| S 100010 | Issue | Source | Comment | Reference |
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| **S 100020** | **Issue** | **Source** | **Comment** | **Reference** |
| (a) | Covered stem cell line | SWG | Scientists on the SWG were asked to consider these issues and suggest a definition that captured the activities of interest for the purpose of the CIRM Regulations. | Working_Notes_7 |
| (b) | Acceptably derived | SWG | Regulatory term see section 100007. Authority derived from CA H&S code 125290.55. | CIRM MES Regulations<br>CA_H&S_12590.55 (b)(2) |
| (c) | Permissible expenses | P71 & SWG | The ICOC shall establish "standards prohibiting compensation to research donors or participants, while permitting reimbursement of expenses." | CA_H&S_Code_125290.35(b)(3)<br><br>SWG 01/30/06 Transcript P205.L24 |
| (d) | Research | HHS | From the Federal Common Rule. | 45CFR Part 46<br>NA Guidelines 3.1 |
| (e) | Funded research | P71 | | CA Constitution XXXV |
| (f) | Human subjects | HHS | From the Federal Common Rule. | 45CFR Part 46<br>NA Guidelines 3.1 |
| (g) | Institution | HHS | From the Federal Common Rule. | 45CFR Part 46<br>NA Guidelines 3.1 |
| (h) | Stem Cell Research Oversight committee (SCRO) | NAG | Based on NAG recommendation. | NA Guidelines 2.0 |
| (i) | Somatic Cell Nuclear Transfer (SCNY) | NIH | From *NIH Report on Stem Cells* appendix F. | NIH_Appendix_F |
| **S 100030** | **Issue** | **Source** | **Comment** | **Reference** |
| (a) | Human reproductive cloning | P71 & NAG | "human reproductive cloning" is defined in P71. Alternative definitions in H&S Code 24185. NA recommended that "Human reproductive cloning should not now be practiced. It is dangerous and likely to fail." | H&S Code 125292.10<br>NA Guidelines 1.1(b) |
| (b) | Culture of embryo, product of SCNT, 12 day limit | P71 & NAG | NA Guidelines have a 14 day limit, P71 says "8 to 12 days after cell division begins." | H & S Code 125290.35(b)(6) |
| (c) | Stem cells into primate embryos | NAG | Direct recommendation of NAG. | NA Guidelines 1.2(c)(2) |

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| (d) | Stem cells into human embryos | NAG | Direct recommendation of NAG. | NA Guidelines 1.2(c)(2) |
| (e) | Breeding animals with human stem cells | NAG | Direct recommendation of NAG. | NA Guidelines 1.2(c)(3) |
| **S 100040** | **Issue** | **Source** | **Comment** | **Reference** |
| (a) | Designate responsible official | NAG | "All scientific investigators and their institutions, regardless of their field, bear the ultimate responsibility for ensuring that they conduct themselves in accordance with professional standards and with integrity." | NA Guidelines 1.3 |
| (b) | Designate SCRO | NAG | "To provide oversight of all issues related to derivation and use of hES cell lines and to facilitate education of investigators involved in hES cell research, each institution involved in hES cell research should establish an Embryonic Stem Cell Research Oversight (ESCRO) committee." | NA Guidelines 2.0 |
| (c) | Designate IRB | NAG & CA | "An IRB, as described in federal regulations at 45 CFR 46.107, should review the procurement of all gametes, blastocysts, or somatic cells for the purpose of generating new hES cell lines."<br>Consistent with CA Health & Safety Code 125300(b). | NA Guidelines 3.1<br>H & S Code 125300(b) |
| (d) | Conscientious objection | NAG | "Clinical personnel who have a conscientious objection to hES cell research should not be required to participate in providing donor information or securing donor consent for research use of gametes or blastocysts." | NA Guidelines 3.7 |
| **S 100050** | **Issue** | **Source** | **Comment** | **Reference** |
| (a-h) | Compliance | NIH | These provisions are based on the NIH Grants Policy Statement (12/03). This document serves as the basis for the CIRM Grants Administration Policy. | NIH_Policy 12_03 |
| **S 100060** | **Issue** | **Source** | **Comment** | **Reference** |
| (a) | SCRO membership | NAG | "The committee should include representatives of the public and persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in hES cell research." | NA Guidelines 2.0 |
| (b) | SCRO function | NAG | "It must have suitable scientific, medical, and ethical expertise to conduct its own review and should have the resources needed to coordinate the management of the various other reviews required for a particular protocol." | NA Guidelines 2.0 |
| (c) | SCRO investigator | NAG | The ESCRO should facilitate education of investigators involved in | NA Guidelines 2.0(5) |

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| | education | | hES [stem] cell research. | |
| (d) | SCRO for two or more institutions | SWG | Numerous commentators indicated it may be difficult for all institution to have the necessary expertise. | Public Session 03 12/14/05 Workshop<br>SWG 10/24/06 Transcript P105.L7 |
| (e) | SCRO may be convened by group of institutions or state agency | SWG | Based on similar rationale as 100005(d); SWG expressed desire to provide multiple options. | SWG 10/24/05 Transcript P90.L23 |
| **S 100070** | **Issue** | **Source** | **Comment** | **Reference** |
| (a)(1) | SCRO approval for CIRM-funded derivation | NAG | "The scientific rationale for the need to generate new hES cell lines, by whatever means, must be clearly presented." | NA Guidelines 4.2 |
| (a)(2) | Demonstrate expertise | NAG | "Research teams should demonstrate appropriate expertise or training in derivation or culture of either human or nonhuman ES [stem] cells" | NA Guidelines 4.3 |
| (a)(3) | Document compliance with necessary review | NAG | "An IRB, as described in federal regulations at 45 CFR 46.107, should review the procurement of all gametes, blastocysts, or somatic cells for the purpose of generating new hES cell lines…" | NA Guidelines 1.2(b)<br>NA Guidelines 3.1 |
| (a)(4) | Document how cell lines will be characterized | NAG | "Investigators must document how they will characterize, validate, store, and distribute any new hES cell lines.." | NA Guidelines 4.6 |
| (b)(1) | Cell lines introduced to humans or animals are acceptably derived | NAG | Section 1.2(a) is applicable to all cell lines used by researchers. | NA Guidelines 1.2(a) |
| (b)(2) | Evaluate probable pattern of differentiation | NAG & SWG | "particular attention should be paid to the probable pattern and effects of differentiation and integration of the human cells into the nonhuman animal tissues." SWG comment that introduction to humans also be covered [1/16/06 call]. | NA Guidelines 1.2(b)(2) |
| (b)(3) | Document compliance with necessary review | | Consistent with 100005(a)(3). | NA Guidelines 1.2(b)<br>NA Guidelines 3.1 |
| (c)(1) | Document cells are acceptably derived | NAG & SWG | "Purely in vitro hES cell research that uses previously derived hES cell lines is permissible provided that the ESCRO committee or equivalent body.." | NA Guidelines 1.2(a) |
| (c)(2) | Document compliance with necessary review | | Consistent with 100005(a)(3). | NA Guidelines 1.2(b)<br>NA Guidelines 3.1 |
| **S 100080** | **Issue** | **Source** | **Comment** | **Reference** |

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| (a)(b)(c) | NIH approved lines | SWG | SWG resolution to Exempt the NIH, HFEA, and UK stem cell lines form documentation. HFEA standards view as equivalent. | SWG 8/30/05 Transcript P102.L22 HFEA_Decision_Tree |
| (d) | CIHR licensed lines | SWG | CIHR license requirements meet standard discussed by SWG. | CIHR_Guidelines |
| (e)(1) | Voluntary & informed consent | HHS & NAG | Fundamental protection under Federal law & major recommendation of NA. | 45CFR Part 46 NA Guidelines 3.1 |
| (e)(2) | Donors did not receive valuable consideration | P71 & NAG | The ICOC shall establish "standards prohibiting compensation to research donors or participants, while permitting reimbursement of expenses."<br><br>Reimbursement standard developed by SWG on 12/30/06. | CA_H&S_Code_1252 90.35(b)(3)<br><br>SWG 01/30/06 Transcript P205.L24&P220.L9 |
| (e)(3) | Persons did not receive valuable considerations | P71, ICOC | Provision intended to make prohibition on compensation consistent with 100007(e)(2).<br>P 71 sets limitations on payments for cells: "Standards limiting payments for the purchase of stem cells or stem cell lines to reasonable payment for the removal, processing, disposal, preservation, quality control, storage, transplantation, or implantation or legal transaction or other administrative costs associated with these medical procedures and specifically including any required payments for medical or scientific technologies, products, or processes for royalties, patent, or licensing fees or other costs for intellectual property." | ICOC_2_10_06_#3<br><br>CA_H&S_Code_1252 90.35(b)(5)<br><br>CA_H&S_Code_1253 20_(b) |
| (e)(4) | Donation overseen by IRB | HHS, NAG & CA | IRB responsible for ensuring fundamental protection under Federal law & major recommendation of NA. Consistent with existing state regulation where IRB oversees aspects of donation of gametes, embryos and tissue. | 45CFR Part 46 NA Guidelines 3.1 CA_H&S_Code_125300 |
| (e)(5) | No compensation for storage costs | NAG | "People who elect to donate stored blastocysts for research should not be reimbursed for the costs of storage prior to the decision to donate." | NA Guidelines 3.4(a) |
| **S 100090** | **Issue** | **Source** | **Comment** | **Reference** |
| (a) | Voluntary & informed consent | | See S100009. | |
| (b)(1) | Shall not compromise optimal reproductive success | SWG | Provision intended to provide additional protections to prospective donors. | SWG 12/01/05 Transcript P140.L14 |
| (b)(2) | Assume cost of medical care | SWG | Provision intended to provide economic protections to prospective donors. | SWG 01/30/06 Transcript P218.L9 |
| (b)(3) | Physician and PI not the | NAG | "Whenever it is practicable, the attending physician responsible for the | NA Guidelines 3.5 |

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| | same individual | | infertility treatment and the investigator deriving or proposing to use hES cells should not be the same person." | |
| (b)(4) | Physician not have financial interest in research outcome | SWG | Provision intended to protect prospective donors from undue influence. | SWG 01/31/06 Transcript P325.L12 & SWG 01/31/06 Transcript P347.L11 |
| **S 100100** | **Issue** | **Source** | **Comment** | **Reference** |
| (a) | Do not violate the preferences of donors | NAG & SWG | Provision developed to be consistent with an aspirational goal of the NAG. "Donors could be offered the option of agreeing to some forms of hES cell research but not others…The consent process should fully explore whether donors have objections to any specific forms of research to ensure that their wishes are honored." | NA Guidelines 3.6<br><br>SWG 12/01/05 Transcript P90.L4 |
| (a) | Informed consent requirements | NAG, SWG & CA | The informed consent requirements are consistent with the NAG and existing CA regulations. | NA Guidelines 3.2 CA_H&S_Code_125315 Working_Notes_3 |
| (a)(1) | Cells may be kept for many years | NAG & CA | NAG: "A statement that derived hES cells and/or cell lines might be kept for many years." [3.6(f)] Same standard applies in existing CA regulations. | NA Guidelines 3.6(f) CA_H&S_Code_125315 (c)(4) |
| (a)(2) | Recontact of donors | NAG | NAG: "If the identities of the donors are retained (even if coded), a statement as to whether donors wish to be contacted in the future to receive information obtained through studies of the cell lines." [3.6(d)] | NA Guidelines 3.6(d) SWG 12/01/05 Transcript P59.L23 |
| (a)(3) | Cells used in future studies | SWG | SWG indicated the need to emphasize all future uses could not be anticipated at time of donation. | SWG 12/01/05 Transcript P83.L9 |
| (a)(4) | May be used in research involving genetic manipulation | NAG | NAG: "A statement that the hES cells and/or cell lines might be used in research involving genetic manipulation of the cells or the mixing of human and nonhuman cells in animal models." [3.6(g)] | NA Guidelines 3.6(g) SWG 12/01/05 Transcript P87.L18 Working_Notes_8 |
| (a)(5) | May be transplanted into humans or animals | NAG | NAG: "A statement that the hES cells and/or cell lines might be used in research involving genetic manipulation of the cells or the mixing of human and nonhuman cells in animal models." [3.6(g)] | NA Guidelines 3.6(g) Working_Notes_8 |
| (a)(6) | No direct medical benefit except autologous | NAG & CA | NAG: "A statement that the research is not intended to provide direct medical benefit to the donor(s) except in the case of autologous donation." [3.6(i)] | NA Guidelines 3.6(i)<br><br>CA_H&S_Code_125315 (c)(6) |
| (a)(7) | Donation without any restriction on recipient | NAG | NAG: "A statement that the donation is made without any restriction or direction regarding who may be the recipient of transplants of the cells derived, except in the case of autologous donation." [3.6(b)] | NA Guidelines 3.6(b) |

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| (a)(8) | Consenting or refusing will not affect quality of care | NAG | NAG: "A statement that neither consenting nor refusing to donate embryos for research will affect the quality of any future care provided to potential donors." [3.6(k)] | NA Guidelines 3.6(k) |
| (a)(9) | Cells may have commercial potential | NAG & CA | NAG: "Disclosure of the possibility that the results of study of the hES cells may have commercial potential and a statement that the donor will not receive financial or any other benefits from any future commercial development." | NA Guidelines 3.6(h)<br><br>CA H&S Code 125315 (c)(5) |
| (b) | Opportunity to document preferences | NAG & SWG | Consistent with NA principle "The consent process should fully explore whether donors have objections to any specific forms of research to ensure that their wishes are honored." | NA Guidelines 3.6<br><br>SWG 01/30/06 Transcript P269.L22 |
| (c) | Additional requirements for donation of oocytes | SWG | SWG identified oocyte donor issues as "complex" and "controversial" requiring special standards. | SWG 12/01/05 Transcript P92.L15 |
| (1) | Description of foreseeable risks | HHS, SWG & CA | Description of risks fundamental to all informed consent; SWG identified specific risks associated with egg donation. | 45CFR Part 46<br>SWG 01/30/06 Transcript P257.L17 |
| (2) | Physician must disclose relationship to researcher | SWG & CA | Consistent with existing regulations that require that "material financial stake or interest, if any, that the investigator or research institution has in the outcome of the medical experiment" to be disclosed. | CA H&S Code 24173 (c) (11) |
| (3) | Steps to enhance informed consent | SWG | Requirement intended to ensure donor fully understands what they are consenting to. | SWG 12/01/05 Transcript P93.L7 |
| (4) | Ascertain donor understands essential aspects of research | SWG | SWG agreed in principal to assessment at 12/1/05 meeting. | SWG 12/01/05 Transcript P118.L11 |
| (4)(A-H) | Essential aspects | SWG | SWG identified critical elements from 100009(a)(1-9) that are essential for oocyte donors understand. | |
| (d) | Statement that embryos will be destroyed | NAG | NAG: "A statement that embryos will be destroyed in the process of deriving hES cells." [3.6(j)] | NA Guidelines 3.6(j) |
| (e) | Consent from legal parent guardian or progenitor. | SWG | NAG did not address cord blood and placenta. | SWG 01/30/06 Transcript P260.L10 |
| (f) | For SCNT disclose whether cell available for autologous treatment | SWG | Based on NAG requirement that availability of SCNT cell lines for autologuos treatment be addressed. | NA Guidelines 3.6(i) |

| S 100110 | Issue | Source | Comment | Reference |
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| | CA Health Research Fairness Act & Inclusion of Women and Minorities | CA & SWG | SWG identified fairness and inclusion in research as a priority. Provision adopts existing CA policy by reference. | SWG 08/30/05 Transcript P22.L15<br><br>CA H&S Code 100237 |
| **S 100120** | **Issue** | **Source** | **Comment** | **Reference** |
| | Record keeping | NAG & CIRM | This section contains general record keeping requirements. Such requirements are also contained in the Grants Administration Policy pursuant to CIRM's general obligations to track use of funds. | NA Guidelines 6.1 |
| **S 100130** | **Issue** | **Source** | **Comment** | **Reference** |
| | Materials Sharing | ICOC IP Policy | This section reiterates a core principle of the proposed intellectual property policy. See: http://www.cirm.ca.gov/policies/pdf/IPPNPO.pdf | SWG 01/30/06 Transcript P24.L10 |