INDIANA UNIVERSITY

Standard Operating Procedure

Institutional Biosafety Committee (IBC)

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Our Mission

The mission of the Institutional Biosafety Committees at Indiana University is to protect the health of laboratory scientists and the greater community by assuring that biological research is conducted in accordance with all appropriate guidelines, regulations, and best safety practices. The committees promote research by guiding scientists through the complexities of regulatory requirements and helping them establish safe working conditions. In service of this mission, the IBCs endeavor to:

- Continue to inform researchers about the application of the federal regulations in an effort to keep researchers current with evolving standards;
- Educate faculty, staff, and students who conduct research with recombinant DNA (rDNA) or synthetic nucleic acid molecules, infectious agents (pathogens), biological toxins, nanotechnology, or select agents;
- Develop new approaches that better serve the overarching mission of the IBCs and assess the overall effectiveness of the program.

Charge of the Committees

The Indiana University Bloomington (IUB) and Indiana University Purdue University Indianapolis (IUPUI) IBCs are charged with the responsibility of review, approval, and monitoring of all research and teaching activities involving the use of recombinant DNA (rDNA) or synthetic nucleic acids and the use of any Biosafety Level (BL) 2 or greater, non-recombinant biological materials. Regardless of whether an activity has external financial support, all research and teaching activities with rDNA or synthetic nucleic acid molecules or ≥BL-2 biological materials, including materials covered by the Bloodborne Pathogen Standard and animal tissues suspected to be contaminated with infectious agents, must be reviewed as set forth in this Standard Operating Procedure Manual.

These materials include, but are not limited to the following:

- All use of rDNA or synthetic nucleic acid molecules, regardless of Biosafety Level (subject to the *NIH Guidelines*)
    - Viral vectors or plasmid vectors
    - Transgenic/Knock-in/Knock-Out animals (see OSP Transgenic Animal FAQs)
    - Genetically modified plants
    - Transfer of rDNA or synthetic nucleic acid molecules into human participants
    - Transactive or infectious proteins
- Use of any Biosafety Level 2 or greater non-recombinant biological material
    - Infectious agents
    - Prion proteins
    - Biohazards (e.g., human or non-human primate tissues or fluids)
    - Select agents or toxins

Both the IUB and IUPUI IBCs meet once a month. A calendar of important dates can be found on the IBC Upcoming Deadlines & Meeting Dates webpage.

Committee Membership

1. Composition

The Vice President for Research or designee, in consultation with the IBC Chair, has the authority to appointment members to the IBC. Per the *NIH Guidelines*, the committee must be comprised of no fewer than five members, so selected that they collectively have experience and expertise in recombinant or synthetic nucleic acid molecule technology and the capability to assess the safety of recombinant or synthetic nucleic acid molecules research, and to identify any potential risk to public health or the environment. At least two members shall not be affiliated with the institution. The committee shall also include at least one individual with expertise in plant, plant pathogen, or plant pest containment principles, at least one scientist with expertise in animal containment principles, and a designated staff member from Environmental Health and Safety (EHS) - Biological Safety Program, who shall serve as a Biological Safety Officer. Membership reflects basic federal requirements for expertise and advocacy; additional members are added as necessary or appropriate. Members who are designated as “Alternate” are voting members and count towards reaching a quorum, but do not raise the overall quorum. Membership may include non-voting members. A Co-Chair or Vice-Chair may be called upon to serve in the Chair’s absence.

2. IBC Training

The training of IBC members is an on-going process and begins for new members through training during a regularly convened meeting of the IBC or with an orientation session conducted by the IBC Administrator, Biological Safety Officer, or designee. This session includes an explanation of the *NIH Guidelines* and the institutional policies and procedures of the IBC. The training of new members continues when they attend the regularly scheduled meetings of the IBC where they observe how members review and present the submissions that they were responsible for reviewing. The training of IBC members continues through the discussion, which takes place over substantive issues during the review of submissions and special topic presentations during convened IBC meetings.

3. Meeting Attendance

IBC members are expected to attend the regularly scheduled meetings unless they have notified the IBC Administrator that they are unable to do so. Members and alternate members should attend no fewer than 60% of convened IBC meetings. If a committee member has been assigned as a reviewer and is unable to attend the IBC meeting, that committee member should find another member to present their review.

Committee Meeting Process

Convened meetings of the IBC typically occur monthly. Meetings must reach quorum in order for research protocols to be approved. Quorum for the IU IBCs is defined as a majority of full voting members. In order for protocol submissions to be added to the agenda for a convened meeting, the Principal Investigator (PI) should submit no later than 2 weeks and 1 day before the scheduled meeting. If the submission is received on time but, during the course of the IBC Office's administrative review, is shown to require significant revisions, the PI may be asked to make corrections and submit for review at a later meeting. If the PI has satisfactorily addressed any issues raised during the administrative review, and the due date for submissions has not passed, the submission may be added to the agenda for the upcoming meeting. IBC members assigned to a submission review ("reviewers") are expected to provide a reviewer sheet detailing any comments or revisions required of the PI and to provide an overview of the submission at the convened meeting. Typically, a committee member will provide a primary review, a Biological Safety Officer will provide a secondary review, and, for protocols with animal work, a member representing the Laboratory Animal Research Center (LARC) will provide a tertiary review. A Veterans Affairs (VA) reviewer will be assigned if the protocol is related to work performed by the VA. Reviewer sheets should be submitted to the IBC Administrator no later than 48 hours before the scheduled IBC meeting. If a reviewer is unable to attend a meeting, the reviewer should make every attempt to find an alternate member to present their review.

Meeting minutes will be taken in accordance with the Office of Science Policy (OSP) *NIH Guidelines* requirements.

Responsibilities

1. The IBC is responsible for:

- Reviewing research and teaching activities conducted on all Indiana University campuses involving recombinant or synthetic nucleic acid molecules or non-recombinant ≥BL-2 biological materials for compliance with the *NIH Guidelines,* recommendations in the Biosafety in

Microbiological and Biomedical Laboratories (BMBL), and the policies of the Indiana University IBC;

- Notifying the Principal Investigator of the results of the IBC's review and approval;
- Setting containment levels for experiments involving recombinant DNA or synthetic nucleic acid molecules and/or non-recombinant, BL-2 and higher biological materials;
- Periodically reviewing recombinant or synthetic nucleic acid molecules research conducted at the institution to ensure compliance with the *NIH Guidelines*;
- Reporting any significant problems with or violation of the *NIH Guidelines* and any significant research-related accidents or illnesses to the appropriate institutional official and NIH's Office of Science Policy within 30 days, unless the IBC determines that a report has already been filed by the PI;
- Immediately reporting any suspected BL-3 or confirmed BL-2 research-related illnesses, accidents, or significant problems with, or violations of the *NIH Guidelines* to the appropriate institutional officials and NIH's Office of Science Policy;
- Reviewing any reports of spills or accidents that fall under the "IBC Policy on Reporting Laboratory Incidents"; and
- The IBC may not authorize initiation of experiments that are not explicitly covered by the *NIH Guidelines* until the NIH establishes the containment requirement.

2. The IBC Chair is responsible for:

The IBC Chair approves the agenda for the convened meetings of the IBC, approves attendees other than IBC members or staff, and directs the meeting deliberations of the committee. The Chair calls the meeting to order, requests motions and seconds, and closes the meeting once it has concluded its business. The Chair assigns subcommittees (i.e., a subset of IBC members) as needed to review an issue or topic prior to official committee review at a convened IBC meeting.

3. The Principal Investigator is responsible for:

On behalf of the institution, the Principal Investigator, the faculty member responsible for research and teaching activities that involve recombinant or synthetic nucleic acid molecules and/or biological materials, is responsible for full compliance with the *NIH Guidelines* and for adherence to the policies and procedures of Indiana University IBC. The PI should take particular note of the following responsibilities:

- The PI should make the initial determination of the required levels of physical and biological containment in accordance with the *NIH Guidelines* and the most recent edition of the BMBL;
- The PI should select the appropriate microbiological practices and laboratory techniques to be used for the research;
- The PI should ensure that all staff listed has access to the currently approved protocol and have read the protocol before beginning work;
- The PI should ensure that all staff listed on the protocol have sufficient knowledge and are sufficiently trained to safely perform the responsibilities for which they have been assigned;
- The PI should ensure that the protocol personnel fully understand the steps necessary following any spills or potential exposures with the agents described in the protocol;

- The PI should immediately report any suspected BL-3 or confirmed BL-2 research-related illnesses as well as reporting any accidents, significant problems with or violation of the *NIH Guidelines* to the Biosafety Office and Office of Research Compliance immediately; and
- Report to the Biosafety Office spills or accidents that fall under the "IBC Policy on Reporting Laboratory Incidents".

4. The Biological Safety Officer, or Designee, is responsible for:

The responsibilities of the Biological Safety Officer include, but are not limited to:

- Serving as a voting Member of Institutional Biosafety Committee;
- Conducting periodic laboratory inspections to ensure that appropriate laboratory standards as determined by the IBC are rigorously followed;
- Reporting to the IBC, The Office of Research Compliance, and the institution any significant problems, violations of the *NIH Guidelines*, and any significant research-related accidents or illnesses of which the Biological Safety Officer becomes aware unless the Biological Safety Officer determines that a report has already been filed by the PI;
- Developing emergency plans for handling accidental spills and personnel contamination and investigating laboratory accidents involving recombinant or synthetic nucleic acid molecules or biological materials research or teaching activities;
- Providing advice on laboratory security, providing technical advice to PIs and the IBC on research safety procedures;
- Developing, and implementing a comprehensive biosafety program for Indiana University campuses;
- Together with the IBC, overseeing review of BL-1, BL-2, and BL-3 research projects and teaching activities on campus and conducting all relevant inspections for these facilities;
- Conducting biosafety risk assessments and training to ensure the University is in compliance with all applicable federal biosafety laws and regulations;
- Collaborating with investigators and staff in all matters related to biosafety;
- Providing expertise for the design and management of containment facilities; and
- Serving the University as a resource in all aspects of education and training in biosafety.

Submitting a New Protocol, Protocol Amendment, Annual Continuing Review, 5 Year Resubmission, or Protocol Termination

The Indiana University IBC Protocol Registration Form is used to register, amend, renew, and approve research and teaching protocols, and to evaluate the Biological Safety Level (BL) and Risk Group (RG) of the materials therein.

1. Submitting a New Protocol

The Indiana University IBC protocol registration form must be submitted to the IBC and, in some cases, approved, prior to initiating research or teaching activities involving any BL-1, BL-2, or BL-3 recombinant or synthetic nucleic acid molecules and/or any ≥BL-2 non-recombinant biological materials.

Based on the *NIH Guidelines*, all research that falls under sections III-A through III-D require approval of the IBC and/or other regulatory bodies before the research can begin. Research that falls under section III-E of the *NIH Guidelines* may begin upon submission of an IBC Protocol Application Form to the IBC. All research that falls under section III-F of the *NIH Guidelines*, any teaching activities involving ≥BL-2 recombinant or synthetic nucleic acid molecules, and any research or teaching activities involving ≥BL-2 non-recombinant biological materials must be registered with the IBC, but does not require approval before initiation.

For more information on IBC protocol registration, please visit the IBC website at https://research.iu.edu/compliance/biosafety/submissions/index.html.

2. Amending a Protocol

Any change to your existing Institutional Biosafety Committee protocol at IU must be submitted to the IBC Office for review.

Amendments (major and minor) made to previously approved protocols should be made directly to the protocol form. When preparing your submission, please make sure to complete Section I-C-2 (Submission Record) and incorporate all changes into the body of the protocol form. All edits should be made using track changes. Amendments submitted without track changes will be returned to the PI as an incomplete submission.

A comprehensive description of the proposed change is necessary for any amendment to be considered.

For more information on amending an IBC protocol, please visit the IBC website at https://research.iu.edu/compliance/biosafety/submissions/protocol-amendments.html.

3. Annual Continuing Review

All previously approved research and teaching protocols at IU require an annual review to assess any changes that have been made during the previous year. This review also verifies that all work has been conducted in accordance with the approved protocol. An Institutional Biosafety Committee continuing review must be submitted during the month in which your initial protocol was approved.

Continuing reviews should be made directly to your protocol form, in Section I-C-2.b – Annual Continuing Review.

If a change to your initial protocol has occurred during the previous year and an amendment is required, an amendment must accompany your continuing review.

The final approval of your continuing review is dependent on the completion of required training for all personnel listed on your protocol.

Annual continuing reviews should be submitted as a Word document, emailed to IBC@iu.edu.

For more information on annual continuing reviews, please visit the IBC website at https://research.iu.edu/compliance/biosafety/submissions/reviews.html.

4. 5 Year Resubmission or Protocol Termination

Institutional Biosafety Committee protocols are approved for five years. At the end of that period, a new protocol must be reviewed and approved by the IBC. Your five-year renewal must be submitted during

the month in which your original protocol was approved. The submission process is the same as a new protocol.

You may terminate an IBC protocol at any time, although notification of research termination is usually given at the time of annual review or five-year renewal. If previously approved research has been completed, you may send an email to your campus committee address, stating that the work covered by your protocol has been completed and that it may be terminated. Your IBC protocol number must be referenced in the email. If the email is being sent by a lab manager, postdoc, graduate student, or any other alternate contact, then the principal investigator must be copied on the notification email.

For more information on 5 year resubmissions and protocol termination, please visit the IBC website at https://research.iu.edu/compliance/biosafety/submissions/closure.html.

IBC Review

1. Administrative Review

Upon receipt, all IBC protocol forms will undergo an administrative review by the IBC Administrator or IBC Office Staff to ensure that the PI has provided all appropriate information and that the form contains sufficient detail to perform a complete risk assessment and review. A complete initial submission must be received for the protocol to move through the review process. The PI must only utilize the latest form from the IBC Website.

The IBC Administrator or IBC Office Staff will determine which type of review is required (i.e., Exempt submissions require Expedited review; Non-Exempt submissions require Full Committee Review). If the IBC submission involves the use of animals, the IBC Administrator will confirm that there is an associated Institutional Animal Care and Use Committee (IACUC) protocol. If the IBC submission involves the administration of biological materials or recombinant or synthetic nucleic acid molecules to humans or the acquisition of materials covered under Bloodborne Pathogens Standard, the IBC Administrator will confirm with the Institutional Review Board (IRB) that there is an associated IRB submission form (pending or approved). If not, the PI will be informed that an IRB approval is also required.

2. Expedited Review (IBC Office/Biological Safety Officer Review and Approval)

Expedited review is performed for all exempt research and teaching activities. Exempt research includes research that falls under section III-F of the *NIH Guidelines*, any research or teaching activities that involve Biosafety Level 2 or higher biological materials, or teaching activities that involve Biosafety Level 2 or higher rDNA or synthetic nucleic acid molecules regardless of biosafety level. When a protocol that involves exempt research or teaching activities is submitted, the IBC office and the Environmental Health and Safety - Biological Safety Program will review the work. If, during the course of the expedited review, the work is found to be non-exempt or of greater concern, it will be reassigned for Full Committee Review by the IBC.

For more information on the expedited review process, please visit the IBC website at https://research.iu.edu/compliance/biosafety/submissions/index.html.

3. Full Committee Review

Full committee review is required for all non-exempt research. Non-exempt research is any research that falls under sections III-A through III-E of the NIH Guidelines. When you submit a protocol that

involves non-exempt research, the IBC office will add it to the agenda of an IBC meeting and assign it to reviewers. Protocols must be received 2 weeks and 1 day prior to an IBC meeting to be considered for review that month.

For more information on the Full Committee Review process, please visit the IBC website at https://research.iu.edu/compliance/biosafety/submissions/index.html.

4. Delinquent PI Responses to IBC Review and Requested Revisions

The Office of Research Compliance and the IBC determined that the following steps would be taken in instances when a PI fails to respond to IBC related items or review letters (e.g., IBC questions or comments provided to the PI before or after a convened meeting) in a timely manner.

Steps taken for past-due items when no response is received:

Reminder Date	Action Taken	Personnel Copied
90, 60, 30 days	Email reminders sent	PI and Alt Contact
Due date	Email courtesy reminder sent	PI, Alt Contact
1 week post due date	Email courtesy reminder sent	PI, Alt Contact
1 month post due date	Phone Call giving 1 additional week	PI or Alt Contact
1 month + 1 week post due date (1 week after phone call)	"Urgent Response Requested" email sent	PI, Alt Contact, Department Head
2 months + 1 week post due date	"Committee Review" warning email	PI, Alt Contact, Department Head, Chairs, and, IBC Administrator
Reviewed by Committee	Committee Letter sent, from Committee Chair, with request to cease research	PI, Alt Contact, Department Head, Chairs, IBC, BSO, SoM Research Affairs Office, any IUB oversight department (TBD)

Steps taken for past-due items when a response is received but remains incomplete (complete submission, training, requested revisions, PI clarification):

Reminder Date	Action Taken	Personnel Copied
90, 60, 30 days	Email reminders sent	PI and Alt Contact
Upon Receipt	Receipt Confirmation with reminder	PI and Alt Contact, and personnel with outstanding training
Due date or date of Administrative Withdrawal	Email courtesy reminder sent	PI, Alt Contact, and personnel with outstanding training
1 week post Admin. Withdrawal	Phone Call giving 1 additional week	PI or Alt Contact

1 week after phone call	"Urgent Response Requested" email sent	PI, Alt Contact, personnel with outstanding training, and Department Head
1 week after "Urgent Resp. Req." email	"Committee Review" warning email sent	PI, Alt Contact, personnel with outstanding training, Department Head, Chairs, and, IBC Administrator

Specific IBC Policies

1. Conflict of Interest

No member of the IBC may be involved in the IBC's deliberation, review, or approval of a submission in which he or she, or his/her spouse or domestic partner, is listed as an investigator, otherwise expects to be engaged, or has a financial interest, except to provide information requested by the IBC (including information requested during a convened IBC meeting). IBC members are obligated to report their conflict of interest to the IBC Chair or IBC Administrator prior to discussion of the protocol in question, and to leave the meeting room during discussion and voting on that protocol, unless requested by the IBC Chair to remain to answer questions or provide additional information.

2. Antibiotic Sensitivity

Research involving organisms with known human biosafety concerns (i.e., Risk Group 2 and above), which may be partially or fully resistant to clinical treatment in humans, animals, or plants by such agents as antibiotics, antivirals, and antifungals, must be described in detail, providing human safety health risks, available treatments, proposed containment measures, and, if appropriate, specialized testing procedures.

3. Reportable Events

Any accident, spill, or exposure involving a Biological or Recombinant or Synthetic Nucleic Acid Molecule Materials must be reported to the Environmental Health and Safety - Biological Safety Program.

For more information on Reportable Events, please visit the IBC website at https://research.iu.edu/compliance/biosafety/reportable-events/index.html.

4. Non-Compliance with the *NIH Guidelines*, State or Federal regulations, or other Institutional Policies

The IBC investigates all concerns brought to its attention. Reports of suspected non-compliance with *NIH Guidelines*, Select Agent Regulations, or any other regulatory agency concerns can be made to any IBC member or through internal audit's anonymous reporting hotline. Reports should indicate times, dates, places, and procedures of concern. The more specific information provided, the more effective the IBC evaluations.

Initial Evaluation and Actions:

- Whoever receives an allegation of non-compliance or other concern will immediately notify the IBC Administrator, Biological Safety Manager, or Executive Director of RIICE (Radiation Safety, IACUC, IBC, Conflict of Interest, and Export Control), and other appropriate institutional officials.
- Unless involved in the alleged non-compliance, the Biological Safety Manager will conduct the initial review and submit a report to the IBC Administrator, IBC Chair, or to the Vice or Co-Chair if the Chair is not available, or if the Chair is involved with the protocol to which the concern is related. If appropriate to the particular concern, or if the Chair and Vice or Co-Chair are both not available, other IBC members will be notified and charged with acting on behalf of the Chair in implementing this procedure. The Chair, Vice or Co-Chair, or other IBC member acting on behalf of the Chair, will promptly initiate an investigation of the circumstances underlying the concern.

Investigation:

A subcommittee appointed by the IBC Chair or Vice or Co-Chair should conduct the investigation of the circumstances underlying the concern and report findings to the IBC. It is important to avoid actual or perceived conflicts of interest in this process and to protect the identity of the complainant. The IBC should charge the subcommittee to gather information and should impose a deadline for reporting to the IBC. The time allowed will depend on the initial determination of whether immediate action may be required.

The nature and sources of the information required will vary depending on the circumstances, but may involve:

- Interviewing complainants (if known), any persons against whom allegations were directed, and pertinent program officials;
- Observing the environment; and
- Reviewing any pertinent records, (e.g., protocol submissions and other documents).

The subcommittee investigator(s) should provide a report to the IBC that summarizes:

- the concern(s) as reported to the IBC;
- the results of interviews;
- the condition of the environment;
- the results of records and other document reviews;
- any supporting documentation such as correspondence, reports, and animal records;
- conclusions regarding the substance of the concerns vis-à-vis requirements of the NIH;
- any institutional policies, procedures, and protocols; and
- recommend corrective actions and deadlines, if appropriate.

The IBC should consider the concern and determine corrective actions:

- The report of the subcommittee investigation should be provided to all IBC members;
- The IBC may vote electronically to accept the recommendations of the investigating subcommittee, offer further suggestions or comments, or request convened meeting to discuss the concern and/or the report; and
- Any member request for a convened meeting to consider a concern must result in a convened meeting.

Based upon the report of investigation the IBC will determine required actions, if any. IBC determinations may include, but are not limited to:

- investigation did not reveal an issue of non-compliance;
- investigation revealed non-compliance;
- related aspects of the program require further review; and
- other related institutional programs may require review.

For any noncompliance with standards accepted by the IBC, the IBC must prescribe corrective actions along with appropriate deadlines and reporting requirements. The IBC must also determine whether the noncompliance meets the criteria “serious or continuing noncompliance” or “serious deviation” so as to require reporting to NIH as discussed below.

Notification in Writing:

- IBC Chair will communicate, in writing, the results of the IBC evaluation of a reported concern to the person(s) responsible for the situation reported, the Institutional Official (IO), the Executive Director of RIICE, and the person reporting the concern if they wish to be notified of the outcome. The communication will contain a summary of the concern, the findings of the investigation, the determinations of the IBC, and the recommended corrective actions/sanctions. The letter will also inform the person(s) responsible for the situation reported of his/her option to appeal the decision by writing the IBC Chair, within 10 days of receipt of this letter detailing the basis of the appeal and requesting a meeting with the IBC.

Examples of IBC actions that may be appropriate in response to situations that constitute non-compliance are:

- terminate approval of the respective research study;
- suspend approval of the respective research study pending completion and acceptance by the IBC of an independent audit of the study and/or the submission, by the Principal Investigator, of a written plan for the correction and/or prevention of the problem;
- institute an IBC-mandated corrective action plan and independent audit of the study; and
- take such other action as the IBC deems appropriate.

The IBC is obligated to report any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses to NIH's Office of Science Policy within 30 days; unless the institution determines that a report has already been filed by the Principal Investigator, Biological Safety Officer, or Director of Biosafety.