

NIH Guidelines on Human Stem Cell Research

March 9, 2009:

- President Obama issued Executive Order
 - “removing barriers to responsible scientific research”

April 23, 2009:

- Draft Guidelines released
 - 30 day public comment period

July 7, 2009:

- Final Guidelines released
 - establishes new NIH Stem Cell Registry

August 25, 2009:

- Draft submission form released
 - request for inclusion on NIH Stem Cell Registry

September 21, 2009:

- NIH announces members of the Working Group of the Advisory Committee
 - online submission form became active

September 23, 2009:

- WiCell submits WA01 (H1) as the first hES cell line for review



Section II (B). Applicant institutions proposing research using hESCs derived from embryos donated in the U.S. **before the effective date of these Guidelines** may establish eligibility for NIH funding in one of two ways:

- 1) By complying with Section II (A) of the Guidelines; or
 - 2) By submitting materials to a Working Group of the Advisory Committee to the Director (ACD)
- The materials submitted 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 review submitted materials, e.g., consent forms, written policies or other documentation, taking into account the **principles articulated in Section II (A)**, 45 C.F.R. Part 46, Subpart A, and the following additional points to consider. That is, 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.**

Add New hESC Registry Request for Advisory Committee to the Director (ACD) Review

Request for Human Embryonic Stem Cell Line to be Approved for Use in NIH Funded Research - Working Group of the ACD Review

The [instructions for completing this form](#) should be read prior to entering any information.

* Required fields are marked with a red asterisk.

Login Information: Commons\erikforsberg (10/08/2009)

Administrative Information ?

* 1. Signing Official (SO):

A. SO Name:
B. SO Phone Number:
C. SO Email Address:

2. Submitter of Request:
(* Complete only if different from Signing Official)

A. Submitter Name:
B. Submitter Phone Number:
C. Submitter Email Address:

(Important Note: If submitted by anyone other than the Signing Official, a copy of a letter signed by the SO must be provided as one of the documents in the Supporting Information section below. See the [sample letter](#) (MS Word - 41 KB) for appropriate language. In addition, users have the ability to send the SO or other individuals a copy of the draft request upon saving draft changes and from the main [NIH Form 2890 selection screen](#) in the "Edit Draft Request(s)" section.)

* 3. Organization Name:
DUNS Number:

Assurance, Certification, Authority and Final Submission ?

Note: If you are a Signing Official with formal designated or delegated authority to sign on behalf of the organization, check the Assurance, Certification, and Authority boxes to provide the required certifications. If you are not a Signing Official with formal designated or delegated authority to sign on behalf of the organization, do not check the boxes, but provide, as one of the attached supporting documents, a letter signed by the SO that provides the required certifications (see [Sample Letter](#) (MS Word - 41 KB)).

* Select the appropriate Assurance Statement from the two options below:

Assurance in accord with [Section II\(B\)](#) of the NIH Guidelines:

The applicant organization identified above assures that the embryo from which the cell line identified in item 6 was derived was donated prior to July 7, 2009, and the embryo : 1) was created using in vitro fertilization for reproductive purposes and was no longer needed for this purpose; and 2) was donated by donor(s) who gave voluntary written consent for the human embryo to be used for research purposes. The applicant is advised that the Working Group of the Advisory Committee to the NIH Director will consider submitted materials taking into account the principles articulated in [Section II\(A\)](#) of the NIH Guidelines for Human for Human Stem Cell Research, [45 CFR 46 Subpart A](#), and the following points to consider: during the informed consent process, including written and oral communications, whether the donor(s) were: (1) informed of other available options pertaining to the use of the embryo ; (2) offered any inducements for the donation of the embryo ; and (3) informed about what would happen to the embryo after the donation for research.

OR

Assurance in accord with [Section II\(C\)](#) of the NIH Guidelines:

The applicant organization identified above assures that the embryo from which the cell line identified in item 6 was derived was donated outside the United States on or after July 7, 2009, and 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 on Human Stem Cell Research.

Summary of Supporting Information Provided for WA01 (H1)

Document 1: Summary of Supporting Information – WA01 (H1)

This, the current document, is intended to provide the Working Group of the Advisory Committee to the [NIH] Director (ACD) with an explanation of how the supporting information provided address the materials that the Working Group will consider during its review of the use of the WA01 (H1) human Embryonic Stem Cell line with NIH funding.

Document 2: 1997 Thomson IRB Approval Notice

The derivation of the WA01 (H1) human Embryonic Stem Cell (hESC) line was conducted with the approval of the University of Wisconsin-Madison Health Sciences Institutional Review Board (IRB). This research protocol (95-623-239) was originally approved on July 24, 1995 and reapproved on an annual basis until the study was completed in 2000. The “1997 Thomson IRB Approval Notice” is a copy of the approval notice which was in affect during the time that the embryos used for the derivation of the WA01 (H1) hESC line were donated (January, 1998). Therefore the ACD should consider this document as demonstration that the derivation of the WA01 (H1) hESC line was conducted under IRB review and therefore meets the Health and Human Services regulations for the Protection of Human Research Subjects (45 C.F.R. 46, Subpart A).

Document 3: 1997 Thomson Consent Form

University of Wisconsin-Madison Health Sciences Institutional Review Board reviewed and approved the consent form (Protocol # 95-623-239) that was signed by the donors of the embryos used for the derivation of the WA01 (H1) hESC line. The “1997 Thomson Consent Form” is a blank copy of this consent form which was signed in January of 1998 by both the male and female gamete donors, for whom the embryos were originally created for reproductive purposes.

While this consent form does not contain all of the elements listed in Section IIA of the July 7, 2009 NIH Guidelines on Human Stem Cell Research, it does contain the following elements:

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.

“Preimplantation embryos that are not chosen to be placed in the uterus will be cultured in various conditions in the laboratory for 10 days or less.”

Element 4. No payments, cash or in kind, were offered for the donated embryos.

“You will not be financially compensated for participation.”

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).

“If you choose not to take part in this study, your medical care will not be affected in any way.”

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.

“You are free at any time to refuse permission for the use of any of your excess embryos, up until the moment when the inner cells of the embryos are isolated for culture.”

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

Element 9. The embryos would be used to derive hESCs for research.

While the term “human Embryonic Stem Cell Research” is not used in the consent, the research is described in lay terms as follows:

“Because these embryonic cells will be from the preimplantation embryo before the development of any specific tissue type they are called “undifferentiated”. These cells can be cultured in this undifferentiated state in the laboratory, potentially indefinitely. However, by changing how they are cultured, they will sometimes randomly develop into “differentiated” cells (for example, cells that look and behave like the cells of the placenta, bone, skin, or blood). By studying how these embryonic cells differentiate, in the future it may be possible to direct their differentiation to specific cell types in culture. Because many diseases (such as diabetes mellitus or Parkinson’s disease) result from the death or dysfunction of specific cell types, it might one day be possible to treat many diseases by the transplantation of differentiated cells derived in tissue culture from embryonic cell lines.”

Element 10. What would happen to the embryos in the derivation of hESCs for research.

“Preimplantation embryos that are not chosen to be placed in the uterus will be cultured in various conditions in the laboratory for 10 days or less. This incubation time is not long enough for the development of any fetal structures. During this incubation the embryo will be photographed. After this period of time, the outer cells of the embryo will be separated from the inner cells of the embryo and discarded. The inner cells will then be cultured for an indefinite time (“cell lines”) and studied. Note that the inner cells are not a complete embryo; as such they would not develop into a fetus if transferred to a uterus.”

Element 11. hESCs derived from the embryos might be kept for many years.

“The inner cells will then be cultured for an indefinite time (“cell lines”) and studied.”

“These cell lines will be permanent, that is they will continue to divide in culture indefinitely.”

Element 13. The research was not intended to provide direct medical benefit to the donor(s).

“You will not directly benefit from participation, but future patients may benefit from this study.”

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.

“You will not be financially compensated for participation. If embryonic cell lines are successfully isolated, the cell lines would become the property of the University of Wisconsin Alumni Research Foundation (WARF). Because of the possibility that differentiated cells derived from embryonic cell lines might one day be used to treat human disease, embryonic cell lines might have significant commercial value, and WARF may apply for patent protection for the isolation technique of the cell lines and on the properties of the cell lines. If a patent is granted, WARF would own the patent.”

Element 15. Whether information that could identify the donor(s) would be available to researchers.

“Nothing discovered about the donors from this research will be conveyed to the donor’s physician in a way that could be personally identified.”

“Neither the men nor women who provide the gametes for the embryos used in this study will be identified in any communication or publication that may result from this study.”

Document 4: Letter of Assurance – WA01 – Sept 2009

A letter of assurance was obtained from the attending physician responsible for obtaining consent from the embryo donors whose embryos resulted in the derivation of the WA01 (H1) hESC line.

In addition to other information, this document provides supporting information demonstrating that the WA01 (H1) hESC line was 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.

It also provides the Working Group with written assurances that the principles articulated in Section IIA of the July 7, 2009 NIH Guidelines on Human Stem Cell Research as well as the HHS regulations for the Protection of Human Research Subjects (45 C.F.R. 46, Subpart A) were followed.

Additionally this document provides written assurances that during the informed consent process (written and oral) that the donor(s):

1. were informed of other available options pertaining to the use of the embryos;
2. would not be offered any inducements for the donation of the embryos; and
3. were informed about what would happen to the embryos after the donation for research.

Therefore the ACD should consider this document as demonstration that the derivation of the WA01 (H1) hESC line was conducted in accordance with all of the eligibility requirements specified in Section IIB of the July 7, 2009 NIH Guidelines on Human Stem Cell Research.

Document 5: 2009 SCRO Approval Notice

The University of Wisconsin-Madison Stem Cell Research Oversight (SCRO) committee had not yet been established at the time (1998) when the WA01 (H1) hESC line was derived, however this committee has reviewed and approved (SC-2008-0014) the derivation of new hESC lines as well as the use of the WA01 (H1) hESC line by researchers at the University of Wisconsin-Madison.

Document 6: Thomson – Science - 1998

The derivation of the WA01 (H1) hESC line, along with four additional hESC lines was published in 1998:

Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz, MA, Swiergiel JJ, Marshall VS, and Jones JM. “Embryonic stem cell lines derived from human blastocysts”. *Science* 282:1145-1147, 1998.

Document 7: Use of hESC Lines – Nat Biotech Aug 2009

As reported in the August 2009 issue of *Nature Biotechnology*, 60.9% of all hESC publications reported using the WA01 (H1) hESC line. Additionally, of the 1,217 unique requests for National Stem Cell Bank lines, fully 77% asked for just two lines (H1, H9).

Scott CT, McCormick JB, and Owen-Smith J. “And then there were two: use of hESC lines”. *Nature Biotechnology* 27(8):696-697, 2009.

Therefore the ACD should consider this information as demonstration that the WA01 (H1) hESC line has been and will likely remain an important cell line for hESC research and that both the WA01 (H1) and the WA09 (H9) hESC lines will continue to be important reference standards for newly derived hESC as well as iPS cell lines.

Assurance of Conditions of Consent
for human Embryonic Stem Cell line
WA01 (H1)

As the attending physician _____ responsible for
obtaining consent from the embryo donors whose embryos resulted in the derivation of the WA01 (H1)
human Embryonic Stem Cell (hESC) line, I, _____ hereby provide the following
written assurances that the embryos used for the derivation of the WA01 (H1) cell line:

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

Furthermore, during the consent process:

- a. All disposition options available at UWHC at the time treatment was sought pertaining to the embryos no longer needed for reproductive purposes were explained to the individual(s) who sought reproductive treatment.
- b. No payments, cash or in kind, were offered for the donated embryos.
- c. While no specific written policies or procedures were in place at UWHC at the time of donation, I hereby provide assurance that neither consenting nor refusing to donate embryos for research affected the quality of care provided to potential donor(s).
- d. There was a clear separation between my discussions related to a prospective donor's decision to create human embryos for reproductive purposes and a prospective donor's decision to donate human embryos for research purposes. Specifically:
 - i. Decisions related to the creation of human embryos for reproductive purposes were made free from the influence of researchers proposing to derive or utilize human Embryonic Stem Cells (hESCs) in research. As the attending physician of individuals who sought reproductive treatment, I was responsible for their reproductive clinical care and obtaining informed consent from the donor(s). I was not directly involved in the laboratory procedures that resulted in the derivation of the WA01 (H1) cell line and did not plan to utilize hESCs in my own research.
 - ii. At the time of embryo donation, consent for that donation was 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 was given at the time of the donation.
 - iii. Potential donor(s) were informed that they retained the right to withdraw consent for the donation of the embryo until the embryos were actually used to derive hESCs.
- e. During the consent process, each donor was informed of the following:
 - i. that the embryos would be used to derive hESCs for research;
 - ii. what would happen to the embryos in the derivation of hESCs for research;
 - iii. that hESCs derived from the embryos could be kept for many years;
 - iv. that the donation of the embryos was made without any restrictions or directions as to the individual(s) who may receive medical benefit from the use of the hESCs, such as who may be the recipients of cell transplants;

CP 9/8/97
Principal Investigator: James Thomson
(608) 263-3585

Consent to Use Excess Pre-implantation Embryos for Cell Line Isolation

YOU ARE INVITED TO TAKE PART IN A RESEARCH STUDY OF HUMAN CELL DIFFERENTIATION.

Purpose

All human tissues and organs are composed of small building blocks called cells. By growing cells from embryos which have not yet implanted in the uterus (preimplantation embryos) we hope to better understand normal embryo development, and ultimately find important clues for the treatment of infertility, miscarriage, birth defects, and other conditions.

What Will Be Done With The Embryos?

Preimplantation embryos that are not chosen to be placed in the uterus will be cultured in various conditions in the laboratory for 10 days or less. This incubation time is not long enough for the development of any fetal structures. During this incubation the embryos will be photographed. After this period of culture, the outer cells of the embryo will be separated from the inner cells of the embryo and discarded. The inner cells will then be cultured for an indefinite time ("cell lines") and studied. Note that the inner cells are not a complete embryo; as such they would not develop into a fetus if transferred to a uterus.

Why Are These Embryonic Cells Important?

Because these embryonic cells will be from the preimplantation embryo before the development of any specific tissue type they are called "undifferentiated". These cells can be cultured in this undifferentiated state in the laboratory, potentially indefinitely. However, by changing how they are cultured, they will sometimes randomly develop into "differentiated" cells (for example, cells that look and behave like the cells of placenta, bone, skin, or blood). By studying how these embryonic cells differentiate, in the future it may be possible to direct their differentiation to specific cell types in culture. Because many diseases (such as diabetes mellitus or Parkinson's disease) result from the death or dysfunction of specific cell types, it might one day be possible to treat many diseases by the transplantation of differentiated cells derived in tissue culture from embryonic cell lines. Although the potential for treating human diseases is great, significant biomedical advances will be needed before such treatments are possible.

NIH Human Embryonic Stem Cell Registry

Submitted hESC Lines Pending Review

The following is a list of human embryonic stem cell lines submitted to NIH, which are PENDING review to determine if they may be used in NIH-supported research.

Cell Line Name	Organization	Type of Review *	Date Submitted
CHB-1	Children's Hospital Corporation	ACD	09/24/2009
CHB-10	Children's Hospital Corporation	ACD	09/24/2009
CHB-11	Children's Hospital Corporation	ACD	09/24/2009
CHB-12	Children's Hospital Corporation	ACD	09/24/2009
CHB-2	Children's Hospital Corporation	ACD	09/24/2009
CHB-3	Children's Hospital Corporation	ACD	09/24/2009
CHB-4	Children's Hospital Corporation	ACD	09/24/2009
CHB-5	Children's Hospital Corporation	ACD	09/24/2009

Related Resources

hESC Line Listings:

- [Lines in Draft Status](#)
- [Lines Eligible for Use](#)
- [Lines Previously Reviewed by NIH](#)

NIH Form 2890:

- [Login Page](#)
(Authorization Required)

Stem Cell Information:

- [NIH Stem Cell Information Page](#)

Contact Us:

- Email questions to: hescregistry@mail.nih.gov



HUES 3	Harvard University	ACD	10/02/2009
HUES 4	Harvard University	ACD	10/02/2009
HUES 5	Harvard University	ACD	10/02/2009
HUES 6	Harvard University	ACD	10/02/2009
HUES 7	Harvard University	ACD	10/02/2009
HUES 8	Harvard University	ACD	10/02/2009
HUES 9	Harvard University	ACD	10/02/2009
WA01 (H1)	WiCell Research Institute	ACD	09/23/2009

* Type of Review:

- ADM = NIH Administrative Review
- ACD = Review by a Working Group of the Advisory Committee to the [NIH] Director (ACD)

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Draft Guideline Category

Cell Line Provider Cell lines	Draft Guideline Category														
	B1	B2	B3	B4	B5	B6	B7								
							a	b	c	d	e	f	g	h	i
Cellartis SA01, SA02	Yellow	Green	Green	Red	Red	Yellow	Green	Red	Green	Red	Red	Red	Red	Red	Red
ES Cell International ES01, ES02, ES03, ES04, ES05, ES06	Yellow	Green	Yellow	Green	Green	Yellow	Green	Red	Green	Red	Green	Red	Green	Green	Green
Bresagen/Novocell BG01, BG02, BG03	Yellow	Green	Yellow	Red	Red	Yellow	Red	Red	Red	Red	Red	Red	Red	Red	Red
Technion TE03, TE04, TE06	Yellow	Green	Yellow	Yellow	Green	Green	Red	Red	Green	Red	Green	Red	Green	Red	Red
University of California San Francisco UC01, UC06	Green	Green	Green	Red	Red	Yellow	Red	Green	Green	Green	Green	Green	Green	Green	Green
WiCell Research Institute WA01, WA07, WA09, WA13, WA14	Green	Green	Green	Red	Green	Green	Green	Red	Green	Green	Green	Red	Green	Green	Green

= Non-compliant



= Unsure



= Compliant



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Section II (A), hESCs should have been derived from human embryos:

- 1) that were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose;
- 2) that were donated by individuals who sought reproductive treatment (hereafter referred to as "donor(s)") and who gave voluntary written consent for the human embryos to be used for research purposes; and
- 3) for which all of the following can be assured and documentation provided, such as consent forms, written policies, or other documentation, provided:

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- a) 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.
- b) No payments, cash or in kind, were offered for the donated embryos.
- c) 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).

d) 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:

- i. 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.
- ii. 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.
- iii. Donor(s) should have been informed that they retained the right to withdraw consent for the donation of the embryo until the embryos were actually used to derive embryonic stem cells or until information which could link the identity of the donor(s) with the embryo was no longer retained, if applicable.

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- e) During the consent process, the donor(s) were informed of the following:
 - i. that the embryos would be used to derive hESCs for research;
 - ii. what would happen to the embryos in the derivation of hESCs for research;
 - iii. that hESCs derived from the embryos might be kept for many years;
 - iv. that 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 cell transplants.;
 - v. that the research was not intended to provide direct medical benefit to the donor(s);
 - vi. that 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;
 - vii. whether information that could identify the donor(s) would be available to researchers.