Instructions for Completing NIH Form 2890

Request for Human Embryonic Stem Cell Line to be Approved for Use in NIH Funded Research

OMB Approval 0925-XXXX

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Introduction

NIH Guidelines on Human Stem Cell Research, effective July 7, 2009, establish a new NIH Human Embryonic Stem Cell Registry listing human embryonic stem cells (hESCs) eligible for use in NIH funded research. Only hESCs that have been reviewed and deemed eligible by the NIH in accordance with the Guidelines may be used in NIH supported research.

NIH Form 2890 is provided for the purposes of submitting information about hESC lines to the NIH, along with assurances and supporting documentation of compliance with the NIH Guidelines. NIH will conduct either an Administrative Review, or review by a Working Group of the Advisory Committee to the [NIH] Director (ACD). The Working Group of the ACD will make recommendations to the ACD, which will advise the NIH Director who will make the final determine whether a hESC line may be approved for use in NIH funded research. All approved lines will be listed on the NIH Registry. The Registry will also contain basic information about organizations intending to submit lines to the Registry, lines pending NIH review and lines that have been reviewed and not approved for use in NIH funding.

Submission of hESC line through the NIH Form 2890 Web Site

NIH Form 2890 is a web-based form only, and must be submitted electronically through this web site: [insert link]

eRA Commons Registration: An organization wishing to submit a hESC line for review must be registered in the eRA Commons. This is a one-time registration and is necessary for NIH validation purposes. Organizations may verify their current registration status by accessing the *List of Grantee Organizations Registered in NIH eRA Commons* at http://era.nih.gov/userreports/ipf_com_org_list.cfm. To register an Organization in the eRA Commons follow these instructions: https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp. Note that a DUNS number must be included in the Institutional Profile. Instructions for obtaining a DUNS number are available through the eRA Commons registration process.

Signing Official Authority: Only an individual with a Signing Official (SO) role in the eRA Commons may submit a request that NIH review a hESC line to be approved for use in NIH funded research. To log into the system and complete NIH 2890, the SO must provide his/her eRA Commons UserID and password.

eRA Commons Support: For questions or problems concerning obtaining an eRA Commons account, please contact Commons Support at 1-866-504-9552, or email commons@od.nih.gov and a customer service representative will be in contact with you.

General Information about Submission

Upon successful log-in to the NIH 2890 web site, you will be required to select the method of NIH review of your request. The two methods of review are Administrative Review, or review by the Working Group of the ACD. Your selection is based on a number of factors, including where and when the embryo from which the stem cells were derived was donated, and whether you are able to provide supporting documentation that the embryo was donated in accordance with Section II(A) of the NIH Guidelines.

Please use the Guidelines to determine the appropriate method of review. A cell line that meets the requirements of Section II(A) should be reviewed by NIH Administrative Review. Review by the Working Group of the ACD is only appropriate for:

- cell lines donated prior to July 7, 2009 which do not meet the exact specifications of Section II(A) but for which the embryos 1) were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose; and 2) that were donated by donor(s) who gave voluntary written consent for the human embryos to be used for research purposes, and
- cell lines from embryos donated outside the US on or after July 7, 2009 that do not meet the exact specifications of Section II(A) but for which the applicant believes the procedural standards of the foreign country provide protections at least equivalent to Section II(A) and were followed.

It is important that you make the selection of method of review carefully. Once you have made a selection you cannot change your selection without exiting the system and logging in again. After a request is submitted, NIH does not have the ability to change the method of review. You may contact the NIH Registry at: hescregistry@mail.nih.gov and request that a submission be deleted.

Following your selection of method of review, you will be directed to complete the remaining sections of Form 2890, where administrative and stem cell line information will be entered, and you will upload supporting documentation for Administrative Review or review by the Working Group of the ACD.

Form 2890 provides the ability to submit multiple hESC lines in one submission, when all of the following circumstances are present:

1. the same organization and Signing Official is submitting all of the hESC lines;
2. the method of review for all of the hESC lines is the same (either Administrative Review or Working Group of the ACD review), and
3. the supporting information for all of the hESC lines included in the submission is exactly identical.

When multiple hESC lines are part of one submission, NIH will review the request as a single submission. If the request is approved then each hESC line will receive a separate NIH approval number and be listed separately on the NIH Registry. It is critical that the supporting information for all of the hESCs included in a single submission is identical.

All information submitted will be subject to the Freedom of Information Act. Do not submit consent documents with the personally identifying information of donor(s) of the embryos (the individuals(s) who sought reproductive treatment). Submission of consent documents with such information will cause the submission to be invalidated and NIH to delete all submitted information.

The last section of Form 2890 is the Assurance, Certification, Authority and Final Submission section. If you have selected review by the Working Group of the ACD you will be required to indicate, by selection of the appropriate assurance, whether you are requesting review by the Working Group under Section II(B) or II(C) of the NIH Guidelines.

Saving Data, Freedom of Information Act, and Intent to Submit

Users have the ability to save data to avoid a timeout of the session and potential data loss. A session lasts approximately one hour, but each time the user clicks the "Save Data for Further Editing" button, the session in restarted.

In addition, if you start a session and click the "Save Data for Further Editing" button, then the session will be saved on the NIH server as a draft. You may come back at a later time or date and complete the submission. However, all drafts, including final submissions, are subject to the Freedom of Information Act.

In order to provide the community with information about plans to submit a particular cell line, if you do not complete a session, and have clicked the "Save Data for Further Editing" button, the name of the applicant organization (item 3) and the same of any stem cell lines that have been entered (item 6), will be posted on the NIH Registry under "Institutions Intending to Submit hESC Lines." If you decide not to complete the submission, please contact **hescregistry@mail.nih.gov** and request that the draft(s) be purged and removed from this list. If you do not complete a session within 6 months from the last time you click "Save Data for Further Editing" then the draft will automatically be purged and removed from the list of "Institutions Intending to Submit hESC Lines."

Form 2890 Support

Questions concerning the NIH Guidelines and use of Form 2890 should be addressed to the NIH Registry at: hescregistry@mail.nih.gov.

Selection of Method of NIH Review

The two methods of NIH review, NIH administrative review and review by the working group of the Advisory Committee to Director of NIH (ACD), and the criteria and supporting information required for each are described below. A simplified decision tree [link to tree] is also available to assist with your selection.

NIH Administrative Review

NIH Administrative Review should be selected if the organization has documentation related to the embryo donation that demonstrates compliance with all of the elements of Section II(A) of the NIH Guidelines. Regardless of where or when the embryo was donated, this option is available for all hESC lines for which there is supporting documentation. For embryos donated in the United States on or after July 7, 2009, compliance with Section II(A) is mandatory and therefore the only method of review available for such cell lines is NIH Administrative Review.

Examples of supporting documents include sample consent forms, written policies, or other documents such as a copy of the Embryonic Stem Cell Research Oversight (ESCRO) or Institutional Review Board (IRB) or ethics committee approval to use the line or documentation of a committee's exemption from review

The supporting information must provide evidence of compliance with each of the following elements of Section II(A) of the NIH Guidelines:

> **Element 1.** hESCs were derived from human embryos that were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose.
> **Element 2.** hESCs were derived from human embryos that were donated by individuals who sought reproductive treatment (donor(s)) and who gave voluntary written consent for the human embryos to be used for research purposes.

Element 3. All options available in the health care facility where treatment was sought pertaining to the embryos no longer needed for reproductive purposes were explained to the individual(s) who sought reproductive treatment.
Element 4. No payments, cash or in kind, were offered for the donated embryos.
Element 5. Policies and/or procedures were in place at the health care facility where the embryos were donated that neither consenting nor refusing to donate embryos for research would affect the quality of care provided to potential donor(s).

There was a clear separation between the prospective donor(s)'s decision to create human embryos for reproductive purposes and the prospective donor(s)'s decision to donate human embryos for research purposes. Specifically:

Element 6. Decisions related to the creation of human embryos for reproductive purposes should have been made free from the influence of researchers proposing to derive or utilize hESCs in research. The attending physician responsible for reproductive clinical care and the researcher deriving and/or proposing to utilize hESCs should not have been the same person unless separation was not practicable.
Element 7. At the time of donation, consent for that donation should have been obtained from the individual(s) who had sought reproductive treatment. That is, even if potential donor(s) had given prior indication of their intent to donate to research any embryos that remained after reproductive treatment, consent for the donation for research purposes should have been given at the time of the donation.
Element 8. Donor(s) should have been informed that they retained the right to withdraw consent until the embryos were actually used to derive embryonic stem cells or until information that could identify the donor(s) was no longer retained by the researchers, if applicable.

During the consent process, the donor(s) were informed of the following:

Element 9. The embryos would be used to derive hESCs for research.
Element 10. What would happen to the embryos in the derivation of hESCs for research.
Element 11. hESCs derived from the embryos might be kept for many years.
Element 12. The donation was made without any restriction or direction regarding the individual(s) who may receive medical benefit from the use of the hESCs, such as who may be the recipients of transplants of the cells.
Element 13. The research was not intended to provide direct medical benefit to the donor(s).
Element 14. The results of research using the hESCs may have commercial potential, and that the donor(s) would not receive financial or any other benefits from any such commercial development.
Element 15. Whether information that could identify the donor(s) would be available to researchers

Working Group of the ACD Review

With the exception of embryos donated in the United States on or after July 7, 2009, review by the Working Group of the ACD is possible. The Working Group will review the materials as described below, and make recommendations regarding eligibility for NIH funding to its parent group, the Advisory Committee to the Director (ACD) of NIH. The ACD will make recommendations to the NIH Director, who will make final decisions about eligibility for NIH funding.

Embryos donated prior to July 7, 2009. Working Group of the ACD review is possible for embryos donated prior to July 7, 2009, in any country, under Section II(B) of the NIH Guidelines. Supporting information will be similar to that provided for Administrative Review (e.g., consent forms, written policies, or other documents such as a copy of the Embryonic Stem Cell Research

Oversight (ESCRO) or Institutional Review Board (IRB) or ethics committee approval to use the line, or documentation of a committee's exemption from review).

Under Section II(B) of the NIH Guidelines, the supporting documentation must demonstrate that the hESCs were derived from human embryos:

1. that were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose; and
2. that were donated by donor(s) who gave voluntary written consent for the human embryos to be used for research purposes.

The Working Group will consider the submitted materials taking into account the principles articulated in Section II(A) of the Guidelines, HHS regulations for the protection of human subjects (45 CFR 46 Subpart A), and the following additional points to consider: during the informed consent process, including written or oral communications, whether the donor(s) were:

1. informed of other available options pertaining to the use of the embryos;
2. offered any inducements for the donation of the embryos; and
3. informed about what would happen to the embryos after the donation for research.

Embryos donated outside of the United States on or after July 7, 2009. Working Group of the ACD review is possible for embryos donated outside the United States on or after July 7, 2009, under Section II(C) of the NIH Guidelines. Supporting documentation demonstrating that the alternative procedural standards of the foreign country where the embryo was donated provide protections at least equivalent to those provided by Section II(A) of the Guidelines will be required.

Completing NIH Form 2890

Please review the instructions below prior to completing the form, uploading supporting documentation, and final submission.

Remember that if you click "Save Data for Further Editing" and do not complete the submission, the data entered thus far is saved on the NIH server as a draft and the name of the applicant organization (item 3) and the same of any stem cell lines that have been entered (item 6), will be posted on the NIH Registry under "Institutions Intending to Submit hESC Lines."

Administrative Information

1. Signing Official. Enter the name, phone number and email address of the Signing Official (SO, also known as the Authorized Organizational Representative) who logged into the system.

2. Point of Contact. If you would like to designate a point of contact (POC) for the request other than the Signing Official, please enter the name, phone and email address of a POC. NIH questions about the submission will be directed to the SO unless a POC is designated.

3. Applicant Organization Name and DUNS Number. Enter the applicant organization name and DUNS number. This information should match the information in the eRA Commons account.

4. Applicant Organization Address. Enter the applicant organization's address.

5. NIH Grant or Application Number. If there is an NIH grant or pending NIH application that would potentially use the stem cell line(s) that is(are) the subject of the request, please provide the numbers, using the following format: HL123456, AI654321, AG345678. If you

are requesting approval for multiple stem cell lines, you may enter multiple application numbers. The response to this question will have no bearing on the NIH review or approval of the submission.

Stem Cell Line Information

Note: If the hESC line is approved for use in NIH funding, information entered into items 6-9 below will appear on the NIH Registry, a public website.

6. Name of Stem Cell Line. Enter the cell line's common or official name.

7. Cell Line Availability. Check yes or no to indicate whether the cell line will be available for use by the research community if approved for use in NIH funded research. NIH strongly encourages that hESC lines be made widely available to facilitate the advancement of new scientific knowledge. NIH Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources stress the importance of sharing unique research resources and dissemination of research tools to advance science and further discovery. Similarly, NIH Best Practices for the Licensing of Genomic Inventions encourage licensing policies and strategies that maximize access of genomic technologies.

If you answer "yes" to item 7 you must complete items 8 and 9. If a hESC line is approved for use in NIH funding, information entered into items 8 and 9 will appear on the NIH Registry.

If it is unknown at this time whether the cell line will be available for distribution, check "other" and provide a brief explanation, e.g., unknown at this time, potentially available in the future, etc.

8. Restrictions (if any) on Use of Stem Cell Line. If there are any limitations on the use of the hESC line (e.g., no commercial use, in-vitro research only, diabetes research only), please describe those restrictions in the space available. If the line is approved this information will appear on the NIH Registry.

9. Provider of Stem Cell Line. Enter contact information for researchers wishing to obtain the hESC line(s). You may provide the name of an individual, organization, or stem cell bank, and a phone number, email address or url. If the line is approved this information will appear on the NIH Registry.

10. Embryo Donation. Indicate whether the embryo was donated in the United States or outside the United States, and the year in which the embryo was donated. This information may be relevant to the NIH review of the hESC line. The answers to item 11 will not appear on the NIH Registry.

Adding Additional Related Cell Lines

Click "Add Another Cell Line with the Same Admin and Supporting Information" to add another hESC line. The method of review, and the supporting information (see next section Uploading Supporting Information) must be ***precisely identical*** to the information for the hESC line identified in item 6. If the method of review or any of the supporting information for another hESC would differ in any way (even in a non-substantive way), you must complete separate requests.

You will be directed to complete items 6-10 for each additional hESC. After you have entered all hESCs, you will have the opportunity to upload one set of supporting documentation for all of the hESCs included in the submission.

Supporting Information (Document Attachments)

11. Supporting Information. All requests for NIH review require that you upload supporting information. All supporting information must be in English.

All materials uploaded and saved or submitted will be subject to the Freedom of Information Act. Do not submit consent or other documents with the personally identifying information of donor(s) of the embryos (the individuals who sought reproductive treatment). Submission of consent documents with such information will cause the request to be invalidated and NIH to delete all submitted information.

Supporting Information for NIH Administrative Review. (If you did not select NIH Administrative Review, go to Supporting Information for Working Group of the ACD Review below.)

If you selected NIH Administrative Review, then you must provide information demonstrating compliance with each element of Section II(A). Supporting materials may include anonymous or sample consent documents, written policies, or other documentation such as a copy of the Embryonic Stem Cell Research Oversight (ESCRO) or Institutional Review Board (IRB) or ethics committee approval to use the line, or documentation of a committee's exemption from review.

Failure to provide documentation for any one element of Section II(A) will result in the cell line not being approved for NIH funding under the NIH Administrative Review process.

To upload supporting information:

- Click the "Browse" buttons below to select a file from your computer. Valid attachment file type extensions are doc, xls, wpd, rtf, pdf, ppt, gif, jpg or txt.
- Provide a brief description (limit 100 characters) of the file (e.g., consent document, clinic policy, etc.) in the box provided.

Select which of the 15 element(s) of Section II (A) of the Guidelines are supported by the document. You may choose multiple elements for each document. Up to 10 supporting documents may be attached.

Supporting Information for Working Group of the ACD Review. Applicants are encouraged to provide, as document 1, a summary document explaining how the attachments address the materials that the Working Group will consider (see below).

If the embryos were donated prior to July 7, 2009, in any country, upload supporting information demonstrating that the hESCs were derived from human embryos:

1. that were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose; and
2. that were donated by donor(s) who gave voluntary written consent for the human embryos to be used for research purposes.

Additional information that will be relevant to the review of the Working Group includes documentation addressing the principles articulated in Section II(A) of the NIH Guidelines, the HHS regulations for the protection of human research subjects (45 CFR 46 Subpart A), and the following additional points to consider: during the informed consent process, including written or oral communications, whether the donor(s) were:

1. informed of other available options pertaining to the use of the embryos;
2. offered any inducements for the donation of the embryos; and
3. informed about what would happen to the embryos after the donation for research.

If the embryos were donated on or after July 7, 2009, in a country other than the United States, the supporting documentation is expected to demonstrate that the alternative procedural standards of the foreign country where the embryo was donated provide protections at least equivalent to those provided by Section II(A) of the NIH Guidelines.

To upload supporting information:

- Click the "Browse" button below to select a file from your computer. Valid attachment file type extensions are doc, xls, wpd, rtf, pdf, ppt, gif, jpg or txt.
- Provide a brief description (limit 100 characters) of the file (e.g., consent document, clinic policy, etc.) in the box provided.

Up to 10 supporting documents may be attached.

Comments

12. Comments. If there is any additional information you wish to provide regarding this submission, you may enter it here. If your comments exceed 1,000 characters and spaces, you may upload additional information as one of the attachments above.

Assurance, Certification, Authority and Final Submission

The Signing Official (SO) registered in the eRA Commons is the only official with the authority to submit NIH Form 2890 and provide the necessary Assurance. If you selected review by the Working Group of the ACD, you will have two Assurance options and must make a selection as to which Assurance is relevant.

Read the Assurance, Certification, Authority and Final Submission paragraphs carefully. By submitting the form you are certifying to NIH compliance with the Assurance statement, that you have the legal authority or rights to make the request to NIH, and the accuracy and validity of all information, including attached supporting documentation.

Email Confirmation

After clicking "Submit FINAL Registry Application" button, you will receive an email confirmation and an NIH assigned number that pertains to the submission. The email will go to the Signing Official to the point of contact if one is identified in item 2.

If you have questions concerning your submission, please contact the NIH Registry at hescregistry@mail.nih.gov, and reference the assigned request number. NIH will not revise or edit any information provided as part of the submission.

The name of the organization submitting the request (item 3), the name(s) of the hESC cell line(s) provided in item 6, and the method of NIH review selected (Administrative Review or Working Group of the ACD) will appear on the NIH Registry under *Submitted hESC Lines Pending Review*.

Printing Your Submission

The email confirmation will include the entire text of the application, with all data you have entered and the names of the uploaded files. Print or save this email as a record of your submission.

Notification of NIH Determination

The results of the NIH review of the submission will be emailed to the SO and to the point of contact, if one is identified in item 2.

NIH decisions are final and may not be appealed. NIH will provide the reason(s) for non-approval. If a hESC line undergoes Administrative Review and is not approved, the hESC may be submitted as a new request with additional documentation for Administrative Review, or may be submitted for review by the Working Group of the ACD (unless the embryos were donated in the United States on or after 7/7/2009). In either situation, the submission will be considered a new submission and not a resubmission of a previous request.