university of washington

OFFICE OF RESEARCH

**Frequently Asked Questions**

1. If my research uses differentiated progeny of hESCs and are no longer pluripotent, do I need to submit a new application?'

ESCRO does not require further review and approval of your hESC research if you have established that the differentiated hESCs are no longer pluripotent. For example, your previous ESCRO application involved inducing the differentiation of hESCs and you have now grown the cells over many passages using media conditions that ensure the loss of pluripotency. These growth conditions are published and are widely accepted by the scientific community as demonstrating that pluripotency of the hESCs no longer exists. Finally, you have shown that your differentiated hESCs no longer express pluripotency markers but rather express markers of a differentiated cell type. If these criteria are met, your research with these cells no longer requires ESCRO review and approval.

If you are no longer working with the original pluripotent hESC lines, please work with

the ESCRO office to close your existing ESCRO application.

1. What if I want to use derivatives from hESC lines or create genetically different cells from hESC lines (e.g. cardiomyocytes)?

It depends. A new cell line derived from a hESC is of interest to ESCRO, only if the new derived line is pluripotent. In other words, if cells of more than one lineage can be developed from the new cell line and they retain characteristics of embryonic stem cells, the new line requires ESCRO approval. If the line has a narrow differentiation path, ESCRO approval is not needed.

Use of derivatives from hESC lines may also require ESCRO approval if they are pluripotent.

1. What type of information should I provide to justify the significance of the research for human health? (Section II of application “Proposed Study”)

Describe how the potential benefits should outweigh the potential impacts and risks. Explain how the research is intended to advance science and medical knowledge and/or benefit human health.

1. Do you have an example of what type of information I should provide in the “Abstract”?' (Section II of application “Proposed Study”)

Below is an example of an ideal Abstract:

**Goals of the research:** The goal of this research is to derive clinically valuable blood cells from hiPSCs. Another goal of this project is to model blood disorders using patient hiPSCs.

**Brief description of the approach:** We start with hiPSCs from normal individuals and patients with blood disorders. We differentiate hiPSCs into hematopoietic stem and progenitor cells. In some cases, we further differentiate progenitors into blood cell types, or generate stable hematopoietic cell lines. We assay them in vitro or in vivo by transplantation into immunodeficient mice to test their function. To model disease, we differentiate normal and patient-derived hiPSCs into hematopoietic progenitors and attempt to recapitulate the patient phenotype in vitro and after transplantation into immunodeficient mice. We then aim to rescue the phenotype by using drug screens to identify therapeutic compounds.

**Rationale for using source of cells:** Since primary cells from patients are very limiting, hiPSCs provide a way of overcoming this limitation to model disease and discover treatments.

**Significance of the research for human health:** this research has significant potential benefits for patients affected by blood disorders.

1. Appendix A: “Source information” - Do I need to include commercial sources from which I obtain somatic cells?'

ESCRO does not review the use of somatic cells unless the investigator plans to induce pluripotency and manipulate the hESC-like line further *in vivo*, in which case provenance documentation is needed. Therefore, with this one exception, the ESCRO application does not require you to list sources of somatic cells.

1. Why do I need to provide the blank consent-of-origin (also known as provenance) and IRB approval for lines that are not listed on the NIH hESC Registry or for hIPSC research requiring ESCRO approval? (All Appendices)

The ESCRO Committee will review the consent and IRB documents to ensure that individual decisions about donation will not affect the quality of care the donor or that donors were made aware of potential future research. ESCRO reviews the consent-of-origin to ensure that individual donations were made free from undue influence. Please include original donor consent forms in original language as well as English translation for:

* egg donations made in context of research;
* egg donations made in the context of fertility treatment;
* sperm donor consent form for research;
* sperm donor consent form made in context of fertility treatment, consent form from donor of blastocyst if different from above;
* somatic cell donor consent form.

GIM 36 prohibits payment to a donor solely for the purpose of creating a human embryo to be used in hESC research.

1. What rationale is acceptable to ESCRO for requesting to waive provenance?

In general, provenance documentation is required for any non-federally approved hESC-line(s). An exception to this requirement may include when induced pluripotent stem cell lines are created from anonymized somatic cell sources where the PI cannot ascertain the identity of the individual who donated the somatic cell. In such cases, the PI should briefly explain the history of the cell line and cite relevant literature supporting the origin of the cell line. (All Appendices.)

1. What if my proposal requires IACUC and/or EH&S approval but I have not received an IACUC protocol # or EH&S protocol #? (Section IV. Additional Oversight.)

ESCRO review will occur concurrently with other Oversight Office reviews. If you have submitted an application to another Oversight Office but have not received an Oversight Office protocol # yet for that application, please email the ESCRO office (escro@uw.edu) with the following information:

* Title of the application applicable to the hESC research
* Applicable Oversight Office relevant to your ESCRO application
* Date of submission

Although the ESCRO office will work as much as possible with existing Oversight Offices to obtain protocol # information and approval information, some of the Oversight Offices cannot issue final approval until they receive confirmation of ESCRO review and approval. For example, if your proposal involves EH&S and/or IACUC, they cannot issue final approval until ESCRO has approved your protocol.

1. When do I need IRB approval?

There are four steps to determine if IRB review may be needed. Review the steps at Human Subject’s Division (HSD) website at <https://www.washington.edu/research/hsd/do-i-need-irb-review/>. See HSD’s main contact page [here](https://www.washington.edu/research/contact-us/?keyword=508) to assist you in locating support.

1. How do I know when the specimens I’ve received contain codes that are considered identifiable would require IRB review?

Part of the four steps referenced above describes research involving human subjects. Review at <https://www.washington.edu/research/hsd/do-i-need-irb-review/does-your-research-involve-human-subjects/>and contact HSD with any questions. HSD’s main contact page is [here](https://www.washington.edu/research/hsd/hsd-contact/). See HSD’s main contact page [here](https://www.washington.edu/research/contact-us/?keyword=508) to assist you in locating support.

1. Why am I asked about CoMotion (our office of Technology Transfer)?

CoMotion is listed in the table to serve as a prompt to remind you to contact them in the event that any specimens or materials are or will be exchanged between you and collaborators.

1. Why do I have to justify the number of human embryos I may use for my research proposal? (Appendix B)

We ask for this justification because we recognize that scientists are the legitimate stewards of these resources and the public trust depends on demonstrating judicious use of human embryonic, or fetal tissues.

1. Why am I asked to provide rationale for using certain genotypes? (Appendix B)p

Such justification helps ensure that vulnerable populations are not enlisted for research without scientific justification and without the promise that these populations will benefit from research in the future. It is important to specify how you plan to assure the confidentiality and anonymity of donors.

1. Why am I asked to provide scientific justification for generating human embryos from hESC or hESC-like lines? The cells came from human embryos of human tissue originally (Appendix D).

Creating embryos specifically for research purposes raises many ethical concerns with the public. In addition, such embryos must also be destroyed by day 14 of development.

1. What type of information do I provide to justify the transplantation of hESCs and/or hIPSCs into animals? (Appendix C.)

If there is a reasonable possibility that, after transplantation of hESCs or hIPSCs, the animal will generate human gametes or neural pathways, discuss the procedures that will be implemented for management, documentation and reporting of such occurrences to IACUC and ESCRO.

As a reminder, prohibited research includes the following:

* Implanting a chimeric embryo containing non-human cells, including ESCs, into the uterus of a human;
* Implanting a chimeric embryo containing hESCs into a uterus of a nonhuman primate and allowing the resulting pregnancy to progress to the point of independent viability;
* Breeding of a chimeric animal having hESCs that were introduced during any stage of the animal’s embryonic or fetal development;
* Breeding of a chimerical animal having hESCs where there is a reasonable possibility that human genetic material could be incorporated into the animal’s germ cells.

In addition, ESCRO has determined that certain categories of induced, pluripotent stem-cell research (iPSC research) require ESCRO review and approval. These categories include the following:

* Transplantation of iPSCs into research animals;
* Transplantation of iPSCs into humans;
* Use of iPSCs to create an embryo.