to or control of listed Select Agents or Select Agent Toxins. **Note: Currently no work involving non-exempt Select Agents and Select Agent Toxins is being conducted, and none is permitted at Creighton University (see section 1.5).**

3.6 Reporting Laboratory Accidents and Exposures

All adverse events, illnesses, or significant accidents leading to or potentially leading to illness or that is environmentally dangerous to humans, or plants shall be reported within 24 hours to the IBC Chair and the Department of Environmental Health and Safety. The report shall be made by completing IBC Form 3 "Adverse Biosafety Event Report Form" (see IBC Appendix A), and sending it by email or fax to the IBC Chair and the Department of Environmental Health and Safety.

Incidents involving biohazardous materials contained at a BL-3 containment level must be immediately reported to Public Safety (280-2911) and the Department of Environmental Health and Safety (546-6269). The IBC Form 3, *Adverse Biosafety Event Report*, must be emailed or faxed to the IBC Chair and the Department of Environmental Health and Safety within 24 hours of the incident.

3.7 Access to Laboratories

Faculty members shall allow access to their laboratories registered for biohazardous materials to the IBC, the Biological Safety Officer, the RO or Director of EHS for routine laboratory inspections.

4.0 Registration and IBC Review

4.1 IBC Registration

Any faculty member (Principal Investigator) that desires to possess or use biohazardous materials shall, unless otherwise exempt under these IBC Policies, submit an appropriate registration document with the IBC. No one shall obtain or use biohazardous materials subject to registration with the IBC until the registration has been approved by the IBC. Modifications of approved registrations shall not occur until approved by the IBC.

4.1.1 Registration of Infectious Agents

Any Principal Investigator that desires to possess or use infectious agents that fall within a risk category of RG-2 to RG-4 shall submit an original signed copy and an electronic copy of IBC Form 1, Infectious Agents Registration Document (IBC Appendix A) along with all attachments, to the IBC Office. The foregoing notwithstanding, infectious agents used in conjunction with a r/s NA project can be registered with the r/s NA project using only IBC Form 2, Recombinant or Synthetic Nucleic Acid Molecule Registration Document, or IBC Form 2a, Exempt Recombinant or Synthetic Nucleic Acid Molecule Registration Document, (IBC Appendix A) as set forth below; IBC Form 1 is not required in this setting. No infectious agents in risk category RG-2 to RG-4 shall be obtained or used until the IBC has approved the registration. The following information shall be included with the registration as attachments (one hard copy and an electronic copy if available):

- A copy of relevant sections of the research protocol describing the use of infectious agents;
- Written summary that describes the potential biohazards related to the use of the infectious agents and the precautions that will be taken when working with the infectious agents;
- An emergency plan for the handling of accidental spills and personnel contamination;
- Documentation for all personnel who will work on the project indicating level of training or experience with Infectious Agents.

4.1.1.1 RG-1 Infectious Agents

RG-1 infectious agents do not need to be registered with the IBC. Principal investigators who are uncertain of the risk category of an infectious agent should review IBC Appendix D and/or contact the IBC Chair for further guidance.

4.1.2 Registration of Select Agents or Select Agent Toxins

At this time only registrations involving Select Agents or Toxins that are exempt shall be eligible for review and approval by the IBC. Those that are non-exempt are prohibited (see section 1.5). Any Principal Investigator that desires to receive, use, store or transfer a Select Agent or Select Agent Toxin, whether or not exempt or excluded from federal registration and regardless of risk category or biosafety level shall submit an original signed copy and an electronic copy of IBC Form 1a, *Select Agent or Select Agent Toxin Registration* (IBC Appendix A), to the RO and the IBC Office. RO and IBC approval must be obtained before procuring, using, transferring or destroying any Select Agent or Select Agent Toxin. Principal Investigators approved to use or store Select Agent Toxins must track its use using IBC Form 4, *IBC Tracking Sheet for Select Agent Toxins Only*. The following information shall be included with the registration as an attachment (one hard copy and an electronic copy if available):

- A copy of relevant sections of the research protocol describing the use of Select Agents/Select Agent Toxins;
- Written protocol or biohazardous manual that describes the potential biohazards related to the use of the Select Agents/Select Agent Toxins and the precautions that must be taken when working with the Select Agents/Select Agent Toxins;
- An emergency plan for the handling of accidental spills and personnel contamination;
- Documentation for all personnel who will work on the project indicating level of training or experience with Infectious Agents.

4.1.3 Registration of Recombinant or Synthetic Nucleic Acid Molecules (r/s NA)

Principal Investigators conducting any r/s NA research shall submit an original signed copy and an electronic copy of IBC Form 2, Recombinant or Synthetic Nucleic Acid Molecules Registration Document (IBC Appendix A), to the IBC Office. IBC approval must be obtained before initiating any r/s NA research. The following information shall be included with the registration as an attachment (one hard copy and an electronic copy if available):

- A copy of relevant sections of the research protocol describing the use of recombinant or synthetic nucleic acid molecules;
- Written protocol or biohazardous manual that describes the potential biohazards related to the use of the recombinant or synthetic nucleic acid molecules and the precautions that must be taken when working with the recombinant or synthetic nucleic acid molecules (non-exempt, RG 2-4 experiments only);
- An emergency plan for the handling of accidental spills and personnel contamination (non-exempt, RG 2-4 experiments only);
- Documentation for all personnel who will work on the project indicating level of training or experience with recombinant or synthetic nucleic acid molecules; and
- For any human gene transfer protocol, a copy of the proposed informed consent document.

The following paragraphs summarize r/s NA experiments covered by the NIH Guidelines; refer directly to the NIH Guidelines for a more detailed description of experiments and specific requirements:

- **Experiments Requiring IBC Approval, RAC Review, and NIH Director Approval Before Initiation (Section III-A) –** This includes experiments considered as *Major Actions* under the NIH Guidelines and experiments involving the deliberate transfer of a drug resistance trait to microorganisms that do not acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease in humans, veterinary medicine, or agriculture;
- **Experiments Requiring NIH/OBA and IBC Approval before Initiation (Section III-B) –** This covers Experiments involving the cloning of toxin molecules with LD_{50} of less than 100 nanograms per kilogram body weight. IBC approval is required *prior to initiation* of the experiments. This also covers proposed experiments that are equivalent to an experiment previously approved by the NIH Director as a Major Action;
- **Experiments Requiring IBC and IRB Approvals and RAC Review Before Research Participant Enrollment (Section III-C) –** These experiments involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into human subjects (human gene transfer);
- **Experiments Requiring IBC Approval Before Initiation (Section III-D) –** This category covers the following subsections: (a) experiments using RG2, RG3, RG4 or restricted agents as host-vector systems; (b) experiments in which DNA from RG2, RG3, RG4, or restricted agents is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems; (c) 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; (d) experiments involving whole animals and/or whole plants; and (e) experiments involving more than 10 liters of culture;
- **Experiments Requiring IBC Notice Simultaneous with Initiation (Section III-E) –** This includes experiments not included in Sections III-A, III-B, III-D, III-F and their subsections. Under these IBC Policies, IBC approval is required ***prior to initiation*** of the research;
- **Exempt Experiments (Section III-F) –** Refer to Appendix B for a list of r/s NA experiments that are exempt from the NIH Guidelines. Under these IBC Policies, registration and approval of the exempt status by the IBC is required ***prior to initiation*** of the research.

If a r/s NA experiment falls into Section III-F (Exempt) and into either Sections III-D or III-E as well, the experiment is considered exempt from NIH Guidelines, but is still subject to IBC registration and approval of exempt status prior to initiation of the research.

4.2 IBC Initial Review of Registrations

IBC approval must be obtained for possession or use of any biohazardous material, except for infectious agents in a risk category RG-1. Such approval must be obtained prior to obtaining the biohazardous material or using it in a research project. All members of the IBC shall receive a copy of the Registration and supporting materials (written or electronic) including those of investigators requesting Expedited Review. In the absence of a scheduled IBC meeting, the IBC Chair shall schedule a full meeting of the IBC unless a majority of members of the IBC agree to Expedited Review pursuant to 4.2.2 below.

4.2.1 Full IBC Review

Except as otherwise allowed under paragraph 4.2.2 below, all registrations shall be reviewed by the full IBC at its regular monthly meetings. As part of its review, the IBC shall:

- Ensure that proposed research activity or use of biohazardous materials are in compliance with applicable federal and state requirements and that any research involving r/s NA molecules or infectious agents is in compliance with Section III of the NIH Guidelines;
- Conduct an independent assessment of the containment levels recommended by the Principal Investigator, as well as those required by the NIH Guidelines for any proposed research involving r/s NA molecules or infectious agents;
- Conduct an assessment of the facilities, procedures, practices, training and expertise of personnel involved in r/s NA or infectious agent research; and
- Ensure that all required approvals under the NIH Guidelines have been obtained from NIH/OBA and RAC prior to initiation of r/s NA or infectious agent research.

Once IBC review is complete, the IBC may do one or more of the following:

- Approve the registration without modification;
- Approve the registration subject to modification;
- Table the decision pending additional information;
- Disapprove the registration.

In the event a registration is approved subject to modification, the IBC may either require the Investigator to submit proof that the modifications have been made and submit the revised registration for review at the next convened meeting of the IBC or permit the IBC Chair to verify that the modifications in the revised registration have been made. If the IBC Chair verifies that modifications have been made, the IBC Chair will report this to the IBC at the next convened meeting.

4.2.2 Expedited Review Process

The Principal Investigator may request that the IBC conduct an expedited review of a registration. The IBC may allow the IBC Chair to conduct an expedited review and approve registrations of (i) infectious agents in a risk category of RG-2 or that require containment at a BL-2 or lower, or (ii) r/s NA experiments that are exempt under NIH Guidelines. Non-exempt r/s NA registrations are not eligible for expedited review. A majority of members of the IBC must specifically approve (via e-mail or written response to the IBC Chair), within 5 days of receipt, the request for expedited review under this provision. If the request for expedited review is approved by a majority of the IBC members, the IBC Chair shall review the registration using the criteria set forth in 4.2.1 above. The IBC Chair may either approve the registration or schedule a full meeting of the IBC to review and approve the registration. If the IBC Chair approves the registration, the investigators may initiate the research. The registration shall then be submitted to the full IBC at its next scheduled meeting, at which time the IBC may do one or more of the following:

- Approve the Chair's decision without modification;
- Conduct its own review and either approve the Chair's decision or modify the Chair's approval;
- Disapprove the registration.

4.2.3 Notice of IBC Action

The IBC Chair shall provide written notification of the Chair's/IBC's decision to the Principal Investigator.

4.2.4 Length of Approval

4.2.4.1 Non-Exempt Recombinant or Synthetic Nucleic Acid Molecules and Infectious Agents (Excluding Select Agents and Select Agent Toxins)

IBC approval of non-exempt r/s NA and infectious agents (excluding Select Agents and Select Agent Toxins) is valid for two (2) years. All IBC approvals of non-exempt r/s NA and infectious agents are subject to continuing review (see Section 4.4), which will occur within the first 2 year period after the initial IBC approval at a regular monthly IBC meeting and then every 2 years thereafter at the appropriate monthly IBC meeting.

4.2.4.2 Exempt Recombinant or Synthetic Nucleic Acid Molecules

IBC registration and approval of exempt status for r/s NA experiments exempt from the NIH guidelines do not expire and such experiments are not subject to continuing review. Principal

Investigators are required to notify the IBC of any and all modifications, terminations, and transfers of exempt r/s NA experiments as otherwise set forth below. The foregoing notwithstanding, r/s NA experiments that also include an infectious agent in a Risk Groups 2, 3 or 4 must undergo continuing review for purposes of the infectious agent.

4.2.4.3 Select Agents and Select Agent Toxins

RO and IBC approval of exempt Select Agents and Select Agent Toxins is valid for one year. RO and IBC approval of Select Agents and Select Agent Toxins is subject to continuing review (see Section 4.4.1), which will occur within the first 12 months after the initial approval date at a regular monthly IBC meeting and then every year thereafter at the appropriate monthly IBC meeting.

4.3 Modifications to Approved Registrations

4.3.1 Non-Exempt Registrations

Principal Investigators shall not initiate or implement any changes or modifications of IBC approved registrations without the prior review and approval of the IBC. This includes, but is not limited to, modification of biohazardous materials, procedure changes (including change of the Principal Investigator), changes in laboratory, or changes that increase the risk of the project and/or the Biosafety Level. A revised registration form (IBC Form 1, 1a and/or IBC Form 2) shall be submitted to the IBC for review and approval. Modifications to approved registrations involving a change in personnel only (exclusive of the principal investigator) may be reviewed and approved by the IBC Chair (IBC Form 5) as long as there is documentation that the appropriate training for new personnel has been completed. The IBC Chair shall then report such changes to the full IBC at the next regularly scheduled IBC meeting.

4.3.2 Exempt Registrations

Principal Investigators shall not initiate or implement any changes or modifications of exempt registrations without prior notification and review by the IBC. The IBC Chair will review the proposed changes and/or modifications to determine if any may potentially change the exempt status of the registration. If a change in exempt status is possible, the IBC Chair shall require that the Principal Investigator submit IBC Form 1, 1a, 2, or 2a, as appropriate, with all proposed changes/modifications described. The modified registration will then be considered for approval at the next scheduled meeting of the full IBC. If the proposed changes/modifications are minor in nature and do not endanger the exempt status of the registration, e.g. change in personnel only, the IBC Chair will so inform the Principal Investigator, document the changes in the registration's file and update the status of the registration as an informational item on the agenda of the next scheduled IBC meeting.

4.4 CONTINUING REVIEW OF APPROVED REGISTRATIONS AND NOTICE OF TERMINATION

4.4.1 Continuing Review of Approved Registrations

Principal Investigators who wish to continue their non-exempt activity with biohazardous materials beyond the initial or subsequent length of approval must complete and submit IBC Form 5, IBC Continuing Review (Appendix A), to the IBC Office at least one month prior to next scheduled IBC meeting occurring *before* the approval term expires. IBC Form 5 should only be submitted *if there are no modifications or revisions*. If there are modifications or revisions, then a new IBC Form 1, IBC Form 1a and/or IBC Form 2 must be submitted for review (see Section 4.3). In any of the above cases, a short summary (e.g. a paragraph) of the project should be included so that the committee members are aware of the activities covered by the registration. The full IBC conducts Continuing Review of registrations during its regular monthly meetings. The IBC Chair shall notify the Principal Investigator in writing of the IBC's decision. PIs are not required to submit exempt registrations for continuing review.

4.4.2 Notice of Termination or Transfer

4.4.2.1 Termination

Principal Investigators shall complete IBC Form 6, IBC Notice of Termination, and file it with the IBC Office when a research project involving registered biohazardous materials is completed or no longer active or when the biohazardous material is properly disposed of or no longer in the possession of the Principal Investigator. The IBC Chair shall contact the Principal Investigator if there are any questions or concerns regarding Termination of Approval. The IBC Chair shall review and approve the request to terminate registration.

4.4.2.2 Full or Partial Transfer

Principal Investigators who wish to transfer biohazardous materials to another principal investigator or entity must complete IBC Form 7, IBC Notice of Transfer and file it with the IBC Chair. A transfer of biohazardous materials among Creighton faculty members also requires completion and submission of IBC Form 1, IBC Form 1a and/or IBC Form 2 by the new Principal Investigator, i.e. the transferee. No biohazardous materials shall be transferred until IBC approval has been granted for all submissions related to the requested transfer. Transfers of biohazardous materials shall be reviewed by the IBC pursuant to Sections 4.2.1 (full review) or 4.2.2 (expedited review). Principal Investigators transferring any select toxin must also complete IBC Form 4, IBC Tracking Sheet for Select Agent Toxins.

5.0 Training

5.1 Training of IBC Members

All members of the IBC shall receive initial and on-going training on the possession and use of biohazardous materials and orientation to the IBC Policies. IBC members shall receive updates at IBC meetings on changes affecting the possession and/or use of biohazardous materials.

5.2 Faculty Registering for Possession and/or Use of Biohazardous Materials

The IBC through the Research Compliance Office shall provide initial and on-going training to faculty and research personnel on the use of biohazardous material and orientation to the IBC Policies. Accordingly, the IBC has implemented the use of the new CITI Biosafety/Biosecurity training course for anyone conducting research involving biohazardous material, including Infectious Biological Agents, Recombinant or Synthetic Nucleic Acid Molecules and Select Agents. All Principal Investigators, Co-Investigators, Laboratory Technicians, and Research Staff involved in research using biohazardous material in their laboratories are required to complete the CITI Basic Biosafety Training course. "Research Staff" refers to anyone, including students of any kind, conducting research on or otherwise handling biohazardous material, including Infectious Biological Agents, Recombinant or Synthetic Nucleic Acid Molecules, and Select Agents.

6.0 Appendix A

INSTITUTIONAL BIOSAFETY COMMITTEE FORMS

http://www.creighton.edu/researchservices/rcocommittees/ibc/forms/

Form 1 – *Infectious Agent Registration*
Form 1a – *Select Agent or Select Agent Toxin Registration*
Form 2 – *Non-Exempt Recombinant or Synthetic Nucleic Acid Molecule Registration*
Form 2a – *Exempt Recombinant or Synthetic Nucleic Acid Molecule Registration*
Form 3 – *Adverse Biosafety Event Report Form*
Form 4 – *IBC Tracking Sheet for Select Agent Toxins Only*
Form 5 – *Continuing Review*
Form 6 – *Notice of Termination*
Form 7 – *Notice of Transfer*

7.0 Appendix B

EXPERIMENTS EXEMPT FROM NIH GUIDELINES

General Exemptions

Certain recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines. Experiments that employ r/s NA with the characteristics listed below are generally exempt from the NIH Guidelines and IBC review unless they also involve, for example; (1) deliberate transfer of a drug resistant 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; (2) deliberate formation of r/s NA containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD_{50} (median lethal dose) of less than 100 nanograms per kilogram of body weight; or (3) the deliberate transfer of r/s NA, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research subjects. Otherwise, per Section III-F of the NIH Guidelines, the following recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines; however, other federal and state standards of biosafety may apply to such research (e.g. BMBL):

- 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 LD_{50} 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 of the NIH Guidelines, it is not exempt.

- 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.

- Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.

- 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.

- 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).

- 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 NIH Guidelines Section IV-C-1-b-(1)-(c), Major Actions). See NIH Guidelines 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.

- Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.

- Those that do not present a significant risk to health or the environment (see NIH Guidelines 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 NIH Guidelines Appendix C, Exemptions under Section III-F-8 for other classes of experiments that are exempt from the NIH Guidelines.

Tissue Culture Experiments with Recombinant or Synthetic Nucleic Acid Molecules

Many tissue experiments with recombinant or synthetic nucleic acid molecules (r/s NA) molecules are exempt from the NIH Guidelines. If the answer to ***all five*** of the following questions is ***No,*** then the tissue culture experiments are exempt under Appendix C of the NIH Guidelines.

- Do any r/s NA molecules contain one-half or more of any eukaryotic viral genome?
- Do any experiments involve Risk Group 2, 3, or 4 organisms or nucleic acids from Risk Group 2, 3, or 4? (See Appendix B of the NIH Guidelines for definitions of Risk Groups 2, 3, and 4)
- Do any experiments involve introduction of genes coding for the biosynthesis of molecules toxic for vertebrates?
- Do any experiments involve infectious viruses? (See Appendix B of the NIH Guidelines for infectious viruses)
- Do any experiments involve defective viruses in the presence of helper viruses? (See Section III-D-3 of the NIH Guidelines)

Note: If the answer to any of the above questions is ***Yes,*** the project may still be exempt; consult with the IBC office.

Escherichia coli K-12 and Yeast

Most experiments involving *Escherichia coli* K-12 host vector systems, *Saccharomyces cerevisiae* and *Saccharomyces uvarum* and *Kluyveromyces lactis* host vector systems are exempt from the NIH Guidelines. If the answer to ***all three*** of the following questions is ***No,*** then the experiments are exempt under the NIH Guidelines (Appendix C-II and C-III).

- Do any experiments involve Risk Group 2, 3, or 4 organisms or nucleic acids from Risk Group 2, 3, or 4 organisms? (See Appendix B of the NIH Guidelines for Risk Groups)
- Do any experiments involve introduction of genes coding for molecules toxic for vertebrates? (See Section III-B-1 and Appendix F of the NIH Guidelines)
- Will there be any large-scale experiments (more than 10 liters of culture)?

Bacillus subtilis or *Bacillus licheniformis* Host-Vector Systems

Any asporogenic *Bacillus subtilis* or asporogenic *Bacillus licheniformis* strain that does not revert to a sporeformer with a frequency greater than 10^{-7} may be used for cloning DNA with the exception of those experiments listed below. For these exempt laboratory experiments, BL-1 physical containment conditions are recommended. For large-scale fermentation experiments, the appropriate physical containment conditions need be no greater than those for the unmodified host organism; the Institutional Biosafety Committee can specify higher containment if it deems necessary.

The following categories are not exempt from the NIH Guidelines: (i) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B of the NIH Guidelines, Classification of Human Etiologic Agents on the Basis of Hazard, and Sections V-G and V-L, Footnotes and References of Sections I through IV) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval, (ii) large-scale experiments (e.g. more than 10 liters of culture), and (iv) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F of the NIH Guidelines, Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates).

Extrachromosomal Elements of Gram Positive Organisms

Recombinant or synthetic nucleic acid molecules derived entirely from extrachromosomal elements of the organisms listed below (including shuttle vectors constructed from vectors described in Appendix C of the NIH Guidelines), propagated and maintained in organisms listed below are exempt from the NIH Guidelines.

Bacillus amyloliquefaciens
Bacillus amylosacchariticus
Bacillus anthracis
Bacillus aterrimus

Bacillus brevis
Bacillus cereus
Bacillus globigii
Bacillus licheniformis
Bacillus megaterium
Bacillus natto
Bacillus niger
Bacillus pumilus
Bacillus sphaericus
Bacillus stearothermophilis
Bacillus subtilis
Bacillus thuringiensis
Clostridium acetobutylicum
Lactobacillus casei
Listeria grayi
Listeria monocytogenes
Listeria murrayi
Pediococcus acidilactici
Pediococcus damnosus
Pediococcus pentosaceus
Staphylococcus aureus
Staphylococcus carnosus
Staphylococcus epidermidis
Streptococcus agalactiae
Streptococcus anginosus
Streptococcus avium
Streptococcus cremoris
Streptococcus dorans
Streptococcus equisimilis
Streptococcus faecalis
Streptococcus ferus
Streptococcus lactis
Streptococcus ferns
Streptococcus mitior
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus salivarious
Streptococcus sanguis
Streptococcus sobrinus
Streptococcus thermophylus

However, the following categories are not exempt from the NIH Guidelines: (i) experiments involving DNA from Risk Groups 3, 4, or restricted organisms (see Appendix B of the NIH Guidelines, Classification of Human Etiologic Agents on the Basis of Hazard, and Sections V-G and V-L, Footnotes and References of Sections I through IV) or cells known to be infected with these agents may be conducted under containment conditions specified in Section III-D-2 with prior Institutional Biosafety Committee review and approval, (ii) large-scale experiments (e.g., more than 10 liters of culture), and (iii) experiments involving the deliberate cloning of genes coding for the biosynthesis of molecules toxic for vertebrates (see Appendix F of the NIH Guidelines, Containment Conditions for Cloning of Genes Coding for the Biosynthesis of Molecules Toxic for Vertebrates).

The Purchase or Transfer of Transgenic Rodents

The purchase or transfer of transgenic rodents for experiments that require BL-1 containment (See NIH Guidelines Appendix GIII- M, Footnotes and References of Appendix G) are exempt from the NIH Guidelines.

Generation of BSL-1 Transgenic Rodents via Breeding

The breeding of two different transgenic rodents or the breeding of a transgenic rodent and a non-transgenic rodent with the intent of creating a new strain of transgenic rodent that can be housed at BL-1 containment will be exempt from the NIH Guidelines if:
(1) Both parental rodents can be housed under BL1 containment; and
(2) Neither parental transgenic rodent contains the following genetic modifications:
    (i) Incorporation of more than one-half of the genome of an exogenous eukaryotic virus from a single family of viruses; or
    (ii) Incorporation of a transgene that is under the control of a gamma-retroviral long terminal repeat (LTR); and
(3) The transgenic rodent that results from this breeding is not expected to contain more than one half of an exogenous viral genome from a single family of viruses.

NOTE:

If your project does not fall within any of the above exemptions, then you must register with the IBC and obtain approval prior to initiating your project. Exempt projects still must register. Please consult the IBC with any questions.

8.0 Appendix C

LIST OF SELECT AGENTS AND SELECT AGENT TOXINS (INCLUDING EXEMPTIONS/EXCLUSIONS)

The list of select agents and toxins can be found at:

http://www.selectagents.gov/SelectAgentsandToxinsList.html

The list of excluded agents and toxins can be found at:

http://www.selectagents.gov/SelectAgentsandToxinsExclusions.html

9.0 Appendix D

RISK GROUP 1 INFECTIOUS AGENTS

RG1 agents are not associated with disease in healthy adult humans. Examples of RG1 agents include asporogenic *Bacillus subtilis* or *Bacillus licheniformis* (see NIH Guidelines Appendix C-IV-A, *Bacillus subtilis* or *Bacillus licheniformis* Host-Vector Systems, Exceptions); adeno-associated virus (AAV) all serotypes; and recombinant or synthetic AAV constructs, in which the transgene does not encode either a potentially tumorigenic gene product or a toxin molecule and are produced in the absence of a helper virus. A strain of *Escherichia coli* (see NIH Guidelines Appendix C-II-A, *Escherichia coli* K-12 Host Vector Systems, Exceptions) is an RG1 agent if it (1) does not possess a complete lipopolysaccharide (i.e. lacks the O antigen); and (2) does not carry any active virulence factor (e.g. toxins) or colonization factors and does not carry any genes encoding these factors.

The following list of animal etiologic agents is appended to the list of human etiologic agents. None of these agents is associated with disease in healthy adult humans; they are commonly used in laboratory experimental work. A containment level appropriate for RG1 human agents is recommended for their use. For agents that are infectious to human cells, e.g. amphotropic and xenotropic strains of murine leukemia virus, a containment level appropriate for RG2 human agents is recommended.

Baculoviruses

Herpesviruses
--Herpesvirus ateles
--Herpesvirus saimiri
--Marek's disease virus
--Murine cytomegalovirus

Papovaviruses
--Bovine papilloma virus
--Polyoma virus
--Shope papilloma virus
--Simian virus 40 (SV40)

Retroviruses
--Avian leukosis virus
--Avian sarcoma virus
--Bovine leukemia virus
--Feline leukemia virus
--Feline sarcoma virus
--Gibbon leukemia virus
--Mason-Pfizer monkey virus
--Mouse mammary tumor virus
--Murine leukemia virus
--Murine sarcoma virus
--Rat leukemia virus

Murine retroviral vectors to be used for human transfer experiments (less than 10 liters) that contain less than 50% of their respective parental viral genome and that have been demonstrated to be free of detectable replication competent retrovirus can be maintained, handled, and administered, under BL1 containment.

For lists of Risk Groups 2-4 agents, see NIH Guidelines (Appendix B).

10.0 Appendix E

USEFUL WEB SITES

National Institutes of Health Guidelines:

http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines

Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition:

http://www.cdc.gov/biosafety/publications/bmbl5/

Select agents and select agent toxins:

http://www.selectagents.gov/SelectAgentsandToxinsList.html

Occupational Safety and Health Administration Regulations

https://www.osha.gov/law-regs.html

Creighton University IBC web site:

http://www.creighton.edu/researchservices/rcocommittees/ibc/

Creighton University downloadable IBC forms:

http://www.creighton.edu/researchservices/rcocommittees/ibc/forms/

Creighton University IBC Policies & Procedures:

http://www.creighton.edu/researchservices/rcocommittees/ibc/policies/