

1 **University of Wisconsin Policy for Human Pluripotent Stem Cell Research**

2 Revised 25 April 2008

3 WHEREAS the University of Wisconsin-Madison (“University”) has reviewed the  
4 “Guidelines for Human Embryonic Stem Cell Research”, the report and  
5 recommendations by the COMMITTEE ON GUIDELINES FOR HUMAN  
6 EMBRYONIC STEM CELL RESEARCH of the National Academies of Science, the  
7 2007 Amendments to the National Academies' Guidelines for Human Embryonic Stem  
8 Cell Research, and the International Society for Stem Cell Research Guidelines for the  
9 conduct of Human Embryonic Stem Cell Research (Version I), and has determined that  
10 the Guidelines will guide our policy on human embryonic stem cell (hESC) research at  
11 the University and that certain other kinds of human pluripotent stem cell (hPSC)  
12 research also merit additional review; and,

13 WHEREAS in addition to specific requirements adopted for application to hESC research  
14 at the University, we endorse several general provisions set forth in the Guidelines as  
15 follows:

16 The University encourages the establishment of a national body to assess  
17 periodically the adequacy of the guidelines proposed in this document and to  
18 provide a forum for a continuing discussion of issues involved in hESC research;  
19 and,

20 The hESC research community should ensure that there is sufficient genetic  
21 diversity among cell lines to allow for potential translation into health care  
22 services for all groups in our society and the University recognizes that ensuring  
23 genetic diversity may require the generation of new hESC lines; and,

24 The investigator, institution, and appropriate institutional review boards, must  
25 ensure that authorizations are received from donors, as appropriate and required  
26 by federal human subjects protections and the Health Insurance Portability and  
27 Accountability Act for the confidential transmission of personal health  
28 information to repositories or to investigators who are using hESC lines derived  
29 from donated materials; and,

30 To facilitate autonomous choice, decisions related to the production of embryos  
31 for infertility treatment will be free of the influence of any investigator who  
32 proposes to derive or use hESCs in research; and,

33 Consenting or refusing to donate gametes or embryos for research should not  
34 affect or alter in any way the quality of care provided to prospective donors.  
35 Clinical staff must provide appropriate care to patients without prejudice  
36 regarding their decisions about disposition of their embryos; and,

37 Clinical personnel who have a conscientious objection to hESC research should  
38 not be required to participate in providing donor information or securing donor  
39 consent for research use of gametes or preimplantation embryos, however, in  
40 some circumstances, a refusal to engage in stem cell research may be relevant to  
41 the assessment of job performance and job qualifications. The privilege to not  
42 participate does not extend to the care of a donor or recipient.

## 43 **SECTION 1**

44 The University establishes a Stem Cell Research Oversight (SCRO) committee. The  
45 committee will include at least one representative of the public and persons with  
46 expertise in developmental biology, stem cell research, molecular biology, assisted  
47 reproduction, and ethical and legal issues in hPSC research. The SCRO committee will  
48 not substitute for the appropriate Institutional Review Board (IRB) but will provide an  
49 additional level of review and scrutiny warranted by the complex issues raised by hPSC  
50 research.

51 The SCRO Committee will provide oversight for all research on campus or involving  
52 campus faculty or staff that involves either:

- 53 (a) the use of hESCs or their derivatives; or
- 54 (b) the introduction of hPSCs, or their derivatives, obtained from a non-  
55 embryonic source, into non-human animals at any embryonic, fetal, or  
56 postnatal stage, if an expected effect is that human cells will be integrated into  
57 the central nervous system, testes, or ovaries of the animal.

58 SCRO committee review applies regardless of the source of funding and the applicability  
59 of federal regulations.

## 60 **SECTION 2**

61 To ensure adherence to the basic ethical and legal principles of informed consent and  
62 protection of confidentiality, hESCs may only be used after documentation of their  
63 provenance has been provided to and approved by the UW-Madison SCRO committee.  
64 Documentation of provenance only needs to be provided prior to the first use of the  
65 hESCs in research falling with the UW-Madison SCRO committee's purview.  
66 Documentation requirements are as follows:

- 67 (a) *hESC Lines on the NIH Embryonic Stem Cell Registry as of May 9, 2007:*  
68 presence on the NIH Embryonic Stem Cell Registry as of May 9, 2007  
69 constitutes adequate documentation of the provenance of those cell lines.
- 70 (b) *hESC Lines Derived from Embryos Created for Research Purposes through*  
71 *Conventional (Standard or ICSI insemination) In Vitro Fertilization (IVF).*  
72 The UW-Madison SCRO committee must receive documentation that the  
73 sperm and oocyte procurement processes were approved by an appropriate

74 IRB and must receive a copy of the IRB-approved consent form(s) used  
75 during the sperm and oocyte procurement processes.

76 (c) *hESC Lines Derived from Embryos Created for Research Purposes through*  
77 *Somatic Cell Nuclear Transfer (SCNT)*. The UW-Madison SCRO committee  
78 must receive documentation that the oocyte and somatic cell procurement  
79 processes were approved by an appropriate IRB and must receive a copy of  
80 the IRB-approved consent form(s) used during the oocyte and somatic cell  
81 procurement processes.

82 (d) *hESC Lines Derived from Embryos Originally Created for Therapeutic*  
83 *Reproductive Purposes but which Are Now in Excess of Clinical Need*. The  
84 UW-Madison SCRO committee must receive documentation that the embryo  
85 procurement process was approved by an appropriate IRB and must receive a  
86 copy of the IRB-approved consent form(s) used during the embryo  
87 procurement process. If sperm or oocyte donors were used in this process,  
88 documentation of their consent to donate these excess embryos for research is  
89 not required.<sup>1</sup>

### 90 **Section 3**

91 Human embryos in existence at the University of Wisconsin as of the date of the approval  
92 of this policy may be used for the derivation of new stem cell lines so long as the consent  
93 process for such use utilized a consent form approved by the University's Health  
94 Sciences IRB. Any request for generation of new hESC lines from these embryos and the  
95 protocol for research using the derived lines are still subject to SCRO review.

96 The procurement processes for gametes or embryos used in the derivation of hESC lines  
97 in existence prior to the date of the approval of this policy are not required to fully  
98 comply with this policy. However, the provenance of pre-existing hESC lines must still  
99 be documented in accordance with section 2.

### 100 **SECTION 4**

101 Research falling within the scope of SCRO committee review can only be initiated after  
102 an on-line application has been submitted and the PI has received notification of SCRO  
103 Committee approval. The SCRO committee shall divide research proposals into three  
104 categories in setting limits on research and determining the requisite level of oversight:

105 (a) Research that is permissible after expedited review consisting of review by  
106 one SCRO staff person and one committee member. Purely *in vitro* hESC

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<sup>1</sup> Differs from National Academies of Science, Guidelines for Humans Embryonic Stem Cell Research, Recommendation 3.3 which provided "When donor gametes have been used in the *in vitro* fertilization process, resulting blastocysts may not be used for research without consent of all gamete donors."

107 research with pre-existing coded or anonymous hESC lines in general is  
108 approvable provided that notice of the research, documentation of the  
109 provenance of the cell lines, and evidence of compliance with any required  
110 Institutional Review Board, Institutional Animal Care and Use Committee,  
111 Institutional Biosafety Committee, or other mandated reviews is provided to  
112 the SCRO committee.

113 (b) Research that is permissible only after additional review and approval by the  
114 SCRO committee. The SCRO committee will evaluate all requests for  
115 permission to attempt derivation of new hESC lines by any means, including  
116 from donated preimplantation embryos, from *in vitro* fertilized oocytes, or by  
117 nuclear transfer. The scientific rationale for the need to generate new hESC  
118 lines, by whatever means, must be clearly presented, and the basis for the  
119 numbers of preimplantation embryos and oocytes needed should be justified.  
120 Such requests should be accompanied by evidence of Institutional Review  
121 Board approval of the procurement process and a copy of the consent form  
122 used during the embryo procurement process. The SCRO committee will  
123 review all research involving the introduction of hESCs into nonhuman  
124 animals at any embryonic, fetal, or postnatal stage, and all research involving  
125 the introduction of hPSCs, or their derivatives, obtained from a  
126 nonembryonic source, into nonhuman animals at any embryonic, fetal, or  
127 postnatal stage, if an expected effect is that human cells will be integrated into  
128 the central nervous system, testes, or ovaries of the animal. Particular attention  
129 will be paid to the probable pattern and effects of differentiation and  
130 integration of the human cells into the nonhuman animal tissues. Research in  
131 which personally identifiable information about the donors of the  
132 preimplantation embryos, gametes, or somatic cells from which the hESCs  
133 were derived is readily ascertainable by the investigator requires IRB and  
134 SCRO committee review and approval.

135 (c) Research that will not be permitted at this time:

136 (i) Research involving *in vitro* culture of any intact human embryo,  
137 regardless of derivation method, for longer than 14 days or until  
138 formation of the primitive streak begins, whichever occurs first.

139 (ii) Research in which hPSCs are introduced into nonhuman primate  
140 preimplantation embryos or in which pluripotent stem cells from any  
141 species are introduced into human preimplantation embryos.

142 In addition:

143 (iii) No animal into which hPSCs have been introduced at any stage will be  
144 allowed to breed.

145 **SECTION 5**

146 The SCRO committee will establish and maintain a registry, the UW hESC Registry,<sup>2</sup> of  
147 University investigators conducting hESC research and record descriptive information (a  
148 brief research abstract) about the types of research being performed and the hESC lines in  
149 use. The registry shall include all NIH-approved cell lines that are used at the University  
150 after the date of the approval of this policy.

151 **SECTION 6**

152 If a University investigator collaborates with an investigator in another country, the  
153 SCRO committee may determine that the procedures prescribed by the foreign institution  
154 afford protections consistent with these guidelines and may approve the substitution of  
155 some or all of the foreign procedures for its own.

156 **SECTION 7**

157 All applicable laws, policies, and guidelines pertaining to recombinant DNA research and  
158 animal care will apply to hESC research. As appropriate, Good Laboratory Practice  
159 standards will be required for hESC research.

160 **SECTION 8**

161 hESC research directly for clinical application will be in compliance with all applicable  
162 Food and Drug Administration (FDA) regulations. If FDA requires that a link to the  
163 donor source be maintained, investigators and the University will document that the  
164 confidentiality of the donor is protected, that the donor is notified that a link will be  
165 maintained, and that, where applicable, federal human subjects protections and Health  
166 Insurance Portability and Accountability Act or other privacy protections are followed.

167 **SECTION 9**

168 Whenever it is practicable, the attending physician responsible for the infertility treatment  
169 and the investigator deriving or proposing to use hESCs will not be the same person.

170 **SECTION 10**

171 No cash or in kind payments may be provided for donating preimplantation embryos in  
172 excess of clinical need for research purposes.

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<sup>2</sup> The UW hESC Registry should not be confused with the NIH Human Embryonic Stem Cell Registry.

173 **SECTION 11<sup>3</sup>**

174 Women who undergo hormonal induction to generate oocytes specifically for research  
175 purposes (such as for nuclear transfer) may be reimbursed for direct expenses incurred as  
176 a result of the procedure, as determined by an appropriate Institutional Review Board.  
177 Oocytes and sperm donors may be compensated at a level consistent with compensation  
178 provided for *in vitro* fertilization donors at the locale where the donation occurs. In  
179 locales where reimbursement for research participation is allowed, there must be a  
180 detailed and rigorous review to ensure that reimbursement of direct expenses or financial  
181 considerations of any kind do not constitute an undue inducement. Due to the unknown  
182 long-term effects of ovulation induction, women should not undergo an excessive number  
183 of hormonally induced ovarian stimulation cycles in a lifetime.<sup>4</sup>

184 **SECTION 12**

185 Potential donors of preimplantation embryos should be informed of all available options  
186 for the disposition of their embryos, including donation to others for reproductive  
187 purposes as well as destruction. Donors who may have specified their intent to donate  
188 embryos to research prior to completion of their clinical care must provide specific  
189 informed consent for donation to stem cell research after their clinical care has been  
190 completed. Donors must also be informed that they retain the right to withdraw consent  
191 until the preimplantation embryo is actually transferred to a researcher for use in the  
192 derivation of human embryonic stem cells.

193 **SECTION 13**

194 In the context of donation of gametes or preimplantation embryos for hESC research, the  
195 informed consent process, will, at a minimum, provide the following information:

- 196 (a) A statement that the preimplantation embryo or gametes will be used to derive  
197 hESCs for research that may include research on human transplantation.
- 198 (b) A statement that the donation is made without any restriction or direction  
199 regarding who may be the recipient of transplants of the cells derived, except  
200 in the case of autologous donation.
- 201 (c) A statement as to whether the identities of the donors will be readily  
202 ascertainable to those who derive or work with the resulting hESC lines.

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<sup>3</sup> Differs from National Academies of Science, Guidelines for Humans Embryonic Stem Cell Research, Recommendation X.X which provided “X.”

<sup>4</sup> Based on International Society for Stem Cell Research, Guidelines for the Conduct of Human Embryonic Stem Cell Research Recommendations 11.5b(ii) and (v).

- 203 (d) If the identities of the donors are retained (even if coded), a statement as to  
204 whether donors wish to be contacted in the future to receive information  
205 obtained through studies of the cell lines.
- 206 (e) An assurance that participants in research projects will follow applicable and  
207 appropriate best practices for donation, procurement, culture, and storage of  
208 cells and tissues to ensure, in particular, the traceability of stem cells.  
209 (Traceable information, however, must be secured to ensure confidentiality.)
- 210 (f) A statement that derived hESCs and/or cell lines might be kept for many  
211 years.
- 212 (g) A statement that the hESCs and/or cell lines might be used in research  
213 involving genetic manipulation of the cells or the mixing of human and  
214 nonhuman cells in animal models subject to approval of the appropriate  
215 institutional committee.
- 216 (h) Disclosure of the possibility that the results of study of the hESCs may have  
217 commercial potential and a statement that the donor will not receive financial  
218 or any other benefits from any future commercial development.
- 219 (i) A statement that the research is not intended to provide direct medical benefit  
220 to the donor(s) except in the case of autologous donation.
- 221 (j) j. A statement that embryos may be destroyed in the process of deriving  
222 hESCs.
- 223 (k) k. A statement that neither consenting nor refusing to donate embryos for  
224 research will affect the quality of any future care provided to potential donors.
- 225 (l) A statement of the risks involved to the donor.

226 **SECTION 14**

227 Researchers may not ask members of the infertility treatment team to generate more  
228 oocytes than necessary for the optimal chance of reproductive success. An infertility  
229 clinic or other third party responsible for obtaining consent or collecting materials will  
230 not pay for or be paid for the material obtained (except for specifically defined cost-based  
231 reimbursements and payments for professional services).

232 **SECTION 15**

233 Any facility engaged in banking hESC lines at or for the University must receive prior  
234 certification by the SCRO Committee and will:

- 235 (a) Establish policies and procedures to ensure that donors of material gave  
236 informed consent through a process approved by an appropriate Institutional  
237 Review Board,
- 238 (b) Maintain records about all aspects of cell culture, and
- 239 (c) Establish a uniform tracking systems and common guidelines for distribution  
240 of cells.

241 **SECTION 16**

242 Any centralized facility at the University or any University designated cell repository  
243 engaged in obtaining, storing, and distributing hESC lines will conform with the  
244 following standards:

- 245 (a) The SCRO Committee, in consultation with any University designated cell  
246 repository will provide policy and oversight and will review and certify  
247 creation of clear and standardized protocols for banking and withdrawals.
- 248 (b) Documentation requirements for investigators and sites that deposit cell lines,  
249 will include
- 250 (i) A copy of the donor consent form.
- 251 (ii) Proof of Institutional Review Board approval of the procurement  
252 process.
- 253 (iii) Available medical information on the donors, including results of  
254 infectious-disease screening.
- 255 (iv) Available clinical, observational, or diagnostic information about the  
256 donor(s).
- 257 (v) Critical information about culture conditions (such as media, cell  
258 passage, and safety information).
- 259 (vi) Available cell line characterization (such as karyotype and genetic  
260 markers).
- 261 (c) A secure system for protecting the privacy of donors when materials retain  
262 codes or identifiable information will be provided, including but not limited to
- 263 (i) A scheme for maintaining confidentiality (such as a coding system).
- 264 (ii) A system for a secure audit trail from primary cell lines to those  
265 submitted to the repository.

- 266 (iii) A policy governing whether and how to deliver clinically significant  
267 information back to donors.
- 268 (d) The following standard practices will apply:
- 269 (i) Assignment of a unique identifier to each sample
- 270 (ii) A process for characterizing cell lines.
- 271 (iii) A process for expanding, maintaining, and storing cell lines.
- 272 (iv) A system for quality assurance and control.
- 273 (v) A website that contains scientific descriptions and data related to the cell  
274 lines available.
- 275 (vi) A procedure for reviewing applications for cell lines.
- 276 (vii) A process for tracking disbursed cell lines and recording their status  
277 when shipped (such as number of passages).
- 278 (viii) A system for auditing compliance.
- 279 (ix) A schedule of charges.
- 280 (x) A statement of intellectual property policies.
- 281 (xi) When appropriate, creation of a clear Material Transfer Agreement or  
282 user agreement.
- 283 (xii) A liability statement.
- 284 (xiii) A system for disposal of material.
- 285 (e) Clear criteria for distribution of cell lines, including but not limited to  
286 evidence of approval of the research by any embryonic stem cell research  
287 oversight committee or equivalent body if such exists at the recipient  
288 institution.
- 289 (f) The University or any University designated repository may refuse to accept  
290 hESC lines if prior culture conditions or other items do not meet these  
291 standards.

292 **SECTION 17**

293 This policy may be amended by action of the SCRO committee subject to the written  
294 approval of the amendment by the Associate Dean for Research Policy of the Graduate  
295 School.