Getting Started…With Biosafety

Oklahoma State University has an obligation to ensure that activities involving biohazardous material, as defined in the university's Institutional Biosafety Policy, are conducted safely and in accordance with applicable federal regulations, laws, and required guidelines. The University accepts this responsibility and has established certain requirements that may exceed provisions set forth in federal regulations and required guidelines. OSU's Institutional Biosafety Committee (IBC) is charged with ensuring that the university remains in compliance with applicable requirements. The IBC oversees all research and instructional activities involving the use of biohazardous materials. Noncompliance places researchers and the university in jeopardy and could cause the university to lose federal funding for certain activities.

Who Must Apply to the IBC for Approval of a Research or Teaching Project?

All research and teaching activities conducted by faculty, staff, students, post docs, visiting scientists and other personnel on Oklahoma State University property or involving the use of OSU-owned equipment are subject to IBC review if the activities involve biohazardous materials, as defined by the university's Institutional Biosafety Policy.

All activities involving recombinant or synthetic nucleic acid molecules, biological agents, and biologically-derived toxins must receive IBC approval prior to beginning the work. All work with recombinant or synthetic nucleic acid molecules must adhere to the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules whether or not they receive funding through the NIH.

Biological agents fall into one of four risk groups. To assist you in determining which NIH classification or risk group the research will fall in, please consult the risk group descriptions or contact the Biological Safety Officer at 744-3203.

The Institutional Biosafety Committee (IBC)

The Institutional Biosafety Committee (IBC) is composed of no fewer than five members whose responsibility is to review, approve, and oversee all teaching and research activities involving recombinant or synthetic nucleic acids, infectious agents, and biologically-derived toxins. Members are selected so that collectively they have the experience and expertise to review protocols and assess the potential risk to people, animals, and plants. The IBC meets no less frequently than quarterly and normally, bimonthly. The schedule for the IBC meetings and deadlines for submitting protocols is available under the IBC Meeting Dates webpage. No official business may be conducted without a quorum of the current voting membership. Certain activities may be reviewed by a subset of the IBC.

The IBC may approve protocols and/or the facility containment level required with or without modifications. Additionally, the IBC may withhold approval for all or any portion of a protocol pending satisfactory completion of any requirements imposed by the IBC. Any change in organisms, project scope, methodology, or project personnel must be pre-approved by the IBC. The Office of University Research Compliance maintains records of protocols, minutes of IBC

meetings, laboratory inspection reports, and other documentation relevant to IBC business. No member of an IBC may be involved (except to provide information requested by the IBC) in the review or approval of a project in which he/she expects to be engaged or has a financial interest.

Coordination with Other University Research Compliance Committees

Depending on the specific activity, the investigator or instructor may be required to seek prior or concurrent approval(s) from other compliance committees, including the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Radiation Safety Committee, and/or the Laser Safety Committee.

Categories of Biomaterials Needing IBC Review and Approval

1. Recombinant or Synthetic Nucleic Acid Molecules

Recombinant or synthetic nucleic acid experiments involving animal, plant or microbial pathogens, whole plants or animals, or humans require IBC approval before initiation of the activities. If your research or teaching activity includes recombinant or synthetic nucleic acid and/or artificial gene transfers (to include gene therapy clinical trials and the creation of transgenic animals), you should consult the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* for specific information on the requirements for registering your particular activity.

Recombinant or synthetic nucleic acid use in 'exempt experiments,' as defined by NIH Guidelines, is required to be reviewed and approved by a subset of the Institutional Biosafety Committee before the research is started. Agents (e.g., faculty, researchers, staff, students, and employees) of OSU may ONLY self-exempt for activities involving synthetic nucleic acids that cannot replicate or generate nucleic acids that can subsequently replicate in any living cell (e.g., oligonucleotides). Subcommittee reviews can normally be conducted within two weeks following submission of the protocol to the Office of University Research Compliance. Protocols involving non-exempt recombinant or synthetic nucleic acids will be reviewed at a convened meeting of the IBC. Experiments may only be initiated after IBC approval and receipt of approval notification from the Office of University Research Compliance.

The Recombinant/Synthetic Nucleic Acid Registration Form may be found in the Forms and Permits section of the Office of University Research Compliance (URC) website. Complete the form and submit a paper copy to the Office of University Research Compliance. This office will coordinate IBC review.

2. Biohazardous Agents: Humans, Animals, Plants

Activities involving Risk Group 2, Risk Group 3, and Risk Group 4 biohazardous agents must be reviewed and approved by the IBC prior to the initiation the project. Risk group classification information is available via the URC website.

A risk group designation is assigned to each biological agent based on the risk of acquiring the disease and the degree of severity from the disease. Regardless of the Risk Group classification the appropriate biosafety level is determined through a risk assessment. The BMBL provides further information regarding the determination of the appropriate biosafety level. Complete the biological agent protocol registration form and submit it to the Office of University Research Compliance in 223 Scott Hall. This office will coordinate IBC review.

3. Toxins

The use of any biological-derived toxins requires IBC review. Use of select agent toxins, **in any quantity,** must receive prior approval from the IBC before the project is started. Specific procedures are in place for ordering and receiving select toxins of any quantity and for keeping accurate records regarding use and disposal. It is the responsibility of the investigator to ensure that these procedures are understood and followed. Questions should be directed to the Biological Safety Officer (BSO) at 744-3203.

Toxin quantities, per investigator, not exceeding those limits shown in the following table are exempt from federal select agent registration and regulation. However, labs using or possessing exempt quantities of a select agent toxin must notify the IBC of its use and follow Oklahoma State University procedures. These procedures include keeping a current inventory of the toxin at all times in an effort to avoid the severe penalties associated with non-compliance with the Select Agent Final Rule. Additionally, this inventory is subject to review by the BSO at any time to ensure that the total amount of toxin per PI in a laboratory is maintained below the exempt limit at all times.

HHS Toxins	Amount
Abrin	100 mg
Botulinum neurotoxins	0.5 mg
Short, paralytic alpha conotoxins	100 mg
Diacetoxyscirpenol (DAS)	1000 mg
Ricin	100 mg
Saxitoxin	100 mg
Staphylococcal Enterotoxins (Subtypes A, B, C, D, and E)	5 mg
T-2 toxin	1000 mg
Tetrodotoxin	100 mg

The PI should complete the biological agent protocol registration form and submit it to the Office of University Research Compliance. This office will coordinate IBC review.

4. Prions

All research involving prions must be reviewed by the Institutional Biosafety Committee. Biosafety level of 2 containment should be expected as a minimum requirement from the IBC. Depending on the nature of the research, BSL-3 containment may be required.

There are additional links to resources concerned with prions listed on the Helpful Links page of the biosafety webpage of the Office of University Research Compliance website.

The PI should complete the biological agent protocol registration form and submit it to the Office of University Research Compliance. This office will coordinate IBC review.

The University has additional oversight procedures for research involving prions. Investigators should contact the Biological Safety Officer at 744-3203 for more information about IBC approval to conduct this type of research.

5. Select Biological Agents and/or Their Toxins

On June 12, 2002, President George W. Bush signed into law the Public Health Security and Bioterrorism Preparedness Response Act of 2002. The Act (PL 107-188) is designed to improve the ability of the United States to prevent, prepare for, and respond to bioterrorism. The law requires persons possessing biological agents or toxins deemed a threat to public health (List of Select Agents and Toxins) to register with the Centers for Disease Control and Prevention (CDC) or the United States Department of Agriculture (USDA).

Compliance Requirements for Select Agent Research

The requirements for institutions and investigators that possess, use, and/or transfer these select agents and toxins are delineated in Title 42, CFR, Part 73 ; Title 9 CFR, Part 121; and Title 7, CFR, Part 331. Investigators should review these regulations thoroughly prior to seeking registration and approval to conduct research with select agents and/or toxins.. Guidance for meeting these requirements is available via the Select Agent Program section of the URC website.

The primary oversight agency for Oklahoma State University is the Centers for Disease Control and Prevention (CDC). Oklahoma State University has approval from the CDC to conduct research using select agents and/or toxins at research facilities in Stillwater. Additional requirements must be followed when shipping and receiving select agents and/or toxins.

All Oklahoma State University personnel working with and/or storing select agents and/or toxins must be included on OSU's Certificate of Registration with the CDC, and must follow all applicable federal regulations and University policies. It is recommended that all investigators interested in conducting research falling into this category consult the federal regulations and the Office of University Research Compliance for guidance.

6. **Plants**

Activities involving recombinant or synthetic nucleic acid molecule-containing plants, plant-associated microorganisms, and small animals shall be conducted in accordance with Appendix P, Physical and Biological Containment for Recombinant or Synthetic Nucleic Molecules Research Involving Plants, as contained in the latest copy of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*.

Appendix P specifies physical and biological containment conditions and practices suitable to the greenhouse conduct of experiments involving recombinant or synthetic nucleic acid molecule-containing plants, plant-associated microorganisms, and small animals. Appendix P supersedes standard recombinant or synthetic nucleic acid molecule containment requirements (Appendix G of the NIH Guidelines) when research plants are of a size, number, or have growth requirements that preclude the use of standard laboratory containment conditions.

Plants covered in Appendix P include, but are not limited to, mosses, liverworts, macroscopic algae, and vascular plants including terrestrial corps, forest, and ornamental species. Plant-associated microorganisms include viroids, virusoids, viruses, bacteria, fungi, protozoans, certain small algae, and microorganisms that have a benign or beneficial association with plants, such as certain Rhizobium species and microorganisms known to cause plant diseases. The appendix applies to microorganisms which are modified with the objective of fostering an association with plants. Plant associated small animals include those arthropods that:

- Are in obligate association with plants,
- Are plant pests,
- Are plant pollinators, or
- Transmit plant disease agents.

Other small animals include nematodes for which tests of biological properties necessitate the use of plants. Microorganisms associated with such small animals (e.g., pathogens or symbionts) are included. Researchers handling similar organisms (plants, plant-associated microorganisms, and small animals) for which a USDA, APHIS, U.S. Department of the Interior or U. S. Public Health Service permit is required, must first notify the IBC of its research by filing a protocol application, and submit it to the Office of University Research Compliance. This office will coordinate its review by the IBC.

Risk Assessment

A risk assessment is performed in order to assign the appropriate containment level. The responsibility for assessing the risks associated with the use of biohazardous materials or obtaining an initial assessment lies with the investigator. The assessment helps reduce the risk of handling the materials plus provides protection to lab workers and to the environment.

The risk assessment seeks to determine both the probability of particular risks and the consequences if a risk occurs.

The risk assessment is to be performed by the PI before the initiation of each protocol. The Institutional Biosafety Committee (IBC) will confirm during its review that the proposed risk group(s) is appropriate for the proposed protocol. The risk assessment is to be evaluated based on requirements for using recombinant DNA, as well as biological agents and toxins, particularly select agents. The following criteria must be considered when determining risk.

Factors considered in the assessment of risk are:

- Agent Characteristics
    - Pathogenicity
    - Transmissibility and mode of transmission
    - Infectious dose
    - Environmental stability
    - Host range
    - Vectors
    - Recombinants
    - Availability of therapeutic treatments
- Personnel
    - Level of training and experience
    - Health status
    - Ability to wear required PPE
    - Allergies
- Experimental Factors
    - Aerosol generating activities
    - Potential for self-innoculation
    - Concentration and nature of samples
    - Techniques
    - Decontamination procedures
    - Contingency plan
- Environmental
    - Level of containment available vs. required
    - Biosecurity
    - Lab facility conditions
    - Factors affecting containment (i.e. air flow)
    - Availability of emergency support (i.e. eye wash, spill kits)
    - Access by public (i.e. students, visitors)
- Equipment
    - Maintenance
    - Decontamination
    - Training
    - Standard operating procedures
    - Location within lab
    - Equipment specific hazards

Laboratory Security

All laboratories should adopt laboratory security practices to minimize opportunities for unauthorized entry and the unauthorized removal of infectious materials from their facilities. Security requirements for facilities handling infectious agents become more stringent as the risk and biosafety levels increase. Refer to the Security Plans link or contact the Biological Safety Officer at 744-3203 for specific requirements for lab security.

Biological Safety Procedures

Each laboratory should develop or adopt a biosafety or operations manual that identifies the hazards that will or may be encountered, and that specifies practices and procedures designed to minimize or eliminate exposures to these hazards. Personnel should be advised of special hazards and should be required to read and follow the required practices and procedures outlined in the lab specific manuals. The Office of University Research Compliance has organized materials into a user-friendly biological research safety plan that can be utilized as reference along with the IBC Policy. Additionally, investigators are encouraged to consult the CDC's *Biosafety in Microbiological and Biomedical Laboratories* and the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* for supplementary guidance. The following is NOT an all inclusive outline of items that can be included in the lab specific manual:

- Contact and Emergency Contact Information
- Lab specific protocols and SOPs
- Copies of the IBC, IRB, IACUC, RSC, and/or LSC protocols
- Laboratory Inspection Reports
- Emergency Plan – including response to spills and personnel contamination
- Reference Material
    - MSDS sheets for specific agents
    - OSU Biological Research Safety Plan
    - IBC Policy and SOPs

Biosafety Containment Levels

The term "containment" is used to describe safe methods for managing infectious agents and organisms containing recombinant or synthetic nucleic acid molecules in the laboratory environment. The purpose of containment is to reduce or eliminate exposure of laboratory workers, other persons, and the outside environment to potentially hazardous agents. The elements of containment include laboratory practices, containment equipment, and special laboratory design. The risk assessment of the work to be done with a specific agent will determine the appropriate containment level.

*Biosafety in Microbiological and Biomedical Laboratories (*BMBL) 5th Edition describes four levels of general containment in Section IV on pages 41-71. Additionally, this same manual provides guidance on Animal Biosafety Containment levels located Section V on pages 72-114. If the research activities involve recombinant DNA, we recommend that you review the guiding principles outlined for containment levels in the NIH Guidelines. General biocontainment levels are outlined in Appendix G, the animal biocontainment levels are outlined in Appendix Q, and the plant biocontainment levels are outlined in Appendix P. OSU does not allow any research to be conducted at a BSL-4 containment level.

Protocol Application, Submission and Review Process

The OSU Office of University Research Compliance (URC) coordinates the Institutional Biosafety Committee's (IBC) review process and maintains all relevant records. The OSU IBC application forms are available electronically and can be downloaded by visiting the Forms and Permits section of the URC website. Incomplete protocol applications will delay the review process. The IBC meets bi-monthly. The biosafety web pages provide the current schedule of meetings and deadlines for protocol submission. The investigator is responsible for having a current lab inspection report. This report is required before a protocol will be approved. The research activity may not begin until approval is granted by the IBC. Biosafety Office staff is available to answer questions regarding the applications.

Application Submission

What to Submit:

The investigator should complete the appropriate Institutional Biosafety Committee IBC protocol application found on the Forms and Permits link located on the URC website. The application should then be submitted to the Office of University Research Compliance located at 223 Scott Hall. The form can be completed electronically, but a paper copy, complete with signatures and all supporting documentation, is required for processing and IBC review.

1. The application **must** include a project summary, the project goals, and procedures. The following supporting documents should also be included:
    a. safety and security procedures
    b. description of required training
    c. an overall risk assessment that includes:
        i. Identification of all potential hazards, to include such things as excretion by animals, aerosol generation, use of sharps, etc.
        ii. Discussion of engineering controls, safety procedures and personal protective equipment that will be employed to minimize risk for exposure.
        iii. Discussion of accidental spill or exposure procedures specific to your project.
    d. Material Safety Data Sheets (MSDS)

    Note: Remember that federal regulations require that the IBC be composed of persons with a broad diversity of backgrounds. Not all committee members are scientists and

others will not be that knowledgeable about the specific discipline. It is the responsibility of the principal investigator to write the summary in such a way that its technical merit and methodology can be judged by persons with varying disciplinary expertise.

2. The application must have all applicable signatures to be reviewed.

3. All project personnel listed on the application must initial by their names acknowledging their responsibilities in this project.

4. A copy of the most recent lab inspection should be attached.

Application Review

The IBC will review the protocol to determine if the proposed project is in compliance with appropriate policies and regulations. The review will consist of, but not be limited to:

- An overall assessment of the proposed project to determine if any conditions associated with the project would prohibit initiation of the proposed plan.
- An assessment of the containment levels proposed to ensure that the levels are sufficient for the type of activity being conducted.
- An assessment of the facilities, procedures, practices, and training relative to the proposed level of containment.

Besides reviewing the proposal, a physical inspection will be conducted for laboratories, research or teaching facilities, or farms if the inspection report is not current. Biosafety containment level 1 laboratories will be inspected by the BSO/ABSO as a team and approved for a term of 5 years. Biosafety containment level 2 laboratories will be inspected by the BSO/ABSO as a team or in conjunction with IBC members and approved for a term of 3 years. Biosafety containment level 3 laboratories will be inspected annually by the BSO/ABSO with members of the IBC. It is imperative that the investigator and the lab manager be present to answer questions for an inspection regarding a BSL-3 laboratory. In the inspection of a BSL-1 or BSL-2 laboratory, it is only required that either the investigator or a lab manager be present. The BSO, or designee, will certify in writing the findings to the IBC.

The IBC will meet to discuss the review and vote on accepting or rejecting the proposed research. Rejection may be overturned based on satisfactory completion of identified deficiencies. The IBC results will be conveyed to the investigator. The project may not start until the investigator receives a full or provisional approval letter from the IBC through the Office of University Research Compliance.

Types of Review

Types of review (e.g., full Institutional Biosafety Committee or subset of IBC) depend on the specific project. For example, experiments exempt from *NIH Guidelines* may be reviewed by a subcommittee of the IBC and granted full approval. Other protocols involving Risk Group I or Risk Group 2 organisms may be similarly reviewed by a subset of the IBC. Protocols involving

non-exempt recombinant or synthetic nucleic acid molecules or involving the use of any Risk Group 3 or higher organisms will require review by the full IBC. Approvals for exempt recombinant or synthetic nucleic acid and BSL-1 protocols will not exceed five years. All other protocols will be approved on a three years basis. All investigators and instructors will complete an annual protocol review questionnaire conducted by the Office of University Research Compliance.

Protocol Modification

If an approved protocol is modified in any way, a Protocol Modification Request form must be submitted to the IBC reporting any variance from the originally approved protocol. Changes in research facilities, personnel, as well as any significant modification to methods or biological materials subsequent to initial approval of protocol must be reported to the IBC. The Biosafety Officer, on behalf of the IBC, will review the proposed changes to determine whether the changes alter the risk and/or biosafety level assessment, which would require subsequent review by the IBC. If no change in risk, biosafety level, or containment level is noted, the Biosafety Officer (BSO) will grant approval of the modification.

Renewal of Protocol

Protocols that are classified at BSL-2 or BSL-3 are subject to renewal every three years either through the annual protocol review or through the use of the modification form. Protocols that are classified as exempt recombinant or synthetic nucleic acid or BSL-1 research are subject to renewal every five years. Research involving select agents is subject to review and approval each year. Investigators and instructors will be notified of the protocol expiration date at the time the project is approved. It is the investigator's responsibility to ensure a protocol is current.

Termination of a Protocol

If a project is terminated or concluded, the Institutional Biosafety Committee (IBC) requests that the investigator notify the Office of University Research Compliance. This action will allow the protocol to be assigned to a non-active file. If the investigator leaves the University, he/she should notify the Office of University Research Compliance. All correspondence relating to termination of a protocol should be sent in writing or electronically.

An investigator or instructor who willfully or negligently violates Federal or State regulations or Oklahoma State University policies regarding the use of biohazardous materials, including recombinant or synthetic nucleic acid molecules, may have his/her IBC approval suspended or terminated by the IBC. The IBC has the authority to perform an inquiry prior to making a final decision regarding suspension or termination of the activities.