Harvard University
Embryonic Stem Cell Research Oversight (ESCRO) Committee

Protocol Application

Use for new protocols and major amendments

Part I. Protocol and Contact Information

A. Protocol Title: _____

Short Title *(optional)*: _____ | **B. Protocol No.**: E_____

C. Submission Type (*choose one*): ☐ New Protocol ☐ Major Amendment
Please also submit a cover letter as well as revised protocol materials ***integrating*** *the changes.*

D. Funding Source(s): _____

E. Principal Investigator* Name and Degree(s): _____

Department: _____ School: _____

Email: _____ Phone: _____

F. ☐ *Check here if this study has **co-PIs**, and include the other PI on the Research Team Form.

G. Administrative or Other Study Contact Name and Degree(s): _____

Email: _____ Phone: _____

Part II. Type of Research

Section A:

Does this protocol involve the **use or creation** of a **human embryo in vitro** to **derive human embryonic stem (hES) cell** lines?

☐ No (*skip to next section*)
☐ Yes (*complete the following*)

If Yes:

1. Does the protocol involve the derivation of new lines from pre-implantation embryos?
   ☐ No ☐ Yes. Estimate the number of embryos you may need: _____

2. Does this protocol involve research in which the **identity of the donors** of embryos, blastocysts, gametes, somatic cells or other tissues from which cells were derived is readily ascertainable or might become known to the investigator?
   No Yes

3. Does the protocol involve research performed with the intention of experimentally creating a human embryo by any means, including, but not limited to parthenogenesis, androgenesis, or nuclear/chromosome transfer?
   ☐ No (*continue to next question*)

☐ Yes (*complete the following*)

If Yes:

a. List method(s) you will use to create the embryos: _____

b. Indicate the tissue(s) needed and the estimated number/amount of each:

4. Please provide the scientific rationale for the need to derive new hES cell lines. Include an explanation of why you cannot use existing lines.

Section B: Use

Does this protocol involve the **use** of **hES** or ESCRO covered uses of **human pluripotent stem (hPS)** cells or **human neural progenitor cells**?

☐ No (*skip to next section*)
☐ Yes (*complete the following*)

If Yes:

5. List all lines you plan to use:

Line Identifier (It is okay to group/batch similar lines below.)	**Type of Line**	**Source (From where will you obtain it?)***
	☐ hES ☐ hPS ☐ Other. Describe:	

*If **hES** cell line is not already registered with ESCRO, also submit hESC Registration Form.

6. Does this protocol involve ***in vitro* use** of hESC lines?
☐ No ☐ Yes

7. Does this protocol involve the use of hES, hPS or human neural progenitor cells in non-human animals, *except* for teratoma formation to test for pluripotency?
☐ No (*continue to next question*)
☐ Yes (*complete the following*)

If Yes:

a. Does the protocol involve the introduction of human pluripotent cells (from any source, including but not limited to hES cells, those derived from human somatic cells, amniotic fluid, or fetal tissue) into any **non-human animal** at any stage of **prenatal development**? (Teratoma formation to test for pluripotency does not require ESCRO review. Insertion of human pluripotent cells into human or non-human primate blastocysts is prohibited.)
☐ No ☐ Yes

b. Does the protocol involve research involving the insertion of **human pluripotent cells** or **human neural progenitor cells** into the **central nervous system** of any non-human animal?
☐ No
☐ Yes

8. Does this protocol involve research involving the introduction of human pluripotent cells into humans?

☐ No
☐ Yes

Section C: Other Protocols

1. **Other embryo Use/Creation:**

   a. Does this protocol involve the use of a human embryo, **other than** to derive human embryonic stem cells?

   ☐ No

   ☐ Yes

   If Yes:

   a. Estimate the number of embryos you may need for this protocol:

   b. Does this protocol involve the creation of a human embryo[1], or human embryo-like structure[2], by any means other than fertilization?

   ☐ No

   ☐ Yes

   Please provide the scientific rationale for the need to use or create new embryos for this protocol.

2. Is this a banking protocol?

   ☐ No

   ☐ Yes

Part III. Research Summary

In addition to this form, and other approvals documentation, please submit the following for review:

1. **Biosketches or CVs for all key personnel, and**
2. **A Research Summary, as described below:**

Research Summary: Please describe the research or educational aim(s)/objective(s) of the project and its significance. Provide its potential value and risks in obtaining or establishing significant information relevant to the understanding of humans or animals and/or improvement to human or animal health, or achievement of educational objectives.

[1] Under Massachusetts law, the creation of an embryo by the method of fertilization for purpose of research is prohibited, and criminal penalties may result. M.G.L. c 111L, Section 8(b).

[2] An embryo-like structure, as defined in the ISSCR Guidelines, is an experimentally generated structure that manifests human organismal form, integrated organ system development, and autonomous developmental capacity. Under MA law, and for Harvard ESCRO purposes, the term "embryo-like" is meant to capture entities that do not result from human fertilization and includes parthenotes, the products of nuclear transfer, "synthetic embryos", and other poorly-defined *in vitro* entities that, while demonstrating some features of embryonic patterning, are not embryos in a biologically functional sense.

- **Clearly state the purpose and questions to be studied, and the key research procedures that will be used to answer these questions.**
- **Define all abbreviations and acronyms.**
- **If there is more than one aim/objective, they should be stated in numbered sequence**
- **Please justify the estimated numbers for this study, including number of subjects to recruit, number of tissue samples (embryos, blastocysts, oocytes, skin biopsies, etc.) to be collected to derive stem cell lines, number of cells implanted (for research involving transplantation of human stem cells into non-human animals).**
- **For research involving transplantation of human stem cells or neural progenitor cells into non-human animals:**
    - **Indicate the age of the animal;**
    - **Detail the anatomical location of the injection site /introduction of human cells in the animal;**
    - **Discuss how you will track the potential migration of transplanted human cells in the animal; and**
    - **Describe how you will prevent transplanted animals from breeding**
    - **Additionally, the ESCRO Committee is concerned with the human biology outcome of such transplantation protocols, for instance, inadvertently creating a chimera with enhanced cognitive function or altering the germline of an animal. Discuss the likelihood that the non-human animal might acquire cognitive functions thought to be distinctly human and, if anticipated, how you might assess and address this during the course of your research.**

Part IV. Other Required Approvals and Documentation

Section A. Indicate approval or status for each of the following (if applicable):

Type of review	Approved	OR	Pending	OR	Not applicable
1. Institutional Review Board (IRB)					☐ no human subjects
2. Institutional Animal Care and Use Committee (IACUC)					☐ no vertebrate animal use
3. Cost Allocation (If not required, please submit written documentation.)					
4. Non-Harvard Review (list details below):					☐ no collaborating institution
a. Collaborating Institution Name: _____ b. Collaborator's Protocol #: _____ c. Type of Review: ☐ ESCRO ☐ IRB ☐ Other, describe: _____ (*Choose as many as apply.*)					
5. Committee on Microbiological Safety (COMS)	☐		☐		

Part V. Principal Investigator's Certification

I have read and agree to abide by the policies of the Harvard University ESCRO. I certify that the information in this form and any supplemental materials is accurate and complete. If this is a hESC line derivation protocol, I agree to register any lines derived.

_____ _____

Principal Investigator's Signature Date

Instructions for Protocol Application

Skip logic in Part II:

If the answer to a question allows the user to skip the rest of the questions in the section, the directions will say "skip to the next section." If the answer to a question allows the user to skip a sub-question within a section, but more questions in that section must be answered, the directions will say "continue to next question." The "next question" is the next question of the same level as the one just answered, e.g., if the answer to question 3 directs the user to continue to the next question, the user skips questions 3a and 3b but answers question 4.

For all tables, use the 'Tab' key to create more rows as needed.

IRB and IACUC protocols are not required to be appended to the ESCRO application. Presumably the research described in the ESCRO protocol reflects what is described in the other committee's protocol. For studies that are also considered human subjects research and require IRB approval, copies of the informed consent forms must be submitted to the ESCRO as well.

** Under Massachusetts law, No person shall knowingly create an embryo by the method of fertilization with the sole intent of donating the embryo for research.