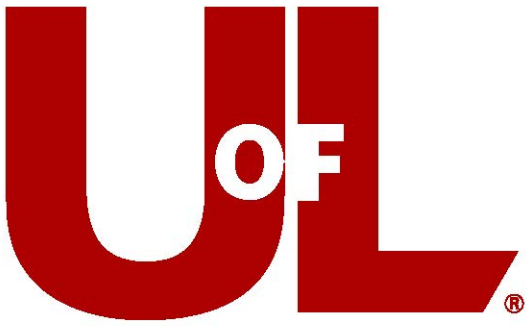

Institutional Biosafety Committee Procedures

Approved by IBC on 9/1/2021
Reviewed by EVPRI on 4/22/2021

Institutional Biosafety Committee Procedures

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Regulations and Guidelines for Research Involving Hazardous Biological Materials

Compliance

Research involving recombinant and synthetic nucleic acids (r/s NA) and other hazardous biological materials that may pose safety, health or environmental risk to animals, humans or plants must comply with the federal, state, and local regulation and guidelines such as the National Institute of Health's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), the Occupational Safety & Health Administration's General Duty Clause and Bloodborne Pathogen Standard as published in the Federal Register.

Applicability

NIH Guidelines

The NIH guidelines are applicable to all recombinant and synthetic nucleic acid (r/s NA) research within the United States or its territories, which is conducted at or sponsored by an institution that receives any support for r/s NA research from the NIH.

Any individual receiving support for research involving r/s NA must be associated with or sponsored by an institution that can and does assume the responsibilities assigned in the NIH Guidelines. The safe conduct of experiments involving r/s NA depends on the individual conducting such activities.

Bloodborne Pathogen Standard

The Bloodborne Pathogen Standard (29 CFR 1910.1030) applies to all occupational exposure to blood or other potentially infectious materials found in body fluids and tissue/organ culture

Responsibility

It is the responsibility of University of Louisville (U of L) through its Institutional Biosafety Committee (IBC) and all personnel to adhere to applicable federal, state and local laws, regulations, and guidelines when performing research involving hazardous biological materials as well as to ensure best work practices to furnish a research environment which controls recognized hazards that are causing or are likely to cause death or serious harm to employees and the environment at large.

Definition: hazardous biological materials

U of L considers the following agents hazardous biological materials:

- Risk Group 2 and Risk Group 3 organisms
- Synthetic and recombinant nucleic acid as defined by the NIH Guidelines
- Use of transgenic plants such as Arabidopsis lines created by

T-DNA insertion
- Select agents and toxins (as defined in 7 CFR Part 331, 9CFR Part 121, and 42 CFR Part 73)
- Other biological materials such as microorganisms, plants or animals with a recognized potential for significant detrimental impact on local managed or natural ecosystems
- Biological toxins
- Prions

- Materials of human or primate origin
- Established human cell lines
- Materials that could be considered Dual Use Research of Concern

Regulations and guidelines

IBC procedures are based upon the following regulations and guidelines:

Publication	Description
Research Involving Recombinant and synthetic NA Molecules - NIH Guidelines	This document: • Provides guidelines for constructing and handling: – r/s NA molecules – Organisms containing r/s NA molecules • Requires that each institution establish an IBC with the authority to approve proposed r/s NA research using NIH Guidelines as a minimum standard
Biosafety in Microbiological and Biomedical Laboratories (BMBL) – published by the Centers for Disease Control and Prevention (CDC) and NIH	This document: • Contains guidelines for: – Microbiological practices – Safety equipment – Facilities • Constitutes the four established biosafety levels • Generally, is considered the standard for biosafety

Arthropod Containment Guidelines published by American Society of Tropical Medicine and Hygiene/American Committee of Medical Entomology	This document: • Contains guidelines for: – Handling practices – Safety equipment – Facilities • Constitutes four Arthropod Containment levels Generally, is considered the standard for work with a variety of uninfected arthropods and those carrying infectious agents, and for work with transgenic vector arthropods in laboratory settings.
A *Practical* Guide to Containment: Greenhouse Research with Transgenic Plants and Microbes	This document provides guidelines for constructing and handling genetically modified: • Plants • Plant-associated organisms such as viruses, bacteria, fungi, protozoa, nematodes, insects, mites, and others
U of L Biosafety Manual	This document provides practical guidance on biosafety techniques for use in U of L laboratories at all levels. The U of L Biosafety Manual must be readily available to employees and employee representatives through their principal investigator, supervisor or departmental office. This document is available on the Biological Safety website.

Types of Activities that Require IBC Approval

Types

For purposes of the U of L IBC**,** research involving hazardous biological materials includes the following types of research:

Lab/benchtop	Lab/benchtop use in experiments involving biological materials hazardous to human or with a recognized potential for significant detrimental impact on local managed or natural ecosystems such as: • Recombinant or synthetic nucleic acids • Toxins • Prions • Viruses • Bacteria • Fungi • Protozoans • Primary cells, cell lines
Animals	Animals used in experiments such as: • Whole animals in which the animal's genome has been altered by stable introduction of recombinant or synthetic nucleic acid into the germ-line (transgenic animals) or somatic cells and CRISPR/Cas technology. • Viable wild-type or genetically-modified microorganisms tested on whole animals • Viable wild-type or genetically-modified arthropods tested on whole animals • Animals with a recognized potential for significant detrimental impact on local managed or natural ecosystems • Cells (primary and cultured) tested on whole animals • Toxins tested on whole animals • Prions tested on whole animals
Plants	Plants used in experiments such as: • Experiments to genetically engineer plants

	• Use of genetically engineered plants for other experimental purposes (e.g. response to stress) • Propagating such genetically engineered plants • Use of genetically engineered plants together with wild-type or genetically modified microorganisms or animals • Plant pathogens tested on whole plants • Infectious agents tested on whole plants • Plants with a recognized potential for significant detrimental impact on local managed or natural ecosystems
Human subject research	Humans participating in clinical trials involving human gene transfer which is defined as: Deliberate in vivo or ex vivo transfer of r/s NA, or r/s NA or RNA derived from r/s NA, or viable r/s NA-modified microorganisms into human research participants.

Location

U of L personnel are required to seek U of L IBC approval for research involving hazardous biological materials in any U of L or non-U of L location. The following are requirements of U of L personnel when work is conducted at various locations:

Location	Requirements
Affiliate institutions	Contact the U of L IBC office to find out if U of L provides the services of its IBC for research using biological hazardous materials conducted under the direction of U of L investigators at affiliate institutions.
Unaffiliated institutions	Research using biological hazardous materials conducted under the direction of U of L investigators at unaffiliated institutions needs review and approval of the U of L IBC and the IBC of the unaffiliated institution. To comply with the requirements of that institution, contact the unaffiliated institution's research office/research compliance office.

Principal Investigator Responsibilities

Primary

The Principal Investigator (PI) has the following primary responsibilities:

- To submit the initial registration and any subsequent changes to the use of hazardous biological materials in a research study prior to initiation of research or changes
- To safely use hazardous biological materials in her/his laboratory

Additional

The table below describes additional PI responsibilities:

Type	Responsibilities
Procedures	• Review the applicable guidelines/regulations and become familiar with the safety procedures and requirements • Perform an initial risk assessment of the hazardous biological material(s) to determine the appropriate biosafety containment level and safety practices • Follow institutional policy and procedure in the procurement of hazardous biological materials • Develop laboratory safety procedures to minimize the risk of exposure specific to the laboratories or registration • Require adherence to good laboratory work practices • If animals are used, ensure: – Appropriate Special Animal Safety Protocols (SASPs) are completed and current – Ensures that appropriate hazard signage is posted on cage level and room level • If involved with Human Gene Transfer (HGT), ensure that research cannot be initiated until Institutional Biosafety Committee and all other applicable institutional and regulatory authorization(s) and approvals have been

	obtained.
Safety	• If needed, consult with the Campus Health Services on appropriate medical surveillance for the work to be performed • Consult with the Department of Environmental Health and Safety (DEHS) on the appropriate biosafety level for the work to be performed • Request consultation with the IBC, if needed, to assist with planning of project safety and occupational health • Ensure that all persons entering the facility are advised of the potential hazards, are instructed on the appropriate safeguards, and read and follow instructions on practices and procedures • Ensure the availability of medical surveillance services to all laboratory personnel if required by risk assessment • Maintain inventories of all hazardous biological agents used in the laboratory • Provide for safe transportation of hazardous biological agents in accordance with transport/shipping regulations • Ensure that waste is properly prepared for disposal
Reporting	• Immediately report significant problems and safety issues according to IBC procedures. See Significant Problems, Spills, Accidents and Safety Reporting. • Incident reports should include sufficient information to allow for an understanding of the nature and consequences of the incident, as well as its root cause.
Training	• Be adequately trained in good microbiological practices and laboratory techniques as described in the BMBL • Personally train or arrange for the training of all employees and students who are directly or indirectly involved in experiments using hazardous biological materials before the personnel begin experiments using these agents. At a minimum, these instructions include

	training in aseptic techniques and in the biology of the organisms used in the experiments so that the potential biohazards are known and understood. • If animals are used - personally train or arrange for the training of research personnel, veterinary staff and animal husbandry staff working with these animals regarding specific safety techniques and work practices to be used so that the potential biohazards are known and understood • Inform research staff of the reasons and provisions for any precautionary medical practices advised or requested • Make available to all research staff, including veterinary and animal husbandry staff, and nursing and pharmacy staff who may be involved in human gene transfer studies, the registrations that describe the potential biohazards and precautions to be taken such as: – Hazards and risks – Immunizations – Personal protective equipment required – Decontamination – Storage and disposal – Spill procedures – Dealing with accidents • Provide adequate personal protective equipment and instruction on its proper use

Research Staff Responsibilities

Date of Last Revision/Review:

Laboratory personnel

Laboratory personnel have the following responsibilities:

- Ensure that:
  - All known biological hazards are appropriately identified and mitigated
  - Labels on materials and equipment in the laboratory are current and accurate
  - Individuals are knowledgeable of decontamination and emergency procedures
- All required training is completed.
- Segregate and collect laboratory wastes in accordance with applicable regulations (local, state and federal). Maintain records per regulatory requirements.
- Consult with DEHS for guidance regarding best safety practices.
- Immediately report significant problems and safety issues according to IBC procedures. See Significant Problems, Spills, Accidents and Safety Reporting.
- Incident reports should include sufficient information to allow an understanding of the nature and consequences of the incident, as well as its cause. See IBC Incident Reporting Template and Adverse Event Template.

Institutional Biosafety Committee Roles and Responsibilities

Authority granted to the IBC

The U of L Institutional Biosafety Committee (IBC) is responsible for oversight of University research and teaching activities that involves hazardous biological materials, to ensure these materials are received, used, stored, transferred and disposed of in accordance with applicable laws and regulations and to provide appropriate safeguards for human health and the environment.

The IBC reviews and approves all activity involving hazardous biological materials unless otherwise exempted under federal regulations.

This authority applies to activities and/or research involving hazardous biological materials that are any of the following:

- Sponsored by U of L
- Conducted by U of L faculty members
- Conducted using U of L property or facilities
- Stored at any U of L facilities

The IBC procedures apply to all faculty, staff, students, visitors, and agents and their employees engaged in activities and/or research involving hazardous biological materials.

Institutional official

The Institutional Official (Executive Vice President of Research and Innovation) has the responsibility for establishing and maintaining the IBC bylaws and policies that provide for the safe conduct of hazardous biological materials research and that ensure compliance with the NIH Guidelines. The Institutional Official may delegate the day-to-day responsibility for the review and oversight activities as s/he deems appropriate.

To this end, the Institutional Official ensures that sufficient resources, including meeting space and staff, are provided to support the IBC's review and responsibilities.

Chair

The IBC Chair is appointed according to the IBC bylaws. The Chair shall be an experienced scientific investigator with respect to research involving hazardous biological materials.

The Chair conducts each meeting in an orderly manner as follows:

- Chairs the IBC meetings
- Conducts business so that each proposal is fairly and completely reviewed

- Sees that the IBC reaches a decision on the disposition of each proposal
- Ensures that these decisions are communicated to the individuals who submitted the proposal
- Acts as liaison between the academic community and the IBC
- Designates an IBC member to serve as interim Chair in the Chair's absence

The IBC Chair has these duties:

- Ensures that members are adequately trained to fulfill their responsibilities
- Reviews IBC policies and procedures periodically to confirm current compliance with the federal, state, and local laws and regulations
- Works in collaboration with the BSO to establish and implement IBC procedures and practices

The IBC Chair may be removed by the Institutional Official for failure to fulfill the duties listed above or:

- For failure to perform the duties of an IBC member, including failure to attend at least 80% of the IBC meetings held within any 12-month period
- For conflict of interest or conduct that obstructs or otherwise impedes review of research by the IBC.

Biosafety officer

The NIH Guidelines require a Biological Safety Officer (BSO) when the institution:

- Conducts recombinant DNA research at Biosafety Level (BSL) 3 or BSL 4
- Engages in large-scale research

The BSO has the following authority and responsibilities:

- Serves as a reviewing member of the IBC
- Conducts initial and periodic inspections of laboratories and of facilities where research is done using hazardous biological materials
- Reports results of these inspections to the IBC
- Provides:
    - Advice on laboratory security
    - Technical advice to Principal Investigators and the IBC on research safety procedures
- Develops template emergency plans for handling accidental spills and personnel contamination for review and approval of the IBC for each r/s NA registration invoking such plans
- Reports to the IBC and the institution any of the following that have not already been reported by the Principal Investigator:

- Significant problems
- Violations of the NIH Guidelines
- Significant research-related accidents or illnesses

Note - Reports according to the IBC procedures: Significant Problems, Spills, Accidents and Safety Reporting, and Handling Significant or Continuing Non-Compliance as applicable

Membership

The Institutional Biosafety Committee (IBC) is appointed by the Executive Vice President for Research and Innovation (EVPRI) in consultation with or at the request of the IBC chair and BSO to ensure membership composition requirements are met. The committee shall be made up of at least eight members with expertise in:

- Synthetic and recombinant nucleic acid technology
- Assessment of the safety of research using r/s NA and other biological hazardous agents
- Identification of any potential risk to public health or the environment

Individuals on the committee include:

- Faculty and staff (at least five of which must be faculty)
- At least one individual with expertise in plant, plant pathogen, or plant pest containment principles when experiments utilizing Appendix L of the NIH Guidelines
- At least one scientist with expertise in animal containment principles when experiments utilizing Appendix M of the NIH Guidelines
- At least one individual with adequate expertise and training when participating in or sponsoring recombinant or synthetic nucleic acid molecule research involving human research participants
- BSO
- At least two members from the local community not otherwise affiliated with U of L
- Any others invited to serve when their expertise is required
- *Ex officio* members shall include representatives from the following offices:
    - Chair or designate of the University of Louisville IACUC and IRB
    - DEHS director or designate
    - Director of the Comparative Medicine Research Unit or designate

The term of membership on the committee is 3 year, which may be renewable for additional three-year terms.

Committee responsibilities

The IBC is charged with the following responsibilities which are further delineated in the relevant sections of this manual:

Type	Description
Registrations	• Review research that uses hazardous biological agents and is conducted at or sponsored by U of L for compliance with the NIH Guidelines and other applicable laws and regulations as well as best practices. This review includes at a minimum: o Independent assessment and assignment of the containment levels for the proposed research. o Assessment of the facilities, procedures, practices, and training and expertise of personnel involved in research to assure appropriate safety. o For human gene transfer: – No research shall be initiated until Institutional Biosafety Committee approval has been obtained and all other applicable institutional and regulatory authorization(s) and approvals have been obtained; – Assessment focused on biosafety issues (e.g., administration, shedding); – Oversight may conclude after the last participant is administered the final dose of product or the IBC may choose to establish other end points for oversight, based on their biosafety assessment of the proposed research. • The regular IBC member may provide his/her review without being present at the fully convened IBC meeting. • Set containment levels and modify containment levels for ongoing experiments. • Periodically re-review of ongoing research

	using hazardous biological materials conducted at the institution to ensure compliance with the NIH Guidelines and other applicable laws and regulation. • Notify the principal investigator of IBC review and approval.
Inspections	• Periodic inspections of laboratories where research using hazardous biological materials is performed to ensure that the laboratory standards as described in the NIH Guidelines and the BMBL are rigorously followed • Individual(s) performing inspections must have at least the following expertise: – Biological safety techniques and practices – Containment practices – Familiarity with BMBL and Appendices G, K, L, and N of the NIH Guidelines
Reports	• Reports according to the IBC procedures, see Significant Problems, Spills, Accidents and Safety Reporting: – Substantial problems – Violations of the NIH Guidelines – Significant research-related accidents or illnesses • Reviews all accident reports for: – Instances of deviations from safety rules and security regulations – Violations of NIH requirements – Determination of the course of corrective action(s) to be taken • Receives and reviews periodic reports on: – Laboratory Assessment – Other biosafety matters
Plans	• Adopting emergency plans for handling: – Accidental spills – Personal contamination resulting from research using hazardous biological agents • Oversees the development and maintenance of written biological safety/infectious disease control plans: – Makes the plans available to the

	institutional community – Recommends updates to the plan as needed • Oversees the development of educational programs related to safety when working with hazardous biological materials
Seeks consultation	• May consult with the University Counsel to address issues pertaining to institutional policies, applicable laws, and standards of conduct and practice • Invites consultants knowledgeable in community attitudes and the environment to its meetings as necessary to assist in any review, but such consultants shall not vote
Meetings	• Conducts IBC meetings on a regular basis

List of members Contact the BSO for names of IBC Committee members and contact information.

Support Staff Organizational Structure

Introduction

This topic describes the organizational structure of the IBC support staff.

Reporting lines and supervision

The reporting lines and supervision for the IBC organization follow:

- The IBC Administrator reports to the Biosafety Officer
- The IBC Administrator takes direction from the IBC Chair regarding hazardous biological materials research issues

Staff training and development

This table lists the initial requirements for the training and professional development of the IBC staff:

Position	Requirement
IBC administrator	• Must complete the Biosafety Office on-the-job training • Are expected to attend if funding is available: – National or regional IBC conferences on a periodic basis – Continuing education opportunities at the U of L or neighboring institutions

Responsibilities of the IBC Administrator and Staff

Introduction This topic discusses the responsibilities of those persons who support the IBC members.

Requirement The IBC Administrator is responsible for ensuring that IBC functions are in compliance with all relevant regulatory requirements.

Responsibilities This table lists the responsibilities by area of responsibility:

Area	Responsibilities
Initial review	Conducting a limited pre-review of incoming applications to ensure completeness and as otherwise directed by the IBC
Before meetings	• Assisting new IBC members in completing orientation procedures and meeting required education standards • Scheduling IBC meetings • Distributing pre-meeting materials with sufficient time to allow IBC members an opportunity to review them in preparation for the meeting • Tracking the progress of each research registration submitted to the IBC
Communication	• Serving as a resource for investigators on general regulatory information and providing guidance about forms, submission procedures, and general research related issues • Facilitating communication between investigators and the IBC • Drafting reports and correspondence to research investigators on behalf of the IBC or IBC Chair regarding: – The status of the research – Including conditions for initial or continuing approval of research and responses to reports of adverse events or unanticipated problems – Research related accidents or illnesses • Assisting in evaluation, audit, and monitoring

	of hazardous biological material research as directed by the Biosafety Officer, IBC and/or other institutional officials
Records	• Maintaining the official roster of IBC members • Compiling the minutes of IBC meetings in compliance with regulatory requirements • Securely and properly archiving all IBC records • Maintaining all IBC documentation and records in accordance with regulatory requirements

Record Requirements

Introduction

This topic discusses the requirements for records to maintain the IBC reviews.

Document flow procedures

The IBC Administrator is responsible for developing and implementing procedures for efficient document flow.

Findings and determinations

IBC records include documentation of all IBC findings and determinations.

IBC records defined

At a minimum, IBC records must include all information:

- Required under the NIH Guidelines
- Recommended by official (written) National Institutes of Health Office of Science Policy (OSP) guidance

File organization

IBC files are organized such that the following information may be readily accessed:

File	Contents
General	• Written IBC operating procedures • Research (registration) tracking system • IBC membership roster • IBC research application (registration) files
Review results	Documentation of: • Exemptions from NIH Guidelines • Biosafety Office reviews • IBC findings and review
After review documentation	• Documentation of convened IBC meetings – minutes • All correspondence to and from the IBC • Adverse event reports • Significant problems with or violations of the NIH Guidelines • Any significant research-related accidents or illnesses

IBC membership rosters

IBC membership rosters include at least the following information:

- Names of IBC members
- Earned degrees and specialties of each member, if applicable
- The representative capacity of each member or *ad hoc* member as:
    - Scientist or non-scientist, affiliated or non-affiliated
- CV, Resume, or biosketch
- Any employment or other relationship with the university or its components

Changes

Any changes in IBC membership are reported as required by applicable OSP guidance.

Voting and Non-Voting Members

Voting members include: IBC Chair, IBC Vice-Chair(s), BSO, and appointed Members.

Non-voting members include: *Ex officio* members (i.e. consultants such as compliance personnel) and *ad hoc* members.

File Requirements

Introduction

This topic discusses the files required to support the IBC reviews.

IBC research application (registration) files

The IBC maintains a separate file for each research application (registration) that it receives for review.

Retention

Such files are kept for a period no less than three years after closure.

File contents

Each IBC research application (registration) file contains at least the following materials:

Classification	Materials
IBC approval review	• The IBC Research Application (Registration) • Documentation of type of IBC review • For human gene transfer applications: – Investigator brochure or full protocol, if sponsored trial
Changes	• Applications for registration amendments or modifications • Continuing review progress reports and related information
Special challenges	• Reports of significant events and injuries • Reports of injuries to subjects and adverse events related to an IBC registration occurring within the University or its components (or involving its employees or agents) and reported to any regulatory agency • Reports of external adverse events and safety reports received from sponsors or cooperative groups
Continuing review and monitoring	• All IBC correspondence to and from research investigators, government agencies, or sponsors • All other IBC correspondence related to the research • Documentation of all IBC review and approval actions, including initial and continuing convened (full) or Biosafety Office review of research

	• Documentation of type of IBC review
Upon completion	• Documentation of registration closeout

Materials for Submission and Review

Forms

All forms for use in this procedure may be accessed on-line on the IBC website.

Submission deadlines can be obtained from the IBC website. The table below indicates the application types:

Type	Procedure
Initial Review	• Principal Investigators must complete and submit the appropriate form in iRIS to request authorization for experimentation involving hazardous biological agents to the IBC • Important: Human Gene Transfer requires additional document submissions of: – Investigator brochure and the full protocol
Amendment	The U of L defines an amendment to be any change to an approved registration regardless of how minor. • Investigators must seek the approval of IBC before changing the conduct of the study, since these modifications may change the risk to human health or the environment
Continuing Review	After one, three, or five years, the entire application must be resubmitted and reviewed by the committee.
Problem/Safety Report	Spills, accidents, non-compliance and other problems must be reported according to IBC Incident Reporting Template.
HGT Serious Adverse Event Reporting	Serious adverse events, illnesses and safety reports that may be associated with the use of the gene transfer product in human gene transfer must be reported to the IBC
Closure Report	Principal Investigators must notify the IBC and DEHS of intentions to close an IBC approved research activity when: • A principal investigator commits to departure from U of L • A project is completed

	• The project is no longer active • Proper disposal of the hazardous biological material has occurred • When the Principal Investigator is no longer in possession of the material

Proprietary information

The Principal Investigator must notify the IBC and the Office of Technology Transfer of any proprietary information within the registration as soon as possible, including:

- New and/or novel ideas
- Information specified as proprietary in any written contract or agreement
- New commercial uses of a process, device, or chemical
- Potentially patentable items

Questions related to proprietary information should be directed to the Office of Technology Transfer.

Risk Assessment

How is risk determined?

Determining the risk group (RG) classification and assessing risk factors are both component in assigning an appropriate biosafety level (BSL) to a research project.

PI responsibilities

It is the Principal Investigator's responsibility to:

- Use NIH Guidelines, Appendix B (Classification of Human Etiologic Agents on the Basis of Hazard), BMBL or other available sources to assess risk level
- Prior to initiating research involving hazardous biological materials, conduct a risk assessment to determine the appropriate level of:
  – Perceived risk
  – Biological and physical containment level
- Contact the DEHS for more information on classifications of:
  – Risk group
  – Biosafety level

Risk group classification

The Principal Investigator determines the risk group (RG) classification of an agent to prevent or reduce the risk of laboratory-associated infections.

The table below lists the risk group number and the likelihood that an agent will harm, injure, or cause disease in humans:

Risk Group #	Agents are...
RG-1	Not associated with disease in healthy adult humans
RG-2	Associated with human disease which is rarely serious Preventive or therapeutic interventions are often available
RG-3	Associated with serious or lethal human disease Preventive or therapeutic interventions may be available
RG-4	Likely to cause serious or lethal human disease Preventive or therapeutic interventions are not usually available

Risk factors The Principal Investigator considers the following biohazard risk factors when assessing risk to determine the level of containment needed:

Biohazard Factors	Description
Pathogenicity	Consideration should include: • Disease incidence • Severity
Route of transmission	Examples: parenteral, airborne, by ingestion Strongly consider the potential for aerosol transmission when planning to work with: • A relatively uncharacterized agent • Uncertain mode of transmission
Agent stability	Consider factors such as: • Desiccation • Exposure to: – Sunlight – Ultraviolet light – Chemical disinfectants
Infectious dose 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 • Activity planned Examples: • Solid Tissue • Viscous blood or sputum • Liquid medium

Origin	Consider factors such as: • Geographic location • Host • Nature of the source
Availability of animal studies	This information may be useful in the absence of human data
Availability of immunization, vaccine, or treatment	The unavailability of immunization, vaccine or treatment may impact the risk involved in the use of biohazardous materials
Gene product effects	Consider the following: • Toxicity • Physiological activity • Allergenicity
Special consideration should be used in the evaluation of containment levels and conditions of experiments that: • Involve transgenic animals • Are likely to enhance pathogenicity • Extend the host range or viral vectors under conditions that permit a productive infection Note: Upon review, the IBC may require an increased containment/safety level.	

Biosafety levels

The determination of the risk group and risk factors are used to set the appropriate biosafety level (BSL).

The biosafety level describes the degree of physical containment required to:

- Confine biohazardous materials
- Reduce the potential for exposure to:
    - Laboratory workers
    - Persons outside the lab
    - The environment

The table below describes the biosafety containment levels (from BMBL, 6th ed.):

BSL	Agents are …	Practices	Primary Barrier and PPE	Facilities (secondary Barrier)
1	Well-characterized agents not known to consistently cause disease in immunocompetent adult humans and present minimal potential hazard to laboratory personnel and the environment.	Standard microbiological practices	No primary barriers required; protective laboratory clothing; protective face, eyewear, as needed	Laboratory doors; sink for handwashing; laboratory bench; windows fitted with screens; lighting adequate for all activities
2	Agents associated with human disease and pose moderate hazards to personnel and the environment	Limited access; occupational medical services including medical evaluation, surveillance, and treatment, as appropriate; all procedures that may generate an aerosol or splash conducted in a BSC; decontamination process needed for laboratory equipment	BSCs or other primary containment device used for manipulations of agents that may cause splashes or aerosols; protective laboratory clothing; other PPE, including respiratory protection, as needed	Self-closing doors; sink located near exit; windows sealed or fitted with screens; autoclave available
3	Indigenous or exotic agents; may cause serious or potentially lethal disease through the inhalation route of exposure	Access limited to those with need to enter; viable material removed from laboratory in primary and secondary containers; opened only in BSL-3 or	BSCs for all procedures with viable agents; solid front gowns, scrubs, or coveralls; two pairs of gloves, when appropriate; protective eyewear, respiratory	Physical separation from access corridors; access through two consecutive self-closing doors; hands-free sink near exit; windows are sealed;

		ABSL-3 laboratories; all procedures with infectious materials performed in a BSC	protection, as needed	ducted air ventilation system with negative airflow into laboratory; autoclave available, preferably in laboratory
4	Dangerous and exotic agents that pose high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that are frequently fatal, for which there are no vaccines or treatments; and related agents with unknown risk of transmission Important **U of L:** • **Does not have any laboratories certified for BSL-4** • **Does not allow possession or use of biohazardous materials requiring this level**	Not permitted at UofL	Not permitted at UofL	Not permitted at UofL

Final BSL determination

The biosafety level may be:

- Equivalent to the risk group (RG) classification of the agent
- Raised or lowered based on the evaluation of risk factors

The IBC:

- Makes the final determination of the appropriate biosafety level
- Answers any questions regarding the risk assessment or appropriate containment level

Animal biosafety levels

The animal facility director establishes policies and procedures for emergency situations. Animal protocols describing research involving hazardous biological agents are subject to approval by the IACUC and IBC and any special practices must be approved by each committee.

Below is a summary of animal biosafety levels (ABSL) for protocols using vertebrate animals:
More detailed information is available in the BMBL.

Animal Biosafety Level	Agents are...	Practices	Primary Barriers and PPE	Facilities (Secondary Barriers)
ABSL-1	Not known to cause disease in healthy human adults	Standard animal care and management practices, including appropriate medical surveillance programs	As required for normal care of each species	Standard animal facility: • Non-recirculation of exhaust air • Directional air flow recommended
ABSL-2	Associated with human disease Hazard: • Percutaneous exposure • Ingestion • Mucous membrane exposure	ABSL-1 practices plus: • Limited access • Biohazard warning signs • Sharps precautions • Biosafety manual • Decontamination of all infectious wastes and of animal cages prior to washing	ABSL-1 equipment plus: • Primary barriers • Containment equipment appropriate for animal species PPEs: • Laboratory coats • Gloves • Face and respiratory protection as needed	ABSL-1 facility plus: • Autoclave available • Handwashing sink available in the animal room
ABSL-3	Indigenous or exotic agents with potential for aerosol transmission; disease may have serious health effects	ABSL-2 practices plus: • Controlled access • Decontamination of clothing before laundering • Cages decontaminated before bedding removed • Disinfectant foot bath as needed	ABSL-2 equipment plus: • Containment equipment for housing animals and cage dumping activities • Class I or II BSCs available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols	ABSL-2 facility plus: • Physical separation from access corridors • Self-closing, double door access • Sealed penetrations • Sealed windows • Autoclave available in facility

			• PPEs:Appropriate respiratory protection	
ABSL-4	• Dangerous or exotic agents which pose high risk of life- threatening disease or aerosol transmission Related agents with unknown risk of transmission **U of L:** • **Does not have any laboratories certified for ABSL-4** • **Does not allow possession or use of biohazardous materials requiring this level**	• Not permitted at UofL	Not permitted at UofL	Not permitted at UofL

Plant biosafety levels

The table below describes plant biosafety containment levels (from "A Practical Guide to Containment / Plant Biosafety in Research Greenhouses" and NIH Guidelines):

Biosafety Level	Agents are ….	Practices	Primary Barriers and PPE
BL-1P	• Transgenic plants in which there is no evidence that the modified organism would be able to survive and spread in the environment and, if accidentally released, would pose no environmental risk • Sterile plants or those rendered non-propagative • DNA-modified common	• Access to the greenhouse shall be limited or restricted, at the discretion of the Greenhouse Director, when experiments are in progress • A record shall be kept of experiments currently in progress in the greenhouse facility. • Experimental organisms shall be	• The term "greenhouse" refers to a structure with walls, a roof, and a floor designed and used principally for growing plants in a controlled and protected environment • The greenhouse floor may be composed of gravel or other porous material. At a minimum, impervious (e.g., concrete)

	microorganisms, arthropods, or small associated with plants that cannot spread rapidly and are not known to have any negative effects on plants in either natural or managed ecosystems	rendered biologically inactive by appropriate methods before disposal outside of the greenhouse facility • A program shall be implemented to control undesired species (e.g., weed, rodent, or arthropod pests and pathogens), by methods appropriate to the organisms • Arthropods and other motile macro-organisms shall be housed in appropriate cages. If macro-organisms (e.g., flying arthropods or nematodes) are released within the greenhouse, precautions shall be taken to minimize escape from the greenhouse facility.	walkways are recommended • Windows and other openings in the walls and roof of the greenhouse facility may be open for ventilation as needed for proper operation and do not require any special barrier to contain or exclude pollen, microorganisms, or small flying animals (e.g., arthropods and birds); however, screens are recommended.
BL-2P	• Transgenic plants and associated organisms, which, if released outside the greenhouse, could be viable in the surrounding environment but would have a negligible impact or could be readily managed • Entire genome of an indigenous infectious agent or pathogen potentially harmful to the environment but manageable, or are exotic but have no potential for causing serious harm to managed or natural ecosystems • Plant-associated transgenic insects or small animals if they pose no threat to managed or natural ecosystems	BL-1P plus these additional practices: • Access to the greenhouse is limited or restricted to individuals directly involved with the experiments when they are in progress • Personnel shall be required to read and follow instructions on BL2P practices and procedures. All procedures shall be conducted in accordance with accepted greenhouse practices that are appropriate to the experimental organisms • A greenhouse practices manual shall be prepared or adopted • A record shall be kept of experimental plants, microorganisms, or small animals that are brought into or removed from the greenhouse facility	• Greenhouse floor must be composed of an impervious material. Concrete is recommended, but gravel or other porous material under benches is acceptable unless propagules of experimental organisms are readily disseminated through soil. Soil beds are acceptable unless propagules of experimental organisms are readily disseminated through soil • If part of the greenhouse is composed of gravel or similar material, appropriate treatments should be made periodically to eliminate, or render inactive, any organisms potentially entrapped by the gravel • Windows and other openings in the walls and roof of the greenhouse facility may be open

		• A record shall be kept of experimental plants, microorganisms, or small animals that are brought into or removed from the greenhouse facility • An autoclave shall be available for the treatment of contaminated greenhouse materials	for ventilation as needed for proper operation and do not require any special barrier to exclude pollen or microorganisms; however, screens are required to exclude small flying animals (e.g., arthropods and birds) • If intake fans are used, measures shall be taken to minimize the ingress of arthropods. Louvers or fans shall be constructed such that they can only be opened when the fan is in operation • BL2-P greenhouse containment requirements may be satisfied by using a growth chamber or growth room within a building provided that the external physical structure limits access and escape of microorganisms and macro-organisms in a manner that satisfies the intent of the foregoing clauses
BL-3P	• Transgenic plants, plant pathogens, or other organisms that have a recognized potential for significant detrimental impact on the environment • Plant associated exotic infectious agents capable of causing serious environmental harm • Transgenic plants containing genes from an exotic infectious agent in which a complete functional genome of the infectious agent could possibly be reconstituted • Transgenic plants or organisms that contain genes coding for	BL-2P plus these additional practices • Authorized entry into the greenhouse shall be restricted to individuals who are required for program or support purposes • Prior to entering the greenhouse, personnel shall be required to read and follow instructions on BL3P practices and procedures • All experimental materials shall be sterilized in an autoclave or rendered biologically inactive by appropriate methods before disposal, except those that are to remain in a viable or intact state for experimental purposes;	BLS-2P plus these additional features: • The greenhouse floor shall be composed of concrete or other impervious material with provision for collection and decontamination of liquid run-off. • Windows must be closed and sealed. All glazing shall be resistant to breakage (e.g., double-pane tempered glass or equivalent). • The greenhouse shall be a closed self-contained structure with a continuous covering that is separated from areas that are open

	vertebrate toxins • Transgenic microbial pathogens of insects or small animals that associate with plants, if the pathogen has the potential to cause harm to the local environment	including water that comes in contact with experimental microorganisms or with material exposed to such microorganisms, and contaminated equipment and supplies • When using arthropods and other motile macro-organisms, experiments shall be conducted within cages designed to contain the motile organisms • Personnel are required to thoroughly wash their hands upon exiting the greenhouse. • All procedures shall be performed carefully to minimize the creation of aerosols and excessive splashing of potting material/soil during watering, transplanting, and all experimental manipulations.	to unrestricted traffic flow. The minimum requirement for greenhouse entry shall be passage through two sets of self-closing locking doors. • The greenhouse facility must be surrounded by a security fence or protected by equivalent security measures. • Internal walls, ceilings, and floors shall be resistant to penetration by liquids and chemicals to facilitate cleaning and decontamination of the area. All penetrations into these structures and surfaces (e.g., plumbing and utilities) must be sealed. • Bench tops and other work surfaces should have seamless surfaces that are impervious to water and resistant to acids, alkalis, organic solvents, and moderate heat. • The greenhouse contains a foot, elbow, or automatically operated sink, which is located near the exit door for handwashing • An autoclave shall be available for decontaminating materials within the greenhouse facility. A double-door autoclave is recommended (not required) for the decontamination of materials passing out of the greenhouse facility. • An individual supply and exhaust air ventilation must be provided. The system maintains pressure differentials and directional airflow, as required, to assure

			inward (or zero) airflow from areas outside of the greenhouse. • The exhaust air from the greenhouse facility must be filtered through high efficiency particulate air-HEPA filters and discharged to the outside. The supply and exhaust airflow shall be interlocked to assure inward (or zero) airflow at all times. • Vacuum lines shall be protected with high efficiency particulate air/HEPA or equivalent filters and liquid disinfectant traps. • Disposable clothing (e.g., solid front or wrap-around gowns, scrub suits, or other appropriate clothing) must be worn in the greenhouse if deemed necessary by the Greenhouse Director because of potential dissemination of the experimental microorganisms. • Protective clothing must be removed before exiting the greenhouse and decontaminated prior to laundering or disposal.
BL-4P (not allowed at UofL)	• Certain exotic, readily transmissible infectious agents that are potentially serious pathogens of major US crops • Human pathogens or vaccines made in plants could, in some cases, cause serious human illness **U of L:** • **Does not have any laboratories certified for BS-4P** • **Does not allow possession or**	Not permitted at UofL	Not permitted at UofL

	use of biohazardous materials requiring this level		

More information

Visit the IBC website or the DEHS website for additional information on handling and disposal recommendations involving:

- Infectious biological agents
- r/s NA
- Toxins

U of L related standards

U of L Biosafety Manual

Approved by IBC on 9/1/2021
Reviewed by EVPRI on 4/22/2021

Initial Review for Exemptions

Introduction	This topic discusses the process used to determine that an activity is exempt from IBC review.
PI's submission	The Principal Investigator may request on the IBC registration form in iRIS that a research activity be considered exempt from IBC review indicating that the activity meets the following criteria for exemption.
Exempt review categories of research	Below are listed the experiments under which an exemption may be determined as set forth by Section III-F of the NIH Guidelines. The following r/s NA molecules are exempt from the NIH Guidelines (Section III F) but registration with the Institutional Biosafety Committee is required: • Those synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to integrate into DNA, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 Nano grams per kilogram body weight. If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III-C, it is not exempt under this Section. • 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 NA sequence from a single source that exists contemporaneously in nature. • Those that consist entirely of NA 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 after appropriate notice and opportunity for public comment (see Section IV-C-1-b-(1)-(c), Major Actions). See Appendices A-I through A-VI, Exemptions under Section III-

	F-6--Sublists of Natural Exchangers, for a list of natural exchangers that are exempt from the NIH Guidelines. • 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 as determined by the NIH Director following appropriate notice and opportunity for public comment. See NIH Guidelines Appendix C, Exemptions under Section III-F-8 for other classes of experiments which are exempt from the NIH Guidelines.
Who verifies	All exemptions requested for proposed activities using hazardous biological material conducted at the U of L or by its employees or agents must be reviewed to determine if they meet the regulatory criteria for exempt research. Exemption of these research activities must be verified by one of the following: • The IBC Chairperson • The BSO or designee • An experienced current member of the IBC, in consultation with the BSO or IBC Chairperson The determination of whether hazardous biological research activities are exempt from IBC review requires a sophisticated level of expertise and is made by the institution, not by the individual investigators proposing the activities.
Documentation for exemptions	Documentation of the verified exemptions consists of the reviewer's written concurrence in the IBC Research Review File that the activity described in the Investigator's Application for Exempt Research satisfies the conditions of the cited exemption category. The investigator proposing the activities will receive a notification stating the determination.

Designated Review of Research

Introduction	Date of Last Revision/Review: 05/2016 This topic discusses the Biosafety Office path for a review of the research.
IBC review	Under the Biosafety Office review procedure, the Biosafety Officer or other members of the Biosafety Office designated by the Biosafety Officer may: • Review and approve the research on behalf of the IBC • Review and approve the research on behalf of the IBC requiring modifications (to secure approval) • Request additional information • Forward the application to the fully convened IBC when, in the opinion of the Biosafety Office reviewer(s), the research does not meet the Biosafety Office review criteria described above in the applicable section
Criteria	Certain categories of research may be reviewed by the IBC using the Biosafety Office review procedure: • Use of RG-1 organisms • Use of human or primate materials • Use of established human cell lines • Minor changes to previously approved research
Definition of minor changes	U of L defines a minor change to be one that makes no substantial alteration in any of the following: • The source(s) or DNA • The nature of the inserted DNA sequences • The host(s) and vector(s) to be used • If an attempt will be made to obtain expression of a foreign gene, and if so, indicate the protein that will be produced • The containment level • The assessment of the facilities, procedures, practices, and training and expertise of personnel involved in hazardous biological agent research • The compliance with all surveillance, data reporting, and adverse event reporting requirements

	• Any other factor that might warrant full committee review
Documentation	Documentation for Biosafety Office reviews is maintained in IBC records and includes the circumstances that justify using Biosafety Office review procedures.
Reporting	The IBC staff keeps all IBC members advised of research that has been approved under Biosafety Office procedures.

Criteria for Full Board Review of Research

Criteria for full board review	The following hazardous biological material research requires review and approval at a convened meeting of the majority of the IBC members: • The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally • The deliberate formation of r/s NA containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD_{50} of less than 100 Nano grams per kilogram body weight (e.g., microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin, and *Shigella dysenteriae* neurotoxin) • The deliberate transfer of r/s NA, or DNA or RNA derived from r/s NA, into human research participants) • Experiments using Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents as host-vector system or experiments in which DNA from Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems • 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 • Experiments involving whole animals or plants and r/s NA, or DNA or RNA derived from r/s NA • Experiments involving more than 10 Liters of culture of r/s NA, or DNA or RNA derived from r/s NA • Experiments involving the formation of r/s NA molecules containing more than two-thirds of the genome of any eukaryotic virus • Experiments involving Risk Group 2 or Risk Group 3 organisms • Experiments involving Select Agents or Toxins • Experiments involving biological toxins • Experiments involving biological materials such as microorganisms, plant or animals with a recognized potential for significant detrimental impact on local managed or natural ecosystems

IBC Meeting Rules of Conduct

Meeting Frequency	Meetings are held regularly with a minimum of 4 per year, see Meeting Dates.
Ad hoc	The IBC Chair may call an *ad hoc* meeting of the IBC as necessary to address the following issues involving hazardous biological materials research at U of L: • Non-compliance • Serious and/or unexpected events • Essential research needing expedited review
Materials	Prior to the regular meeting, each member shall receive a copy of materials to be reviewed at the meeting.
Meeting	The IBC conducts initial and continuing reviews of research that do not meet Biosafety Office review criteria at a fully convened IBC meeting. • At least 8 members or, if committee consist of 14 members or less, the simple majority of the committee must be present to have a quorum for a convened IBC meeting. • IBC members may participate in convened IBC meetings via telephonic and video conferencing • The IBC Administrator or designee is responsible for making the determination of whether an IBC meeting is appropriately convened with a quorum and when the convened IBC meeting loses quorum • All IBC members are afforded full opportunity to discuss each research proposal during the convened meeting • For research to be approved, it must receive the approval of a majority of those members present
Attendance	The IBC may open its meetings to the public when possible and consistent with the protection of privacy and proprietary interest. Anyone interested in participating must contact the IBC to coordinate their attendance. Contact: IBC Administrator Department of Environmental Health and Safety 1800 Arthur Street

	Louisville, KY 40208 E-mail: biosafe@louisville.edu Phone: 502-852-6670

Primary and Team Reviewer System

Introduction	The IBC utilizes the Primary and Team Reviewer System to assist in the initial and continuing review of research by the convened IBC.
Primary/team reviewers	The Primary, Secondary and Team Reviewer(s) are considered to be the lead reviewers for research proposals assigned to them. All IBC members are expected to review the materials provided to them in order to make an informed decision regarding the research at the convened meeting. Note: Continuing reviews and amendments may be reviewed by a single primary reviewer.
Assignment	The IBC Administrator in consultation with the IBC Chair assigns registrations upon receipt of a complete set of IBC application materials: • To one primary and a secondary reviewer based on their scientific and scholarly expertise • To an additional and/or consultant member identified by the chair in consultation with the BSO if members request additional expertise • Approximately 5 days before the meeting date when that registration is to be discussed and voted upon
Reviewer responsibilities	The Primary and Secondary Reviewers • Review for all elements required for approval. See Approval Criteria. • Ask the IBC staff to seek clarification from the investigator as needed before the convened meeting or contact individual investigators for clarification • Prepare a brief summary of the registration to the committee as follows: – The summary must include the discussion basis for the approval of the research, requiring changes in (approved with modifications or tabled) the research registration; or disapproving the research registration – The summary may include a pre-meeting motion based on the review of the registration. • Lead the discussion of the proposed research at the convened meeting of the IBC giving a brief summary of the registration and facilitating any discussion prompted by the summary and the comments available at the meeting with the assistance of the Chairperson

	Note: The primary reviewer typically makes the motion to approve, request modifications in, table, or disapprove the research registration. Team Reviewer(s) • Review for all elements required for approval • Contact individual investigators for clarification as needed before the convened meeting or ask the IBC staff to seek this clarification from the investigator • Assist in leading the discussion of the proposed research at the convened meeting of the IBC and facilitating any discussion prompted by the summary and the comments available at the meeting with the assistance of the Chairperson Note: In the absence of the primary reviewer at the meeting, the secondary reviewer of the registration will be asked to present the findings.
Use of subcommittees	The IBC may utilize subcommittees to support IBC review activities. The IBC Chairperson may appoint subcommittees: • To perform Biosafety Office reviews • To fulfill the duties of Primary and Team reviewers • On an *ad hoc* basis to perform additional functions as needed

Required Research Materials

Access to research files

Except for unusual circumstances, at least 5 business days before the convened meeting, the complete IBC file for all research to be discussed during the meeting is provided to all IBC members for their review, and the entire IBC file is present in the meeting room during the meeting.

Reason: To provide sufficient time for all IBC members to review each proposed project before the meeting so they can discuss each project adequately and determine the appropriate action during the convened review.

All IBC members are expected to review the materials provided to them in order to make an informed decision regarding the research at the convened meeting.

Materials IBC members review

The following table lists the materials IBC members review depending on their role and the type of submission they are reviewing:

Type of submission	Members review…
Initial submissions	• The complete registration • Application form • For human gene transfer clinical trials: – Investigator brochure and full protocol
Continuing review submissions	• The complete registration • Application form • For human gene transfer clinical trials: – Investigator brochure and full protocol
Amendments	• A summary of the proposed amendment(s) • The complete registration with proposed revisions • Application form • For human gene transfer clinical trials: – Investigator brochure and full protocol with proposed revisions

Meeting documentation	The minutes of IBC meetings will document separate deliberations, actions, and votes for each registration undergoing initial and continuing review by the convened IBC.

Approval Criteria

Introduction

The IBC reviews use of hazardous biological materials and determines that requirements in all of the following areas are satisfied before approving proposed research:

- Containment levels
- Facility design and construction
- Training and expertise
- Human gene transfer experiments

Containment levels

Containment levels are sufficient to:

- Avoid unintentional:
  - Transmission or release of hazardous biological materials
  - Spread of a serious pathogen from a greenhouse to a local agricultural crop
  - Introduction and establishment of an organism in a new ecosystem
- Minimize the possibility of unanticipated deleterious effects on organisms and ecosystems outside of the experimental facility

Facility design and construction

Facility design and construction is appropriate:

- To:
  - Contribute to the laboratory workers' protection
  - Provide a barrier to protect persons outside the laboratory
  - Protect persons, animals or plants in the community from transmission of or release of hazardous biological materials from the laboratory
- For institutional procedures and practices based on assigned biosafety levels

Training and expertise

Training and expertise of personnel are as follows:

- Assurances are in place that laboratory personnel have specific training in the procedures conducted in the laboratory and are supervised by a scientist with training in microbiology or a related science
- Before entering the facility, all staff working with and around hazardous biological materials should be fully informed about the containment measures applicable to a given research project

Human gene transfer experiments	For human gene transfer experiments, the IBC is also responsible for establishing end points for oversight, based on their biosafety assessment of the proposed research

Conflicts of Interest in IBC Review

Introduction

This topic discusses conflict of interest (COI) for members of the IBC and consultants to the IBC.

Member requirements

Conflict by participation

IBC members are prohibited from participating in the review of, deliberative discussion on, or vote relative to any research in which they (or their immediate family members) participate in any way, including but not limited to the following:

- Study planning and design
- Conduct of the study
- Data analysis
- Subject recruitment
- Subject consent
- Authorship

Conflict by financial interest

For further information see U of L COI policy.

Member responsibility

IBC members are expected to use their best judgment to ensure that all IBC deliberations take place without any appearance or possibility of Conflict of Interest.

Issues for IBC members

The following issues govern the management of Conflicts of Interest in the review of research by the IBC:

Issue	Description
Member or consultant recusal and absence	IBC staff and the IBC Chair assist members or consultants by making them aware of the conflict of interest requirements and assist in determining whether recusal would be necessary. • If an IBC member has a conflicting interest that might affect or appear to have an impact on IBC deliberations, the member must declare the presence of the conflict to the IBC and recuse/absent himself or herself from any review

	(Biosafety Office or full board), deliberative IBC discussion, or vote on the research • Members with any (financial or non-financial) interest in the research under consideration are recused from participation in, or voting on the initial or continuing review of research • The member may be present to answer questions posed by the IBC, but any other IBC activity, including the final discussion in which a determination is made as to how the IBC will vote on the registration, must be conducted without the presence or participation of the conflicted IBC member Important: There are no exceptions from this requirement.
Documentation of recusals	All recusals and absences of IBC members for Conflict of Interest must be noted as such in the official IBC minutes. See Minutes of an IBC Meeting.

Actions Taken at the IBC Meeting

Introduction

This topic provides guidance regarding the actions taken at the IBC meeting, including the following:
IBC minutes include all actions taken by the convened IBC and the votes underlying those actions.

Required IBC findings and determinations

The IBC must make the following specific findings and determinations based on registration-specific information:

Item	Description
Containment level	Assessment of the containment levels
Research practice and expertise	Assessment of the facilities, procedures, practices, and training and expertise of the personnel involved in research using hazardous biological materials
Agent characteristics	Identification of host(s), vector(s), toxins to be used (e.g. virulence, pathogenicity, environmental stability)
Inserted DNA sequences (e.g. species)	Characterization of sources of the inserted DNA sequences (e.g. species) and nature of the inserted DNA sequences (e.g. structural gene, oncogene)
Expression of foreign genes	Whether an attempt will be made to obtain expression of a foreign gene, and if so, the protein that will be produced
Section of the NIH Guidelines	Applicable section of the NIH Guidelines (e.g. Section III-D-1, Section III-E-1, etc.)
Human gene transfer	• Establish end points for oversight, based on their biosafety assessment of the proposed research • Review adverse events potentially related to the gene therapy product
Approval period	The approval period for the research, including identification of research that warrants review more often than every one, three or five years
Other items	Any IBC discussions or determinations regarding any other items on which the IBC takes formal action including:

	• Unanticipated problems involving risks to subjects or others • Serious adverse events

IBC actions

This table describes the actions the IBC may take:

When the research is …	Then …
Approved (no changes/additional changes required)	The research may proceed.
Required modifications to obtain approval	The research may proceed after the required changes are verified: • Such minor changes must be clearly delineated by the IBC so the investigator may simply concur with the IBC's stipulations • Such minor changes require the review and approval of BSO or designated voting IBC member
Tabled	The research may proceed only after the same fully convened IBC has reviewed and approved: • They require substantive changes to the research • Additional substantive information that was lacking in the application
Disapproved	The IBC has determined that the research cannot be conducted at U of L or by its employees or agents. Reasons for the decision are included.

IBC registration approval dates

Follow these steps to determine approval and expiration dates for each type of registration review:

Types of Review	Dates
Full board	For all full board reviews: • Approved: Date of approval • Expires: 1, 3, or 5 year(s) from date of approval
Biosafety Office	For Biosafety Office reviews: • Approved: Date of approval • Expires: 5 year(s) from date of approval

Minutes of an IBC Meeting

Introduction

This topic provides an overview of the documentation requirements for the minutes of an IBC meeting.

Content overview

The meeting minutes are a record of the following specific information:

- Attendance
- Member and consultant recusals and absences due to conflicts of interest
- Quorum
- Activities conducted by the IBC on the initial or continuing review of research:
  Examples
  – Review of registration modifications or amendments
  – Unanticipated problems involving risks to subjects or others
  – Adverse event reports
  – Reports from sponsors, cooperative groups, or DSMBs
  – Reports of continuing non-compliance with regulations or IBC determinations
  – Suspensions or terminations of research
- Registration-specific votes for any action taken by the IBC after the review of research registrations
- Separate votes for other IBC actions
- The basis for requiring changes in or disapproving research
- Summary of major points of discussion and the rationale for decisions
- Required IBC findings and determinations. See IBC Approval Criteria and Actions Taken at the IBC Meeting.
- Once the IBC approves the minutes, they may not be altered

IBC Records

Retention

The IBC retains the following registration records for 3 years after completion of the research or project:

- Initial submissions and any attachments
- Continuing review submissions
- Amendments to the initial and continuing review submission

The IBC retains the following records for 3 years:

- Meeting minutes
- IBC roster

Until such time as the IBC is no longer registered with the NIH/OSP, the IBC must retain its:

- Initial NIH/OSP registration
- Annual reports to OSP

Public access to records

U of L and the IBC may provide public access to records as outlined in the NIH Guidelines upon written authorization from the:

- University Counsel or designee

Certain information, though part of the IBC meeting summary, is not to be made available to the public. Redaction of information is applied consistently in consultation with the Associate University Counsel.

Types of redacted information include:

- Trade secrets or other confidential commercial information
- Proprietary information
- Personal information such as home phone numbers, addresses, e-mails, etc. of IBC members, staff or other representatives
- Information that would compromise institutional or national security
- Protected Health Information (PHI) as defined under HIPAA
- Personaly Identifiable Information (PII) as defined in federal and state laws There may be a cost for photocopying of documents.

Reviews After Approval

Re-evaluation

During the approval period, any member of the IBC may request a re-evaluation of a registration based on new information pertaining to a specific agent that has been released to the research community.
The Principal Investigator may request a re-evaluation of a disapproved registration provided that new information is presented that was not available at the time of review.

Changes in previously approved research - amendments

Revisions, modifications, or amendments to a research registration must be incorporated into the written registration for review by the IBC.

The IBC reviews and determines that the changes to the previously approved research satisfy all of the approval criteria, as explained for designated and convened IBC review. See Biosafety Office review of Research and Criteria for Full Board Review of Research before approving the proposed changes.
The table below defines the following terms:

Term	Definition
Amendment	U of L defines an amendment to be any change to an approved registration regardless of how minor it is. Investigators must report to the IBC planned changes in the conduct of the study, since these may change the risk to human health or the environment.
Minor Change	UofL IBC defines a minor change to be one that makes no substantial alteration in any of the following: • The source(s) of DNA • The nature of the inserted DNA sequences • The host(s) and vector(s) to be used • If an attempt will be made to obtain expression of a foreign gene, and if so, indicate the protein that will be produced • The containment level • The assessment of the facilities, procedures, practices, and training and expertise of personnel involved in r/s NA research • Any factor warranting full committee review

Biosafety Office review of changes in previously approved research

The IBC may utilize Biosafety Office review procedures to review a proposed change to previously approved research if it represents changes to research as outlined by Section III-E of the NIH Guidelines or represents a minor change to research as set forth by Sections III-A through III-D to be implemented during the previously authorized approval period.

Note: When a proposed change in a research study is not minor, then the IBC must review and approve changes at a convened meeting before changes may be implemented.

Review of changes by the fully convened IBC

The IBC utilizes the Primary and Team Reviewer System to assist in the review of changes to previously approved research by the convened IBC.

Continuing review

To ensure compliance with its guidelines, the NIH requires that the IBC periodically review ongoing research using biological materials that is conducted at U of L.

U of L procedures require that the IBC conduct substantive and meaningful continuing review of research every one, three or five year(s).

Investigators submit the Required Research Materials to the IBC. The IBC utilizes the Primary and Team Reviewer System to assist in continuing and determines that research still meets Approval Criteria.

Suspension or termination of IBC approval

The IBC may vote to suspend or terminate approval of research that is not being conducted in accordance with IBC or regulatory requirements or that has been associated with serious unexpected problems or serious harm to personnel and surrounding community.

- Where the IBC Chairperson determines that such action is necessary to protect subjects, personnel, or the surrounding community, the Chairperson in consultation with the DEHS director and BSO may require an immediate, temporary suspension of research, pending review of the situation by the convened IBC
- The IBC notifies the principal investigator orally and in writing of such suspensions or terminations and includes a statement of the reasons for the IBC's actions.
  Result: The investigator is provided with an opportunity to respond in person or in writing.
- See Handling Significant or Continuing Non-compliance for details of the notification process
- See Reporting for timelines for reporting suspensions or terminations

Closure

Closure notice

Principal Investigators must notify the IBC and DEHS of intentions to close an IBC-approved research activity when:

- A principal investigator is to depart from U of L
- A project is completed
- The project is no longer active
- Proper disposal of the r/s NA material has occurred
- When the Principal Investigator is no longer in possession of the material

Should a Principal Investigator fail to notify the appropriate committees prior to departure, the Department Chair shall be contacted. Following direction of the Department Chair, a registration may be transferred to another investigator or administratively closed.

Handling Significant or Continuing Non-compliance

Introduction

The U of L IBC has the responsibility and authority to oversee the use of r/s NA and other biohazardous agent(s) in research that is under its jurisdiction. As part of the IBC's oversight responsibilities, procedures exist for the reporting of any significant or continuing non-compliance with federal regulations, institutional policies, and suspension or termination of IBC approval.

Scope

This procedure applies to all research activities of faculty, staff, students, or others who are involved in research using r/s NA and other biohazardous agent(s) that fall under the jurisdiction of the U of L IBC.

Definitions

The following table defines terms used in this procedure:

Terms	Definitions
Non-compliance	Conducting research involving r/s NA and other biohazardous agent(s) in a manner that violates federal regulations or institutional policies governing such research. Note: This includes the failure to comply with IBC determinations and the failure of the IBC to follow regulations.
Significant non-compliance	Violations that pose a significant risk to research subjects, research personnel and the surrounding community
Continuing non-compliance	A pattern of non-compliance that has the potential to compromise safeguards protecting research subjects, research personnel and the surrounding community.

Suspected non-compliance reporting process

Below is a description of the reporting process for suspected non-compliance on the part of an investigator or research staff as described in U of L's Procedure for Investigating and Reporting Potential Violation(s) of the NIH Guidelines:

Questions	Answers
Who may report?	Reports can come from a number of different sources, including: • Investigators • Research personnel

	• Oversight committees/staff members • Subjects/family of subjects • Institutional personnel • The media • The public • Anonymous sources
Where do reports go?	Verbal or written reports may be made to either of the following: • IBC administrator • Anonymous through the "Compliance Hotline Reporting All reports will be referred to the IBC Chair, DEHS director and BSO to determine whether the allegation is a possible IBC non-compliance issue.
How is suspected non-compliance reported?	• Since these types of reports may arrive in various formats (phone call, letter, e-mail) there is not a requirement regarding specific information that must be reported • In most cases, the complainant is asked to submit the concern(s) in writing
What happens next?	The IBC Chair, DEHS director and BSO investigate to determine whether the allegation, if true, is a possible IBC non-compliance issue, and may refer the issue to other Committees (i.e. Scientific Integrity, Conflict of Interest) as appropriate. If the allegation is considered possible IBC non-compliance, IBC Chair, DEHS director and BSO will select one or more additional IBC members as soon as possible to constitute a subcommittee to investigate and, where concerns are substantiated, take the appropriate steps to address, correct, and/or resolve the reported concern.

Investigating allegations

The process for IBC review of allegations of suspected non-compliance for an investigator or research staff as described in U of L's Procedure for Investigating and Reporting Potential Violation(s) of the NIH Guideline is as follows:

<table>
<tr><th>Step</th><th>Action</th></tr>
<tr><td>1</td><td>The IBC Subcommittee on Compliance:
Conducts a preliminary review of the IBC files
Determines whether an assessment is warranted
If warranted, defines the scope of the assessment
May interview the person who filed compliance concern
May notify, in writing, the individual that is the subject of the concern</td></tr>
<tr><td>2</td><td>Note: If concerns pose a significant risk to personnel and/or the surrounding community, the IBC Chair may temporarily suspend conduct of a study pending full IBC review. See Suspension or termination of IBC approval for more information regarding suspensions and required reporting of suspensions by the IBC Chair and the Institution.</td></tr>
<tr><td>3</td><td>The IBC Subcommittee on Compliance:
May requests information related to the incident from the PI and, if necessary, a meeting with the PI will be scheduled.
Upon completion of the investigation, communicates the preliminary findings to the Principal Investigator of the research in question
Offers the Principal Investigator an opportunity to correct any errors of fact and respond to the subcommittee within ten business days
Upon completion of the investigation, communicates the findings to complainant
Note: If the PI does not respond or cooperate with the investigation within 10 business days of initial notification, the incident will escalate up the chain of command (i.e. Department Chair, School Dean, EVPRI, etc.) until the investigation can be completed.</td></tr>
<tr><td>4</td><td>Reviews the findings and investigator’s response above and makes a formal recommendation.
Prepares a report using the NIH/OSP “Incident Reporting Template” as guidance.</td></tr>
<tr><td>5</td><td><table><tr><th>If...</th><th>Then the IBC Subcommittee ...</th></tr><tr><td>Substantiated</td><td>Decides:
Whether it is…
– Significant
– Continuing
– Or both of the above</td></tr></table></td></tr>
</table>

		• What corrective actions are required to bring the study into compliance
	Not substantiated	• Dismisses the allegation • Notifies the Principal Investigator that the assessment is closed • This communication may include comments or recommendations from the IBC

- If applicable, the IBC chair will ensure that notification and the incident report signed by the IBC chair will be sent to the NIH/OSP
- The incident report will be openly discussed at the first available meeting convened of the IBC.
    - The IBC chair will notify the PI of the date of said meeting and request that they advise the IBC chair if they plan to appear at that meeting.
    - After open discussion of the incident report, the IBC will determine if refinement of University procedures are necessary to prevent future incidents.

6	To whom is an allegation referred if it cannot be investigated adequately? • If an allegation is within the purview of the IBC and is handled inadequately by IBC subcommittee, then the complainant may report this concern to the: – Compliance Hotline Reporting – EVPR, or – President of the University • If the allegation is not within the purview of the IBC (e.g. scientific misconduct or conflict of interest), the concern is forwarded to appropriate oversight officials

Actions the IBC Subcommittee on Compliance may take	After the IBC Subcommittee has made a final determination, it may take any reasonable corrective action it deems appropriate. Below are examples of possible actions, but should not be construed as an all-encompassing list: • Approval of the investigator's proposal for correction – no further action • Notification and involvement from other individuals from U of L (e.g.: Dean, Department Chair)

- Restricting the use of research data for publication
- Requiring:
  – Modification to the research registration
  – Additional registrations be submitted to the IBC
  – Remediation, mentoring, or educational measures such as; increased reporting by the investigator, or increased monitoring of the research
- Modifying the continuing review cycle
- Restricting the investigator's research activities, including suspension
- Suspension of approval or the termination of one or more of the investigator's research activities
- Refer the issue to other committees responsible for possible further review and action
- Requesting assistance from University Counsel
- Any other action the IBC deems appropriate to ensure compliance with federal regulations and U of L policies

Significant Problems, Spills, Accidents and Safety Reporting

Introduction

This topic provides the reporting process for significant problems, accidents/illnesses in the laboratory as well as safety reporting in human gene transfer research.

See Materials for Submission and Review for further information on forms to use for such reporting.

Definitions

The table below defines the following terms:

Term	Definition
Overt exposure	Any accident or spill involving organisms containing recombinant DNA molecules may be considered an **overt exposure** if the release of the material results in ingestion, inhalation, or assimilation into any person, either directly from the environment or indirectly by ingestion through food chains Reference: Derived in part from OSHA Regulations: 29 CFR 1910.120(a)(3), definition of "hazardous substance".
Potential exposure	Any accident or spill that has the **potential** for ingestion, inhalation, or assimilation into any person, either directly from the environment or indirectly by ingestion through food chains Reference: Derived in part from OSHA Regulations: 29 CFR 1910.120(a)(3), definition of "hazardous substance".
Violations of the NIH Guidelines	• A substantial deviation from or lack of adherence to the NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules; or • A pattern of non-adherence (including repeated minor violations) to the NIH guidelines
Significant problem	A problem related to the research which, is or has the potential to be a threat to the health or safety of animal or human subjects, research personnel, and/or the environment
Significant research-related accidents or illnesses	• Any serious, unexpected adverse events related to the use of a gene therapy product • Any accident falling into the overt exposure category

Reporting

The table below indicates who reports, the description of the report, and the timeframe for reporting:

Who reports	Description	Must report to	Timeframe
Investigator	**Spills or accidents** resulting in overt or potential exposures to BSL-3 organisms containing recombinant DNA molecules	IBC, DEHS Director or BSO	Immediately
	Spills or accidents resulting in overt exposures to BSL-2 organisms containing recombinant DNA molecules		
	Release of a Risk Group 2 or 3 agent/genetic material from a primary containment device (e.g. biological safety cabinet, centrifuge, or primary container into the laboratory)		Within 1 business day
	Spills or accidents that lead to personal injury or illness or breach of containment (e.g. aerosols released outside of containment)		
	Failure to adhere to the containment and biosafety practices described in the NIH Guidelines		

	Serious adverse event in human gene transfer that is: • fatal or life-threatening, • unexpected, and associated with the use of the gene transfer product	IBC	Within 7 calendar days after the sponsor's initial receipt of the information
	Serious adverse event in human gene transfer (not fatal or life-threatening) that is: • unexpected and associated with the use of the gene transfer product		Within 15 calendar days after the sponsor's initial receipt of the information
	Concerns regarding possible violations of the NIH Guidelines	IBC, DEHS Director or BSO	Within 5 business days
DEHS Director and BSO	**Spills or accidents** resulting in overt or potential exposures to BSL-3 organisms containing recombinant DNA molecules	Office of Science Policy	Immediately
	Spills or accidents resulting in overt exposure to BSL-2 organisms containing recombinant DNA molecules		
	Release of a Risk Group 2 or 3 agent/genetic		As soon as possible

	material from a primary containment device (e.g. biological safety cabinet, centrifuge, or primary container into the laboratory)		
	Spills or accidents that lead to personal injury or illness or breach of containment (e.g. aerosols released outside of containment)		
	Failure to adhere to the containment and biosafety practices described in the NIH Guidelines.		
IBC Chair	**IBC-substantiated**: • Significant problems • Violations of NIH Guidelines • Significant research-related accidents or illnesses	• Principal Investigator • Department Chair • DEHS Director • BSO • IBC • University Counsel	Within 30 days from notification of the IBC, DEHS Director, or BSO