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GUIDELINES FOR IBC REVIEW OF HUMAN GENE TRANSFER**Table of Contents**

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GUIDELINES FOR IBC REVIEW OF HUMAN GENE TRANSFER

1. Introduction

1.1. Purpose

The purpose of this document is to provide guidance on the IBC review process to clinical investigators who will be conducting trials or studies involving recombinant or synthetic nucleic acids in human subjects.

1.2. Definitions

Recombinant DNA Advisory Committee (RAC):

Section I-E-4 of the NIH Guidelines defines RAC as “the public advisory committee that advises the Department of Health and Human Services (DHHS) Secretary, the DHHS Assistant Secretary for Health, and the NIH Director concerning recombinant or synthetic nucleic acid molecule research.

Serious Adverse Events (SAE)

Section I-E-8 of the NIH Guidelines defines SAE as any event occurring at any dose that results in any of the following outcomes: death, a life-threatening event, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

Oversight body

Section I-E-11 of the NIH Guidelines defines the oversight body as an institutional entity (an Institutional Biosafety Committee or an Institutional Review Board) that must review and approve a human gene transfer trial. At Emory University the oversight body is the Institutional Biosafety Committee.

Human Gene Transfer (HGT)

Section III-C-1 of the NIH Guidelines defines HGT as 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.

Initial Site

An Institution where the investigational product will be used for the first time in human subjects and the clinical trial has not been reviewed by an oversight body. There may be multiple initial sites.

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2. Regulatory framework

In April 2016, the NIH amended the NIH Guidelines in the following areas:

- The criteria for selecting protocols for in-depth review and public discussion by the NIH Recombinant DNA Advisory Committee (RAC),
- The process by which human gene transfer protocols are reviewed by the institutional oversight body and registered with the NIH Office of Science Policy (OSP), and
- The streamlining of the NIH protocol submission requirements under Appendix M–I–A of the NIH Guidelines.

3. Responsibilities

3.1. Environmental Health and Safety Office (EHSO)

At Emory University, the Biosafety Officer (BSO) or Associate Biosafety Officer (ABSO) have the following responsibilities:

- Assist the Principal Investigator in the submission of all required documentation.
- Ensure that all documentation is available for review.
- Notify the Chair of the IBC of the submission of a new clinical trial where Emory University is an initial site.
- Coordinate the review of the clinical trial by the IBC and IRB chairs and/or a subcommittee.
- Ensure that IBC members reviewing HGT studies have the adequate expertise and training.
- Issue an approval letter after the IBC review has been completed and all administrative requirements have been fulfilled.

3.2. Principal Investigators (PIs)

- Complete the project and associated forms in the electronic platform.
- Submit documentation for review by uploading documents to the electronic platform.
- Submit appropriate and timely follow up information to the NIH as outlined in the NIH Guidelines (e.g., protocol amendments, serious adverse events, annual reports with cumulative safety data).
- Review and update annually, or when any change has occurred in the study, i.e. addition of another investigational product.
- ***All HGT studies to be conducted at Emory University must be reviewed by the Emory IBC.***
- ***All HGT studies subject to the NIH Guidelines must be registered with NIH OSP.***

3.3. Laboratory Personnel (All Staff associated with the clinical trial)

- Report all incidents and accidents during the administration or handling of the recombinant or synthetic product.
- Update annual training for Bloodborne pathogens, if applicable.
- Update the EHSO Biosafety training.

3.4. IBC Chair

- Convene with the IRB chair when studies or trials where Emory University is an initial site to determine if the clinical trial would benefit from RAC review.
- Assist in the selection of IBC members for the subcommittee to review further the

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merits of the initial recommendation of the IBC and IRB Chairs regarding the need for RAC review.

4. General Guidelines

4.1. What is the criteria for RAC review?

- An oversight body (an Institutional Biosafety Committee (IBC) or an Institutional Review Board (IRB)) involved in the initial site(s) review determines that a human gene transfer protocol submitted to it for approval would significantly benefit from RAC review, and
 - One or more of the criteria below are satisfied:
 - The protocol uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience, thus presenting an unknown risk.
 - The protocol relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value.
 - The proposed vector, gene construct, or method of delivery is associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies to evaluate the protocol rigorously.

4.2. Who requests RAC review?

The chair of the Emory University IBC requests RAC review to NIH OSP after concurring with the IRB Chair and the IBC sub-committee's recommendation.

4.3. When does a clinical trial need to be registered with NIH OSP?

All HGT studies subject to the NIH Guidelines must be registered with NIH OSP.

4.4. What documentation is required for IBC review?

According to Section III-C-1 and Appendix M of the NIH Guidelines, the following documents need to be submitted:

- 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;
- A description of the investigational product;
- The proposed informed consent document(s);
- The Principal Investigator shall provide additional documentation originating from oversight bodies involved in the review, if available
- Emory University IBC requires the additional documentation:
 - Completion of the project form and pathogen or viral vector form associated with the investigational product in the electronic platform
 - Investigational Brochure
 - Pharmacy Manual, or related document

4.5. What if Emory University is an additional site?

Emory University IBC reviews all clinical trials involving recombinant or synthetic nucleic acids, even if Emory University is not an initial site. Thus, submission must be completed

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in the electronic platform.

In addition, the PI will provide documentation that the initial site (if there is another initial site) has completed the IBC review.

For a clinical trial site that is added after the completion of the NIH protocol registration process, no research participant shall be enrolled (see definition of enrollment in Section I-E-7) at the clinical trial site until IBC approval and IRB approval from that site have been obtained. Within 30 days of enrollment (see definition of enrollment in Section I-E-7) at a clinical trial site, the following documentation shall be submitted to NIH OSP:

- Institutional Biosafety Committee approval (from the initial clinical trial site);
- Institutional Review Board approval;
- Institutional Review Board-approved informed consent document(s); and
- NIH grant number(s) if applicable.

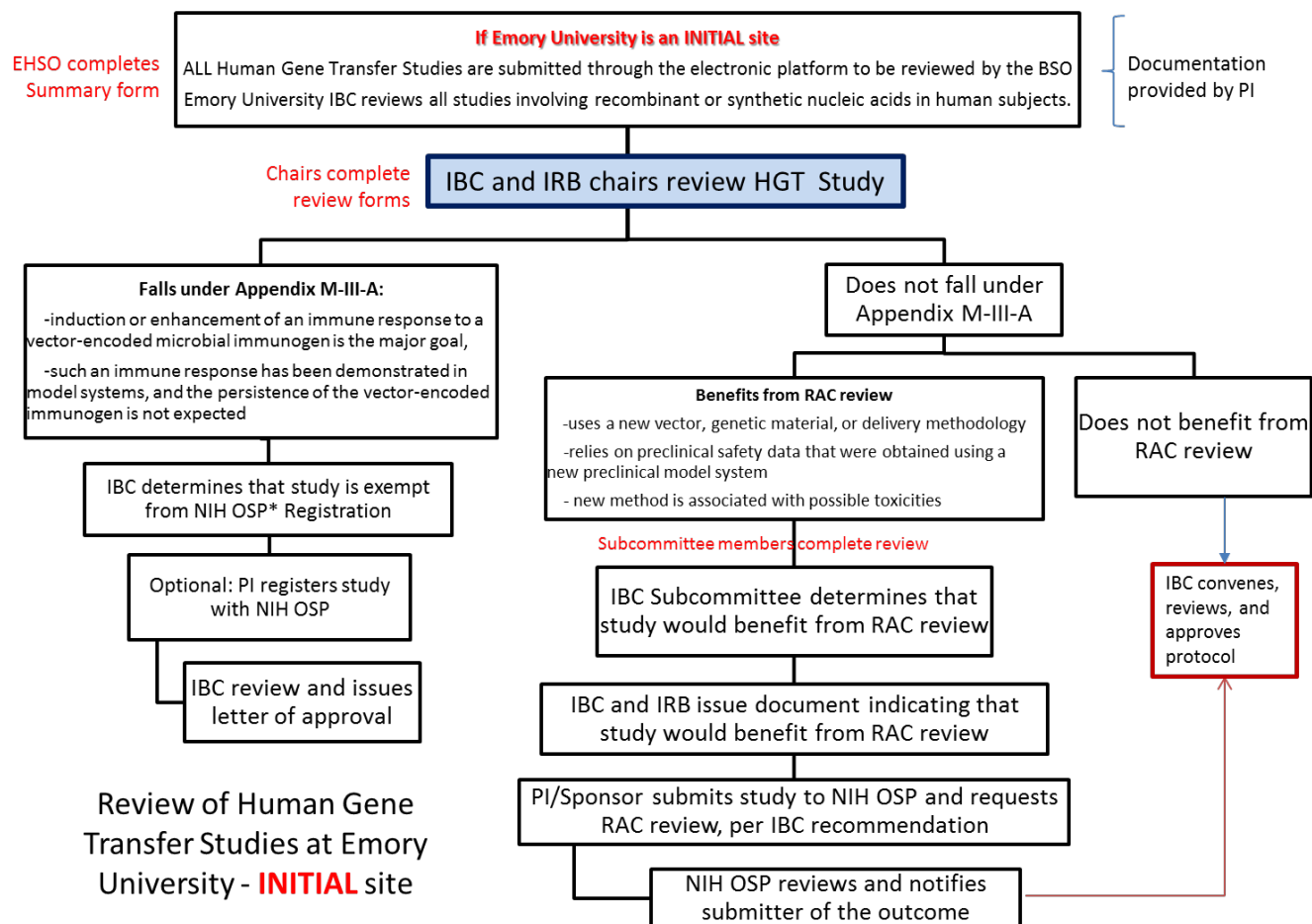
5. References

- NIH Guidelines: https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.html#_Toc446948309
- NIH The NIH Review Process for Human Gene Transfer Trials: <https://osp.od.nih.gov/biotechnology/faq-onthe-nih-review-process-for-human-gene-transfer-trials/>
- Emory University IBC Standard Operating Procedure
- Emory University IBC Charter

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Appendix A: Review process for a clinical study involving recombinant or synthetic nucleic acids when Emory University is an Initial Site.



*OSP= Office of Science Policy