IBC Requirements for Human Gene Transfer (HGT) Studies

I. INTRODUCTION

The purpose of this document is to establish the Institutional Biosafety Committee (IBC) requirements for HGT studies based on the most current version of the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (*NIH Guidelines*).

Per the *NIH Guidelines*:

Section III-C: Experiments Involving Human Gene Transfer that Require Institutional Biosafety Committee Approval Prior to Initiation.

Section III-C-1: Experiments Involving the Deliberate Transfer of Recombinant or Synthetic Nucleic Acid Molecules, or DNA or RNA Derived from Recombinant or Synthetic Nucleic Acid Molecules, into One or More Human Research Participants.

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

1. Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
2. Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria:
    a. Contain more than 100 nucleotides; or
    b. Possess biological properties that enable integration into the genome (e.g., cis elements involved in integration); or
    c. Have the potential to replicate in a cell; or
    d. Can be translated or transcribed.

Research cannot be initiated until the IBC and all other applicable institutional and regulatory authorization(s) and approvals have been obtained.

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.

II. HGT REVIEW UPDATES

In 2019, the NIH approved an Amendment to the *NIH Guidelines* to streamline the review of gene therapy trials**.** The NIH eliminated the Recombinant DNA Advisory Committee (RAC) and removed the requirement to register and report human gene therapy protocols to the NIH Office of Science Policy (OSP), thereby granting full authority over this research to local oversight bodies: The Institutional Biosafety Committee (IBC) and Institutional Review Board (IRB).

HGT studies are still covered under the *NIH Guidelines* (see Section III-C), as protocols must still be reviewed and approved by the IBC to assess biosafety considerations associated with the study agent at the clinical trial site. In addition, all other applicable institutional (e.g., IRB) and regulatory authorization(s) and approvals must be obtained before any research with human participants can be initiated.

UPDATES IN NIH REPORTING REQUIREMENTS

Under the *NIH Guidelines*, individual HGT protocol submission and reporting to NIH/OSP are no longer required. Specifically, NIH/OSP will not:

- accept or register new HGT protocols
- convene the RAC to review individual HGT protocols
- accept annual reports, safety reports, amendments, or other documentation for any HGT protocols previously registered under the *NIH Guidelines* (formerly, Appendix M-I-C)

It is important to note that while NIH is streamlining individual HGT protocol reporting requirements, robust oversight over HGT research will continue through both Federal and local oversight bodies. HGT research remains subject to Food and Drug Administration (FDA) oversight. In addition, as with all NIH-supported research, HGT research will remain subject to NIH oversight, as well as applicable policies and regulations for the protection of human subjects in research—such as the Common Rule and the NIH policy on Certificates of Confidentiality—and rigorous local oversight will continue to be provided by IRB and IBC.

https://osp.od.nih.gov/biotechnology/faqs-on-the-nih-guidelines-research-synthetic-nucleic-acid-molecules/

III. ROLE OF THE IBC

The focus of the IBC's review of HGT research is equivalent to their review of the biosafety aspects of other covered research, and includes (but is not limited to):

- → required biocontainment levels,
- → potential for virus shedding,
- → safety and training of laboratory/technical personnel involved in the clinical protocol,
- → details of the facilities,
- → adequacy and maintenance of safety equipment that may be used in support of the clinical protocol,
- → safety procedures and practices when working with the product and during administration to a protocol participant,
- → reporting of biosafety accidents and incidents occurring during conduct of the protocol, and
- → approving emergency response plans for accidental spills and personnel contamination.

IBC oversight may conclude after the last participant is administered the final dose of product. However, IBCs may choose to establish other end points for oversight, based on their biosafety assessment of the proposed research. See section VII (Study Closure and Long-Term Follow-Up) below for more information regarding UCLA IBC policy for HGT study closures.

IV. HGT REVIEW PROCESS

The Principal Investigator (or designee) must notify the IBC of new HGT studies by submitting a Biological Use Authorization (BUA) application and supporting documents through SafetyNet.

When submitting an application to the UCLA IBC, the following documentation must be submitted in SafetyNet for review.

Document	Additional Information
Clinical Protocol	
Investigator's Brochure	
Pharmacy Manual/Instructions	
Bloodborne Pathogen Exposure Control Plan (If study involves collection of clinical specimens or delivery of materials covered under the Cal/OSHA BBP Standard)	For Health Systems locations, follow Policy IC 006 For non-Health Systems locations, complete the BBP Exposure Control Plan template
Aerosol Transmissible Disease Exposure Control Plan (If study involves aerosol transmissible diseases or pathogens)	ATD Exposure Control Plan template

Concurrent with the review of their BUA, the PI must also submit a protocol to the IRB for review. No research participant may be enrolled in a HGT study until IBC and IRB approvals and any other applicable regulatory authorizations are obtained.

V. BUA CONTINUING RENEWALS AND AMENDMENTS

Continuing Renewals

An Annual Continuing Review process begins one year after the initial protocol is approved by the IBC. The annual continuing review will assess any changes that have been made during the previous year and confirm any study updates.

Specifically, you must outline:

- Any significant incidents or SAEs related to the investigational product.
- A summary of the research progress and enrollment in the last year.

Please note: An amendment must be submitted alongside the continuing renewal when there are updates made to the study protocol that are directly related to the investigational product and/or its administration. More detail is outlined below describing amendment criteria for the IBC.

Amendments

After initiation of an approved HGT Study, if a change to your initial protocol has occurred during the previous year an amendment is required. The following information and documents need to be submitted to the UCLA IBC.

Changes that Could Impact the Biosafety Risk Assessment

Any changes that could potentially impact the initial biosafety risk assessment must be submitted to the IBC for review prior to initiating these changes by creating an amendment in SafetyNet. This may include, but is not limited to:

- Changes to the gene transfer product.
- Changes to any procedures involving handling the gene transfer product at UCLA.
  Changes to the locations where the gene transfer product will be handled, stored, administered.
- Changes to the personnel who will handle, transport, or administer the gene transfer product or specimens collected from subjects.
- Any new safety information related to the gene transfer product.
- Changes in the monitoring/surveillance tests and/or procedures at UCLA.

Contact the IBC administrative team if there are questions about whether a change requires an amendment.

VI. REPORTING REQUIREMENTS

Incidents (Biosafety-Related)

The IBC requires that study teams submit a report to the IBC and EH&S Biosafety for any significant incident or event that occurs involving the hazardous biological materials or r/sNAs described in the BUA, including:

- Serious Adverse Events (SAEs) determined to be associated with the gene transfer product.
- All accidents that result in an exposure or potential exposure to the biological materials.
- Any illness that may be caused by the biological materials.
- Theft or loss of the biological materials.
- All biological material spills outside of containment equipment (e.g., outside biosafety cabinet, centrifuge).
- Environmental contamination/release of the biological materials.
- Improper disposal of the biological materials.
- Near misses that could have resulted in any of the above.

VII. STUDY CLOSURE AND LONG-TERM FOLLOW-UP

A study may be closed in SafetyNet by submitting a Closure Request if the criteria listed below have been met. Additionally, new studies which look at long-term follow-up of subjects previously enrolled in a HGT study do not need to be submitted to the IBC if the following criteria have been met:

1. The study is closed to enrollment
2. Subjects are not actively being dosed with recombinant materials
3. There is no gene transfer product on site[a/b]

[a] If the product is stored on site, but all other criteria have been met, you may submit a BUA for storage only.
[b] If long-term follow-up involves collection of clinical specimens, a BUA is still needed to cover the Bloodborne Pathogen exposure risks; however, the IBC will not need to review all the documentation associated with the study. Additionally, IRB approval may still be required. Please consult with UCLA OHRPP to discuss IRB requirements.

VIII. ATTACHMENTS

- HGT SOP Template
  Please note that the HGT is no longer a requirement for IBC approval, but you can use this template for your records.

IX. REGULATIONS

- NIH Guidelines
- April 2019 Amendment of the NIH Guidelines FAQs
- Points to Consider: Institutional Biosafety Committee (IBC) Review of Human Gene Transfer Protocols

X. ADDITIONAL GUIDANCE

- SafetyNet Quick Reference Guides & Training Materials
- https://rsawa.research.ucla.edu/ibc/ibc-policies-guidance/

Any questions should be directed to the IBC Administrative Staff at ibc@research.ucla.edu.