KUMC Procedure for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (Including Human Gene Transfer Research)

I. Purpose:

This procedure sets forth the requirements for review, approval and oversight of the use of recombinant or synthetic nucleic acid molecules in teaching, research or testing activities conducted by KUMC facilities or research personnel. All such activity, regardless of funding source, must be conducted in accordance with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (NIH Guidelines).

II. Applies to:

- Principal Investigators, research personnel, IBC Members, the BSO and all staff supporting IBC functions.

- All KUMC campus and reporting units

III. Definitions:

BSO: KUMC's Biological Safety Officer. The BSO carries out the duties specified in Section IV-B-3 of the NIH Guidelines. The BSO serves as a member of the IBC.

IBC Chair: The individual appointed by the Vice Chancellor for Administration to serve as Chair of the KUMC IBC. The IBC Chair must be an experienced scientific investigator with significant knowledge of issues related to biosafety, especially as it pertains to working with recombinant DNA.

Human gene transfer: the deliberate transfer into human research participants of either: (a) recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or (b) synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria: (i) contain more than 100 nucleotides; or (ii) possess biological properties that enable integration into the genome (e.g., *cis* elements involved in integration); (iii) have the potential to replicate in a cell; or (iv) can be translated or transcribed. See NIH Guidelines, Section III-C-1.

Institutional Biosafety Committee (IBC): the committee appointed by the Vice Chancellor for Administration in accordance with NIH Guidelines to review KUMC activities involving recombinant and synthetic nucleic acid molecules or other biological agents.

Recombinant and Synthetic Nucleic Acid Molecules: (a) molecules that (i) are constructed by joining nucleic acid molecules and (ii) can replicate in a living cell (i.e. recombinant nucleic acids); (b) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can abase pair with naturally occurring nucleic acid molecules (i.e. synthetic nucleic acids); or (c) molecules that result from the replication of those described in (i) or (ii) above. See NIH Guidelines, Section I-B.

IV. IBC Meetings and Minutes:

A. Timing of Meetings. IBC meetings will generally occur monthly. At the discretion of the IBC Chair, meetings may occur on more frequent basis. Prior to each meeting, all voting members of the IBC will receive copies of IBC Registration Forms, IBC Amendment Forms and other materials for consideration by the IBC, along with a copy of the agenda and draft minutes from the previous meeting. Special meetings may be called by the IBC Chair or any member of the IBC.

B. Open Meetings. Except where necessary to protect privacy and proprietary interests (to the extent consistent with the NIH Guidelines), or when the BSL 3 Subcommittee of the IBC is meeting to consider research that is not subject to the NIH Guidelines, IBC meetings shall be open to the public**.** All meetings will be conducted in person or by phone or video-conference.

C. Quorum. A majority of the voting members must be present to conduct the business of the IBC. If a quorum is lost at any time during the meeting, no further action will be taken by the IBC until a quorum is attained. Anticipated absences from an IBC meeting should be communicated to the BSO and IBC administrative at least 48 hours before a meeting.

D. Conflict of Interest. No member of the IBC may be involved in the review or approval of a project in which he or she has a conflict of interest, except to provide information requested by the IBC. This includes, but is not limited to, situations where the IBC member is currently engaged in or expects to be engaged in the research project under review, the IBC member has a direct financial interest in the research project, the IBC member has a significant financial interest in the research sponsor as defined in KUMC's Individual Conflict of Interest Policy and Procedures, or the IBC member has reason to feel that he or she cannot render an independent assessment of the application. The IBC member with the conflict of interest must disclose the conflict when he or she is assigned to participate in the review of the project, and prior to discussion of the project at a convened meeting. The IBC member who has disclosed a conflict will be recused

from voting on the specific matter, but may provide information requested by the IBC. The absence will be noted in the IBC meeting minutes.

E. Board Actions. Board Actions will be determined by a simple majority of votes. The IBC Chair or his/her designee will notify the Principal Investigator of the IBC's determination. Board actions may include the following:

- Approved: accepted as submitted;
- Modifications Required: Approval conditional upon IBC directed changes. The conditions for approval and the time frame (if any) within which the conditions must be met will be clearly stated in the approval letter.
- Deferral: IBC conditions consist of requiring substantive response from the investigator; response must come back to the IBC for review at a convened meeting; or
- Disapproval: IBC finds that no revision to the study would permit the possibility of approval.

F. Meeting Minutes: The Committee will prepare minutes of its meetings showing the date and place of the meeting (including the time the meeting begins and ends), whether minutes of the prior meeting were approved, individuals in attendance, and all substantive committee actions (e.g. all major motions, major points of order, whether motions were approved, and the time of meeting adjournment). Draft minutes will be circulated to the IBC members prior to the next meeting. Once ratified, a copy of the approved minutes will be maintained by the BSO. Minutes should offer sufficient detail to document that the IBC is fulfilling the performance expectations set forth in the NIH Guidelines. Specifically, the minutes should reflect the IBC's review and consideration of the following aspects of the proposed research:

- Principal Investigator and project title,
- Agent characteristics (e.g., virulence, pathogenicity, environmental stability)
- Types of manipulations planned
- Source(s) of the nucleic sequences (e.g., species)
- Nature of the nucleic acid sequences (e.g., structural gene, oncogene)
- Host(s) and vector(s) to be used
- Whether an attempt will be made to obtain expression of a foreign gene, and if so, the protein that will be produced
- Whether the PI and laboratory staff performing the research have completed the appropriate training
- Applicable section of the NIH Guidelines the research falls under

- Containment conditions to be implemented (biosafety level and any special provisions)

G. Access to Documents: KUMC will make available to the public copies of the IBC's meeting minutes and any other documents that must be made public in accordance with the NIH Guidelines. Consistent with the NIH Guidelines, KUMC may redact certain information from these documents if there are privacy or proprietary concerns. Consistent with the Kansas Open Records Act and the NIH Guidelines, KUMC may charge an amount sufficient to cover the costs of providing minutes. However charges will not be excessive or used a deterrent to access. Requests for access to documents must be referred to the BSO.

V. Protocol Registration and Review

A. Initial Submission

All protocols covered under sections III-A, III-B, III-C, III-D, or III-E of the NIH Guidelines must be submitted to the IBC for review and approval using the IBC Registration Form approved for this purpose. IBC Registration Forms should be submitted to ibc@kumc.edu. Before submitting the IBC Registration Form, the Principal Investigator must make an initial determination whether the subject research is exempt (covered under Section III-F) or non-exempt (covered under sections III-A, III-B, III-C, III-D, or III-E) under the NIH Guidelines. If an experiment falls into Sections III-A, III-B, or III-C and one of the other sections, the rules pertaining to Sections III-A, III-B, or III-C shall be followed. Certain experiments may also require prior approval of NIH as outlined in the NIH Guidelines. It is the Principal Investigator's responsibility to be knowledgeable of and abide by the provisions of the NIH Guidelines when making this determination. Principal Investigators are encouraged to consult the IBC Chair or BSO when uncertain about making the exempt versus non-exempt determination.

Protocols subject to Section III-F will require submission of an IBC Questionnaire in order to validate that it is indeed exempt. Protocols found not to be exempt will require full registration.

- Experiments subject to III-A, III-B, IIIC, or III-D, must be submitted to and approved by the IBC **prior** to initiation of the research.

Experiments covered by Section III-E and Section III-F, must be submitted to the IBC prior to or **at the time** the experiment is initiated. IBC approval will be granted

for a three (3) year period, unless a shorter time period is indicated in the IBC approval letter. After expiration of the approval period, a new IBC Registration Form must be submitted for *de novo* review. If study approval expires, the research activity must stop until approval is re-issued by the IBC.

B. **Continuing Review**

The IBC will periodically re-review research projects for continued compliance with regulatory requirements and policy, as follows.

- **Post Approval Status Review.** On an annual basis PI's will be required to submit a Post Approval Status Form approved by the IBC for this purpose. In the case of human subjects research, annual review will coincide with the IRB continuing review process.

- **De Novo Review.** Every three (3) years (unless a shorter time frame is noted in the IBC approval letter) Principal Investigators will be required to submit a *de novo* application to the IBC.

C. **Amendments**

Modifications of approved non-exempt research protocols require IBC review and approval before implementation of the changes. Amendments should be submitted on the IBC Amendment Form and submitted to ibc@kumc.edu. The IBC Chair and BSO will perform an initial review of the modification. Minor administrative amendments may be approved by the BSO or IBC Chair. Minor non-administrative amendments to IBC-approved studies may be reviewed and approved by the IBC chair. All other amendments shall be reviewed by the IBC at a convened meeting. Examples of situations requiring submission of an amendment for approval include:

- A change in host or vector;
- A change in the donor species or nature of the DNA segment selected;
- A change of project title;
- A change in the location of work/experiments;
- A change of the Principal Investigator or laboratory personnel.
- Generation of a novel mouse line.

D. **Human Gene Transfer Research**

In order for human gene transfer research to be considered, a copy of the consent form, in addition to the protocol, must be provided to the IBC, along with the IBC Registration Form.

Investigators must review Appendix M of the NIH Guidelines**, "**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," which includes mandated adverse event/safety reporting requirements.

VI. Principal Investigator Responsibilities

The Principal Investigator is responsible for the following:

- Not initiating or modifying recombinant DNA research which requires IBC approval prior to initiation (Sections III-A to III-D) until that research or the proposed modification thereof has been approved by the IBC and has met all other requirements of the *NIH Guidelines*;

- Determining whether experiments are covered under Section III-E of the *NIH Guidelines*, (*Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation*) and ensuring that the appropriate procedures are followed;

- Selecting appropriate microbiological practices and laboratory techniques to be used for the research, and completion of required training;

- Making available to all laboratory staff the protocols and IBC Registration Forms that describe the potential biohazards and the precautions to be taken;

- Instructing and training laboratory staff in: (i) the practices, techniques and proper biocontainment levels required to ensure safety; (ii) the procedures for dealing with spills, releases, accidents and exposures; (iii) the types of research covered under the *NIH Guidelines*, and (iv) maintaining records documenting personnel training;

- Informing the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection);

- Adhering to the IBC-approved protocol and promptly reporting proposed changes/amendments to the IBC;

- Remaining in communication with the IBC throughout the entirety of the project and completing the Post-approval Status Form when so requested;

- Reporting any significant problems or violations of the *NIH Guidelines* and any significant research-related accidents or illnesses in accordance with section VII below;

- Adhering to and training research staff on the KUMC Biosafety Plan and IBC Emergency Plan and supervising the safety performance of the laboratory staff to assure that the required safety practices and techniques are employed;

- Investigating and reporting any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the BSO, the Executive Director of Lab Animal Resources (where applicable), IBC, NIH and other appropriate authorities (if applicable);

- Correcting work errors and conditions that may result in the release of recombinant or synthetic nucleic acid molecule material materials;

- Ensuring the integrity of the physical containment (e.g., biological safety cabinets) and the biological containment (e.g., purity and genotypic and phenotypic characteristics);

- Complying with reporting requirements for human gene transfer experiments conducted in compliance with the *NIH Guidelines* (see Appendix M-I-C of the *NIH Guidelines)*; and Reporting any new information bearing on the NIH Guidelines to the IBC and to NIH/OSP.

VII. Incident and Safety Adverse Event Reporting

A. Incident Reporting

1. The Principal Investigator is responsible for immediately reporting to NIH and to the BSO or Director of Environment, Health and Safety, spills and accidents where there has been overt exposure at biosafety level 2 or higher and/or potential exposures at biosafety level 3 or higher. The BSO will immediately report the incident to NIH, if the BSO is unable to confirm that the Principal Investigator has made the required report described above.

2. The Principal investigator is responsible for immediately reporting to the BSO or Director of Environment, Health and Safety, and for reporting to NIH within 30 days, any significant problems or violations of the NIH guidelines and any significant research-related accidents or illness.

3. The IBC shall be responsible for reporting any significant problems with or violations of the NIH Guidelines and any significant research-related accidents or illnesses to the Vice Chancellor for Compliance, Vice Chancellor for Administration, Vice Chancellor for Research, and the NIH OSP within 30 days, unless the IBC determines that a report has already been filed by the Principal Investigator. Reports to NIH OSP shall be sent to the Office of Science Policy, National Institutes of Health, preferably by e-mail to: NIHGuidelines@od.nih.gov;

additional contact information is also available here and on the OSP website (www.osp.od.nih.gov).

4. The Template for Reporting Incidents Related to Research Involving Recombinant or Synthetic Nucleic Acids to the NIH Office of Biotechnology Activities is available for researchers to utilize.

B. Human Gene Transfer; Adverse Event Reporting

1. The Principal Investigator is responsible for reporting any serious adverse events that is **fatal or life-threatening**, that is unexpected, and associated with the use of the gene transfer product (i.e. there is a reasonable possibility that the event may have been caused by the use of the product; investigators should not await definitive proof of association before reporting such events). The report must be submitted to NIH Office of Science Policy (OSP) as soon as possible, but not later than 7 calendar days after the sponsor's initial receipt of the information (i.e. at the same time the event must be reported to the FDA). **The Institutional Review Board (IRB) and other federal agencies may have additional reporting requirements.**

2. Serious adverse events that are unexpected and associated with the use of the gene transfer product, but are **not fatal or life-threatening**, must be reported to the NIH OSP as soon as possible, but not later than 15 calendar days after the sponsor's initial receipt of the information (i.e. at the same time the event must be reported to the FDA). **The Institutional Review Board (IRB) and other federal agencies may have additional reporting requirements.**

3. If, after further evaluation, an adverse event initially considered not to be associated with the use of the gene transfer product is subsequently determined to be associated, then the event must be reported to the NIH OSP within 15 days of the determination. Relevant additional clinical and laboratory data may become available following the initial serious adverse event report. Any follow-up information relevant to a serious adverse event must be reported within 15 calendar days of the sponsor's receipt of the information. If a serious adverse event occurs after the end of a clinical trial and is determined to be associated with the use of the gene transfer product, that event shall be reported to the NIH OSP within 15 calendar days of the determination.

4. Any finding from tests in laboratory animals that suggests a significant risk for human research participants including reports of mutagenicity, teratogenicity, or carcinogenicity must be reported as soon as possible, but not later than 15 calendar days after the sponsor's initial receipt of the information (i.e., at the same time the event must be reported to the FDA).

See the NIH Guidelines, Section M-I-C-4.

VIII. Violations

Non-compliance with the NIH Guidelines, this procedure or the KUMC Policy on *Activities Involving Recombinant or Synthetic Nucleic Acid Molecules or Other Potentially Hazardous Biological Agents* may result in one or more of the following:

- Suspension or termination of use of recombinant or synthetic nucleic acid molecules and/or biohazardous materials, agents or toxins.
- Confiscation or destruction of the recombinant or synthetic nucleic acid molecules and/or biohazardous materials, agents or toxins.
- Other actions necessary to protect the public and/or university, including restricting access to the laboratory in order to suspend activities.
- Loss of approval to conduct research or teaching activities involving use, or generation of recombinant or synthetic nucleic acid molecules and/or biohazardous agents, materials and toxins, or termination.
- Liability under applicable state and federal law, and disciplinary action under applicable faculty, staff or student policies.

Policy Owner: Vice Chancellor for Administration

Contact by Title Only: Vice Chancellor for Administration

Approved by: [Vice Chancellor Administration, EVC, Institutional Biosafety Committee**]**

Review Cycle: Annual

Related Policies:

- Activities Involving Recombinant or Synthetic Nucleic Acid Molecules or Other Potentially Hazardous Biological Agents

Related Procedures:

- IBC Emergency Plan

Related Forms:

- Template for Reporting Incidents Related to Research Subject to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acids to the NIH Office of Biotechnology Activities.

- Template for Reporting Adverse Events In Human Gene Transfer Trials

Related Regulations, Guidance:

- NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

- Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition (http://www.cdc.gov/biosafety/publications/bmbl5/index.htm)

Related Other:

- **The Learning Connection (TLC)**