Institutional Biosafety Committee (IBC)
Standard Operating Procedures

Contents

1 Institutional Biosafety Committee

1.1 Policy

The National Institutes of Health's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (rsNAM) and Institutional Biosafety Committee application requirements (see procedure below) are applicable to all faculty, staff, students, and users of the facilities of this University who propose and conduct research involving recombinant or synthetic nucleic acid molecules, *regardless of source of funding.* The SBU website for Biosafety in Research provides links to the current IBC membership roster, meeting dates, submission deadlines, and links to institutional policies and procedures, NIH Guidelines, and other information relevant to the compliant conduct of rsNAM at SBU.

This institution has an Institutional Biosafety Committee (IBC) whose responsibilities include review of recombinant or synthetic nucleic acid molecule (rsNAM) research. The IBC is in compliance with the requirements of the NIH Guidelines for Research Involving rsNAM ("NIH Guidelines").

The IBC is administered by the Office of Research Compliance, within the Office for Research and Innovation. The institutional official responsible for oversight of the IBC is the Vice President for Research (VPR), who delegates this responsibility to the Assistant Vice President for Research Compliance.

1.2 Definitions

Recombinant and synthetic nucleic acid molecules (rsNAM):
Recombinant nucleic acid molecules: are constructed by joining nucleic acid molecules **and** can replicate in a living cell;

Synthetic nucleic acid molecules: are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules;

Molecules that result from the replication of those described in (1), or (2) above.

Human gene transfer is the deliberate transfer into human research participants of either:

- Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
- Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria:
    - Contain more than 100 nucleotides; or
    - Possess biological properties that enable integration into the genome (e.g., *cis* elements involved in integration); or

- Have the potential to replicate in a cell; or
- Can be translated or transcribed.

1.3 Submission of Application

Stony Brook University uses the MyResearch Safety electronic system for the IBC submission process. Submission via MyResearch Safety of an IBC application, registration "smart" form, and grant application (if external funding exists or is being sought) is required for all experiments involving recombinant or synthetic nucleic acid molecules, *including those falling into the "exempt" experiment category.*

- First time submissions, continuing reviews/progress reports, amendments and annual continuing reviews/progress reports where significant changes to protocol detail or design are proposed (determined by the Office of Research Compliance (ORC) in consultation with the IBC chair will be reviewed at a convened meeting of the IBC consisting of a quorum of members. Action will be determined by a simple majority of votes. Board actions, which are uploaded in MyResearch Safety, may include:
  - Approved: accepted as submitted.
  - Modifications Required: consist of requiring additional information or investigator concurrence as to required changes, and providing applicable uploaded revisions.
  - Deferral: consist of requiring substantive response from the investigator; response must come back to the committee for review at a convened meeting.
  - Disapproval: no revision to the study would permit the possibility of approval.

Once approved, an activity is valid, as written, for a maximum of one year. No changes may be made to the approved activity unless prior approval is first granted by the IBC. Following the review, the IBC Administrator will notify the Principal Investigator of the results of the IBC's review and approval.

Minor, administrative amendments to IBC-approved studies, and studies that are undergoing continuing review for the first or second time with no changes or only personnel changes, are administratively reviewed and an approval is issued by the Office of Research Compliance on behalf of the IBC, pending confirmation from the Principal Investigator that Environmental Health and Safety (EHS) training requirements are met. Minor, non-administrative amendments are reviewed and approved by the IBC chair.

It is the PI's responsibility to maintain continued approval. Courtesy renewal e-reminders are sent in MyResearch Safety at three (3) months, and again at two (2) months before study expiration. During inspections the EHS Biological Safety Officer requires that the approval letter from the Institutional Biosafety Committee (IBC) be posted. Thus, study team members are fully aware of the study expiration date. If the study approval expires, the activity must stop until approval is re-issued by the IBC.

The completion or termination of the study, is a change in activity and should be reported to the IBC via the electronic management system. A final report to the IBC allows it to close its files

as well as provides information that may be used by the IBC in the evaluation and approval of related studies.

Upon lapse of approval for an IBC protocol, the PI of the study will receive an automatic notice from MyResearch Safety, with a "cc" to EHS Biological Safety Officer (BSO) and IBC Chair. All work covered under said approved protocol must stop until a **notice of continued approval** has been received from the IBC (via MyResearch Safety). In that notice, the PI will be instructed to reply within 48 hours to the BSO and IBC Chair that specifies either:

- All work covered under the lapsed IBC protocol has been completed and no further approval is required (in which case the BSO will schedule a close-out inspection by EHS within 10 working days); or
- Confirmation and acknowledgement of the requirement to stop all work covered under the protocol until renewed approval has been issued by the IBC.

If the PI response is not received within 48 hours, Bio Safety Officer will post a written notice of the lapse in the approved lab space(s) to notify the PI and all lab staff of the Cease Work Order. The PI will be required to:

- Provide a detailed summary on any work that took place after the date of the lapse in approval,
- Submit a corrective action plan to prevent recurrence of the lapse of the IBC approval to the satisfaction of the IBC,
- Undergo inspection of the laboratory by Environmental Health and Safety, and
- Cooperate with the IBC and the Institution in providing all necessary information for mandated reporting (within 30 days) to National Institutes of Health Office of Science Policy, if applicable. The report will need to include a copy to the relevant chair and dean, and other institutional officials as applicable.

The convened IBC will consider all information and render a decision regarding either project termination or renewed approval.

Any significant problems, violations of the *NIH Guidelines*, or any significant research related accidents and illnesses relating to recombinant or synthetic nucleic acid molecule (rsNAM) work must be reported immediately (and no longer than 24 hours) to the IBC Administrator (within the ORC), the IBC Chair, and the BSO. Examples of problems, accidents or violations include:

- Breaches in biosafety during the conduct of an activity involving rsNAM (i.e., release of rsNAM into the environment)
- Work involving rsNAM that is not covered by an approved IBC protocol.
- rsNAM involving human-infectious viral vectors at BSL2 containment, previously approved by the IBC, that is conducted during a lapsed IBC approval.

Upon receipt of the above report, the IBC Chair and BSO will take any or all of the following actions, depending on the incident:

- Initiate steps to mitigate the incident.

- Initiate an investigation to obtain details of the incident.
- Notify and consult with appropriate SBU officials as deemed necessary.
- Where there have been overt exposures to biosafety level 2 or higher and/or potential exposures at biosafety level 3 or higher, the incident will be reported immediately to NIH/OSP.

The IBC Chair will report to the IBC on the matter either by special meeting or at the regular monthly meeting. The IBC may require an additional investigation, explanation, a corrective action plan, suspend and/or terminate IBC approval, and/or other actions deemed necessary given the known details of the incident.

The IBC will determine if the incident requires a report to OSP (via the Incident Reporting template [https://osp.od.nih.gov/biotechnology/nih-guidelines/]). The relevant chair and dean will be copied on this report. The IBC will consider the OSP Guidance on determining if incidents are reportable.

Reports to other agencies:

- Any incidents that include the use of **Biological Select Agents and Toxins** (BSAT) will be immediately reported by the Bio-Safety Officer to the BSAT Responsible Official (RO) in EHS. Coordination of reports to Center for Disease Control and other agencies for BSAT materials is the responsibility of the Responsible Official.

1.4 Human Gene Transfer Research

In order for human gene transfer research to be considered, the protocol, consent form, and IBC application materials must be uploaded into MyResearch Safety. Research cannot be initiated until Institutional Biosafety Committee and all other applicable institutional and regulatory authorization(s) and approvals have been obtained.

Any required documentation is at the discretion of the IBC, as outlined in the "Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant or Synthetic Nucleic Acid Molecules into One or More Human Research Participants" file:///C:/Users/rdahl/Downloads/appendix_m.pdf

The following information should be included in human gene transfer protocols:

- A scientific abstract.
- The proposed clinical protocol, including tables, figures, and any relevant publications.
- Summary of preclinical studies conducted in support of the proposed clinical trial or reference to the specific section of the protocol providing this information.
- Product description:
    - Derivation of the delivery vector system including the source, associated modifications, and previous clinical experience with the system

- Genetic content of the transgene or nucleic acid delivered, including the species source of the sequence, and whether any modifications have been made
- Any other material to be used in preparation of the agent to be administered to research participants
- Methods for replication-competent virus testing
- Intended *ex vivo* or *in vivo* target cells and transduction efficiency
- Gene transfer agent delivery method

Investigators must review the NIH Guidelines sections III-C and the document "Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant or Synthetic Nucleic Acid Molecules into One or More Human Research Participants". This information includes mandated adverse event/safety reporting requirements. Investigators conducting human gene transfer experiments must additionally accept responsibility for the requirements specified in Section IV.B.7 NIH Guidelines https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.html

The deliberate transfer of recombinant or synthetic nucleic acids into one human research participant, conducted under an FDA regulated individual patient expanded access IND or protocol, including for emergency use, is not research subject to the *NIH Guidelines* and thus does not need to be submitted to an IBC for review and approval.

Investigators who have received approval from the Food and Drug Administration (FDA) to initiate a human gene transfer protocol must report any serious adverse event immediately to the IRB, IBC, Office for Human Research Protections (OHRP), Office of Science Policy of NIH (OSP), and FDA, followed by the submission of a written report filed with each group.

1.5 Transgenic (Vertebrate, Non-vertebrate) Animals Research

The IBC's policy for the Approval of the Creation or Use of Transgenic Animals is available in the MyResearch Safety Library. Transgenic work with *any* animal requires submission to ORC. This includes:

- The registration form for transgenic rodent strain creation requiring BL1 containment; (IACUC approval is also required) or
- A complete IBC application for all other transgenic animal activity.

1.6 Investigator Responsibilities

The IBC requires compliance with Principal Investigator Responsibilities, as outlined in section IV.B.7.d and IV.B.7.e of the NIH guidelines and briefly summarized below:

Responsibilities of the Principal Investigator Prior to Initiating Research:

- Make available to all laboratory staff the protocols that describe the potential biohazards and the precautions to be taken;

- Instruct and train laboratory staff in: (i) the practices and techniques required to ensure safety, and (ii) the procedures for dealing with accidents; and
- Inform the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested

Responsibilities of the Principal Investigator During the Conduct of the Research:

- Supervise the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed;
- Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the Biological Safety Officer (where applicable), Greenhouse/Animal Facility Director (where applicable), Institutional Biosafety Committee, NIH OSP, and other appropriate authorities (if applicable)
- Correct work errors and conditions that may result in the release of recombinant or synthetic nucleic acid molecule materials; and
- Ensure the integrity of the physical containment and the biological containment

Prior to final approval of an IBC application, all investigators and study personnel named on the IBC application must:

- Certify that they have reviewed the NIH (OSP) documents: "Overview of the NIH Guidelines" and "IBC Investigator Responsibilities under the NIH Guidelines".
- Complete Environmental Health and Safety training. Depending on the type of research, investigators are required to complete training in the following:
  - Laboratory Safety for Chemical Hazards
  - Laboratory Safety for Biological Hazards
  - Hazardous Waste Management
  - Regulated Medical Waste Management
  - Bloodborne Pathogens

Incident Reporting

The *NIH Guidelines* require that "any significant problems, violations, or any significant research-related accidents and illnesses" be reported to the Office of Science Policy (OSP) within 30 days. Appendix G of the *NIH Guidelines* specifies certain types of accidents that must be reported on a more expedited basis. Specifically, Appendix G-II-B-2-k requires that spills and accidents in BL2 laboratories resulting in an overt exposure must be **immediately** reported to the OSP (as well as the IBC). In addition, Appendices G-II-C-2-q and G-II-D-2-k require that spills or accidents occurring in high containment (BL3 or BL4) laboratories resulting in an overt or potential exposure must be **immediately** reported to OSP (as well as the IBC and BSO). The form for reporting these types of incidents can be located here: https://osp.od.nih.gov/biotechnology/nih-guidelines/

1.7 Institutional Biosafety Committee Membership

The IBC is comprised of no fewer than five members, appointed by the Assistant Vice President for Research Compliance. The members are selected so 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 molecule research and to identify any potential risk to public health or the environment. The membership includes:

- At least two members that are not affiliated with the institution (apart from their membership on the Institutional Biosafety Committee) and represent the interest of the surrounding community with respect to health and protection of the environment (e.g., officials of state or local public health or environmental protection agencies, members of other local governmental bodies, or persons active in medical, occupational health, or environmental concerns in the community).
- At least one individual with expertise in plant, plant pathogen, or plant pest containment principles when experiments utilizing Appendix L, *Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Plants*, require prior approval by the Institutional Biosafety Committee.
- At least one scientist with expertise in animal containment principles when experiments utilizing Appendix M, *Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Animals*, require Institutional Biosafety Committee approval.
- As Stony Brook conducts certain rsNAM activities (e.g., requiring BSL3 containment), a Biological Safety Officer (BSO) is a member of the Institutional Biosafety Committee.
- As Stony Brook participates in rsNAM research involving human research participants, the IBC ensures that committee membership (or consultants to the IBC) includes adequate expertise and training, including an individual with expertise in human gene transfer principles.
- In order to ensure the competence necessary to review and approve recombinant or synthetic nucleic acid molecule activities, the Institutional Biosafety Committee considers that the membership or consultants include: (i) persons with expertise in biological safety, and physical containment; (ii) persons knowledgeable in institutional commitments and policies, applicable law, standards of professional conduct and practice, community attitudes, and the environment, and (iii) at least one member representing the laboratory technical staff.

Meetings are held on the fourth Tuesday of the month. Members are expected to attend in person or via conference call. Attendance of the following members is required for a meeting to occur:

- Member representing genetics/microbiology
- Member representing animal resources
- Member representing the community (unaffiliated member)
- Member representing biosafety

Meeting minutes will be reviewed and confirmed by the Chair of the Institutional Biosafety Committee. Minutes will contain the date and place of the meeting, whether minutes of the prior meeting were approved, individuals in attendance, whether and why the meeting was open or closed, all major motions, major points of discussion and the committee's rationale for

particular decisions, documenting that the IBC has fulfilled its review and oversight responsibilities as outlined under Section IV-B-2-b of the NIH Guidelines.

If plant pathogens or plant containment research is being reviewed, a member with the necessary expertise must attend the IBC meeting. If animal research is being reviewed, a member with the necessary expertise must attend the IBC meeting. Members who are unable to regularly attend convened meetings of the IBC will be replaced with new members at the recommendation of the IBC Chair to the VPR or his/her designee.

New IBC members will review the following documents:

- NIH Guidelines
- IBC Standard Operating Procedures

Institutional Biosafety Committee members are required to take the Collaborative Institutional Training Initiative (CITI) IBC member training. The course must be retaken every 3 years.

1.8 IBC Responsibilities

On behalf of the institution, the IBC is responsible for:

- Reviewing recombinant or synthetic nucleic acid molecule research conducted at or sponsored by the institution for compliance with the *NIH Guidelines* as specified in Section III, *Experiments Covered by the NIH Guidelines*, and approving those research projects that are found to conform with the *NIH Guidelines*. This review includes:
    - An assessment of the containment levels required by the *NIH Guidelines* for the proposed research;
    - An assessment of the facilities, procedures, practices, and training and expertise of personnel involved in recombinant or synthetic nucleic acid molecule research;
    - Recombinant or synthetic nucleic acid molecule research involving human research participants, assessment is focused on biosafety issues (e.g., administration, shedding). IBC oversight may conclude after the last participant is administered the final dose of product.
- All aspects of Section III-C in the NIH guidelines must be appropriately addressed by the Principal Investigator; no research participant will be enrolled in a human gene transfer experiment until the IBC review process has been completed, unless the deliberate transfer of recombinant or synthetic nucleic acids into one human research participant is conducted under an FDA regulated individual patient expanded access IND or protocol. IBC approval must be obtained from the institution at which recombinant or synthetic nucleic acid molecule material will be administered to human research participants (rather than the site involved in manufacturing gene transfer products).

Additionally, the IBC is responsible for:

- Lowering containment levels for certain experiments as specified in Section III-D-2a, *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*.
- Setting containment levels as specified in Sections III-D-4-b and Appendix M for, *Experiments Involving Whole Animals*, and III-D-5, and Appendix L for *Experiments Involving Whole Plants*.
- Adopting emergency plans covering accidental spills and personnel contamination resulting from recombinant or synthetic nucleic acid molecule research. See the SBU document titled 'Policy and Procedures for Incidents Involving Recombinant or Synthetic Nucleic Acid Molecules (rsNAM) and Materials'
- Reporting any significant problems with or violations of the *NIH Guidelines* and any significant research-related accidents or illnesses
- Performing such other functions as may be delegated to the Institutional Biosafety Committee under Section IV-B-2 in the NIH guidelines, *Institutional Biosafety Committee*.
- The Institutional Biosafety Committee will not authorize initiation of experiments which are not explicitly covered by the NIH Guidelines until NIH establishes the containment requirements.

1.9 Biological Safety Officer (BSO)

The BSO's duties include, but are not be limited to:

- Periodic inspections to ensure that laboratory standards are rigorously followed;
- Reporting to the IBC and the institution any significant problems, violations of the *NIH Guidelines*, and any significant research-related accidents or illnesses of which the BSO becomes aware unless the BSO determines that a report has already been filed by the Principal Investigator;
- Developing emergency plans for handling accidental spills and personnel contamination and investigating laboratory accidents involving recombinant or synthetic nucleic acid molecule research;
- Providing advice on laboratory security;
- Laboratories in which rsNAM activities are conducted undergo inspection by the BSO at the time of application is submitted to the IBC.

1.10 Plant, Plant Pathogen, or Plant Pest Containment Expert

When the institution conducts recombinant or synthetic nucleic acid molecule research that requires Institutional Biosafety Committee approval in accordance with Appendix L, *Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Plants*, the institution shall appoint at least one individual with expertise in plant, plant pathogen, or plant pest containment principles (who is a member of the Institutional Biosafety Committee).

1.11 Animal Containment Expert

When the institution conducts recombinant or synthetic nucleic acid molecule research that requires Institutional Biosafety Committee approval in accordance with Appendix M, *Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Animals*, the institution shall appoint at least one individual with expertise in animal containment principles (who is a member of the Institutional Biosafety Committee).

1.12 Human Gene Transfer Therapy Expert

When the institution participates in or sponsors recombinant or synthetic nucleic acid molecule research involving human subjects, the institution must ensure that: (i) the Institutional Biosafety Committee has adequate expertise and training (using *ad hoc* consultants as deemed necessary) and (ii) all aspects of, *Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant or Synthetic Nucleic Acid Molecules into One or More Human Subjects*, have been appropriately addressed by the Principal Investigator.

The following information is required in **reviewing** human gene transfer protocols:

- A scientific abstract.
- The proposed clinical protocol, including tables, figures, and any relevant publications.
- Summary of preclinical studies conducted in support of the proposed clinical trial or reference to the specific section of the protocol providing this information.
- Product description, for instance:
    - Derivation of the delivery vector system including the source (e.g., viral, bacterial, plasmid), associated modifications (i.e., deletions to attenuate or self-inactivate, encapsulation in any synthetic complex, changes to tropisms), and previous clinical experience with the system
    - Genetic content of the transgene or nucleic acid delivered, including the species source of the sequence, and whether any modifications have been made (e.g., mutations, deletions, truncations)
    - Any other material to be used in preparation of the agent (vector and transgene) to be administered to research participants (e.g., helper virus, packaging cell line, carrier particles)
    - Methods for replication-competent virus testing
    - Intended ex vivo or in vivo target cells and transduction efficiency
    - Gene transfer agent delivery method

1.13 Annual Report to NIH/Office of Biotechnology Activities

Stony Brook files an annual report with NIH/OSP which includes: (i) a roster of all IBC members clearly indicating the IBC Chair, contact person, BSO (if applicable), plant expert (if applicable), animal expert (if applicable), human gene therapy expertise or *ad hoc* consultant (if applicable); and (ii) biographical sketches of all IBC members (including community members).

1.14 Public Considerations

Depending on specific circumstances, and consistent with protection of privacy and proprietary interests of investigators and the institution, SBU will allow the public to attend its IBC meetings. Any member of the general public who wishes to attend an IBC meeting will be welcome to do so for the open portion of the meeting that involves discussion of research with recombinant and synthetic nucleic acid molecules subject to the NIH Guidelines. The Institution reserves the right to restrict access to the portion of the meeting which may include discussions on research activities that do not fall under the NIH Guidelines, or are closed to protect private or proprietary information. Section IV-B-2-a-(6) of the NIH Guidelines acknowledges that the protection of private or proprietary information is a legitimate basis for closing meetings to the public.

Upon request, SBU will make available to the public all IBC meeting minutes and any documents submitted to or received from funding agencies which the latter are required to make available to the public. The Office of Research Compliance, Office of Internal Audit, legal counsel, and others as required will assess the need to redact certain (e.g., proprietary, personal etc.) information prior to release of the document(s) in question.

To ensure redaction is performed consistently, the following redaction procedure has been adopted in accordance with provisions allowed by the NIH Guidelines. Information not released to the Public under this procedure include:

- Private information of IBC members
- Guests names at IBC meetings
- Information whose disclosure is likely to compromise institutional or national security, including, but not limited to:
    - Details related to Select Agent work
    - Locations of laboratories and animal facilities
    - PI Names working with animals
- Proprietary, confidential or trade secret information

1.14.1 NIH Guidelines require the IBC to respond to public comments received, and report such comments with the IBC's response to the NIH. Public comments and the IBC's response shall be forwarded in writing to the NIH Office of Science Policy by the Biosafety Officer in a timely manner.